OBJECTIVES

When you reach the end of this chapter, you should be able to do the following:

1. Briefly discuss the normal anatomy and physiology of the autonomic nervous system, including the events that take place within the sympathetic and parasympathetic divisions and the way they relate to long-term and short-term control of blood pressure.

2. Define hypertension and compare primary and secondary hypertension and their related manifestations.

3. Describe the protocol for treating hypertension as detailed in the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), including the rationale for its use.

4. List the criterion pressure values (in millimeters of mercury) for the new hypertension categories of normal pressure, prehypertension, hypertension stage 1, and hypertension stage 2 as defined in JNC 7.

5. Using the most recent guidelines, compare the various drugs used in the pharmacologic management of hypertension with regard to mechanism of action, specific indications, adverse effects, toxic effects, cautions, contraindications, dosages, and routes of administration.

6. Discuss the rationale for the nonpharmacologic management of hypertension.

7. Develop a nursing care plan that includes all phases of the nursing process for patients receiving antihypertensive drugs.

Glossary

**Alpha-blockers** Drugs that primarily cause arterial and venous dilation through their action on peripheral sympathetic neurons. (p. 000)

**Antihypertensive drugs** Medications used to treat hypertension. (p. 000)

**Cardiac output** The amount of blood ejected from the left ventricle, measured in liters per minute. (p. 000)

**Centrally acting adrenergic drugs** Drugs that modify the function of the sympathetic nervous system in the brain by stimulating alpha receptors, which has a reverse sympathetic effect that causes decreased blood pressure. (p. 000)

**Essential hypertension** Elevated systemic arterial pressure for which no cause can be found and which is often the only significant clinical finding; also called primary or idiopathic hypertension. (p. 000)

**Hypertension** A common, often asymptomatic disorder in which blood pressure persistently exceeds 140/90 mm Hg. (p. 000)

**Orthostatic hypotension** A common adverse effect of adrenergic drugs involving a sudden drop in blood pressure when a person changes position, especially when rising from a seated or horizontal position. (p. 000)

**Prodrug** A drug that is inactive in its administered form and must be metabolized to its active form in the body, generally by the liver, to be effective. (p. 000)

**Secondary hypertension** High blood pressure associated with a primary disease such as renal, pulmonary, endocrine, or vascular disease. (p. 000)

Anatomy, Physiology, and Disease Overview

Significant advances have been made in the detection, evaluation, and treatment of high blood pressure, or hypertension. Over the past 40 years the development of new antihypertensive medications has had an enormous impact on the quality of life of affected persons by reducing the incidence of the various complications associated with hypertension and decreasing the adverse effects associated with these medications. Drug therapy for hypertension first became available in the early 1950s with the introduction of ganglionic blocking drugs. However, unpleasant adverse effects and inconsistent therapeutic effects were common problems with these antihypertensive drugs. In 1953 the vaso-
dilator hydralazine was introduced, and in 1958 the thiazide diuretics became available. These drugs offered important advantages over the previous antihypertensive drug therapies. In addition, with the discovery of these newer drugs came a better understanding of the disease process itself.

Since that time, several additional drug categories have emerged, including loop diuretics (also called potassium-wasting diuretics), potassium-sparing diuretics, beta-blockers (beta receptor antagonists), angiotensin-converting enzyme (ACE) inhibitors, alpha1 antagonists, alpha2 agonists, angiotensin II receptor blockers (ARBs), calcium channel blockers (CCBs), vasodilators, and the newest class, the direct renin inhibitors. Although some of the medications mentioned in this chapter represent older classes of drugs, all are current therapeutic options listed in the treatment guidelines for hypertension published by the National Heart, Lung, and Blood Institute.

**HYPERTENSION**

As many as 50 million people in the United States have some form of hypertension, which makes it the most common disease in the population of the Western hemisphere. Not only does hypertension affect a large portion of our society, but it has many severe consequences if left untreated. Hypertension is a major risk factor for coronary artery disease, cardiovascular disease, and death resulting from cardiovascular causes. It is the most important risk factor for stroke and heart failure, and it is also a major risk factor for renal failure and peripheral vascular disease.

