CHAPTER

16

Alterations in Blood Pressure

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 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 due to its effect on the heart, blood vessels, and kidneys.

CONTROL OF BLOOD PRESSURE

The arterial blood pressure reflects the rhythmic ejection of blood from the left ventricle into the aorta. It rises as the left ventricle contracts and falls as it relaxes. The contour of the arterial pressure tracing shown in Figure 16-1 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; this accounts for the rapid rise in the pressure contour. The end of systole is marked by a brief downward deflection and formation of the dicrotic notch, which occurs when ventricular pressure falls below that in the aorta. The sudden closure of the aortic valve is associated with a small rise in pressure due to continued contraction of the aorta and other large vessels against the closed valve. As the ventricles relax and blood flows into the peripheral vessels during diastole, the arterial pressure falls rapidly at first and then declines slowly as the driving force decreases.

In healthy adults, the highest pressure, called the *systolic pressure*, ideally is less than 120 mm Hg, and the lowest pressure, called the *diastolic pressure*, is less than 80 mm Hg. The
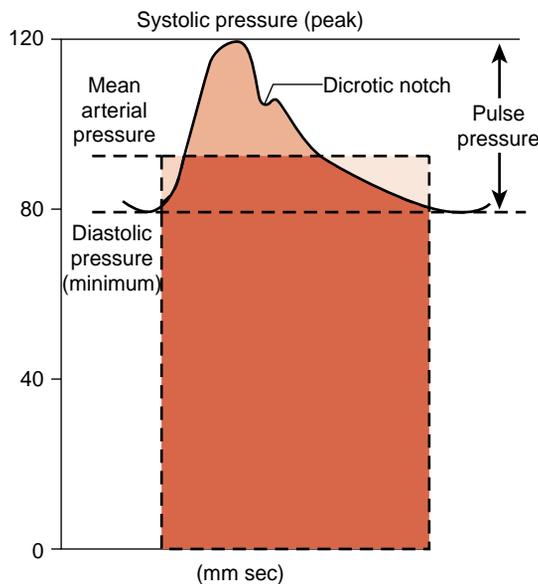
■ **FIGURE 16-1** ■ Intra-arterial pressure tracing made from the brachial artery. Pulse pressure is the difference between systolic and diastolic pressures. The darker area represents the mean arterial pressure, which can be calculated by using the formula of mean arterial pressure = diastolic pressure + pulse pressure/3.

KEY CONCEPTS

DETERMINANTS OF BLOOD PRESSURE

■ The arterial blood pressure represents the pressure of the blood as it moves through the arterial system. It reaches its peak (systolic pressure) as blood is ejected from the heart during systole and its lowest level (diastolic pressure) as the heart relaxes during diastole.

■ Blood pressure is determined by the cardiac output (stroke volume × heart rate) and the resistance that the blood encounters as it moves through the peripheral vessels (peripheral vascular resistance).

■ The systolic blood pressure is largely determined by the characteristics of the stroke volume being ejected from the heart and the ability of the aorta to stretch and accommodate the stroke volume.

■ The diastolic pressure is largely determined by the energy that is stored in the aorta as its elastic fibers are stretched during systole and by the resistance to the runoff of blood from the peripheral blood vessels.

difference between the systolic and diastolic pressure (approximately 40 mm Hg) is the *pulse pressure*. The *mean arterial pressure* (approximately 90 to 100 mm Hg), depicted by the darker area under the pressure tracing in Figure 16-1, represents the average pressure in the arterial system during ventricular contraction and relaxation.

Determinants of Blood Pressure

The systolic and diastolic components of blood pressure are determined by the cardiac output and the peripheral vascular resistance and can be expressed as a product of the two (blood pressure = cardiac output × peripheral vascular resistance). The cardiac output is the product of the stroke volume (amount of blood ejected from the heart with each beat) and the heart rate. The peripheral vascular resistance reflects changes in the radius of the arterioles as well as the viscosity or thickness of the blood. The arterioles often 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 it 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 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.

Systolic Blood Pressure

The systolic blood pressure reflects the rhythmic ejection of blood into the aorta (Fig. 16-2). As blood is ejected into the aorta, it stretches the vessel wall and produces a rise in aortic pressure. The extent to which the systolic pressure rises or falls with each cardiac cycle is determined by the amount of blood ejected into the aorta with each heart beat (*i.e.*, stroke volume), the velocity of ejection, and the elastic properties of the aorta. Systolic pressure increases when there is a rapid ejection of a large stroke volume or when the stroke volume is ejected into a rigid aorta. The elastic walls of the aorta normally stretch to accommodate the varying amounts of blood that are ejected into the aorta; this prevents the pressure from rising excessively during systole and maintains the pressure during diastole. In some elderly persons, the elastic fibers of the aorta lose some of their elasticity, and the aorta becomes more rigid. When this occurs, the aorta is less able to stretch and buffer the pressure that is generated as blood is ejected into the aorta, resulting in an elevated systolic pressure.

Diastolic Blood Pressure

The diastolic blood pressure is maintained by the energy that has been stored in the elastic walls of the aorta during systole (see Fig. 16-2). The level at which the diastolic pressure is maintained depends on the elastic properties of the aorta and large arteries and their ability to stretch and store energy, the resistance of the arterioles that control the outflow of blood into the microcirculation, and the competency of the aortic valve. The small diameter of the arterioles contributes to their effectiveness as resistance vessels because it takes more force to push blood through a smaller vessel than a larger vessel. When
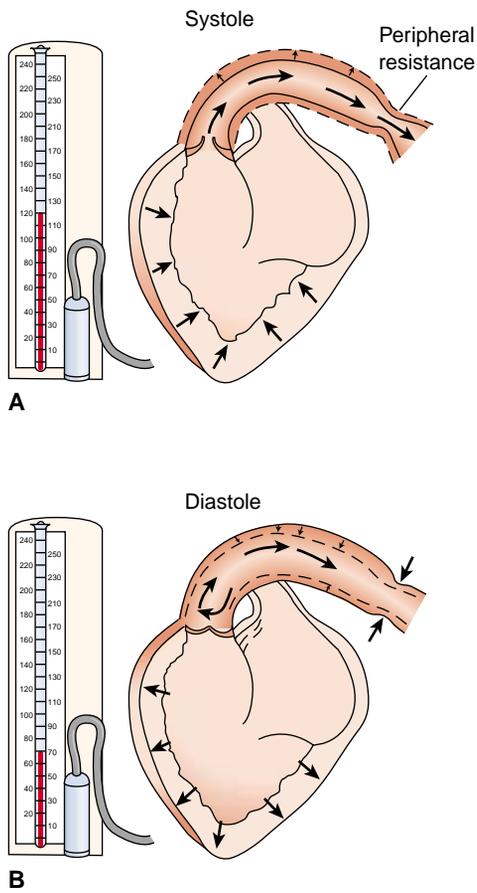
■ **FIGURE 16-2** ■ Diagram of the left side of the heart. (**A**) Systolic blood pressure represents the ejection of blood into the aorta during ventricular systole; it reflects the stroke volume, the distensibility of the aorta, and the velocity with which blood is ejected from the heart. (**B**) Diastolic blood pressure represents the pressure in the arterial system during diastole; it is largely determined by the peripheral vascular resistance.

there is an increase in peripheral vascular resistance, as with sympathetic stimulation, diastolic blood pressure rises. Closure of the aortic valve at the onset of diastole is essential to the maintenance of the diastolic pressure. When there is incomplete closure of the aortic valve, as in aortic regurgitation (see Chapter 17), the diastolic pressure drops as blood flows backward into the left ventricle, rather than moving forward into the arterial system.

