Blood pressure is probably one of the most variable but best-regulated functions of the body. The purpose of the control of blood pressure is to keep blood flow constant to vital organs such as the heart, brain, and kidneys. Without constant blood flow to these organs, death ensues within seconds, minutes, or days. Although a decrease in flow produces an immediate threat to life, the continuous elevation of blood pressure that occurs with hypertension is a contributor to premature death and disability because of its effects on the heart, blood vessels, and kidneys.

The discussion in this chapter focuses on determinants of blood pressure and conditions of altered arterial pressure—hypertension and orthostatic hypotension.

The arterial blood pressure reflects the rhythmic ejection of blood from the left ventricle into the aorta.\(^1\)\(^-\)\(^3\) It rises during systole as the left ventricle contracts and falls as the heart relaxes during diastole. The contour of the arterial pressure tracing shown in Figure 23-1 is typical of the pressure changes that occur in the large arteries of the systemic circulation. There is a rapid rise in the pulse contour during left ventricular contraction, followed by a slower rise to peak pressure. Approximately 70% of the blood that leaves the left ventricle is ejected during the first one third of systole, accounting for the rapid rise in the pressure contour. The end of systole is marked by a brief down-
are referred to as the resistance vessels because they can selectively constrict or relax to control the resistance to outflow of blood into the capillaries. The body maintains its blood pressure by adjusting the cardiac output to compensate for changes in peripheral vascular resistance and changes the peripheral vascular resistance to compensate for changes in cardiac output.

In hypertension and disease conditions that affect blood pressure, changes in blood pressure usually are described in terms of the systolic and diastolic pressures, pulse pressure, and mean arterial pressure. These pressures are influenced by the stroke volume, the rapidity with which blood is ejected from the heart, the elastic properties of the aorta and large arteries and their ability to accept various amounts of blood as it is ejected from the heart, and the properties of the resistance blood vessels that control the runoff of blood into the smaller vessels and capillaries that connect the arterial and venous circulations.

**Mechanisms of Blood Pressure Regulation**

Although different tissues in the body are able to regulate their own blood flow, it is necessary for the arterial pressure to remain relatively constant as blood shifts from one area of the body to another. The mechanisms used to regulate the arterial pressure depend on whether short-term or long-term adaptation is needed (Fig. 23-2).

**Short-Term Regulation**

The mechanisms for short-term regulation of blood pressure, those acting over minutes or hours, are intended to correct temporary imbalances in blood pressure, such as occur during physical exercise and changes in body position. These mechanisms also are responsible for maintenance of blood pressure at survival levels during life-threatening situations such as during an acute hemorrhagic incident. The short-term regulation of blood pressure relies mainly on neural and humoral mechanisms, the most rapid of which are the neural mechanisms.

**Neural Mechanisms.** The neural control centers for the regulation of blood pressure are located in the reticular formation of the medulla and lower third of the pons, where integration and modulation of autonomic nervous system (ANS) responses occur. This area of the brain contains the vasomotor and cardiac control centers and is often collectively referred to as the cardiovascular center. The cardiovascular center transmits parasympathetic impulses to the heart through the vagus nerve and sympathetic impulses to the heart and blood vessels through the spinal cord and peripheral sympathetic nerves. Vagal stimulation of the heart produces a slowing of heart rate, whereas sympathetic stimulation produces an increase in heart rate and cardiac contractility. Blood vessels are selectively innervated by the sympathetic nervous system. Increased sympathetic activity produces constriction of the small arteries and arterioles with a resultant increase in peripheral vascular resistance.
The ANS control of blood pressure is mediated through intrinsic circulatory reflexes, extrinsic reflexes, and higher neural control centers. The intrinsic reflexes, including the baroreceptor and chemoreceptor reflexes, are located in the circulatory system and are essential for rapid and short-term regulation of blood pressure. The sensors for extrinsic reflexes are found outside the circulation. They include blood pressure responses associated with factors such as pain and cold. The neural pathways for these reactions are more diffuse, and their responses are less consistent than those of the intrinsic reflexes. Many of these responses are channeled through the hypothalamus, which plays an essential role in the control of sympathetic nervous system responses. Among higher-center responses are those caused by changes in mood and emotion.

The baroreceptors are pressure-sensitive receptors located in the walls of blood vessels and the heart. The carotid and aortic baroreceptors are located in strategic positions between the heart and the brain (Fig. 23-3). They respond to changes in the stretch of the vessel wall by sending impulses to cardiovascular centers in the brain stem to effect appropriate changes in heart rate and vascular smooth muscle tone. For example, the fall in blood pressure that occurs on moving from the lying to the standing position produces a decrease in the stretch of the baroreceptors with a resultant increase in heart rate and sympathetically induced vasoconstriction that causes an increase in peripheral vascular resistance.

The arterial chemoreceptors are chemosensitive cells that monitor the oxygen, carbon dioxide, and hydrogen ion content of the blood. They are located in the carotid bodies, which lie in the bifurcation of the two common carotids, and in the aortic bodies of the aorta (see Fig. 23-3). Because of their location, these chemoreceptors are always in close contact with the arterial blood. Although the main function of the chemoreceptors is to regulate ventilation, they also communicate with cardiovascular centers in the brain stem and can induce widespread vascular constriction. Whenever the arterial pressure drops below a critical level, the chemoreceptors are stimulated because of diminished oxygen supply and a buildup of carbon dioxide and hydrogen ions. In persons with chronic lung disease, systemic and pulmonary hypertension may develop because of hypoxemia (see Chapter 29). Persons with sleep apnea also may experience an increase in blood pressure because of the hypoxemia that occurs during the apneic periods.

Humoral Mechanisms. A number of humoral mechanisms contribute to blood pressure regulation, including the renin-angiotensin-aldosterone system and vasopressin. Other humoral substances, such as epinephrine, a sympathetic neurotransmitter
**Understanding • Determinants of Blood Pressure**

The arterial blood pressure, which is the force that moves blood through the arterial system, reflects the intermittent contraction and relaxation of the left ventricle. It is determined by (1) the properties of the arterial system and the factors that maintain (2) the systolic and (3) the diastolic components of the blood pressure. These factors include the blood volume, elastic properties of the blood vessels, cardiac output, and peripheral vascular resistance.

### 1 Arterial Blood Pressure

The arterial blood pressure represents the force that distributes blood to the capillaries throughout the body. The highest arterial pressure is the systolic pressure and the lowest is the diastolic pressure. The aorta and its major branches constitute a system of conduits between the heart and the arterioles. The arterioles, which are the terminal components of the arterial system, serve as resistance vessels that regulate the blood pressure at the distribution of blood to the capillary beds. Because the normal arteries are so compliant and the arterioles present such high resistance to flow, the arterial system acts as a filter that converts the intermittent flow generated by the heart into a virtually steady flow through the capillaries. The low-pressure venous system collects blood from the capillaries and returns it to the heart as a means of maintaining the cardiac output needed to sustain arterial pressure.

### 2 Systolic Pressure

The systolic blood pressure reflects the amount of blood (stroke volume) that is ejected from the heart with each beat, the rate and force with which it is ejected, and the elasticity or compliance of the aorta and large arteries. The blood that is ejected from the heart during systole does not move directly through the circulation. Instead, a substantial fraction of the stroke volume is stored in large arteries. Because the walls of these vessels are elastic, they can be stretched to accommodate a large volume of blood without an appreciable change in pressure. The systolic pressure often increases with aging as the aorta and large arteries lose their elasticity and become more rigid.
Diastolic Pressure

The diastolic blood pressure reflects the closure of the aortic valve, the energy that has been stored in the elastic fibers of the large arteries during systole, and the resistance to flow through arterioles into the capillaries. Closure of the aortic valve at the onset of diastole and recoil of the elastic fibers in the aorta and large arteries continue to drive the blood forward, even though the heart is not pumping. These effects, largely restricted to the elastic vessels, convert the discontinuous systolic flow in the ascending aorta into a continuous flow in the peripheral arteries.

released from the adrenal gland, have the effect of directly stimulating an increase in heart rate, cardiac contractility, and vascular tone.

The renin-angiotensin-aldosterone system plays a central role in blood pressure regulation. Renin is an enzyme that is synthesized, stored, and released by the juxtaglomerular cells of the kidneys in response to an increase in sympathetic nervous system activity or a decrease in blood pressure, extracellular fluid volume, or extracellular sodium concentration. Most of the renin that is released leaves the kidney and enters the bloodstream, where it acts enzymatically to convert an inactive circulating plasma protein called angiotensinogen to angiotensin I (Fig. 23-4). Angiotensin I is then converted to angiotensin II. This conversion occurs almost entirely in the lungs, while blood flows through the small vessels of the lung, catalyzed by an enzyme called the angiotensin-converting enzyme that is present in the endothelium of the lung vessels. Although angiotensin II has a half-life of only several minutes, renin persists in the circulation for 30 minutes to 1 hour and continues to cause production of angiotensin II during this time.

Angiotensin II functions in both the short- and long-term regulation of blood pressure. It is a strong vasoconstrictor, particularly of arterioles and, to a lesser extent, of veins. Constriction of the arterioles increases the peripheral vascular resistance, thereby contributing to the short-term regulation of blood pressure. Angiotensin II also reduces sodium excretion by increasing sodium reabsorption by the proximal tubules of the kidney.

A second major function of angiotensin II, stimulation of aldo-
sterone secretion from the adrenal gland, contributes to the long-term regulation of blood pressure by increasing salt and water retention by the kidney.

**Vasopressin**, also known as antidiuretic hormone (ADH), is released from the posterior pituitary gland in response to decreases in blood volume and blood pressure, an increase in the osmolality of body fluids, and other stimuli. The antidiuretic actions of vasopressin are discussed in Chapter 31. Vasopressin has a direct vasoconstrictor effect, particularly on the vessels of the splanchnic circulation that supplies the abdominal viscera. However, long-term increases in vasopressin cannot maintain an increase in blood pressure, and vasopressin does not enhance hypertension produced by sodium-retaining hormones or other vasoconstricting substances. It has been suggested that vasopressin plays a permissive role in hypertension through its water-retaining properties or as a neurotransmitter that serves to modify ANS function.

**Long-Term Regulation**

Long-term mechanisms control the daily, weekly, and monthly regulation of blood pressure. Although the neural and hormonal mechanisms involved in the short-term regulation of blood pressure act rapidly, they are unable to maintain their effectiveness over time. Instead, the long-term regulation of blood pressure is largely vested in the kidneys and their role in the regulation of the extracellular fluid volume. According to the late Arthur Guyton, a noted physiologist, the extracellular fluid volume and arterial blood pressure are regulated around an equilibrium point, which represents the normal pressure for a given individual (Fig. 23-5). When the body contains excess extracellular fluids because of increased water and salt intake, the arterial pressure rises, and the rate at which water (i.e., pressure diuresis) and salt (i.e., pressure natriuresis) are excreted by the kidney is increased. Accordingly, there are two ways that arterial pressure can be increased using this model: one is by shifting the elimination of salt and water to a higher pressure level (see Fig. 23-5A), and the second is by changing the extracellular fluid level at which diuresis and natriuresis occur (see Fig. 23-5B). The function of the kidneys in the long-term regulation of blood pressure can be influenced by a number of factors. For example, excess sympathetic nerve activity or the release of vasoconstrictor substances can alter the transmission of arterial pressure to the kidney. Similarly, changes in neural and humoral control of kidney function can shift the diuresis–natriuresis process to a higher fluid or pressure level, thereby initiating an increase in arterial pressure.