The diagnosis and treatment of hypertension have varied considerably over the years. The *Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7)* was released in May 2003. This report provides treatment guidelines for hypertension assembled by two large expert panels based on a review of the latest clinical research publications on the disease. As with previous such reports, the development of *JNC 7* was sponsored by the National Heart, Lung, and Blood Institute of the National Institutes of Health, the major governmental health research entity of the United States. The efforts of the Joint National Committee are intended to educate both health care professionals and the general public about the dangers of the disease and the importance of its treatment. The *Eighth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 8)* is scheduled to be published in spring 2010 and can be found at [http://www.nhlbi.nih.gov/guidelines/hypertension](http://www.nhlbi.nih.gov/guidelines/hypertension). See [http://evolve.elsevier.com/Lilley](http://evolve.elsevier.com/Lilley) for further information on new JNC 8 guidelines.

One of the major changes that appeared in the earlier guideline *Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 6)* in 1997 was a new classification system for blood pressure. The previously applied term mild hypertension did not adequately reflect the serious nature of this condition. This became evident when it was found that, although the overwhelming majority of patients with hypertension have so-called mild hypertension, most of the morbidity and mortality actually occur in this group. In addition, whereas pre-JNC 6 reports had recommended a stepped-care pharmacologic approach to treating the illness, many practitioners believed that this approach no longer adequately reflected the current range of pharmacologic alternatives or furnished the type of care dictated by the current level of scientific understanding of the disorder. In *JNC 6*, individualized therapy was proposed as a more appropriate treatment strategy, because it allowed specific patient circumstances to be addressed and pharmacologic alternatives to be considered. This individualized approach continues to be emphasized in *JNC 8*, with the recognition that some patients may require two or more medications, even as initial therapy, depending on their individual cardiovascular risk factors such as obesity, diabetes, and family history. Prescribers are therefore encouraged to adopt an individualized approach to the planning of drug therapy that takes into consideration the demographic concerns for the given patient, the presence of more than one disease, the use of concurrent therapies, and the patient’s quality of life.

The classification scheme used to categorize individual cases of hypertension has been simplified to the following four stages based on blood pressure measurements: normal, prehypertension, stage 1 hypertension, and stage 2 hypertension. (The reader is referred to *JNC 8* at [http://www.nhlbi.nih.gov/guidelines/hypertension](http://www.nhlbi.nih.gov/guidelines/hypertension).)

Hypertension can also be defined by its cause. When the specific cause of hypertension is unknown, it may be called essential, idiopathic, or primary hypertension. About 90% of cases of hypertension are of this type. Secondary hypertension accounts for the other 10%. Secondary hypertension is most commonly the result of another disease such as pheochromocytoma (adrenal tumor), preeclampsia of pregnancy (a pregnancy complication involving acute hypertension, among other symptoms), or renal artery disease. It may also result from the use of certain medications. If the cause of secondary hypertension can be eliminated, blood pressure usually returns to normal.

Blood pressure is determined by the product of cardiac output (4 to 8 L/min) and systemic vascular resistance (SVR). Cardiac output is the amount of blood that is ejected from the left ventricle and is measured in liters per minute. SVR is the force (resistance) the left ventricle has to overcome to eject its volume of blood. Numerous factors interact to regulate these two major variables and keep the blood pressure within normal limits. These are illustrated in Figure 25-1. These are the same factors that can cause high blood pressure and are the targets of action of many of the antihypertensive drugs.

**Pharmacology Overview**

The drug therapy for hypertension should be individualized. Important considerations in planning drug therapy are whether the patient has multiple medical problems and what impact drug therapy will have on the patient’s quality of life. For example, one very common adverse effect of almost any antihypertensive drug is sexual dysfunction in male patients, which is the most common reason for nonadherence to drug therapy. Demographic factors, cultural implications, the ease of medication administration (e.g., a once-a-day dosing schedule or transdermal administration), and cost are other important considerations.