Pulse Pressure

The pulse pressure is the difference between the systolic and diastolic pressures. It reflects the pulsatile nature of arterial blood flow and is an important component of blood pressure. During the rapid ejection period of ventricular systole, the volume of blood that is ejected into the aorta exceeds the amount that exits the arterial system. The pulse pressure reflects this difference. The pulse pressure rises when additional amounts of blood are ejected into the arterial circulation, and it falls when the resistance to outflow is decreased. In hypovolemic shock, the pulse pressure declines because of a decrease in stroke volume and systolic pressure. This occurs despite an increase in

peripheral vascular resistance, which maintains the diastolic pressure.

Mean Arterial Pressure

The mean arterial blood pressure represents the average blood pressure in the systemic circulation. The mean arterial pressure can be estimated by adding one third of the pulse pressure to the diastolic pressure (*i.e.*, diastolic blood pressure + pulse pressure/3). Hemodynamic monitoring equipment in intensive and coronary care units measures or computes mean arterial pressure automatically. Because it is a good indicator of tissue perfusion, the mean arterial pressure often is monitored, along with systolic and diastolic blood pressures, in critically ill patients.

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 method by which the arterial pressure is regulated depends on whether short-term or long-term adaptation is needed. The mechanisms of blood pressure regulation are illustrated in Figure 16-3.

Short-Term Regulation

The mechanisms for short-term regulation of blood pressure, those occurring 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. The short-term regulation of blood pressure relies mainly on neural and hormonal mechanisms, the most rapid of which are the neural mechanisms.

Neural Mechanisms. The neural control center for the regulation of blood pressure is located in the reticular formation of the lower pons and medulla of the brain where integration and modulation of autonomic nervous system (ANS) responses occur.[1] 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 transmits 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 *baroreflex* and *chemoreceptor-mediated reflex*, 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 path-

■ **FIGURE 16-3** ■ Mechanisms of blood pressure regulation. The *solid lines* represent the mechanisms for renal and baroreceptor control of blood pressure through changes in cardiac output and peripheral vascular resistance. The *dashed lines* represent the stimulus for regulation of blood pressure by the baroreceptors and the kidneys.

ways 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 due to 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. 16-4). 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 sensitive to changes in 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.16-4). 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 the cardiovascular center and can induce widespread vasoconstriction. When 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 21).

Humoral Mechanisms. A number of hormones and humoral mechanisms contribute to blood pressure regulation, including the renin-angiotensin-aldosterone mechanism and vasopressin. Other humoral substances such as epinephrine, a sympathetic neurotransmitter released from the adrenal gland, has 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 kidneys in response to an increase in sympathetic nervous system activity or a decrease
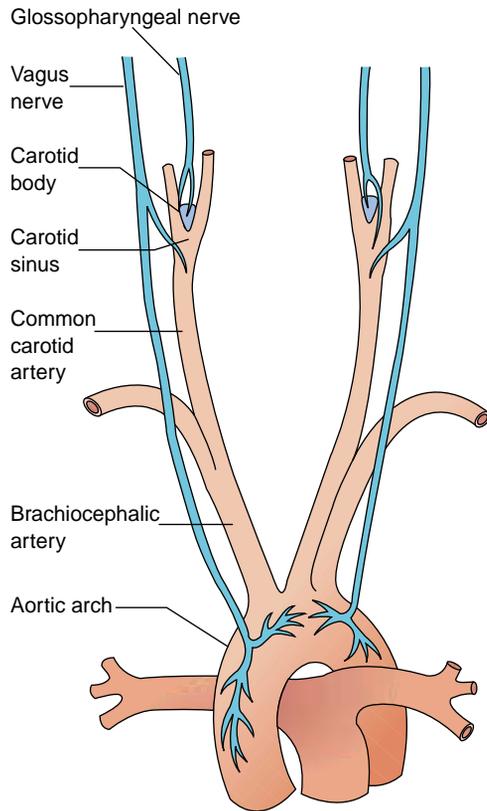
■ FIGURE 16-4 ■ Location and innervation of the aortic arch and carotid sinus baroreceptors and the carotid body chemoreceptors.

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. 16-5). Angiotensin I travels to the small blood vessels of the lung, where it is converted to angiotensin II by the angiotensin-converting enzyme that is present in the endothelium of the lung vessels. Although angiotensin II has a half-life of 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-term and long-term regulation of blood pressure. It is a strong vasoconstrictor, particularly of arterioles and to a lesser extent of veins. The vasoconstrictor response produces an increase in peripheral vascular resistance (and blood pressure) and functions in the short-term regulation of blood pressure. A second major function of angiotensin II, stimulation of aldosterone secretion from the adrenal gland, contributes to the long-term regulation of blood pressure by increasing salt and water retention by the kidney. It also acts directly on the kidney to decrease the elimination of salt and water.