There are two general mechanisms by which an increase in fluid volume can elevate blood pressure. One is through a direct effect on cardiac output and the other is indirect, resulting from the autoregulation of blood flow and its effect on peripheral vascular resistance. Autoregulatory mechanisms function in distributing blood flow to the various tissues of the body according to their metabolic needs (see Chapter 21). When the blood flow to a specific tissue bed is excessive, local blood vessels constrict, and when the flow is deficient, the local vessels dilate. In situations of increased extracellular fluid volume and a resultant increase in cardiac output, all of the tissues of the body are exposed to the same increase in flow. This results in a generalized constriction of arterioles and an increase in the peripheral vascular resistance (and blood pressure).

The role that the kidneys play in blood pressure regulation is emphasized by the fact that many antihypertensive medications produce their blood pressure–lowering effects by increasing sodium and water elimination.
can be certain that the cuff pressure is high enough to avoid a level of 30 mm Hg above the palpated pressure, the observer palpated systolic pressure. By inflating the pressure in the cuff to patation before the actual pressure is measured to get the pal-
artery, occluding the blood flow. This should be done by pal-
der is placed around the upper arm. The bladder of the cuff is blood pressure, a cuff that contains an inflatable rubber blad-
a well-calibrated sphygmomanometer. In the measurement of,
pressures. Blood pressures obtained by automated devices are usually less accurate than those obtained by trained observers using the auscultatory method, and it is recom-
ended that their use be limited to situations in which fre-
quent and less accurate measures of blood pressure trends are needed. They should not be used for the diagnosis and management of hypertension.4

Automated or semiautomated methods of blood pressure measurement use a microphone, arterial pressure pulse sensor (oscillometric method), or Doppler equipment for detecting the equivalent of the Korotkoff sounds. Oscillometric measurement, the most commonly used method, depends on the detection of the pulsatile oscillations of the brachial artery in the blood pressure cuff.6 In contrast to the auscultatory method, this method determines the mean arterial pressure based on the amplitude of the arterial pulsations and then uses an algorithm to calculate the systolic and diastolic pressures. Blood pressures obtained by automated devices are usually less accurate than those obtained by trained observers using the auscultatory method, and it is recom-
ended that their use be limited to situations in which fre-
quent and less accurate measures of blood pressure trends are needed. They should not be used for the diagnosis and management of hypertension.4

Automated devices are useful for the self-monitoring of blood pressure and for 24-hour ambulatory monitoring of blood pressure.7 Ambulatory blood monitors are fully automatic and can record blood pressure for 24 hours or longer while persons go about their normal activities. The monitors are typically programmed to take readings every 15 to 30 minutes through-
out the day and night. The readings are stored and downloaded into a computer for analysis. Automated equipment for self-
monitoring of blood pressure is sold in pharmacies and medical supply stores throughout the country and is available in many styles and price ranges. It is important that the equipment be cer-
tified as accurate and reliable. The equipment should be a vali-
dated aneroid or electronic monitor, should use an appropriate-
size cuff, and be checked at least once a year for accuracy. The accuracy of an electronic device can be checked by compar-
ing its readings with simultaneously obtained auscultatory measurements.

Intra-arterial methods provide for direct measurement of blood pressure. Intra-arterial measurement requires the insertion of a catheter into a peripheral artery. The arterial catheter is con-
ected to a pressure transducer, which converts pressure into a digital signal that can be measured, displayed, and recorded.1 The use of this type of blood pressure monitoring usually is restricted to intensive care units.
IN SUMMARY, the alternating contraction and relaxation of the heart produces a pressure pulse that moves blood through the circulatory system. The elastic walls of the aorta stretch during systole and relax during diastole to maintain the diastolic pressure. The systolic blood pressure denotes the highest point of the pressure pulse and the diastolic pressure the lowest point. The pulse pressure, which reflects the pulsatile nature of arterial blood flow, is the difference between the systolic and diastolic pressures, and the mean arterial pressure, the average blood pressure in the systemic circulation. Systolic pressure is determined primarily by the characteristics of the stroke volume, whereas diastolic pressure is determined largely by the conditions of the arteries and arterioles and their abilities to accept the runoff of blood from the aorta.

The regulation of blood pressure involves both short- and long-term mechanisms. The short-term mechanisms are responsible for regulating blood pressure on a minute-by-minute or hour-by-hour basis during activities such as physical exercise and changes in body position. The short-term regulation of blood pressure relies mainly on neural and humoral mechanisms, the most rapid of which are the neural mechanisms. The long-term mechanisms, those maintaining blood pressure over days, weeks, and even years, are largely vested in the kidney and the regulation of extracellular fluid volume.

Arterial blood pressure measurements usually are obtained by the indirect auscultatory method, which uses a sphygmomanometer and a stethoscope. Automated or semiautomated methods of blood pressure measurement use a microphone, arterial pressure pulse sensor (oscillometric method), or Doppler equipment for detecting the equivalent of the Korotkoff sounds. Ambulatory and self-measurement of blood pressure may provide valuable information outside the clinician’s office regarding a person’s blood pressure and response to treatment. Accurate blood pressure measurement, whether by auscultatory or automated methods, requires the use of accurately calibrated equipment, a properly fitted cuff, and the proper level of cuff inflation and timing for cuff deflation.

Hypertension, or high blood pressure, is probably the most common of all health problems in adults and is the leading risk factor for cardiovascular disorders. It affects approximately 50 million individuals in the United States and approximately 1 billion worldwide. Hypertension is more common in younger men compared with younger women, in blacks compared with whites, in persons from lower socioeconomic groups, and in older persons. Men have higher blood pressures than women until the time of menopause, at which point women quickly lose their protection. The prevalence of hypertension increases with age. Recent data from the Framingham Study suggest that persons who are normotensive at 55 years of age have a 90% lifetime risk for development of hypertension. Thus, the problem of hypertension can be expected to become even greater with the aging of the “baby-boomer” population.

Hypertension is commonly divided into the categories of primary and secondary hypertension. Primary (essential) hypertension is the term applied to 95% of cases in which no cause for hypertension can be identified. In secondary hypertension, the elevation of blood pressure results from some other disorder, such as kidney disease.

Essential Hypertension

The seventh report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) of the National Institutes of Health was published in 2003. According to the JNC 7 recommendations, a systolic pressure of less than 120 mm Hg and a diastolic pressure of less than 80 mm Hg are normal, and systolic pressures between 120 and 139 mm Hg and diastolic pressures between 80 and 89 mm Hg are considered prehypertensive (Table 23-1). A diagnosis of hypertension is made if the systolic blood pressure is 140 mm Hg or higher and the diastolic blood pressure is 90 mm Hg or higher. For adults with diabetes mellitus, the blood pressure goal has been lowered to less than 130/80 mm Hg. Hypertension is further divided into stages 1 and 2 based on systolic and diastolic blood pressure measurements. Systolic hypertension
The constitutional risk factors include a family history of hypertension, race, and age-related increases in blood pressure. Another factor that is thought to contribute to hypertension is insulin resistance and the resultant hyperinsulinemia that occurs in metabolic abnormalities such as type 2 diabetes.

**Family History.** The inclusion of heredity as a contributing factor in the development of hypertension is supported by the fact that hypertension is seen most frequently among persons with a family history of hypertension. The strength of the prediction depends on the definition of positive family history and the age of the person at risk. In studies of twins and family members in which the degree of familial aggregation is compared with the closeness of genetic sharing, the genetic contribution ranges from 30% to 60%. Until now, however, geneticists have failed to identify common genes with large effects on hypertension. It is possible that blood pressure is determined by multiple genes at many loci, each with a small influence or with a contribution differing according to sex, race, age, and lifestyle.

**Age-Related Changes in Blood Pressure.** Maturation and growth are known to cause predictable increases in blood pressure. For example, the arterial blood pressure in the newborn is approximately 50 mm Hg systolic and 40 mm Hg diastolic. Sequentially, blood pressure increases with physical growth from a value of 78 mm Hg systolic at 10 days of age to 120 mm Hg at the end of adolescence. Diastolic pressure increases until 50 years of age and then declines from the sixth decade onward, whereas systolic blood pressure continues to rise with age.

**Race.** Hypertension not only is more prevalent in African Americans than other ethnic groups in the United States, it is more severe. The Third National Health and Nutrition Survey (NHANES) III, from 1988 to 1991, reported that diastolic blood pressures were significantly greater for African Americans than for white men and women 35 years of age and older.

**Constitutional Risk Factors**

Although the cause or causes of essential hypertension are largely unknown, both constitutional and lifestyle factors have been implicated, either singly or collectively, as contributing factors. The constitutional risk factors include a family history of hypertension, race, and age-related increases in blood pressure. Another factor that is thought to contribute to hypertension is insulin resistance and the resultant hyperinsulinemia that occurs in metabolic abnormalities such as type 2 diabetes.

**TABLE 23-1 Classification of Blood Pressure for Adults and Recommendations for Follow-up**

<table>
<thead>
<tr>
<th>BLOOD PRESSURE CLASSIFICATION</th>
<th>SYSTOLIC BLOOD PRESSURE (mm Hg)</th>
<th>DIASTOLIC BLOOD PRESSURE (mm Hg)</th>
<th>FOLLOW-UP RECOMMENDATIONS FOR INITIAL BLOOD PRESSURE*†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>And &lt;80</td>
<td>Recheck in 2 years</td>
</tr>
<tr>
<td>Prehypertensive</td>
<td>120–139</td>
<td>or 80–89</td>
<td>Recheck in 1 year‡</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>140–159</td>
<td>or 90–99</td>
<td>Confirm within 2 months‡</td>
</tr>
<tr>
<td>Stage 2 hypertension</td>
<td>≥160</td>
<td>or ≥100</td>
<td>Evaluate or refer to source of care within 1 month. For those with higher pressure (e.g., &gt;180/110 mm Hg), evaluate and treat immediately or within 1 week, depending on clinical situation and complications.</td>
</tr>
</tbody>
</table>

*Initial blood pressure: If systolic and diastolic categories are different, follow recommendations for shorter follow-up (e.g., 160/86 mm Hg should be evaluated or referred to source of care with 1 month).
†Follow-up blood pressure: Modify the scheduling of follow-up according to reliable information about past blood pressure measurements, other cardiovascular risk factors, or target-organ disease.
‡Provide advice about lifestyle modification.

and that systolic pressures of African American women at every age were greater than those of white women. Hypertension also tends to occur at an earlier age in African Americans than in whites and often is not treated early enough or aggressively enough. Blacks also tend to experience greater cardiovascular and renal damage at any level of pressure. The reasons for the increased incidence of hypertension among African Americans are largely unknown. Studies have shown that many African American persons with hypertension have lower renin levels than white persons with hypertension. The suppression of renin has been considered a secondary response to sodium retention and volume excess. Salt sensitivity, defined as an increase in blood pressure in response to a high-salt diet, is commonly described in both normotensive and hypertensive African Americans. Recent research has focused on potential defects in renal sodium transport to explain this observation. Other factors, such as increased vasomotor function (e.g., sympathetic nervous system overactivity) or abnormalities in endothelium-dependent vasodilation have also been suggested as possible contributing factors.