There are essentially seven main categories of pharmacologic drugs: diuretics, adrenergic drugs, vasodilators, ACE inhibitors, ARBs, CCBs, and direct renin inhibitors. Because all antihypertensive drugs (with the exception of diuretics) have...
some vasodilatory action, and are also called direct vasodilators to differentiate them. Drugs in these classes may be used either alone or in combination. The various categories and subcategories of antihypertensive drugs are listed in Box 25-1. The diuretics are discussed in detail in Chapter 26 and therefore are not covered here.

**REVIEW OF AUTONOMIC NEUROTRANSMISSION**

The stimulation of the two divisions of the autonomic nervous system (ANS), the parasympathetic nervous system (PSNS) and sympathetic nervous system (SNS), is controlled by the neurotransmitters acetylcholine and norepinephrine. The receptors for both divisions of the ANS are located throughout the body in a variety of tissues. ANS physiology is reviewed in greater detail in the introductory sections of Chapters 18 through 21. The receptor located between the postganglionic fiber and the effector cells (i.e., the postganglionic receptor) is called the muscarinic or cholinergic receptor in the PSNS and the adrenergic or noradrenergic receptor (i.e., alpha or beta receptor) in the SNS. Physiologic activity at muscarinic receptors is stimulated by acetylcholine and cholinergic agonist drugs (Chapter 20) and is inhibited by cholinergic antagonists (anticholinergic drugs; Chapter 21). Similarly, physiologic activity at adrenergic receptors is stimulated by norepinephrine and epinephrine and adrenergic agonist drugs (Chapter 18) and inhibited by antiadrenergic drugs (adrenergic blockers, i.e., alpha or beta receptor blockers; Chapter 19). Figure 25-2 shows how these various receptors are arranged in both the PSNS and SNS and indicates their corresponding neurotransmitters.

**ADRENERGIC DRUGS**

Adrenergic drugs are a large group of antihypertensive drugs, as shown in Box 25-1. The alpha-blockers and combined alpha/beta-blockers were described in detail in Chapter 19. The adrenergic drugs discussed here exert their antihypertensive action at different sites.

**Mechanism of Action and Drug Effects**

Five specific drug subcategories are included in the adrenergic antihypertensive drugs as indicated in Box 25-1. Each of these subcategories of drugs can be described as having central action (in the brain) or peripheral action (at the heart and blood vessels). These drugs include the adrenergic neuron blockers (central and peripheral), the alpha2 receptor agonists (central), the alpha1 receptor blockers (peripheral), the beta receptor blockers (peripheral), and the combination alpha1 and beta receptor blockers (peripheral).

The centrally acting alpha2-adrenergic drugs clonidine and methyldopa both act by modifying the function of the SNS. Because SNS stimulation leads to an increase in heart rate and force of contraction, the constriction of blood vessels, and the release of renin from the kidney, the result is hypertension. The centrally acting adrenergic drugs work by stimulating the alpha2-adrenergic receptors in the brain. The alpha2-adrenergic receptors are unique in that receptor stimulation actually reduces sympathetic outflow, in this case from the central nervous system (CNS). The resulting lack of norepinephrine production reduces blood pressure. This stimulation of the alpha2-adrenergic receptors also affects the kidneys, reducing the activity of renin. Renin is the hormone and enzyme that converts the protein precursor angiotensinogen to the protein angiotensin I, the precursor of angiotensin II (AII), a potent vasoconstrictor that raises blood pressure.
are often considered by health care providers in selecting first-line treatment. These responses that include attention to cultural influences. These factors also allow a better understanding of the dynamics of pharmacologic treatment in hypertensive patients of different ethnic groups and also underscore the importance of a thorough nursing assessment.