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 6. Vasopressin has a direct vasoconstrictor effect on blood vessels, particularly those of the splanchnic circulation that supplies the abdomi-
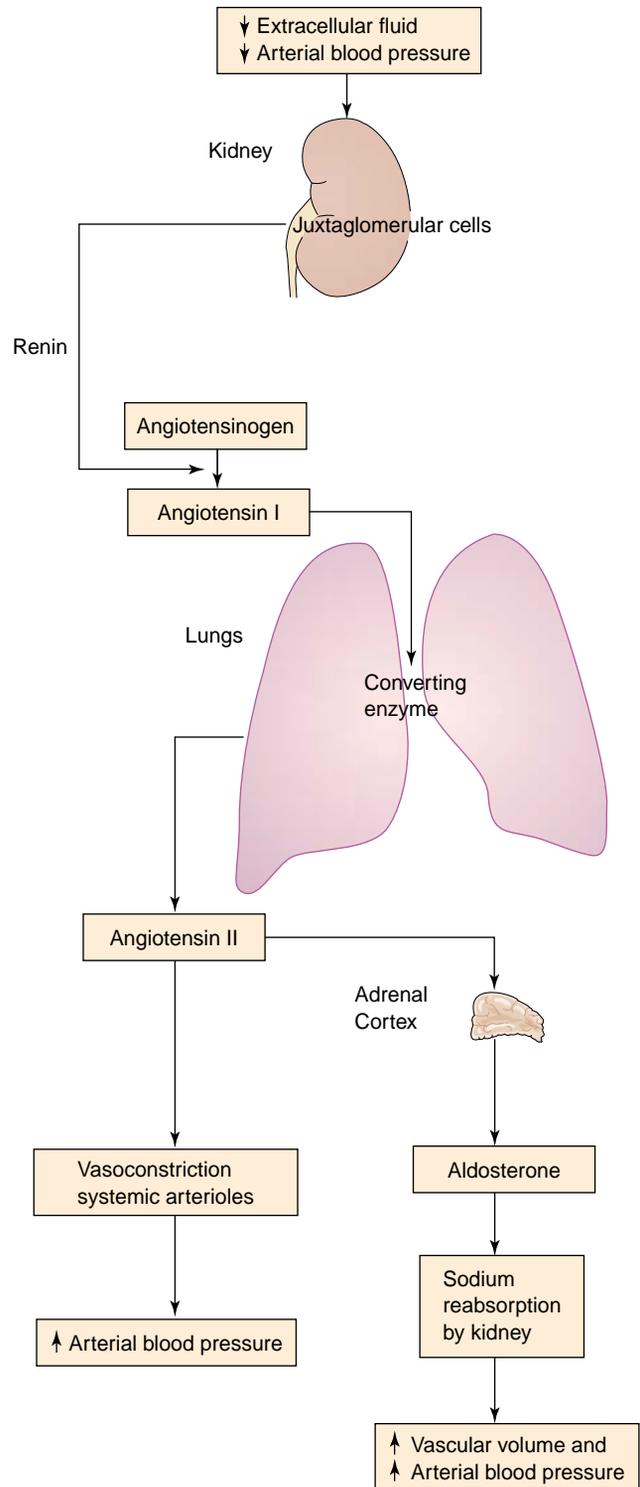
■ FIGURE 16-5 ■ Control of blood pressure by the renin-angiotensin-aldosterone system. Renin enzymatically converts the plasma protein angiotensinogen to angiotensin I; angiotensin-converting enzyme in the lung converts angiotensin I to angiotensin II; and angiotensin II produces vasoconstriction and increases salt and water retention through direct action on the kidney and through increased aldosterone secretion by the adrenal cortex.

nal viscera. However, long-term increases in vasopressin cannot maintain volume expansion or hypertension, and it 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 fluid-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 regulation of extracellular fluid volume.[1] Blood pressure is normally regulated around an equilibrium point, which represents the normal pressure for a given individual. Accordingly, when the body contains too much extracellular fluid, the arterial pressure rises and the rate at which water (*i.e., pressure diuresis*) and salt (*i.e., pressure natruresis*) are excreted by the kidney is increased.[1] When blood pressure returns to its equilibrium point, water and salt excretion return to normal. A fall in blood pressure due to a decrease in extracellular fluid volume has the opposite effect. In persons with hypertension, renal control mechanisms are often altered such that the equilibrium point for blood pressure regulation is maintained at a higher level of salt and water elimination.

There are several ways that extracellular fluid volume serves to regulate blood pressure. One is through a direct effect on cardiac output and another is indirect resulting from 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 14). 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 blood volume and 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.

The role that the kidneys play in blood pressure regulation is emphasized by the fact that many hypertension medications produce their blood pressure-lowering effects by increasing salt and water elimination.

> **In summary,** the arterial blood pressure that moves blood through the circulatory system reflects the alternating contraction and relaxation of the left heart. The systolic pressure denotes the peak pressure that occurs during ventricular contraction, and the diastolic pressure denotes the lowest point that occurs during relaxation. The pulse pressure is the difference between these two pressures, and the mean arterial pressure reflects the average pressure throughout the cardiac cycle.
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> The level to which the arterial blood pressure rises during systole and falls during diastole is determined by the cardiac output (stroke volume × heart rate) and the peripheral vascular resistance. Systolic pressure is determined primarily by the characteristics of the stroke volume and elastic properties of the aorta and large arteries and their ability to stretch and

> accommodate the varying amounts of blood that is ejected from the heart. Diastolic pressure is determined largely by the smaller arteries and their ability to maintain the peripheral vascular resistance and accept the runoff of blood from the larger arteries.
>
> Normally, blood pressure is regulated at levels sufficient to ensure adequate tissue perfusion. Blood pressure regulation requires the use of short-term and long-term mechanisms. Short-term regulation, which occurs over minutes and hours, involves ANS responses associated with baroreceptor and chemoreceptor stimulation and hormonal mechanisms such as the renin-angiotensin-aldosterone system and vasopressin. Long-term mechanisms are involved in the daily, weekly, and monthly regulation of blood pressure. They are largely vested in the kidney and involve regulation of the extracellular fluid volume through the elimination of water (pressure diuresis) and salt (pressure natruresis).

HYPERTENSION

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. In the United States, approximately 25% of all adults older than 18 years of age have high blood pressure.[2] It has been estimated that as many as 60 million adults have cardiovascular disease. In 50 million of these people (83%), the cause of cardiovascular disease is high blood pressure. 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 do women up until the time of menopause, at which point women quickly lose their protection.[2]

Hypertension commonly is divided into the categories of primary and secondary hypertension. In primary, or *essential*, hypertension, which accounts for 90% to 95% of all hypertension, the chronic elevation in blood pressure occurs without evidence of other disease. In secondary hypertension, the elevation of blood pressure results from some other disorder, such as kidney disease. Malignant hypertension, as the name implies, is an accelerated form of hypertension.

Essential Hypertension

The sixth report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC-VI) of the National Institutes of Health was published in 1997.[2] The JNC-VI report classifies blood pressure as optimal, normal, high-normal, and hypertensive (Table 16-1). Hypertension is further divided into stages 1, 2, and 3 based on systolic and diastolic blood pressure measurements. For adults with diabetes mellitus, the blood pressure goal has been lowered to less than 130/80 mm Hg.[3]

Mechanisms of Blood Pressure Elevation

Several factors, including hemodynamic, neural, humoral, and renal mechanisms, are thought to interact in producing long-term elevations in blood pressure. As with other disease

HYPERTENSION

- Essential hypertension is characterized by a chronic elevation in blood pressure that occurs without evidence of other disease and secondary hypertension by an elevation of blood pressure that results from some other disorder, such as kidney disease.

- The pathogenesis of essential hypertension is thought to reside with the kidney and its role regulating vascular volume through salt and water elimination; the renin-angiotensin-aldosterone system through its effects on blood vessel tone, regulation of renal blood flow, and salt metabolism; and the sympathetic nervous system, which regulates the tone of the resistance vessels.