Evidence suggests that African Americans, when provided equal access to diagnosis and treatment, can achieve overall reductions in blood pressure and experience fewer cardiovascular complications, similar to whites. Barriers that limit access to the health care system include inadequate financial support, inconveniently located health care facilities, long waiting times, and lack of access to culturally relevant health education about hypertension. With the high prevalence of salt sensitivity, obesity, and smoking among blacks, health education and lifestyle modifications are particularly important.

**Insulin Resistance and Metabolic Abnormalities.** Insulin resistance and an accompanying compensatory hyperinsulinemia have been suggested as possible etiologic links to the development of hypertension and associated metabolic disturbances such as impaired glucose tolerance, type 2 diabetes, hyperlipidemias, and obesity. This clustering of cardiovascular risk factors has been named the insulin resistance syndrome, cardiometabolic syndrome, or metabolic syndrome (see Chapter 42).

Insulin resistance may be a genetic or acquired trait. For example, it has been shown that insulin-mediated glucose disposal declines by 30% to 40% in persons who are 40% over ideal weight. Nonpharmacologic interventions, such as caloric restriction, weight loss, and exercise, tend to decrease insulin resistance, sympathetic nervous system activity, and blood pressure.

**Lifestyle Risk Factors**

Lifestyle factors can contribute to the development of hypertension by interacting with other risk factors. These lifestyle factors include high salt intake, excessive calorie intake and obesity, excessive alcohol consumption, and low intake of potassium. Although stress can raise blood pressure acutely, there is less evidence linking it to chronic elevations in blood pressure. Smoking and a diet high in saturated fats and cholesterol, although not identified as primary risk factors for hypertension, are independent risk factors for coronary heart disease and should be avoided.

**High Salt Intake.** Increased salt intake has long been suspected as an etiologic factor in the development of hypertension. Just how increased salt intake contributes to the development of hypertension is still unclear. It may be that salt causes an elevation in blood volume, increases the sensitivity of cardiovascular or renal mechanisms to sympathetic nervous system influences, or exerts its effects through some other mechanism such as the renin-angiotensin-aldosterone system. It has also been suggested that it may be the chloride rather than the sodium in salt that is responsible for the rise in blood pressure. This is difficult to study, however, because 95% of sodium in the diet is in the form of sodium chloride.

Regardless of the mechanism, numerous studies have shown that a reduction in salt intake can lower blood pressure. The strongest data come from the INTERSALT study, which measured 24-hour urine sodium excretion (an indirect measure of salt intake) in 10,079 men and women 20 to 59 years of age in 52 locations around the world. In all 52 sites, there was a positive correlation between sodium excretion and both systolic and diastolic blood pressures. Furthermore, the association of sodium and blood pressure was greatest for older (40 to 59 years) subjects compared with younger (20 to 39 years) subjects in the study.

At present, salt intake among adults in the United States and United Kingdom averages at least 9 g/day, with large numbers of people consuming 12 g/day or more. This is far in excess of the maximal intake of 6 g/day for adults recommended by the American Heart Association. Approximately 75% of salt intake comes from salt added in the processing and manufacturing of food; 15% from the discretionary addition in cooking and at the table; and 10% from the natural sodium content of food. The Dietary Approaches to Stop Hypertension (DASH) diet is a nutritional plan that emphasizes fruits, vegetables, low-fat dairy products, whole grains, poultry, fish, and nuts, and is reduced in fat, red meat, sweets, and sugar-containing beverages. Results from studies using the low-sodium DASH diet have shown significant reductions in both systolic and diastolic blood pressures.

**Obesity.** Excessive weight commonly is associated with hypertension. Weight reduction of as little as 4.5 kg (10 lb) can produce a decrease in blood pressure in a large proportion of overweight people with hypertension. It has been suggested that fat distribution might be a more critical indicator of hypertension risk than actual overweight. The waist-to-hip ratio commonly is used to differentiate central or upper body obesity, with fat cells located in the abdomen and viscera, from peripheral or lower body obesity, with fat cell deposits in the buttocks and legs (see Chapter 39). Studies have found an association between hypertension and increased waist-to-hip ratio (i.e., central obesity), even when body mass index and skinfold thickness are taken into account. Abdominal
or visceral fat seems to be more insulin resistant than fat deposited over the buttocks and legs. There is also an evolving understanding of the neuroendocrine effects of excess adipose tissue on blood pressure. Recent evidence indicates that leptin, an adipocyte-derived hormone, may represent a link between adiposity and increased cardiovascular sympathetic activity. Besides its effect on appetite and metabolism, leptin acts on the hypothalamus to increase blood pressure through activation of the sympathetic nervous system. High levels of circulating free fatty acids in obese people also appear to participate in activation of the sympathetic nervous system. There is also research supporting activation of the renin-angiotensin-aldosterone system by adipocyte-derived angiotensinogen and the ability of adipose tissue to increase aldosterone levels through the production of factors that induce aldosterone production.

Excess Alcohol Consumption. Regular alcohol drinking plays a role in the development of hypertension. The effect is seen with different types of alcoholic drinks, in men and women, and in a variety of ethnic groups. One of the first reports of a link between alcohol consumption and hypertension came from the Oakland–San Francisco Kaiser Permanente Medical Care Program study that correlated known drinking patterns and blood pressure levels of 84,000 persons. This study revealed that the regular consumption of three or more drinks per day increases the risk for hypertension. Systolic pressures were more markedly affected than diastolic pressures. Blood pressure may improve or return to normal when alcohol consumption is decreased or eliminated. The mechanism whereby alcohol exerts its effect on blood pressure is unclear. It has been suggested that lifestyle factors such as obesity and lack of exercise may be accompanying factors.

Dietary Intake of Potassium, Calcium, and Magnesium. Low levels of dietary potassium have also been linked to increased blood pressure. The strongest evidence comes from the previously described INTERSALT study. In this study, a 60 mmol/day or greater urinary excretion of potassium (an indirect measure of potassium intake) was associated with a reduction in systolic pressure of 3.4 mm Hg or more and a decrease in diastolic pressure of 1.9 mm Hg or more. Various mechanisms have been proposed to explain the influence of potassium on blood pressure, including a purported change in the ratio of sodium to potassium in the diet, a direct natriuretic effect, and suppression of the renin-angiotensin system. In terms of food intake, a diet high in potassium usually is low in sodium. One of the major benefits of increased potassium intake is increased elimination of sodium (natriuretic effect) through the renin-angiotensin-aldosterone mechanism.

The associations between high blood pressure and calcium and magnesium levels also have been investigated. Although there have been reports of high blood pressure in persons with low calcium intake or lowering of blood pressure with increased calcium intake, the link between low calcium and magnesium intake and hypertension is inconclusive.

Target-Organ Damage

Essential hypertension is typically an asymptomatic disorder. When symptoms do occur, they are usually related to the long-term effects of hypertension on other organ systems such as the kidneys, heart, eyes, and blood vessels. The JNC 7 report uses the term target-organ damage to describe the heart, brain, peripheral vascular, kidney, and retinal complications associated with hypertension9 (Chart 23-1). The excess morbidity and mortality related to hypertension is progressive over the whole range of systolic and diastolic pressures, with target-organ damage varying markedly among persons with similar levels of hypertension.

Hypertension is a major risk factor for atherosclerosis; it predisposes to all major atherosclerotic cardiovascular disorders, including coronary heart disease, heart failure, stroke, and peripheral artery disease. The risk for coronary artery disease and stroke depends to a great extent on other risk factors, such as obesity, smoking, and elevated cholesterol levels. In clinical trials, antihypertensive therapy has been associated with reductions in stroke incidence averaging 30% to 40%, myocardial infarction, 20% to 25%, and heart failure, more than 50%.

An elevation in blood pressure increases the workload of the left ventricle by increasing the pressure against which the heart must pump as it ejects blood into the systemic circulation. As the workload of the heart increases, the left ventricular wall hypertrophies to compensate for the increased pressure work. Despite its adaptive advantage, left ventricular hypertrophy is a major risk factor for coronary heart disease, cardiac dysrhythmias, sudden death, and congestive heart failure. Hypertensive left ventricular hypertrophy regresses with therapy. Regression is most closely related to systolic pressure reduction and does not appear to reflect the particular type of medication used.

Chronic hypertension leads to nephrosclerosis, a common cause of chronic kidney disease (see Chapter 33). Hypertensive kidney disease is more common in blacks than whites. Hypertension also plays an important role in accelerating the

![chart]

**CHART 23-1**

**TARGET ORGAN DAMAGE**

| Heart | • Left ventricular hypertrophy  
|       | • Angina or prior myocardial infarction  
|       | • Prior coronary revascularization  
|       | • Heart failure  
| Brain | • Stroke or transient ischemic attack  
|       | Chronic kidney disease  
|       | Peripheral vascular disease  
|       | Retinopathy  

course of other types of kidney disease, particularly diabetic nephropathy. Because of the risk for diabetic nephropathy, the American Diabetes Association recommends that persons with diabetes maintain their blood pressure at levels less than 130/80 mm Hg (see Chapter 42).

Dementia and cognitive impairment occur more commonly in persons with hypertension. Hypertension, particularly systolic hypertension, is a major risk factor for ischemic stroke and intracerebral hemorrhage (see Chapter 51). Narrowing and sclerosis of small penetrating arteries in the subcortical regions of the brain are common findings on autopsies in person with chronic hypertension. These changes are thought to contribute to hypoperfusion, loss of autoregulation of blood flow, and impairment of the blood-brain barrier, ultimately leading to subcortical white matter demyelination. Magnetic resonance imaging (MRI) studies have revealed more extensive white matter lesions and brain atrophy in hypertensive versus normotensive persons. Effective antihypertensive therapy strongly reduces the risk of development of significant white matter changes; however, existing white matter changes, once established, do not appear to be reversible.

**Diagnosis**

Unlike disorders of other body systems that are diagnosed by methods such as radiography and tissue examination, hypertension and other blood pressure disorders are determined by repeated blood pressure measurement. Laboratory tests, x-ray films, and other diagnostic tests usually are done to exclude secondary hypertension and determine the presence or extent of target-organ damage.