**CULTURAL IMPLICATIONS**

**Antihypertensive Drug Therapy**

The following are some important generalizations about demographics and the drugs used to treat hypertension:

- Beta-blockers and angiotensin-converting enzyme (ACE) inhibitors have been found to be more effective in lowering blood pressure in whites than in African Americans.
- Calcium channel blockers and diuretics have been shown to be more effective in African American patients than in white patients.
- Captopril used as monotherapy to treat hypertension has been found to elicit a lesser response in African American patients, who are considered to be low-renin hypertensives, than in the general treatment population.
- Losartan used as monotherapy for hypertension has been found to be less effective in African American patients than in other racial groups because African American patients are low-renin hypertensives.

These findings are important to remember in the care of patients, whether they are in an inpatient setting, are being seen by a physician, physician’s assistant, or a nurse practitioner; or are being screened by a nurse in the community. The significance of these cultural-ethnic factors is that they allow a better understanding of the dynamics of pharmacologic treatment in hypertensive patients of different ethnic groups and also underscore the importance of a thorough nursing assessment that includes attention to cultural influences. These factors also allow an appreciation of individual responses to drug therapy and aid in achieving more successful treatment of the disease. These responses are often considered by health care providers in selecting first-line therapy.

Results of many studies have supported a difference between African Americans and whites in response to antihypertensive drugs; however, conflicting findings in this area should be mentioned for balance. Although researchers have reported that, on average, African Americans and whites differ slightly in their responses to antihypertensive drugs, a meta-analysis published in the March 2004 issue of Hypertension found that the majority of African Americans and whites in the studies analyzed had similar responses to some of the more commonly used antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors. In this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors, in this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors. In this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors. In this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors. In this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors. In this analysis, which pooled data on the use of common antihypertensives such as diuretics, beta-blockers, calcium channel blockers, and ACE inhibitors.

Two dual-action alpha and beta receptor blockers, which also act in the periphery at the heart and blood vessels, are currently available. These two drugs are labetalol and carvedilol. They have the dual antihypertensive effects of reduction in heart rate (beta 1 receptor blockade) and vasodilation (alpha 1 receptor blockade). Figure 25-3 illustrates the site and mechanisms of action of the various antihypertensive drugs.

**Indications**

All of the drugs mentioned are used primarily for the treatment of hypertension, either alone or in combination with other antihypertensive drugs. Various forms of glaucoma may also respond to treatment with some of these drugs. Clonidine also has several off-label uses (not approved by the U.S. Food and Drug Administration but still common in practice), including prophylaxis against migraine headaches and treatment of severe dysmenorrhea or menopausal flushing. It is also useful in the management of withdrawal symptoms in persons with opioid, nicotine, or alcohol dependency. The alpha 1-blockers doxazosin, prazosin, and terazosin have been used to relieve the symptoms associated with BPH. They have also proved effective in the management of severe heart failure when used with cardiac glycosides (Chapter 22) and diuretics (Chapter 26).

**Contraindications**

Contraindications to the use of the adrenergic antihypertensive drugs include known drug allergy and may also include acute heart failure, concurrent use of monoamine oxidase inhibitors (Chapter 17), severe mental depression, peptic ulcer, colitis, and severe liver or kidney disease. Asthma may also be a contraindication to the use of any noncardioselective beta-blocker (e.g., carvedilol). As mentioned in Chapter 22, the use of vasodilating drugs may also be contraindicated in cases of heart failure that is secondary to diastolic dysfunction.

**Adverse Effects**

The most common adverse effects of adrenergic drugs are bradycardia with reflex tachycardia, postural and postexercise hypotension, dry mouth, drowsiness, sedation, dizziness, edema, constipation, and sexual dysfunction (e.g., impotence). Other effects include headaches, sleep disturbances, nausea, rash, peripheral pooling of blood, and cardiac disturbances such as palpitations. There is also a high incidence of orthostatic hypotension (a sudden drop in blood pressure during changes in position) in patients taking these drugs. Orthostatic hypotension is commonly referred to as postural hypotension. This can lead to a situation known as first-dose syncope, in which the hypotensive effect is severe enough to cause the patient to lose consciousness with even the first dose of medication. This is especially true with alpha-blockers. Patients should be educated to change positions slowly. In addition, the abrupt discontinuation of the centrally acting alpha 2 receptor agonists can result in rebound hypertension. This may also be true for other antihypertensive drug classes, especially beta-blockers. Nonselective blocking drugs are also more commonly associated with bronchoconstriction (due to unrestrained parasympathetic tone) as well as metabolic inhibition of glycogenolysis in the liver, which can lead to hypoglycemia. However, hyperglycemic episodes are also among the adverse effects reported for this drug class. Any change in the dosing regimen for cardiovascular medications should be undertaken gradually and with appropriate patient monitoring and follow-up. Although the same is also true for most other classes of medications, abrupt dosage changes of cardiovascular medications, either up or down, can be especially hazardous for the pa-
Antihypertensive Drugs