- Uncontrolled hypertension increases the work demands on the heart, resulting in left ventricular hypertrophy and heart failure, and on the vessels of the arterial system, leading to atherosclerosis, kidney disease, and stroke.

conditions, it is probable that there is not a single cause of essential hypertension or that the condition is a single disease. Because arterial blood pressure is the product of cardiac output and peripheral vascular resistance, all forms of hypertension involve hemodynamic mechanisms—an increase in either cardiac output or peripheral vascular resistance, or a combination of the two. Other factors, such as sympathetic nervous system activity, kidney function in terms of salt and water retention, the electrolyte composition of the intracellular and extracellular fluids, and humoral influences such as the renin-angiotensin-aldosterone mechanism, play an active or permissive role in regulating the hemodynamic mechanisms that control blood pressure.

Contributing Factors

Risk Factors. Although the cause or causes of essential hypertension are largely unknown, several constitutional factors have been implicated as contributing to its development. These risk factors include family history of hypertension, race, diabetes mellitus, and age-related increases in blood pressure. 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 inherited predisposition does not seem to rely on other risk factors, but when they are present, the risk apparently is additive. Hypertension not only is more prevalent in African Americans than whites, it is more severe, tends to occur earlier, and often is not treated early enough or aggressively enough. Blacks also tend to develop greater cardiovascular and renal damage at any level of pressure.[4] Diabetes mellitus and hypertension are closely interrelated disorders that share similar genetic and life-style factors. Also, persons with both hypertension and diabetes have a greater risk of target organ damage. Maturation and growth are known to cause predictable increases in blood pressure from infancy to adolescence. In adult life, the systolic pressure continues to slowly rise, and hypertension becomes more common with increasing age.

Lifestyle Factors. Lifestyle factors can contribute to the development of hypertension by interacting with the constitutional risk factors. These lifestyle factors include high sodium intake,

TABLE 16-1	Classification and Follow-up of Blood Pressure Measurements for Adults 18 Years of Age and Older*			
Category*	**Systolic Blood Pressure (mm Hg)**		**Diastolic Blood Pressure (mm Hg)**	**Follow-up Recommended**
Optimal†	<120	and	<80	Recheck in 2 years
Normal	<130	and	<85	Recheck in 2 years
High-Normal	130–139	or	85–89	Recheck in 1 year
Hypertension‡				
Stage 1	140–159	or	90–99	Confirm within 2 months
Stage 2	160–179	or	100–109	Evaluate or refer to source of care within 1 month
Stage 3	≥180	or	≥110	Evaluate or refer to source of care immediately or within 1 week, depending on clinical situation

*Not taking antihypertensive drugs and not acutely ill. When systolic and diastolic pressures fall into different categories, the higher category should be selected to classify the individual's blood pressure status. For instance, 160/92 should be classified as stage 2 and 174/120 should be classified as stage 3. Isolated systolic hypertension (ISH) is defined as systolic blood pressure ≥140 mm Hg and diastolic blood pressure <90 mm Hg and staged appropriately (*e.g.,* 170/82 mm Hg is defined as stage 2 ISH). In addition to classifying stages of hypertension on the basis of average blood pressure levels, clinicians should specify presence or absence of target-organ disease and additional risk factors. This specificity is important for risk classification and treatment.
†Optimal blood pressure with respect to cardiovascular risk is below 120/80 mm Hg. However, unusually low readings should be evaluated for clinical significance.
‡Based on the average of two or more readings taken at each of two or more visits after an initial screening.
(Adapted from the National Heart, Lung, and Blood Institute. [1997]. *The sixth report of the National Committee on Detection, Evaluation, and Treatment of High Blood Pressure* [pp. 11, 13]. NIH publication no. 98-4080. Bethesda, MD: National Institutes of Health. Available: http://www.nhlbi.nih.gov/guidelines/hypertension/jncintro.htm)

excessive calorie intake and obesity, physical inactivity, and excessive alcohol consumption. Oral contraceptive drugs also may increase blood pressure in predisposed women. Although stress can raise blood pressure acutely, there is less evidence linking it to chronic elevations in blood pressure. Dietary fats and cholesterol are independent risk factors for cardiovascular disease, but there is no evidence that they raise blood pressure. Smoking, although not identified as a primary risk factor in hypertension, is an independent risk factor in coronary heart disease and should be avoided.

Increased salt intake has long been implicated as an etiologic factor in the development of hypertension.[2,5] 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 stimuli, or exerts its effects through some other mechanisms such as the renin-angiotensin-aldosterone system.

Excessive weight commonly is associated 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 (*i.e.*, fat cell deposits in the abdomen) from peripheral or lower body obesity with fat cell deposits in the buttocks and legs (see Chapter 29).[6]

Regular alcohol consumption can play a role in the development of hypertension. The effect is seen with different types of alcoholic beverages, in men and women, and in a variety of ethnic groups.[7,8] Systolic pressure is usually more markedly affected than diastolic pressure. Blood pressure may improve or return to normal when alcohol consumption is decreased or eliminated.

Oral contraceptives cause a mild increase in blood pressure in many women and overt hypertension in approximately 5%.[9] Why this occurs is largely unknown, although it has been suggested that estrogen and progesterone are responsible for the effect. 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 use of the drug has been discontinued, although it may take as long as 6 months for this to happen. However, in some women the blood pressure may not return to normal; they may be at risk for hypertension. The risk of hypertension-associated cardiovascular complications is found primarily in women older than 35 years of age and in those who smoke.[2]

Manifestations

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 of the body including the kidneys, heart, eyes, and blood vessels.

The 1997 JNC-VI report uses the term *target organ disease* to describe the cardiac, cerebrovascular, peripheral arterial disease, kidney, and retinal complications associated with hypertension (Chart 16-1).[2] The excess morbidity and mortality related to hypertension is progressive over the whole range of systolic and diastolic pressures. Target organ damage varies markedly among persons with similar levels of hypertension.

Hypertension is a major risk factor for atherosclerosis; it predisposes to all major atherosclerotic cardiovascular disorders,

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CHART 16-1 Components of Target Organ Damage/Cardiovascular Disease in Persons With Hypertension

Heart disease
- Left ventricular hypertrophy
- Angina/prior myocardial infarction
- Prior coronary revascularization
- Heart failure

Stroke or transient ischemic attack

Nephropathy

Peripheral arterial disease

Retinopathy

Adapted from National Heart, Lung, and Blood Institute. (1997). *The sixth report of the National Committee on Prevention, Detection, and Treatment of High Blood Pressure* (p. 16). NIH publication no. 98-4080. Bethesda, MD: National Institutes of Health.