Blood pressure measurements should be taken when the person is relaxed and has rested for at least 5 minutes and has not smoked or ingested caffeine within 30 minutes. At least two measurements should be made at each visit in the same arm while the person is seated in a chair (rather than on the examination table) with the feet on the floor and arm supported at heart level. If the first two readings differ by more than 5 mm Hg, additional readings should be taken. Both the systolic and diastolic pressures should be recorded. The increased availability of hypertensive screening clinics provides one of the best means for early detection. Because blood pressure in many individuals is highly variable, blood pressure should be measured on different occasions over a period of several months before a diagnosis of hypertension is made unless the pressure is extremely elevated or associated with symptoms. The JNC 7 recommendations for follow-up of persons with various stages of hypertension are included in Table 23-1.

**Ambulatory Blood Pressure Measurement.** As previously discussed, ambulatory and self/home measurement of blood pressure may provide valuable information outside the clinician’s office regarding the person’s blood pressure and response to treatment. Self/home measurement can help detect “white coat hypertension,” a condition in which the blood pressure is consistently elevated in the health care provider’s office but normal at other times; it can be used to assess the response to treatment methods for hypertension; it can motivate adherence to treatment regimens; and it can potentially reduce health care costs.

The guidelines for the 2005 Canadian Hypertension Education Program recommend short intervals between the initial and subsequent office visits (e.g., up to three visits over 6 months for a blood pressure of >140/90 mm Hg) to confirm the blood pressure elevation before pharmacologic intervention. In addition, the Canadian guidelines stipulate the use of ambulatory and self/home blood pressure measurements as complements to office-based evaluations. According to these guidelines, an ambulatory or self/home awake systolic pressure of 135 mm Hg or more or a diastolic pressure of 85 mm Hg or more, or a 24-hour ambulatory systolic pressure of 130 mm Hg or more or a diastolic pressure of 80 mm Hg or more, is diagnosed as hypertension.

**Circadian Variations in Blood Pressure.** Blood pressure normally varies in a characteristic circadian pattern. It tends to be highest in the early morning, shortly after arising from sleep, and then decreases gradually throughout the day, reaching its lowest point at approximately 2:00 to 5:00 AM. The term dippers is used to refer to persons with a normal circadian blood pressure profile in which blood pressure falls during the night, and nondippers for persons whose 24-hour blood pressure profile is flattened. Ambulatory blood pressure monitoring can be used to determine alterations in a person’s circadian blood pressure profile. Changes in the normal circadian blood pressure profile may occur in a number of conditions, including malignant hypertension, Cushing syndrome, preeclampsia, orthostatic hypotension, congestive heart failure, and sleep apnea. There is increasing evidence that persons with a nondipping pattern of hypertension are at higher risk for development of target-organ damage than those with a dipping pattern; in addition, persons with an excessive morning surge in blood pressure may also be at increased risk.

**Treatment**

The main objective for treatment of essential hypertension is to achieve and maintain arterial blood pressure below 140/90 mm Hg, with the goal of preventing morbidity and mortality. In persons with hypertension and diabetes or renal disease, the goal is below 130/80 mm Hg. The JNC 7 report contains a treatment algorithm for hypertension that includes lifestyle modification and, when necessary, guidelines for the use of pharmacologic agents to achieve and maintain blood pressure within an optimal range. For persons with secondary hypertension, efforts are made to correct or control the disease condition causing the hypertension. Antihypertensive medications and other measures supplement the treatment of the underlying disease.

**Lifestyle Modification.** Lifestyle modification has been shown to reduce blood pressure, enhance the effects of antihypertensive drug therapy, and prevent cardiovascular risk. Major life-
style modifications shown to lower blood pressure include weight reduction in persons who are overweight or obese, regular physical activity, adoption of the DASH eating plan, reduction of dietary salt intake, and limitation of alcohol intake to no more than two drinks per day for most men and one drink for women and persons of lighter weight6 (Table 23-2). Although nicotine has not been associated with long-term elevations in blood pressure as in essential hypertension, it has been shown to increase the risk for heart disease. The fact that smoking and hypertension are major cardiovascular risk factors should be reason enough to encourage the hypertensive smoker to quit. There is conflicting evidence about the direct effects of dietary fats on blood pressure. As with smoking, the interactive effects of saturated fats and high blood pressure as cardiovascular risk factors would seem to warrant dietary modification to reduce the intake of foods high in cholesterol and saturated fats.

Pharmacologic Treatment. The decision to initiate pharmacologic treatment is based on the stage and severity of the hypertension, the presence of target-organ disease, and the existence of other disease conditions and risk factors. The JNC 7 has developed a pharmacologic treatment algorithm for use in the pharmacologic treatment of hypertension6 (see Fig. 23-6). Among the drugs used in the treatment of hypertension are diuretics, β-adrenergic blocking agents, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers, calcium channel blocking agents, α1-adrenoreceptor antagonists, and vasodilators. Diuretics, such as the thiazides, loop diuretics, and the aldosterone antagonist (potassium-sparing) diuretics, lower blood pressure initially by decreasing vascular volume (by suppressing renal reabsorption of sodium and increasing salt and water excretion) and cardiac output. With continued therapy, a
The reduction in peripheral vascular resistance becomes a major mechanism of blood pressure reduction.

The β-adrenergic blockers are effective in treating hypertension because they decrease heart rate and cardiac output. These agents also decrease renin release, thereby decreasing the effect of the renin-angiotensin-aldosterone mechanism on blood pressure. There are two types of β-adrenergic receptors: β₁ and β₂. The β₁-adrenergic blocking drugs are cardioselective, exerting their effects on the heart, whereas the β₂-adrenergic receptor blockers affect bronchodilation, relaxation of skeletal blood vessels, and other β-mediated functions. Both cardioselective (targeting β₁ receptors) and nonselective (targeting β₁ and β₂ receptors) β-adrenergic blockers are used in the treatment of hypertension.

The ACE inhibitors act by inhibiting the conversion of angiotensin I to angiotensin II, thus decreasing angiotensin II levels and reducing its effect on vasoconstriction, aldosterone levels, intrarenal blood flow, and the glomerular filtration rate. They also inhibit the degradation of bradykinin and stimulate the synthesis of vasodilating prostaglandins. The ACE inhibitors are increasingly used as the initial medication in mild to moderate hypertension. Because of their effect on the renin-angiotensin system, these drugs are contraindicated in persons with renal artery stenosis, in which the renin-angiotensin mechanism functions as a compensatory mechanism to maintain adequate renal perfusion. Because they inhibit aldosterone secretion, these agents also can increase serum potassium levels and cause hyperkalemia. A relative newcomer to the field of antihypertensive medications is the angiotensin II receptor blocking agents. Because they do not inhibit bradykinin degradation in the lungs, they are less likely to produce a cough, which is a common side effect of ACE inhibitors.

The calcium channel receptor blocking drugs inhibit the movement of calcium into cardiac and vascular smooth muscle. They are thought to reduce blood pressure by several mechanisms, including a reduction of vascular smooth muscle tone in the venous and arterial systems. Each of the different agents in this group acts in a slightly different way. Some calcium channel blockers have a direct myocardial effect that reduces the cardiac output through a decrease in cardiac contractility and heart rate; others influence venous vasomotor tone and reduce the cardiac output through a decrease in venous return; still others influence arterial vascular smooth muscle tone by inhibiting calcium transport across the cell membrane channels or the vascular response to norepinephrine or angiotensin.

The α₁-adrenergic receptor antagonists block postsynaptic α₁ receptors and reduce the effect of the sympathetic nervous system on the vascular smooth muscle tone of the blood vessels that regulate the peripheral vascular resistance. These drugs produce a pronounced decrease in blood pressure after the first dose; therefore, treatment is initiated with a smaller dose given at bedtime. Postdosing palpitations, headache, and nervousness may continue with chronic treatment. These agents usually are more effective when used in combination with other agents.

The centrally acting adrenergic agonists block sympathetic outflow from the CNS. These agents are α₂-adrenergic agonists that act in a negative-feedback manner to decrease sympathetic outflow from presynaptic sympathetic neurons in the CNS. The α₂-adrenergic agonists are effective as a single...
therapy for some persons, but often are used as second- or third-line agents because of the high incidence of side effects associated with their use. One of the agents, clonidine, is available as a transdermal patch that is replaced weekly.

The direct-acting smooth muscle vasodilators promote a decrease in peripheral vascular resistance by producing relaxation of vascular smooth muscle, particularly of the arterioles. These drugs often produce tachycardia because of an initial stimulation of the sympathetic nervous system, and salt and water retention owing to decreased filling of the vascular compartment. Vasodilators are most effective when used in combination with other antihypertensive drugs that oppose the compensatory cardiovascular responses.

**Treatment Strategies.** Factors to be considered when hypertensive drugs are prescribed are the person’s lifestyle (i.e., someone with a busy schedule may have problems with medications that must be taken two or three times each day); demographics (e.g., some drugs are more effective in elderly or African American persons); motivation for adhering to the drug regimen (e.g., some drugs can produce undesirable and even life-threatening consequences if discontinued abruptly); other disease conditions and therapies; and potential for side effects (e.g., some drugs may impair sexual functioning or mental acuity; others have not been proved safe for women of childbearing age). Particular caution should be used in persons who are at risk for orthostatic hypotension (e.g., those with diabetes, ANS dysfunction, and some older individuals). Another factor to be considered is the cost of the drug in relation to financial resources. There is wide variation in the prices of antihypertensive medications, and this factor should be considered when medications are prescribed. This is particularly important for low-income persons with moderate to severe hypertension because keeping costs at an affordable level may be the key to compliance.8

**Systolic Hypertension**

The JNC 7 report defined systolic hypertension as a systolic pressure of 140 mm Hg or greater and a diastolic pressure of less than 90 mm Hg, indicating a need for increased recognition and control of isolated systolic hypertension.8 Historically, diastolic hypertension was thought to confer a greater risk for cardiovascular events than systolic hypertension.8 However, there is mounting evidence that elevated systolic blood pressure is at least as important, if not more so, than diastolic hypertension.41,42

There are two aspects of systolic hypertension that confer increased risk for cardiovascular events—one is the actual elevation in systolic pressure and the other is the disproportionate rise in pulse pressure. Elevated pressures during systole favor the development of left ventricular hypertrophy, increased myocardial oxygen demands, and eventual left heart failure. At the same time, the absolute or relative lowering of diastolic pressure is a limiting factor in coronary perfusion because coronary perfusion is greatest during diastole. Elevated pulse pressures produce greater stretch of arteries, causing damage to the elastic elements of the vessel and thus predisposing to aneurysms and development of the intimal damage that leads to atherosclerosis and thrombosis.42

**Secondary Hypertension**

Secondary hypertension, which describes an elevation in blood pressure due to another disease condition, accounts for 5% to 10% of hypertension cases.43 Unlike essential hypertension, many of the conditions causing secondary hypertension can be corrected or cured by surgery or specific medical treatment. Secondary hypertension tends to be seen in persons younger than 30 and older than 50 years of age. Cocaine, amphetamines, and other illicit drugs can cause significant hypertension, as can sympathomimetic agents (decongestants, anorectics), erythropoietin, and licorice (including some chewing tobaccos with licorice as an ingredient). Obstructive sleep apnea (see Chapter 52) is an independent risk factor for secondary hypertension.