CHAPTER 25

Some of these drugs can also cause disruptions in blood count as well as in serum electrolyte levels and renal function. Periodic monitoring of white blood cell count, serum potassium and sodium levels, and urinary protein levels is recommended.

Interactions

Adrenergic drugs interact primarily with CNS depressants such as alcohol, benzodiazepines, and opioids. The additive effects of these combinations of drugs increase CNS depression. Other drug interactions that can occur with selected adrenergic drugs are summarized in Table 25-1. This list is merely representative and is not exhaustive. The nurse should always keep a drug information handbook available to check in cases in which a specific drug interaction is suspected. Hospital pharmacists are also excellent resources for the nurse.

Dosages

For information on the dosages of selected adrenergic antihypertensive drugs, see the Dosages table on page 000.

DRUG PROFILES

ALPHA₂-ADRENERGIC RECEPTOR STIMULATORS (AGONISTS)

Of the available alpha₂ receptor agonists—clonidine and methyldopa—clonidine is by far the most commonly used and the prototypical drug for this class. Methyldopa is also administered for the treatment of hypertension and is commonly used to treat hypertension in pregnancy. However, these drugs are not typically prescribed as first-line antihypertensive drugs, because their use is associated with a high incidence of unwanted adverse effects such as orthostatic hypotension, fatigue, and dizziness. They may be
used as adjunct drugs in the treatment of hypertension after other drugs have failed or may be used in conjunction with other antihypertensives such as diuretics.  

◆ clonidine

Clonidine (Catapres) is used primarily for its ability to decrease blood pressure. It is also useful in the management of opioid withdrawal. It has a better safety profile than the other centrally acting adrenergics and has the advantage of being available in several dosage formulations, including both topical and oral preparations. When the patch dosage form is used, it is important to remove the old patch before applying a new one. Clonidine should not be discontinued abruptly, because this will lead to severe rebound hypertension. Its use is contraindicated in patients who have shown hypersensitivity reactions to it. See the table on page 000 for recommended dosages.

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>30-60 min</td>
<td>3-5 hr</td>
<td>6-20 hr</td>
<td>8 hr</td>
</tr>
</tbody>
</table>

ALPHA2-BLOCKERS

The alpha2-blockers are doxazosin (Cardura), prazosin (Minipress), tamsulosin (Flomax), and terazosin (Hytrin). They are the newest of the adrenergics and have the best safety and efficacy profiles, but they are not free of adverse effects. Their use is contraindicated in patients who have shown hypersensitivity reactions to them. They are classified as pregnancy category C drugs. They are available only as oral preparations. Tamsulosin is not used to control blood pressure but is indicated solely for symptomatic control of BPH. This use is described further in Chapter 35.

doxazosin

Doxazosin (Cardura) is the most commonly used alpha1-blocker. It reduces peripheral vascular resistance and blood pressure by dilating both arterial and venous blood vessels. It has been shown to be beneficial in the treatment of hypertension and the relief of the symptoms of obstructive BPH. It is available in immediate- and extended-release formulations. When the drug is released from the extended-release form, the matrix of the capsule is expelled in the stool. Patients should be educated about this and reassured that the active drug has been absorbed. Confusion over this fact could cause patients to take more than the prescribed dosage. Recommended dosages are given in the table on page 000.