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including heart failure, stroke, coronary artery disease, and peripheral artery disease. The risk of coronary artery disease and stroke depends to a great extent on other risk factors, such as obesity, smoking, and elevated cholesterol levels. If all else is favorable, the risk of a coronary event in persons with mild hypertension is no greater than in the average population of the same age. However, if a cluster of risk factors exists, the risk is greatly increased. The same is true for stroke. The risk of stroke in persons with hypertension occurs over an eightfold range, depending on the number of associated risk factors.[10] Cerebrovascular complications are more closely related to systolic than diastolic hypertension.

Hypertension 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 compensatory function, left ventricular hypertrophy is a major risk factor for ischemic heart disease, cardiac dysrhythmias, sudden death, and congestive heart failure. The prevalence of left ventricular hypertrophy increases with age and is highest in persons with blood pressures greater than 160/95 mm Hg.[11] Hypertensive left ventricular hypertrophy usually regresses with therapy. Regression is most closely related to systolic pressure reduction and does not appear to reflect the particular type of medication used.

Hypertension also can lead to nephrosclerosis, a common cause of renal insufficiency (see Chapter 23). Hypertensive kidney disease is more common in blacks than whites. Hypertension also plays an important role in accelerating the course of other types of kidney disease, particularly diabetic nephropathy.[3] Because of the risk of 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 32).

Diagnosis and Treatment

Unlike disorders of organ structure that are diagnosed by methods such as x-rays and tissue examination, hypertension and other blood pressure disorders are determined by repeated blood pressure measurement. The diagnosis of hypertension

in a person who is not taking antihypertensive medications should be based on the average of at least two or more blood pressure readings taken at each of two or more visits after an initial screening visit.[2] 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 disease.

Clinically, blood pressure measurements are usually obtained by the auscultatory method, which uses a sphygmomanometer and a stethoscope. Accuracy of blood pressure measurement requires that persons taking the pressure are adequately trained in blood pressure measurement, that the equipment is properly maintained and calibrated, and the cuff bladder is appropriate for the arm size.[12] The width of the bladder should be at least 40% of arm circumference and the length at least 80% of arm circumference. Undercuffing (using a cuff with a bladder that is too small) can cause an overestimation of blood pressure.[13] This is because a cuff that is too small results in an uneven distribution of pressure across the arm, such that a greater cuff pressure is needed to occlude blood flow. Likewise, overcuffing (using a cuff with a bladder that is too large) can cause an underestimation of blood pressure.

The main objective for treatment of essential hypertension is to achieve and maintain arterial blood pressure of less than 140/90 mm Hg, with the goal of preventing morbidity and mortality. 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 for the underlying disease. The JNC-VI 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 systolic pressure below 140 mm Hg and diastolic pressure below 90 mm Hg.[2]

Lifestyle Modification. Lifestyle modification includes reduction in sodium intake, maintenance of adequate potassium intake, weight reduction if overweight, regular aerobic physical activity, and modification of alcohol intake. A reduction in dietary saturated fats and cholesterol is recommended for overall cardiovascular health. Smoking cessation should be encouraged for people who smoke. For persons with stage 1 hypertension (see Table 16-1), an attempt to control blood pressure with weight loss and other lifestyle modifications should be tried for at least 3 to 6 months before initiating pharmacologic treatment.[4]

The American Heart Association recommends the daily salt intake for adults in the general population should not exceed 6 g/day.[14] Because many prepared foods are high in sodium, it was recommended that persons consult package labels for the sodium content of canned foods, frozen foods, soft drinks, and other foods and beverages to reduce sodium intake adequately. High dietary potassium intake may protect against the development of hypertension or improve blood pressure control in people with hypertension. Therefore, an adequate intake of potassium (approximately 90 mmol per day), preferably from food sources such as fresh fruits and vegetables, is recommended.[2]

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.[2] Because of alcohol's association with high blood pressure, the JNC-VI report recommends restriction of alcohol consumption to no more than 1 oz (30 mL) ethanol per day (equal to 2 oz of 100-proof whiskey, 10 oz of wine, or 24 oz of beer) or 0.5 oz per day for women or lighter weight people.[2]

A regular program of aerobic physical exercise (*e.g.*, walking, biking, swimming) is protective, especially for those at increased risk for cardiovascular disease because of hypertension. Exercise may have additional indirect benefits, such as weight loss or motivation for changing other risk factors.

Pharmacologic Treatment. The decision to initiate pharmacologic treatment is based on the severity of the hypertension, the presence of target organ disease, and the existence of other conditions and risk factors. Drug selection is based on the stage of hypertension. Among the drugs used in the treatment of hypertension are diuretics, β-adrenergic–blocking drugs, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers, the calcium channel-blocking drugs, central α_2-adrenergic agonists, α_1-adrenergic receptor blockers, and vasodilators.

The physiologic mechanisms whereby the different hypertension drugs produce a reduction in blood pressure differ among agents. 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 reduction in peripheral resistance becomes a major mechanism of blood pressure reduction. β-Adrenergic–blocking drugs are effective in treating hypertension because they decrease heart rate, cardiac output, and renin release by the kidney. 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. The calcium channel blockers decrease peripheral vascular resistance by inhibiting the movement of calcium into arterial smooth muscle cells. The centrally acting α_2-adrenergic agonists act in a negative-feedback manner to decrease sympathetic outflow from the central nervous system. The α_1-adrenergic receptor antagonists block α_1 receptors on vascular smooth muscle causing vasodilation and a reduction in peripheral vascular resistance. The direct-acting smooth muscle vasodilators promote a decrease in peripheral vascular resistance by producing relaxation of vascular smooth muscle, particularly of the arterioles.

Pharmacologic treatment of hypertension usually follows a stepwise approach.[2] It is usually initiated with a low dose of a single drug. The dose is slowly increased at a schedule dependent on the person's age, needs, and desired response.[2] If the response to the initial drug is not adequate, one of three approaches can be used: the dose can be increased if the initial dose was below the maximum recommended; a drug with a different mode of action can be added; or the initial drug can be discontinued and another substituted. Combining drugs with different modes of action often allows smaller doses to be used to achieve blood pressure control, while minimizing the dose-dependent side effects from any one drug. In treating stage 3 or 4 hypertension, it often is necessary to add a second or third drug after a short interval if the treatment goal is not achieved.

Systolic Hypertension

Essential hypertension may be classified as systolic/diastolic hypertension in which both the systolic and diastolic pressures are elevated; as diastolic hypertension in which the diastolic pressure is selectively elevated; or as systolic hypertension in which the systolic pressure is selectively elevated. The JNC-VI report defined systolic hypertension as a systolic pressure of 140 mm Hg or greater and a diastolic pressure less than 90 mm Hg and indicated a need for increased recognition and control of isolated systolic hypertension.[2] Historically, diastolic hypertension was thought to confer a greater risk for cardiovascular events than systolic hypertension.[2] However, there is mounting evidence that elevated systolic blood pressure is at least as important, if not more so, than diastolic hypertension.[15,16]

There are two aspects of systolic hypertension that confer increased risk of 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 levels of pulse pressure produce greater stretch of arteries, causing damage to the elastic elements of the vessel and thus predisposing to aneurysms and development of the endothelial cell damage that leads to atherosclerosis and thrombosis.