Among the most common causes of secondary hypertension are kidney disease (i.e., renovascular hypertension), adrenal cortical disorders, pheochromocytoma, and coarctation of the aorta. To avoid duplication in descriptions, the mechanisms associated with elevations of blood pressure in these disorders are discussed briefly, and a more detailed discussion of specific disease disorders is reserved for other sections of this book. Oral contraceptive agents are also implicated as a cause of secondary hypertension.

**Renal Hypertension**

With the dominant role that the kidney assumes in blood pressure regulation, it is not surprising that the largest single cause of secondary hypertension is renal disease. Most acute kidney disorders result in decreased urine formation, retention of salt and water, and hypertension. This includes acute glomerulonephritis, acute renal failure, and acute urinary tract obstruction. Hypertension also is common among persons with chronic pyelonephritis, polycystic kidney disease, diabetic nephropathy, and end-stage renal disease, regardless of cause. In older persons, the sudden onset of secondary hypertension often is associated with atherosclerotic disease of the renal blood vessels.

Renovascular hypertension refers to hypertension caused by reduced renal blood flow and activation of the renin-angiotensin-aldosterone mechanism. It is the most common cause of secondary hypertension, accounting for 1% to 2% of all cases of hypertension.44 The reduced renal blood flow that occurs with renovascular disease causes the affected kidney to release excessive amounts of renin, increasing circulating levels of angiotensin II. Angiotensin II, in turn, acts as a vasoconstrictor to increase peripheral vascular resistance and as a stimulus for increased aldosterone levels and sodium retention by the kidney. One or both of the kidneys may be affected. When the renal artery of only one kidney is involved, the unaffected kidney is subjected to the detrimental effects of the elevated blood pressure.

There are two major types of renovascular disease: atherosclerosis of the proximal renal artery and fibromuscular dyspla-
sia, a noninflammatory vascular disease that affects the renal arteries and branch vessels. Atherosclerotic stenosis of the renal artery accounts for 70% to 90% of cases and is seen most often in older persons, particularly those with diabetes, aortoiliac occlusive disease, coronary artery disease, or hypertension. Fibromuscular dysplasia is more common in women and tends to occur in younger age groups, often persons in their third decade. Genetic factors may be involved, and the incidence tends to increase with risk factors such as smoking and hyperlipidemia.

Renal artery stenosis should be suspected when hypertension develops in a previously normotensive person older than 50 (i.e., atherosclerotic form) or younger than 30 (i.e., fibromuscular dysplasia) years of age, or when accelerated hypertension occurs in a person with previously controlled hypertension. Hypokalemia (due to increased aldosterone levels), the presence of an abdominal bruit, the absence of a family history of hypertension, and a duration of hypertension of less than 1 year help to distinguish renovascular hypertension from essential hypertension. Because renal blood flow depends on the increased blood pressure generated by the renin-angiotensin system, administration of ACE inhibitors can cause a rapid decline in renin function.

Diagnostic tests for renovascular hypertension may include studies to assess overall renal function, physiologic studies to assess the renin-angiotensin system, perfusion studies to evaluate overall renal function, physiologic studies to assess renal artery stenosis. Renal arteriography remains the definitive test for identifying renal artery disease. Duplex ultrasonographic scanning, contrast-enhanced computed tomography (CT), and magnetic resonance angiography (MRA) are other tests that can be used to screen for renovascular hypertension.

The goal of treatment of renal hypertension is to control the blood pressure and stabilize renal function. Angioplasty or revascularization has been shown to be an effective long-term treatment for the disorder. ACE inhibitors may be used in medical management of renal stenosis. However, these agents must be used with caution because of their ability to produce marked hypotension and renal dysfunction.

**Disorders of Adrenocortical Hormones**

Increased levels of adrenocortical hormones also can give rise to hypertension. Primary hyperaldosteronism (excess production of aldosterone due to adrenocortical hyperplasia or adenoma) and excess levels of glucocorticoid (Cushing disease or syndrome) tend to raise the blood pressure (see Chapter 41). These hormones facilitate salt and water retention by the kidney; the hypertension that accompanies excessive levels of either hormone probably is related to this factor. For patients with primary hyperaldosteronism, a salt-restricted diet often produces a reduction in blood pressure. Because aldosterone acts on the distal renal tubule to increase sodium absorption in exchange for potassium elimination in the urine, persons with hyperaldosteronism usually have decreased potassium levels. Screening tests for primary hyperaldosteronism involve the determination of plasma aldosterone concentration and plasma renin activity. CT and MRI scans are used to localize the lesion. Persons with solitary adenomas are usually treated surgically. Potassium-sparing diuretics, such as spironolactone, which is an aldosterone antagonist, often are used in the medical management of persons with bilateral hyperplasia.

Licorice is an extract from the roots of the Glycyrrhiza glabra plant that has been used in medicine since ancient times. European licorice (not licorice flavoring) is associated with sodium retention, edema, hypertension, and hypokalemia. Licorice, which is an effective analog of the steroid 11β-dehydrogenase enzyme that modulates access to the aldosterone receptor in the kidney, produces a syndrome similar to primary hyperaldosteronism.

**Pheochromocytoma**

A pheochromocytoma is a tumor of chromaffin tissue, which contains sympathetic nerve cells that stain with chromium salts. The tumor is most commonly located in the adrenal medulla but can arise in other sites, such as the sympathetic ganglia, where there is chromaffin tissue. Although only 0.1% to 0.5% of persons with hypertension have an underlying pheochromocytoma, the disorder can cause serious hypertensive crises. The tumors are malignant 8% to 10% of the time.

Like adrenal medullary cells, the tumor cells of a pheochromocytoma produce and secrete the catecholamines epinephrine and norepinephrine. The hypertension that develops is a result of the massive release of these catecholamines. Their release may be paroxysmal rather than continuous, causing periodic episodes of headache, excessive sweating, and palpitations. Headache is the most common symptom and can be quite severe. Nervousness, tremor, facial pallor, weakness, fatigue, and weight loss occur less frequently. Marked variability in blood pressure between episodes is typical. Approximately 50% of persons with pheochromocytoma have paroxysmal episodes of hypertension, sometimes to dangerously high levels. The other 50% have sustained hypertension, and some even may be normotensive.

Several tests are available to differentiate hypertension due to pheochromocytoma from other forms of hypertension. The most commonly used diagnostic measure is the determination of urinary catecholamines and their metabolites. Although measurement of plasma catecholamines also may be used, other conditions can cause catecholamines to be elevated. After the presence of a pheochromocytoma has been established, the tumor needs to be located. CT and MRI scans may be used for this purpose. Radioisotopes that localize the chromaffin tissue are available. Surgical removal of operable tumors is usually curative. If the tumor is not resectable, treatment with drugs that block the action or synthesis of catecholamines can be used.

**Coarctation of the Aorta**

Coarctation represents a narrowing of the aorta. In the adult form of aortic coarctation, the narrowing most commonly occurs just distal to the origin of the subclavian arteries (see Chapter 24). Because of the narrowing, blood flow to the lower
parts of the body and kidneys is reduced. In the infantile form of coarctation, the narrowing occurs proximal to the ductus arteriosus, in which case heart failure and other problems may occur. Many affected infants die within their first year of life.

In the adult form of aortic coarctation, the ejection of an increased stroke volume into a narrowed aorta causes an increase in systolic blood pressure and blood flow to the upper part of the body. Blood pressure in the lower extremities may be normal, although it frequently is low. It has been suggested that the increase in stroke volume and maintenance of the pressure to the lower part of the body is achieved through the renin-angiotensin-aldosterone mechanism in response to a decrease in renal blood flow. Pulse pressure in the legs almost always is narrowed, and the femoral pulses are weak. Because the aortic capacity is diminished, there usually is a marked increase in pressure (measured in the arms) during exercise, when the stroke volume and heart rate are increased. For this reason, blood pressures in both arms and one leg should be determined; a pressure that is 20 mm Hg more in the arms than in the legs suggests coarctation of the aorta. Involvement of the left subclavian artery or an anomalous origin of the right subclavian may produce decreased or absent left or right brachial pulses, respectively. Palpation of both brachial pulses and measurement of blood pressure in both arms are important.

Treatment consists of surgical repair or balloon angioplasty. Although balloon angioplasty is a relatively recent form of treatment, it has been used in children and adults with good results. However, there are few data on long-term follow-up.

**Oral Contraceptive Drugs**

The use of oral contraceptive pills is probably the most common cause of secondary hypertension in young women. Women taking oral contraceptive should have their blood pressure taken regularly. The Nurses Health Study (a prospective cohort study of over 70,000 nurses over 4 years between 1989 and 1993) found that current users of oral contraceptives had a significant, moderately increased risk of hypertension. However, among this group, only 41.5 cases per 10,000 person-years could be attributed to oral contraceptive use.

The cause of the increased blood pressure is largely unknown, although it has been suggested that the probable cause is volume expansion because both estrogens and synthetic progestogens used in oral contraceptive pills cause sodium retention. Various contraceptive drugs contain different amounts and combinations of estrogen and progestational agents, and these differences may contribute to the occurrence of hypertension in some women but not others. Fortunately, the hypertension associated with oral contraceptives usually disappears after the drug has been discontinued, although it may take as long as 3 months for this to happen. However, in some women, the blood pressure may not return to normal, and they may be at risk for development of hypertension. The risk for hypertension-associated cardiovascular complications is found primarily in women older than 35 years of age and in those who smoke.

**Malignant Hypertension**

A small number of persons with hypertension develop an accelerated and potentially fatal form of the disease termed malignant hypertension. This usually is a disease of younger persons, particularly young African American men, women with toxemia of pregnancy, and persons with renal and collagen diseases.

Malignant hypertension is characterized by sudden, marked elevations in blood pressure, with diastolic values above 120 mm Hg complicated by evidence of acute or rapidly progressive life-threatening organ dysfunction. There may be intense arterial spasm of the cerebral arteries with hypertensive encephalopathy. Cerebral vasoconstriction probably is an exaggerated homeostatic response designed to protect the brain from excesses of blood pressure and flow. The regulatory mechanisms often are insufficient to protect the capillaries, and cerebral edema frequently develops. As it advances, papilledema (i.e., swelling of the optic nerve at its point of entrance into the eye) ensues, giving evidence of the effects of pressure on the optic nerve and retinal vessels. The patient may have headache, restlessness, confusion, stupor, motor and sensory deficits, and visual disturbances. In severe cases, convulsions and coma follow.

Prolonged and severe exposure to exaggerated levels of blood pressure in malignant hypertension injures the walls of the arterioles, and intravascular coagulation and fragmentation of red blood cells may occur. The renal blood vessels are particularly vulnerable to hypertensive damage. Renal damage due to vascular changes probably is the most important prognostic determinant in malignant hypertension. Elevated levels of blood urea nitrogen and serum creatinine, metabolic acidosis, hypocalcemia, and proteinuria provide evidence of renal impairment.