PHARMACOKINETICS

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>1-2 hr</td>
<td>2-3 hr</td>
<td>15-22 hr</td>
<td>Less than 24 hr</td>
</tr>
</tbody>
</table>
failure in conjunction with digoxin, diuretics, and ACE inhibitors. Its contraindications include known drug allergy, cardiogenic shock, severe bradycardia or heart failure, bronchospastic conditions such as asthma, and various cardiac problems involving the conduction system. Dosage information appears in the table on page 000.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>20-120 min</td>
<td>1-4 hr</td>
<td>6-8 hr</td>
<td>8-24 hr</td>
</tr>
</tbody>
</table>

**NEW BETA RECEPTOR BLOCKER nebivolol**

Nebivolol (Bystolic) is the newest beta-blocker, released in 2008. It is a beta-selective beta blocker approved for use in hypertension. It is also being used for treatment of heart failure. Nebivolol is similar to other beta-selective blockers; however, in addition to blocking beta, receptors, it also produces an endothelium-derived nitric oxide-dependent vasodilatation, which results in a decrease in SVR. It is promoted as causing less sexual dysfunction. Like other beta-blockers, it should not be stopped abruptly but must be tapered over 1 to 2 weeks. Dosing starts at 5 mg/day and may be increased at 2-week intervals to a maximum of 40 mg/day.

**ANGIOTENSIN-CONVERTING ENZYME INHIBITORS**

The ACE inhibitors are a large group of antihypertensive drugs. Currently 10 ACE inhibitors are available for clinical use, in addition to various combination drug products in which a thiazide diuretic or a CCB is combined with an ACE inhibitor. Combination products tend to increase adherence as the patient is taking less number of drugs. The available ACE inhibitors are captopril (Capoten), benazepril (Lotensin), enalapril (Vasotec), fosinopril (Monopril), lisinopril (Prinivil), moexipril (Univasc), perindopril (Aceon), quinapril (Accupril), ramipril (Altace), andtrandolapril (Mavik). These drugs have been reported to have occurred in at least 50 cases in which patients is hindered.

Captopril and lisinopril is an important advantage in treating a patient with liver dysfunction; because all of the other ACE inhibitors are prodrugs, their transformation to active form in such patients is hindered.

Enalapril is the only ACE inhibitor that is available in a parenteral preparation. All of the newer ACE inhibitors, such as benazepril, fosinopril, lisinopril, quinapril, and ramipril, have long half-lives and long durations of action, which allows them to be given only once a day. A once-a-day medication regimen promotes better patient adherence.

All ACE inhibitors have detrimental effects on the unborn fetus and neonate. They are classified as pregnancy category C drugs for women in their first trimester and as pregnancy category D drugs for women in their second or third trimester. ACE inhibitors should be used by pregnant women only if there are no safer alternatives. Fetal and neonatal morbidity and mortality have been reported to have occurred in at least 50 cases in which women received ACE inhibitors during their pregnancies.

**Mechanism of Action and Drug Effects**

As is often the case with pharmaceutical innovations, the development of the ACE inhibitors was spurred by the discovery of an animal substance found to have beneficial effects in humans. This particular substance was the venom of a South American viper, which was found to inhibit kininase activity. Kininase is an enzyme that normally breaks down bradykinin, a potent vasodilator, and preventing the action of renin) to AII. AII is a potent vasoconstrictor and effects. As their name implies, they inhibit angiotensin-converting enzyme, which is responsible for converting AI (formed through the action of renin) to AII. AII is a potent vasoconstrictor and induces aldosterone secretion by the adrenal glands. Aldosterone stimulates sodium and water resorption, which can raise blood pressure. Together, these processes are referred to as the renin-angiotensin-aldosterone system.