Secondary Hypertension

Only 5% to 10% of hypertensive cases are classified as secondary hypertension (*i.e.*, hypertension due to another disease condition). 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 more commonly in persons younger than 30 years and those older than 50 years of age.[17] Among the most common causes of secondary hypertension are kidney disease (*i.e.*, renovascular hypertension), adrenal cortical disorders, pheochromocytoma, and coarctation of the aorta. Cocaine and cocaine-like substances also can cause significant 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.

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. The reduced renal blood flow that occurs with renovascular disease causes the affected kidneys to release excessive amounts of renin, increasing circulating levels of angiotensin II. One or both of the kidneys may be affected.

Manifestations of renovascular hypertension include hypokalemia (caused by increased aldosterone levels), the presence of an abdominal bruit, and a duration of hypertension of less than 1 year (to 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 renal function.

Disorders of Adrenocorticosteroid Hormones

Excess production of aldosterone caused by adrenocortical hyperplasia or adenoma (primary hyperaldosteronism) and excess levels of glucocorticoid (Cushing's disease or syndrome) tend to raise the blood pressure (see Chapter 31). These hormones produce hypertension through increased salt and water retention by the kidney. For persons 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. Potassium-sparing diuretics, such as spironolactone, which is an aldosterone antagonist, often are used in the medical care of persons with the disorder.

Pheochromocytoma

A pheochromocytoma is a tumor of chromaffin tissue, which contains sympathetic nerve cells. The tumor is most commonly located in the adrenal medulla but can arise in other sites, such as sympathetic ganglia, where there is chromaffin tissue.[18] Although only 0.1% to 0.5% of persons with hypertension have an underlying pheochromocytoma, the disorder can cause serious hypertensive crises. Eight percent to 10% of the tumors are malignant.

Like adrenal medullary cells, the tumor cells of a pheochromocytoma produce and secrete the catecholamines epinephrine and norepinephrine. The hypertension that develops is the result of a 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. Some persons with pheochromocytoma have paroxysmal episodes of hypertension, sometimes to dangerously high levels; others may have sustained hypertension; and some may even be normotensive.

Coarctation of the Aorta

Coarctation of the aorta represents a narrowing of the aorta just distal to the origin of the subclavian arteries (see Chapter 17).[19] The ejection of a large stroke volume into a narrowed aorta with limited ability to accept the runoff results in 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 cardiac output 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 exaggerated. It is important that blood pressure be measured in both arms and one leg when coarctation of the aorta is suspected. A 20 mm Hg or higher pressure in the arms than in the legs suggests coarctation of the aorta.

Malignant Hypertension

A small number of persons with secondary hypertension develop an accelerated and potentially fatal form of the disease—malignant hypertension. This usually is a disease of younger persons, particularly young African-American men, women with hypertension 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, renal disorders, vascular changes, and retinopathy. 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 caused by 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 the potential for additional episodes. Because chronic hypertension is associated with autoregulatory changes in cerebral blood flow, care is taken to avoid excessively rapid decreases in blood pressure, which can lead to cerebral hypoperfusion and brain injury.

Hypertension During Pregnancy

Hypertensive disorders complicate 6% to 8% of pregnancies. They are the second leading cause, after embolism, of maternal mortality in the United States, accounting for almost 15% of such deaths. Hypertensive disorders also contribute to stillbirths and neonatal morbidity and mortality. The incidence of hypertensive disorders of pregnancy increases with maternal age and is more common in African-American women.[20]

Classification

The National Institutes of Health Working Group Report on High Blood Pressure in Pregnancy published a revised classification system for high blood pressure in pregnancy that included preeclampsia-eclampsia, preeclampsia superimposed on chronic hypertension, chronic hypertension, and gestational hypertension[21] (Table 16-2).

Preeclampsia-Eclampsia. Preeclampsia-eclampsia is a pregnancy-specific syndrome. It is defined as an elevation in blood pressure and proteinuria developing after the 20th week of gestation. It is defined as an elevation in blood pressure (systolic >140 or diastolic >90 mm Hg) and proteinuria (≥0.3 g/24 hours) developing after the 20th week of gestation. The presence of systolic pressure ≥160 mm Hg, diastolic pressure ≥110 mm Hg; proteinuria (≥2.0 g/24 h); increased serum creatinine (>1.2 mg); platelet counts <100,000 cells/mm³; elevated liver enzymes; persistent headache or cerebral or visual disturbances; and persistent epigastric pain serve to reinforce the diagnosis.[21] Preeclampsia may occur in women who already are hypertensive, in which case the prognosis for the mother and fetus tends

TABLE 16-2	Classification of High Blood Pressure in Pregnancy
Classification	**Description**
Gestational hypertension	Blood pressure elevation, without proteinuria, that is detected for the first time during midpregnancy and returns to normal by 12 weeks postpartum.
Chronic hypertension	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.
Preeclampsia-eclampsia	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).
Preeclampsia superimposed on chronic hypertension	Chronic hypertension (blood pressure ≥140 mm Hg systolic or ≥90 mm Hg diastolic prior to 20th week of pregnancy) with superimposed proteinuria and with or without signs of the preeclampsia syndrome

(Developed using information from National Institutes of Health. [2000]. *Working group report on high blood pressure in pregnancy.* NIH publication no. 00-3029. Bethesda, MD: Author. Available: http://www.nhlbi.gov/health/prof/heart/hbp/hbp_preg.htm)

to be worse than for either condition alone.[21] Eclampsia is the occurence, in a woman with preeclampsia, of seizures that cannot be attributed to other causes.

Preeclampsia occurs primarily during first pregnancies and during subsequent pregnancies in women with multiple fetuses, diabetes mellitus, or coexisting renal disease. It is 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 of preeclampsia and adverse neonatal outcomes, particularly when associated with proteinuria early in pregnancy.[22]

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.[22] 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, cerebral hemorrhage, hepatic failure, and acute renal failure. Thrombocytopenia is the most common hematologic complication of preeclampsia. Platelet counts of less than below 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 most severe forms of preeclampsia occur in the absence of edema. Even when there is extensive edema, the plasma volume usually is lower than that seen in 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 tests, 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 and has been attributed to both increased coagulability and fibrin deposition in the cerebral vessels.