The complications associated with a hypertensive crisis demand immediate and rigorous medical treatment in an intensive care unit with continuous monitoring of arterial blood pressure. With proper therapy, the death rate from this cause can be markedly reduced, as can complications and additional episodes. Because chronic hypertension is associated with autoregulatory changes in coronary artery, cerebral artery, and kidney blood flow, care should be taken to avoid excessively rapid decreases in blood pressure, which can lead to hypoperfusion and ischemic injury. Therefore, the goal of initial treatment measures should be to obtain a partial reduction in blood pressure to a safer, less critical level, rather than to normotensive levels.

**High Blood Pressure in Pregnancy**

Hypertensive disorders of pregnancy complicate 5% to 10% of pregnancies and remain a major cause of maternal and neonatal mortality and morbidity in the United States and worldwide. Most adverse events are attributable directly to the preeclampsia syndrome, characterized by new-onset hypertension with proteinuria that develops in the last half of pregnancy. Women with chronic hypertension can also manifest adverse events.
Classification

In 2000, the National Institutes of Health Working Group on High Blood Pressure in Pregnancy published a revised classification system for high blood pressure in pregnancy that included preeclampsia–eclampsia, gestational hypertension, chronic hypertension, and preeclampsia superimposed on chronic hypertension51 (Table 23-3).

Defining the cause or causes of hypertension that occurs during pregnancy is difficult because of the normal circulatory changes that occur. Blood pressure normally decreases during the first trimester, reaches its lowest point during the second trimester, and gradually rises during the third trimester. The fact that there is a large increase in cardiac output during early pregnancy suggests the decrease in blood pressure that occurs during the first part of pregnancy results from a decrease in peripheral vascular resistance. Because the cardiac output remains high throughout pregnancy, the gradual rise in blood pressure that begins during the second trimester probably represents a return of the peripheral vascular resistance to normal. Pregnancy normally is accompanied by increased levels of renin, angiotensin I and II, estrogen, progesterone, prolactin, and aldosterone, all of which may alter vascular reactivity. Women who experience preeclampsia are thought to be particularly sensitive to the vasoconstrictor activity of the renin-angiotensin-aldosterone system. They also are particularly responsive to other vasoconstrictors, including the catecholamines and vasopressin. It has been proposed that some of the sensitivity may be caused by a prostacyclin–thromboxane imbalance. Thromboxane is a prostaglandin with vasoconstrictor properties, and prostacyclin is a prostaglandin with vasodilator properties. Emerging evidence suggests that insulin resistance, including that which occurs with diabetes, obesity, and the metabolic syndrome, may predispose to the hypertensive disorders of pregnancy.

Preeclampsia–Eclampsia. Preeclampsia–eclampsia is a pregnancy-specific syndrome with both maternal and fetal manifestations.51–54 It is defined as an elevation in blood pressure (systolic blood pressure >140 mm Hg or diastolic pressure >90 mm Hg) and proteinuria (≥300 mg in 24 hours) developing after 20 weeks of gestation. The Working Group recommends that K5 be used for determining diastolic pressure. Edema, which previously was included in definitions of preeclampsia, was excluded from this most recent definition. The presence of a systolic blood pressure of 160 mm Hg or higher or a diastolic pressure of 110 mm Hg or higher; proteinuria greater than 2 g in 24 hours; serum creatinine greater than 1.2 mg/dL; platelet counts less than 100,000 cells/mm³; elevated liver enzymes (alanine aminotransferase [ALT] or aspartate aminotransferase [AST]); persistent headache or cerebral or visual disturbances; and persistent epigastric pain serve to reinforce the diagnosis.53 Eclampsia is the occurrence, in a woman with preeclampsia, of seizures that cannot be attributed to other causes.53

Preeclampsia occurs primarily during first pregnancies and during subsequent pregnancies in women with multiple fetuses, diabetes mellitus, collagen vascular disease, or underlying kidney disease.51 It is also associated with a condition called a hydatidiform mole (i.e., abnormal pregnancy caused by a pathologic ovum, resulting in a mass of cysts). Women with chronic hypertension who become pregnant have an increased risk for preeclampsia and adverse neonatal outcomes, particularly when associated with proteinuria early in pregnancy.

The cause of pregnancy-induced hypertension is largely unknown. Considerable evidence suggests that the placenta is the key factor in all the manifestations because delivery is the only definitive cure for this disease. Pregnancy-induced hypertension is thought to involve a decrease in placental blood flow leading to the release of toxic mediators that alter the function of endothelial cells in blood vessels throughout the body, including those of the kidney, brain, liver, and heart.51,55 The endothelial changes result in signs and symptoms of preeclampsia and, in more severe cases, of intravascular clotting and hypoperfusion of vital organs. There is risk for development of disseminated intravascular coagulation (DIC; see Chapter 13), cerebral hemorrhage, hepatic failure, and acute renal failure. Thrombocytopenia is the most common

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**TABLE 23-3 Classification of High Blood Pressure in Pregnancy**

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>DESCRIPTION</th>
</tr>
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<tbody>
<tr>
<td>Preeclampsia–eclampsia</td>
<td>Pregnancy-specific syndrome of blood pressure elevation (blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic) that occurs after the first 20 weeks of pregnancy and is accompanied by proteinuria (urinary excretion of 0.3 g protein in a 24-hour specimen).</td>
</tr>
<tr>
<td>Gestational hypertension</td>
<td>Blood pressure elevation, without proteinuria, that is detected for the first time during mid-pregnancy and returns to normal by 12 weeks postpartum.</td>
</tr>
<tr>
<td>Chronic hypertension</td>
<td>Blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic that is present and observable before the 20th week of pregnancy. Hypertension that is diagnosed for the first time during pregnancy and does not resolve after pregnancy also is classified as chronic hypertension.</td>
</tr>
<tr>
<td>Preeclampsia superimposed on chronic hypertension</td>
<td>Chronic hypertension (blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic before the 20th week of pregnancy) with superimposed proteinuria and with or without signs of the preeclampsia syndrome.</td>
</tr>
</tbody>
</table>

hematologic complication of preeclampsia. Platelet counts of less than 100,000/mm³ signal serious disease. The cause of thrombocytopenia has been ascribed to platelet deposition at the site of endothelial injury. The renal changes that occur with preeclampsia include a decrease in glomerular filtration rate and renal blood flow. Sodium excretion may be impaired, although this is variable. Edema may or may not be present. Some of the severest forms of preeclampsia occur in the absence of edema. Even when there is extensive edema, the plasma volume usually is lower than that of a normal pregnancy. Liver damage, when it occurs, may range from mild hepatocellular necrosis with elevation of liver enzymes to the more ominous hemolysis, elevated liver function test results, and low platelet count (HELLP) syndrome that is associated with significant maternal mortality. Eclampsia, the convulsive stage of preeclampsia, is a significant cause of maternal mortality. The pathogenesis of eclampsia remains unclear but has been attributed to both increased blood coagulability and fibrin deposition in the cerebral vessels.

The decreased placental flow that occurs with preeclampsia also affects the fetus. It frequently results in intrauterine growth restriction and infants who are small for gestational age. Preeclampsia is one of the leading causes of prematurity because of frequent need for early delivery in affected women.

**Gestational Hypertension.** Gestational hypertension represents a blood pressure elevation without proteinuria that is detected for the first time after mid-pregnancy. It includes women with preeclampsia syndrome who have not yet manifested proteinuria as well as women who do not have the syndrome. The hypertension may be accompanied by other signs of the syndrome. The final determination that a woman does not have the preeclampsia syndrome is made only postpartum. If preeclampsia has not developed and blood pressure has returned to normal by 12 weeks postpartum, the condition is considered to be gestational hypertension. If blood pressure elevation persists, a diagnosis of chronic hypertension is made.

**Chronic Hypertension.** Chronic hypertension is considered to be hypertension that is unrelated to the pregnancy. It is defined as a history of high blood pressure before pregnancy, identification of hypertension before 20 weeks of pregnancy, and hypertension that persists after pregnancy. Hypertension that is diagnosed for the first time during pregnancy and does not resolve after pregnancy also is classified as chronic hypertension. In women with chronic hypertension, blood pressure often decreases in early pregnancy and increases during the last trimester (3 months) of pregnancy, resembling preeclampsia. Consequently, women with undiagnosed chronic hypertension who do not present for medical care until the later months of pregnancy may be incorrectly diagnosed as having preeclampsia.

**Preeclampsia Superimposed on Chronic Hypertension.** Women with chronic hypertension are at increased risk for the development of preeclampsia, in which case the prognosis for the mother and fetus tends to be worse than for either condition alone. Superimposed preeclampsia should be considered in women with hypertension before 20 weeks of gestation who develop new-onset proteinuria; women with hypertension and proteinuria before 20 weeks of gestation; women with previously well-controlled hypertension who experience a sudden increase in blood pressure; and women with chronic hypertension who develop thrombocytopenia or an increase in serum ALT or AST to abnormal levels.

### Diagnosis and Treatment

Early prenatal care is important in the detection of high blood pressure during pregnancy. It is recommended that all pregnant women, including those with hypertension, refrain from alcohol and tobacco use. Salt restriction usually is not recommended during pregnancy because pregnant women with hypertension tend to have lower plasma volumes than normotensive pregnant women and because the severity of hypertension may reflect the degree of volume contraction. The exception is women with preexisting hypertension who have been following a salt-restricted diet.

In women with preeclampsia, delivery of the fetus is curative. The timing of delivery becomes a difficult decision in preterm pregnancies because the welfare of both the mother and the infant must be taken into account. Bed rest is a traditional therapy. Antihypertensive medications, when required, must be carefully chosen because of their potential effects on uteroplacental blood flow and on the fetus. For example, the ACE inhibitors can cause injury and even death of the fetus when given during the second and third trimesters of pregnancy.

#### High Blood Pressure in Children and Adolescents

Until recently, the incidence of hypertension among children has been low, with a range of 1% to 3%. Recent data, however, indicate that the prevalence and rate of diagnosis of hypertension in children and adolescence appear to be increasing. This may be due in part to increasing prevalence of obesity and other lifestyle factors, such as decreased physical activity and increased intake of high-calorie, high-salt foods.

Blood pressure is known to increase from infancy to late adolescence. The average systolic pressure at 1 day of age is approximately 70 mm Hg and increases to approximately 85 mm Hg at 1 month of age. Systolic blood pressure continues to increase with physical growth to about 120 mm Hg at the end of adolescence. During the preschool years, blood pressure begins to follow a pattern that tends to be maintained as the child grows older. This pattern continues into adolescence and adulthood, suggesting that the roots of essential hypertension have their origin early in life. A familial influence on blood pressure often can be identified early in life. Children of parents with high blood pressure tend to have...
higher blood pressures than do children with normotensive parents.