The primary effects of the ACE inhibitors are cardiovascular and renal. Their cardiovascular effects are due to their ability to reduce blood pressure by decreasing SVR. They do this by preventing the breakdown of the vasodilating substance bradykinin and also of substance P (another potent vasodilator), and preventing the

<table>
<thead>
<tr>
<th>Drug (Trade Name)</th>
<th>Combination with Hydrochlorothiazide</th>
<th>Dosing Schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>benazepril (Lotensin)</td>
<td>Lotensin HCT</td>
<td>Once a day</td>
</tr>
<tr>
<td>captopril (Capoten)</td>
<td>Capozide</td>
<td>Multiple</td>
</tr>
<tr>
<td>enalapril (Vasotec)</td>
<td>Vasotec</td>
<td>Multiple</td>
</tr>
<tr>
<td>fosinopril (Monopril)</td>
<td>None</td>
<td>Once a day</td>
</tr>
<tr>
<td>lisinopril (Prinivil)</td>
<td>Prinzide</td>
<td>Once a day</td>
</tr>
<tr>
<td>lisinopril (Zestril)</td>
<td>Zestoretic</td>
<td>Once a day</td>
</tr>
<tr>
<td>moexipril (Univasc)</td>
<td>None</td>
<td>Once a day</td>
</tr>
<tr>
<td>perindopril (Aceon)</td>
<td>None</td>
<td>Once to twice daily</td>
</tr>
<tr>
<td>quinapril (Accupril)</td>
<td>None</td>
<td>Once a day</td>
</tr>
<tr>
<td>ramipril (Altace)</td>
<td>None</td>
<td>Once a day</td>
</tr>
<tr>
<td>tandolapril (Mavik)</td>
<td>None</td>
<td>Once a day</td>
</tr>
</tbody>
</table>

ACE, Angiotensin-converting enzyme.
formulation of AII. These combined effects decrease afterload, or the resistance against which the left ventricle must pump to eject its volume of blood during contraction. The ACE inhibitors are beneficial in the treatment of heart failure because they prevent sodium and water resorption by inhibiting aldosterone secretion. This causes diuresis, which decreases blood volume and return to the heart. This in turn decreases preload, or the left ventricular end-diastolic volume, and the work required of the heart.

**Indications**

The therapeutic effects of the ACE inhibitors are related to their potent cardiovascular effects. They are excellent antihypertensives and adjunctive drugs for the treatment of heart failure. They may be used alone or in combination with other drugs such as diuretics in the treatment of hypertension or heart failure.

The beneficial hemodynamic effects of the ACE inhibitors have been studied extensively. Because of their ability to decrease SVR (a measure of afterload) and preload, ACE inhibitors can stop the progression of left ventricular hypertrophy, which is sometimes seen after a myocardial infarction (MI). This pathologic process is known as ventricular remodeling. The ability of ACE inhibitors to prevent it is termed a cardioprotective effect.

ACE inhibitors have been shown to decrease morbidity and mortality in patients with heart failure. They should be considered the drugs of choice for hypertensive patients with heart failure. ACE inhibitors have also been shown to have a protective effect on the kidneys, because they reduce glomerular filtration pressure. This is one reason that they are among the cardiovascular drugs of choice for diabetic patients. Numerous studies have shown that the ACE inhibitors reduce proteinuria, and they are considered by many to be standard therapy for diabetic nephropathy. The various therapeutic effects of the ACE inhibitors are listed in Table 25-3, which lists the biochemicals on which ACE inhibitors act and the resulting beneficial hemodynamic effects.

**Contraindications**

Contraindications to the use of ACE inhibitors include known drug allergy, especially a previous reaction of angioedema (e.g., laryngeal swelling) to an ACE inhibitor. Patients with a baseline potassium level of 5 mEq/L or higher may not be suitable candidates for ACE inhibitor therapy, because these drugs can promote hyperkalemia (see later). All ACE inhibitors are contraindicated in lactating women, children, and patients with bilateral renal artery stenosis.