Chronic Hypertension. Chronic hypertension is considered in the same manner as 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. In women with chronic hypertension, blood pressure often decreases in early pregnancy and increases during the last trimester (3 months) of pregnancy, resembling preeclampsia. Women with chronic hypertension are at increased risk for the development of preeclampsia.

Gestational Hypertension. Gestational hypertension represents a blood pressure elevation without proteinuria that is detected for the first time after midpregnancy. It includes women with preeclampsia syndrome who have not yet manifested proteinuria, as well as women who do not have 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.

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 do 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.

Hypertension in Children

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.[23,24] 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 children grow older. This pattern continues into adolescence and adulthood, suggesting the roots of essential hypertension are established 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 gender-specific percentiles. The 1996 Task Force updated earlier recommendations by including height as a variable in determination of blood pressure (Table 16-3).[25] The Task Force recommended continued classification of blood pressure into three ranges: normal (*i.e.*, systolic and diastolic pressures below the 90th percentile for age, height, and gender); high normal (*i.e.*, systolic or diastolic blood pressures between the 90th and 95th percentile for age, height, and gender); and high blood pressures, or hypertension (*i.e.*, systolic and diastolic blood pressures equal to or greater than the 95th percentile for age, height, and gender on at least three occasions).

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.[25] 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.[26] Most

| TABLE 16-3 | 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* | | | | | | | |

Blood Pressure Percentiles	Age (yr)	Height Percentile for Boys				Height Percentile for Girls			
		5th	25th	75th	95th	5th	25th	75th	95th
Systolic Pressure									
90th	1	94	97	100	102	97	99	102	104
95th		98	101	104	106	101	103	105	107
90th	3	100	103	107	109	100	102	104	106
95th		104	107	111	113	104	105	108	110
90th	6	105	108	111	114	104	106	109	111
95th		109	112	115	117	108	110	112	114
90th	10	110	113	117	119	112	114	116	118
95th		114	117	121	123	116	117	120	122
90th	13	117	120	124	126	118	119	122	124
95th		121	124	128	130	121	123	126	128
90th	16	125	128	132	134	122	123	126	128
95th		129	132	136	138	125	127	130	132
Diastolic Pressure									
90th	1	50	52	54	55	53	53	55	56
95th		55	56	58	59	57	57	59	60
90th	3	59	60	62	63	61	61	63	64
95th		63	64	66	67	65	65	67	68
90th	6	67	69	70	72	67	68	69	71
95th		72	73	75	76	71	72	73	75
90th	10	73	74	76	78	73	73	75	76
95th		77	79	80	82	77	77	79	80
90th	13	75	76	78	80	76	77	78	80
95th		79	81	83	84	80	81	82	84
90th	16	79	80	82	83	79	79	81	82
95th		83	84	86	87	83	83	85	86

* The height percentiles were determined with standard growth curves. (Data adapted from National Heart, Lung, and Blood Institute. [1996]. Update of the 1987 Task Force Report of the Second Task Force on High Blood Pressure in Children and Adolescents. A working group report from the National High Blood Pressure Education Program. *Pediatrics* 98, 653-654. Available: http://www.nhibi.nih.gov/health/prof/heart/hbp/hbp_ped.htm)

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 females. The nephrotoxicity of the drug cyclosporine, an immunosuppressant used in transplant therapy, may cause hypertension in children after bone marrow, heart, kidney, or liver transplantation. The co-administration of corticosteroid drugs appears to increase the incidence 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. Repeated measurements over time, rather than a single isolated determination, are required to establish consistent and significant observations. Children with high blood pressure should be referred for medical evaluation and treatment as indicated. Treatment includes nonpharmacologic methods and, if necessary, pharmacologic therapy. The Task Force suggested use of the stepped-care approach for drug treatment of children who require antihypertensive medications.[25]

Hypertension in the Elderly

The prevalence of hypertension in the elderly population (65 to 74 years of age) of the United States ranges from 60% for whites to 71% for African Americans.[27] The most common type of hypertension in the elderly is isolated systolic hypertension, in which systolic pressure is elevated while diastolic pressure remains within normal range. A *Clinical Advisory Statement* intended to advance and clarify the JNC-VI guidelines on the importance of systolic pressure in older Americans, issued by the Coordinating Committee of the National High Blood Pressure Education Program in 2000, reaffirmed the importance of lifelong maintenance of a blood pressure of 140/90 mm Hg or less.[28]

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. 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.[29] 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. Differences in the central and peripheral arteries relate to the larger vessels containing 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 diastolic 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 ≥ 140 mm Hg and diastolic < 90 mm Hg) is recognized as an important risk factor for cardiovascular morbidity and mortality in older persons.[29] Stroke is two to three times more common in elderly hypertensive people than in age-matched normotensive subjects. The treatment of hypertension in the elderly has beneficial effects in terms of reducing the incidence of cardiovascular events such as stroke. The Systolic Hypertension in the Elderly Program (SHEP) showed a reduction of 36% in stroke and a 27% reduction in myocardial infarction in persons who were treated for hypertension compared with those who were not.[30]

Diagnosis and Treatment

The recommendations for measurement of blood pressure in the elderly are similar to those for the rest of the population. Blood pressure variability is particularly prevalent among older persons, so it is especially important to obtain multiple measurements on different occasions to establish a diagnosis of hypertension. The effects of food, position, and other environmental factors also are exaggerated in older persons. Although sitting has been the standard position for blood pressure measurement, it is recommended that blood pressure also be taken in the supine and standing positions in the elderly. In some elderly persons with hypertension, a silent interval, called the *auscultatory gap*, may occur between the end of the first and beginning of the third phases of the Korotkoff sounds, providing the potential for underestimating the systolic pressure, sometimes by as much as 50 mm Hg. Because the gap occurs only with auscultation, it is recommended that a preliminary determination of systolic blood pressure be made by palpation and the cuff be inflated 30 mm Hg above this value for auscultatory measurement of blood pressure. In some older persons, the indirect measurement using a blood pressure cuff and the Korotkoff sounds has been shown to give falsely elevated reading compared with the direct intra-arterial method. This is because excessive cuff pressure is needed to compress the rigid vessels of some older persons. Pseudohypertension should be suspected in older persons with hypertension in whom the radial or brachial artery remains palpable but pulseless at higher cuff pressures.

The treatment of hypertension in the elderly is similar to that for younger age groups. However, blood pressure should be reduced slowly and cautiously. When possible, appropriate lifestyle modification measures should be tried first. Antihypertensive medications should be prescribed carefully because the older person may have impaired baroreflex sensitivity and renal function. Usually, medications are initiated at smaller doses, and doses are increased more gradually. There is also the dangers of adverse drug interactions in older persons, who may be taking multiple medications, including over-the-counter drugs.