Blood pressure norms for children are based on age-, height-, and sex-specific percentiles\(^\text{59}\) (Table 23-4). The National High Blood Pressure Education Program (NHBPEP) first published its recommendations in 1977. The fourth Task Force report (published in 2004) recommended classification of blood pressure (systolic or diastolic) for age, height, and gender into four categories: normal (less than the 90th percentile), high normal (between the 90th and 95th percentiles), stage 1 hypertension (between the 95th and 99th percentiles plus 5 mm Hg), and stage 2 hypertension (greater than the 99th percentile plus 5 mm Hg).\(^\text{59}\) The height percentile is determined by using the revised Centers for Disease Control and Prevention (CDC) growth charts.\(^\text{60}\) As with the JNC 7 report, high normal is now considered to be “prehypertensive” and is an indication for lifestyle modification. Children and adolescents with hypertension should be evaluated for target-organ damage.\(^\text{59}\)

Secondary hypertension is the most common form of high blood pressure in infants and children. In later childhood and adolescence, essential hypertension is more common. Approximately 75% to 80% of secondary hypertension in children is caused by kidney abnormalities.\(^\text{51}\) Coarctation of the aorta is another cause of hypertension in children and adolescents. Endocrine causes of hypertension, such as pheochromocytoma and adrenal cortical disorders, are rare. Hypertension in infants is associated most commonly with high umbilical catheterization and renal artery obstruction caused by thrombosis.\(^\text{52}\) Most cases of essential hypertension are associated with obesity or a family history of hypertension.

A number of drugs of abuse, therapeutic agents, and toxins also may increase blood pressure. Alcohol should be considered as a risk factor in adolescents. Oral contraceptives may be a cause of hypertension in adolescent girls. The nephrotoxicity of the drug cyclosporine, an immunosuppressant used in transplant therapy, may cause hypertension in children (and adults) after

### Table 23-4: The 90th and 95th Percentiles of Systolic and Diastolic Blood Pressure for Boys and Girls 1 to 16 Years of Age by Percentiles for Height

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The height percentile is determined by using the newly revised CDC growth charts. Blood pressure levels are based on new data from the 1999–2000 National Health and Nutritional Examination Survey (NHANES) that have been added to the childhood BP database.

bone marrow, heart, kidney, or liver transplantation. The con-
dominance of corticosteroid drugs appears to increase the inci-
dence of hypertension.

**Diagnosis and Treatment**

The Task Force recommended that children 3 years of age
through adolescence should have their blood pressure taken
once each year. The auscultatory method using a cuff of an
appropriate size for the child’s upper arm is recommended.\(^5^9\)
Repeated measurements over time, rather than a single isolated
determination, are required to establish consistent and signifi-
cant observations. Children with high blood pressure should be
referred for medical evaluation and treatment as indicated.
Treatment includes nonpharmacologic methods and, if neces-
sary, pharmacologic therapy.

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**High Blood Pressure in the Elderly**

The prevalence of hypertension increases with advancing age
to the extent that half of people aged 60 to 69 years and approx-
imately three fourths of people 70 years and older are affected.\(^8\)
The age-related rise in systolic blood pressure is primarily
responsible for the increase in hypertension that occurs with
increasing age.

Among the aging processes that contribute to an increase in
blood pressure are a stiffening of the large arteries, particularly
the aorta; decreased baroreceptor sensitivity; increased peripheral
vascular resistance; and decreased renal blood flow.\(^6^2\) Systolic
blood pressure rises almost linearly between 30 and 84 years of
age, whereas diastolic pressure rises until 50 years of age and then
levels off or decreases.\(^6^3\) This rise in systolic pressure is thought
to be related to increased stiffness of the large arteries. With
aging, the elastin fibers in the walls of the arteries are gradually
replaced by collagen fibers that render the vessels stiffer and less
compliant.\(^6^2\) Differences in the central and peripheral arteries
relate to the fact that the larger vessels contain more elastin,
whereas the peripheral resistance vessels have more smooth
muscle and less elastin. Because of increased wall stiffness, the aorta
and large arteries are less able to buffer the increase in systolic
pressure that occurs as blood is ejected from the left heart, and
they are less able to store the energy needed to maintain the dia-
stolic pressure. As a result, the systolic pressure increases, the
diastolic pressure remains unchanged or actually decreases, and
the pulse pressure or difference between the systolic pressure
and diastolic pressure widens.

Isolated systolic hypertension (systolic pressure \(\geq 140\) mm
Hg and diastolic pressure \(< 90\) mm Hg) is recognized as an
important risk factor for cardiovascular morbidity and mortal-
ity in older persons.\(^8\) The treatment of hypertension in the
elderly has beneficial effects in terms of reducing the incidence
of cardiovascular events such as stroke. Studies have shown a
reduction in stroke, coronary heart disease, and congestive heart
failure in persons who were treated for hypertension compared
with those who were not.\(^6^2,^6^4\)

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**IN SUMMARY,** hypertension (systolic pressure \(\geq 140\) mm Hg
and/or diastolic pressure \(\geq 90\) mm Hg) is one of the most com-
mon cardiovascular disorders. It may occur as a primary disor-
der (i.e., essential hypertension) or as a symptom of some other
disease (i.e., secondary hypertension). The incidence of essen-
tial hypertension increases with age; the condition is seen more
frequently among African Americans, and it may be associated
with a family history of high blood pressure, metabolic syn-
drome, obesity, and increased sodium intake. Causes of sec-
ondary hypertension include kidney disease and adrenal
cortical disorders (hyperaldosteronism and Cushing disease),
which increase sodium and water retention; pheochromocytomas, which increase catecholamine levels; and coarctation of the aorta, which produces an increase in blood flow and systolic blood pressure in the arms and a decrease in blood flow and systolic pressure in the legs.

Unlike disorders of other body systems that are diagnosed by methods such as radiography and tissue examination, hypertension and other blood pressure disorders are determined by repeated blood pressure measurements. Uncontrolled hypertension increases the risk of heart disease, renal complications, retinopathy, and stroke. Treatment of essential hypertension focuses on nonpharmacologic methods such as weight reduction, reduction of sodium intake, regular physical activity, and modification of alcohol intake. Among the drugs used in the treatment of hypertension are diuretics, centrally acting inhibitors, calcium channel blocking agents, of hypertension are diuretics, β-adrenergic blocking agents, ACE inhibitors, and vasodilating drugs.

Hypertension that occurs during pregnancy can be divided into four categories: preeclampsia–eclampsia, gestational hypertension, chronic hypertension, and preeclampsia superimposed on chronic hypertension. Preeclampsia–eclampsia is hypertension that develops after 20 weeks' gestation and is accompanied by proteinuria. This form of hypertension, which is thought to result from impaired placental perfusion along with the release of toxic vasoactive substances that alter blood vessel tone and blood clotting mechanisms, poses a particular threat to the mother and the fetus. Gestational hypertension represents a blood pressure elevation without proteinuria that is detected for the first time after mid-pregnancy and returns to normal by 12 weeks postpartum. Chronic hypertension is hypertension that is unrelated to the pregnancy. It is characterized by hypertension that was present before pregnancy or identified before the 20th week of pregnancy and persists after pregnancy.

The prevalence of hypertension in children and adolescents appears to be increasing, partly as a result of an increase in childhood obesity, and lifestyle factors such as physical inactivity and increased intake of high-calorie and high-salt foods. During childhood, blood pressure is influenced by growth and maturation; therefore, blood pressure norms have been established using percentiles specific to age, height, and sex to identify children for further follow-up and treatment. Although hypertension occurs infrequently in children, it is recommended that children 3 years of age through adolescence should have their blood pressure taken once each year.

The most common type of hypertension in elderly persons is isolated systolic hypertension (systolic pressure ≥140 mm Hg and diastolic pressure <90 mm Hg). Its pathogenesis is related to the loss of elastin fibers in the aorta and the inability of the aorta to stretch during systole. Untreated systolic hypertension is recognized as an important risk factor for stroke and other cardiovascular morbidity and mortality in older persons.

Orthostatic or postural hypotension, which is a physical finding and not a disease, is an abnormal drop in blood pressure on assumption of the standing position. In 1995, the Joint Consensus Committee of the American Autonomic Society and the American Academy of Neurology defined orthostatic hypotension as a drop in systolic pressure of 20 mm Hg or more or a drop in diastolic blood pressure of 10 mm Hg or more within 3 minutes of standing. Although this is now the accepted definition, it does not take into account the possibility that different blood pressure declines may be symptomatic or asymptomatic, depending on the resting supine pressure. It also does not account for blood pressure changes that occur after 3 minutes of standing. Therefore, some authorities regard the presence of orthostatic symptoms (e.g., dizziness, syncope) as being more relevant than the numeric decrease in blood pressure.

**ORTHOSTATIC HYPOTENSION**

After completing this section of the chapter, you should be able to meet the following objectives:

- Define the term orthostatic hypotension.
- Describe the cardiovascular, neurohumoral, and muscular responses that serve to maintain blood pressure when moving from the supine to standing position.
- Explain how fluid deficit, medications, aging, disorders of the ANS, and bed rest contribute to the development of orthostatic hypotension.

Orthostatic or postural hypotension represents an abnormal drop in blood pressure on assumption of the upright position due to pooling of blood in the lower part of the body.

Orthostatic hypotension may be accompanied by a decrease in cerebral perfusion that causes a feeling of lightheadedness, dizziness, and, in some cases, fainting. It poses a particular threat for falls in the elderly.

The fall in blood pressure is caused by conditions that decrease vascular volume (dehydration), impair muscle pump function (bed rest and spinal cord injury), or interfere with the cardiovascular reflexes (medications that decrease heart rate or cause vasodilation, disorders of the ANS, effects of aging on baroreflex function).

**Pathophysiology and Causative Factors**

After the assumption of the upright posture from the supine position, approximately 500 to 700 mL of blood is momentar-
ily shifted to the lower part of the body, with an accompany-
ing decrease in central blood volume and arterial pressure. Maintenance of blood pressure during position change is quite complex, involving the rapid initiation of cardiovascular, neurohumoral, and muscular responses. When the standing position is assumed in the absence of normal circulatory reflexes or blood volume, blood pools in the lower part of the body, cardiac output falls, blood pressure drops, and blood flow to the brain is inadequate. As a result, symptoms of decreased blood flow to the CNS may occur, including feelings of weakness, nausea, lightheadedness, dizziness, blurred vision, palpitations, and syncope (i.e., fainting).

The decrease in blood pressure that occurs on standing is usually transient, lasting through several cardiac cycles. Normally, the baroreceptors located in the thorax and carotid sinus area sense the decreased pressure and initiate reflex constriction of the veins and arterioles and an increase in heart rate, which brings blood pressure back to normal (Fig. 23-7). The initial adjustment to orthostatic stress is mediated exclusively by the ANS. Within a few minutes of standing, blood levels of anti-diuretic hormone and sympathetic neuromediators increase as a secondary means of ensuring maintenance of normal blood pressure in the standing position. Under normal conditions, the renin-angiotensin-aldosterone system is also activated when the standing position is assumed, and even more so in situations of hypotensive orthostatic stress.

Muscle movement in the lower extremities also aids venous return to the heart by pumping blood out of the legs. The unconscious slight body and leg movement during standing (postural sway) is recognized as an important factor in moving venous blood back to the heart. Crossing the legs, which involves contraction of the agonist and antagonist muscles, has been shown to be a simple and effective way of increasing cardiac output and, therefore, blood pressure. When leg crossing is practiced routinely by persons with autonomic failure, standing systolic and diastolic pressures can be increased by approximately 20/10 mm Hg.