In summary, hypertension (systolic pressure ≥ 140 mm Hg and/or diastolic pressure >90 mm Hg) is one of the most common cardiovascular disorders. It may occur as a primary disorder (*i.e.*, essential hypertension) or as a symptom of some other disease (*i.e.*, secondary hypertension). Essential hypertension may be classified as systolic/diastolic hypertension in which both the systolic and diastolic pressures are elevated; as diastolic hypertension in which the diastolic pressure is selectively elevated; or as systolic hypertension in which the systolic pressure is selectively elevated. The incidence of essential hypertension increases with age; the condition is seen more frequently among African Americans, and it is linked to a family history of high blood pressure, obesity, and increased salt intake.

Causes of secondary hypertension include renal disorders and adrenal cortical disorders, such as hyperaldosteronism and Cushing's disease, which increase salt and water retention; pheochromocytomas, which increase catecholamine levels; and coarctation of the aorta, which produces a decrease in leg blood pressures and compensatory increase in arm pressures.

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, modification of alcohol intake, and smoking cessation. Among the drugs used in the treatment of hypertension are diuretics, adrenergic inhibitors, vasodilators, ACE inhibitors, and calcium channel-blocking drugs.

Hypertension that occurs during pregnancy can be divided into four categories: chronic hypertension, preeclampsia-eclampsia, chronic hypertension with superimposed preeclampsia-eclampsia, and gestational hypertension. Preeclampsia-eclampsia, which is hypertension that develops after 20 weeks' gestation, is accompanied by proteinuria, and poses a particular threat to the mother and the fetus. Blood pressure norms for children are based on age, height, and gender-specific percentiles. 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. Isolated systolic hypertension is the most common type of hypertension in the elderly. It represents the effects of aging on the distensibility of the aorta and its ability to stretch and accommodate blood being ejected from the left heart during systole. Untreated systolic hypertension is recognized as an important risk factor for stroke and other cardiovascular morbidity and mortality in older persons.

ORTHOSTATIC HYPOTENSION

Orthostatic or postural hypotension is an abnormal drop in blood pressure on assumption of the standing position. In the absence of normal circulatory reflexes or blood volume, blood pools in the lower part of the body; when the standing position is assumed, cardiac output falls, and blood flow to the

brain is inadequate. Dizziness, syncope (*i.e.*, fainting), or both may occur.

After the assumption of the upright posture from the supine position, approximately 500 to 700 mL of blood is momentarily shifted to the lower part of the body, with an accompanying decrease in central blood volume and arterial pressure.[31] Normally, this decrease in blood pressure is transient, lasting through several cardiac cycles, because 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. Within a few minutes of a change to the standing position, blood levels of antidiuretic hormone and sympathetic neuromediators increase as a secondary means of ensuring maintenance of normal blood pressure in the standing position. Muscle movement in the lower extremities also aids venous return to the heart by pumping blood out of the legs.

In persons with healthy blood vessels and normal autonomic nervous system function, cerebral blood flow usually is not reduced on assumption of the upright position unless arterial pressure falls below 70 mm Hg. The strategic location of the arterial baroreceptors between the heart and brain is designed to ensure that the arterial pressure is maintained within a range sufficient to prevent a reduction in cerebral blood flow.

Classification

Although there is no firm agreement on the definition of orthostatic hypotension, many authorities consider a drop in systolic pressure of 20 mm Hg or more or a drop in diastolic blood pressure of 10 mm Hg or more as diagnostic of the condition.[32] Some authorities regard the presence of orthostatic symptoms (*e.g.*, dizziness, syncope) as being more relevant than the numeric decrease in blood pressure.[33]

Causes

A wide variety of conditions, acute and chronic, are associated with orthostatic hypotension. These include reduced blood volume, drug-induced hypotension, altered vascular responses associated with aging, bed rest, and autonomic nervous system dysfunction.

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.

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. If postural hypotension is severe enough to cause light-headedness or dizziness, it is recommended that the dosage of the drug be reduced or a different drug be used.[33]

Aging

Weakness and dizziness on standing are common complaints of elderly persons. Orthostatic hypotension is associated with systolic hypertension, major electrocardiographic abnormalities, and carotid artery stenosis. 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 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.[34] The greatest postprandial changes occur after a 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.

Bed Rest

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. 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 re-entry into the earth's gravitational field.

Disorders of Autonomic Nervous System Function

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 autonomic 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 autonomic nervous system dysfunction: pure autonomic failure, defined as a sporadic, idiopathic cause of persistent orthostatic hypotension and other manifestations of autonomic failure such as urinary retention, impotence, or decreased sweating; Parkinson's disease with autonomic failure; and multiple-system atrophy (Shy-Drager syndrome).[35] The Shy-Drager syndrome usually develops in middle to late life and manifests 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 blood pressure cuff. A reading should be made when the patient is supine, immediately after assumption of the seated or upright position,

and after 2 to 3 minutes following assumption of the standing position. A tilt table also can be used for this purpose. With a tilt table, the recumbent patient 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. Persons with a drop in blood pressure to orthostatic levels should be evaluated to determine the cause and seriousness of the condition. A history should be done 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 autonomic nervous system dysfunction, such as impotence or bladder dysfunction. A physical examination should document blood pressure in both arms and the heart rate while the patient is 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, helping people learn ways to cope with the disorder and prevent falls and injuries. Medications that predispose to postural hypotension should be avoided. Other measures include preventing or correcting the fluid deficit and avoidance of situations that encourage excessive vasodilatation (*e.g.*, drinking alcohol, exercising vigorously in a warm environment). Measures designed to help persons prevent symptomatic orthostatic drops in blood pressure include gradual ambulation (*i.e.*, sitting on the edge of the bed for several minutes and moving the legs to initiate skeletal muscle pump function before standing). 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.[32] Mineralocorticoids can be used to reduce salt and water loss. 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 or on the capacitance vessels may be used. Many of these agents have undesirable side effects.

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 autonomic nervous system, and the effects of immobility. Diagnosis of orthostatic hypotension includes blood pressure measurement in the supine and upright positions, 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 to prevent falls and injuries.

REVIEW QUESTIONS

■ Explain how cardiac output and peripheral vascular resistance interact in determining systolic and diastolic blood pressure.

■ Explain the difference between the essential and secondary forms of hypertension.

■ Cite some of the major contributing factors in the development of hypertension.

■ Cite the risks of hypertension in terms of target organ damage.

■ Explain the changes in blood pressure that accompany normal pregnancy and describe the four types of hypertension that can occur during pregnancy.

■ Cite the criteria for the diagnosis of high blood pressure in children.

■ Define systolic hypertension, characterize the effect of increased systolic and pulse pressure on the production of target organ damage, and explain why systolic hypertension is more common in the elderly.

■ Define the term *orthostatic hypotension.*

■ Explain how fluid deficit, medications, aging, disorders of the autonomic nervous system, and bed rest contribute to the development of orthostatic hypotension

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