Causes

A wide variety of conditions, acute and chronic, are associated with orthostatic hypotension. Although orthostatic hypotension can occur in all age groups, it is seen more frequently in the elderly, especially in persons who are sick and frail. Any disease condition that reduces blood volume, impairs mobility, results in prolonged inactivity, or impairs ANS function may also predispose to orthostatic hypotension. Adverse effects of medications are also commonly encountered causes of orthostatic hypotension.

Aging. Weakness and dizziness on standing are common complaints of elderly persons. Although orthostatic tolerance is well maintained in the healthy elderly, after 70 years of age there is an increasing tendency toward arterial pressure instability and postural hypotension. Although orthostatic hypotension may be either systolic or diastolic, that associated with aging seems more often to be systolic. Several deficiencies in the circulatory response may predispose to this problem in the elderly, including diminished ability to produce an adequate increase in the heart rate, ventricular stroke volume, or peripheral vascular resistance; decreased function of the skeletal muscle pumps; and decreased blood volume. Because cerebral blood flow primarily depends on systolic pressure, patients with impaired cerebral circulation may experience symptoms of weakness, ataxia, dizziness, and syncope when their arterial pressure falls even slightly. This may happen in older persons who are immobilized for even brief periods or whose blood volume is decreased owing to inadequate fluid intake or overzealous use of diuretics.

Postprandial blood pressure often decreases in elderly persons. The greatest postprandial changes occur after a

**FIGURE 23-7** Mechanisms of blood control on immediate assumption of the upright position.
high-carbohydrate meal. Although the mechanism responsible for these changes is not fully understood, it is thought to result from glucose-mediated impairment of baroreflex sensitivity and increased splanchnic blood flow mediated by insulin and vasoactive gastrointestinal hormones.

**Reduced Blood Volume.** Orthostatic hypotension often is an early sign of reduced blood volume or fluid deficit. When blood volume is decreased, the vascular compartment is only partially filled; although cardiac output may be adequate when a person is in the recumbent position, it often decreases to the point of causing weakness and fainting when the person assumes the standing position. Common causes of orthostatic hypotension related to hypovolemia are excessive use of diuretics, excessive diaphoresis, loss of gastrointestinal fluids through vomiting and diarrhea, and loss of fluid volume associated with prolonged bed rest.

**Bed Rest and Impaired Mobility.** Prolonged bed rest promotes a reduction in plasma volume, a decrease in venous tone, failure of peripheral vasoconstriction, and weakness of the skeletal muscles that support the veins and assist in returning blood to the heart (see Chapter 11). Physical deconditioning follows even short periods of bed rest. After 3 to 4 days, the blood volume is decreased. Loss of vascular and skeletal muscle tone is less predictable but probably becomes maximal after approximately 2 weeks of bed rest. Orthostatic intolerance is a recognized problem of space flight—a potential risk after reentry into the earth’s gravitational field.

**Drug-Induced Hypotension.** Antihypertensive drugs and psychotropic drugs are the most common cause of chronic orthostatic hypotension. In most cases, the orthostatic hypotension is well tolerated. However, if the hypotension causes lightheadedness or syncope, the dosage of the drug is usually reduced or a different drug substituted.

**Disorders of the Autonomic Nervous System.** The sympathetic nervous system plays an essential role in adjustment to the upright position. Sympathetic stimulation increases heart rate and cardiac contractility and causes constriction of peripheral veins and arterioles. Orthostatic hypotension caused by altered ANS function is common in peripheral neuropathies associated with diabetes mellitus, after injury or disease of the spinal cord, or as the result of a cerebral vascular accident in which sympathetic outflow from the brain stem is disrupted. The American Autonomic Society and the American Academy of Neurology have distinguished three forms of primary ANS dysfunction: (1) pure autonomic failure, which is defined as a sporadic, idiopathic cause of persistent orthostatic hypotension and other manifestations of autonomic failure such as urinary retention, impotence, or decreased sweating; (2) Parkinson disease with autonomic failure; and (3) multiple-system atrophy (Shy-Drager syndrome). The Shy-Drager syndrome usually develops in middle to late life as orthostatic hypotension associated with uncoordinated movements, urinary incontinence, constipation, and other signs of neurologic deficits referable to the corticospinal, extrapyramidal, corticobulbar, and cerebellar systems.

**Diagnosis and Treatment**

Orthostatic hypotension can be assessed with the auscultatory method of blood pressure measurement. Measurements should be made when the person is supine, after standing for 1 minute, and again after standing for 3 minutes. Because it takes approximately 5 to 10 minutes for the blood pressure to stabilize after lying down, it is recommended that the patient be supine for this period before standing. It is strongly recommended that a second person be available when blood pressure is measured in the standing position to prevent injury should the person become faint. The seated position may be used in persons who are unable to stand; however, the postural blood pressure changes may be missed.

The detection of orthostatic hypotension may require numerous blood pressure measurements under different conditions. The time of day is important because postural hypotension is often worse in the morning when the person rises from bed. Food and alcohol can also exacerbate orthostatic hypotension, as can activities that raise intrathoracic pressure (urination, defecation, coughing). An orthostatic hypotensive response may be immediate or delayed. Prolonged standing or a tilt table test may be needed to detect a delayed response. With a tilt table, the recumbent person can be moved to a head-up position without voluntary movement when the table is tilted. The tilt table also has the advantage of rapidly and safely returning persons with a profound postural drop in blood pressure to the horizontal position.

The heart rate response to postural change may provide valuable information about the cause of orthostatic hypotension. A minimal increase in heart rate (<10 beats/minute) in the face of hypotension suggests impairment of baroreflex function, whereas tachycardia (>100 beats/minute) is suggestive of volume depletion or orthostatic intolerance. Because of the age-related decrease in baroreflex function, the absence of an increase in heart rate does not rule out volume depletion in the elderly person.

Persons with a position-related drop in blood pressure sufficient to qualify as orthostatic hypotension should be evaluated to determine the cause and seriousness of the condition. A history should be taken to elicit information about symptoms, particularly dizziness and history of syncope and falls; medical conditions, particularly those such as diabetes mellitus that predispose to orthostatic hypotension; use of prescription and over-the-counter drugs; and symptoms of ANS dysfunction, such as erectile or bladder dysfunction. A physical examination should document blood pressure in both arms and the heart rate while in the supine, sitting, and standing positions and should note the occurrence of symptoms. Noninvasive, 24-hour ambulatory blood pressure monitoring may be used to determine blood pressure responses to other stimuli of daily life, such as food ingestion and exertion.

Treatment of orthostatic hypotension usually is directed toward alleviating the cause or, if this is not possible, toward
helping people learn ways to cope with the disorder and prevent falls and injuries. Medications that predispose to postural hypotension should be avoided. Correcting the fluid deficit and trying a different antihypertensive medication are examples of measures designed to correct the cause. Measures designed to help persons prevent symptomatic orthostatic drops in blood pressure include gradual ambulation to allow the circulatory system to adjust (i.e., sitting on the edge of the bed for several minutes and moving the legs to initiate skeletal muscle pump function before standing); avoidance of situations that encourage excessive vasodilation (e.g., drinking alcohol, exercising vigorously in a warm environment); and avoidance of excess diuresis (e.g., use of diuretics), diaphoresis, or loss of body fluids. Tight-fitting elastic support hose or an abdominal support garment may help prevent pooling of blood in the lower extremities and abdomen.

Pharmacologic treatment may be used when nonpharmacologic methods are unsuccessful. A number of types of drugs can be used for this purpose.67,69 Mineralocorticoids (e.g., fludrocortisone) can be used to reduce salt and water loss and probably increase α-adrenergic sensitivity. Vasopressin-2 receptor agonists (desmopressin as a nasal spray) may be used to reduce nocturnal polyuria. Sympathomimetic drugs that act directly on the resistance vessels (e.g., phenylephrine, noradrenaline, clonidine) or on the capacitance vessels (e.g., dihydroergotamine) may be used. Many of these agents have undesirable side effects. Octreotide, a somatostatin analog that inhibits the release of vasodilatory gastrointestinal peptides, may prove useful in persons with postprandial hypotension.

**IN SUMMARY,** orthostatic hypotension refers to an abnormal decrease in systolic and diastolic blood pressures that occurs on assumption of the upright position. An important consideration in orthostatic hypotension is the occurrence of dizziness and syncope. Among the factors that contribute to its occurrence are decreased fluid volume, medications, aging, defective function of the ANS, and the effects of immobility. Diagnosis of orthostatic hypotension relies on blood pressure measurements in the supine and upright positions, and a history of symptomatology, medication use, and disease conditions that contribute to a postural drop in blood pressure. Treatment includes correcting the reversible causes and assisting the person to compensate for the disorder and prevent falls and injuries.

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**Review Exercises**

1. A 47-year-old African American man who is an executive in a law firm has his blood pressure taken at a screening program and is told that his pressure is 142/90 mm Hg. His father and older brother have hypertension, and his paternal grandparents had a history of stroke and myocardial infarction. The patient enjoys salty foods and routinely uses a salt shaker to add salt to meals his wife prepares, drinks about four beers while watching television in the evening, and gained 15 pounds in the past year. Although his family has encouraged him to engage in physical activities with them, he states he is either too busy or too tired.

A. According to the JNC 7 guidelines, into what category does the patient’s blood pressure fall?
B. What is his risk factors for hypertension?
C. Explain how an increased salt intake might contribute to his increase in blood pressure.
D. What lifestyle changes would you suggest to the patient? Explain the rationale for your suggestions.

2. A 36-year-old woman enters the clinic complaining of headache and not feeling well. Her blood pressure is 175/90 mm Hg. Her renal test results are abnormal, and follow-up tests confirm that she has a stricture of the left renal artery.

A. Would this woman’s hypertension be classified as primary or secondary?
B. Explain the physiologic mechanisms underlying her blood pressure elevation.

3. A 75-year-old woman residing in an extended care facility has multiple health problems, including diabetes, hypertension, and heart failure. Lately, she has been feeling dizzy when she stands up, and she has almost fallen on several occasions. Her family is concerned and wants to know why this is happening and what they can do to prevent her from falling and breaking her hip.

A. How would you go about assessing this woman for orthostatic hypotension?
B. What are the causes of orthostatic hypotension in elderly persons?
C. How might this woman’s medical conditions and their treatment contribute to her orthostatic hypotension?
D. The woman tells you that she feels particularly dizzy after she has eaten, yet staff members insist that she sit up and socialize with the other residents even though she would rather lie down and rest until the dizziness goes away. Explain the possible reason for her dizziness and what measures might be used to counteract the dizziness.
E. The woman recently had an episode of vomiting and diarrhea on an extremely hot day. She told her family that she was so dizzy that she was sure she would fall. Explain why her dizziness was more severe under these conditions and what might be done to alleviate the situation.
References


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