**Adverse Effects**

Major CNS effects of the ACE inhibitors include fatigue, dizziness, mood changes, and headaches. A characteristic dry, nonproductive cough may occur that is reversible with discontinuation of the therapy. A first-dose hypotensive effect can cause a significant decline in blood pressure. Other adverse effects include loss of taste, hyperkalemia, rash, pruritus, anemia, neutropenia, thrombocytosis, and agranulocytosis. In patients with severe heart failure whose renal function may depend on the activity of the renin-angiotensin-aldosterone system, treatment with ACE inhibitors may cause acute renal failure. ACE inhibitors tend to promote potassium resorption in the kidney, although they also promote sodium excretion due to their reduction of aldosterone secretion. For this reason, serum potassium levels should be monitored regularly. This is especially true when there is concurrent therapy with potassium-sparing diuretics, although many patients tolerate both types of drug therapy with no major problems. One rare, but potentially fatal, adverse effect is angioedema. This is a strong vascular reaction involving inflammation of submucosal tissues, which can progress to anaphylaxis.

**Toxicity and Management of Overdose**

The most pronounced symptom of an overdose of an ACE inhibitor is hypotension. Treatment is symptomatic and supportive and includes the administration of intravenous fluids to expand the blood volume. Hemodialysis is effective for the removal of captopril and lisinopril.

**Interactions**

Nonsteroidal antiinflammatory drugs (NSAIDs), such as ibuprofen, can reduce the antihypertensive effect of ACE inhibitors. The use of NSAIDs and ACE inhibitors may also predispose patients to the development of acute renal failure. Concurrent use of ACE inhibitors and other antihypertensives or diuretics can have hypotensive effects. Giving lithium and ACE inhibitors together can result in lithium toxicity. Potassium supplements and potassium-sparing diuretics, when administered with ACE inhibitors, may result in hyperkalemia. The monitoring of serum potassium levels becomes important in these cases. False-positive results on tests for acetone in the urine may occur in patients taking captopril.

**Dosages**

For information on the dosages for selected ACE inhibitors, see the Dosages table on page 000.

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**TABLE 25-3 ACE Inhibitors: Therapeutic Effects**

<table>
<thead>
<tr>
<th>Body Substance</th>
<th>Effect in Body</th>
<th>ACE Inhibitor Action</th>
<th>Resulting Hemodynamic Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldosterone</td>
<td>Causes sodium and water retention</td>
<td>Prevents its secretion</td>
<td>Diuresis ↓ plasma volume ↓ filling pressures or ↓ preload</td>
</tr>
<tr>
<td>Angiotensin II</td>
<td>Potent vasoconstrictor</td>
<td>Prevents its formation</td>
<td>↓ SVR = ↓ afterload</td>
</tr>
<tr>
<td>Bradykinin</td>
<td>Potent vasodilator</td>
<td>Prevents its breakdown</td>
<td>↓ SVR = ↓ afterload</td>
</tr>
</tbody>
</table>

↓ Decreased; ACE, angiotensin-converting enzyme; SVR, systemic vascular resistance.

---

**DRUG PROFILES**

- **captopril**
  Captopril (Capoten) was the first ACE inhibitor to become available and is considered the prototypical drug for the class. Several large multicenter studies have shown its clinical efficacy in minimizing or preventing the left ventricular dilatation and dysfunction (also called ventricular remodeling) that can arise in the acute period after an
**DOSAGES**

Selected Antihypertensive Drugs: ACE Inhibitors and Angiotensin II Receptor Blockers

<table>
<thead>
<tr>
<th>Drug (Pregnancy Category)</th>
<th>Pharmacologic Class</th>
<th>Usual Dosage Range</th>
<th>Indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>captopril (Capoten, Capozi*(^\text{a})) (C, first trimester; D, second and third trimesters)</td>
<td>ACE inhibitor</td>
<td>Adult: PO: 25-150 mg bid-tid PO (Capozi*(^\text{a})): Usual dosage 1-2 tabs/day or more based on ratio of the two drugs</td>
<td>Hypertension, heart failure</td>
</tr>
<tr>
<td>enalapril (Vasotec, Vaseretic*(^\text{a})) (C, first trimester; D, second and third trimesters)</td>
<td>ACE inhibitor</td>
<td>Adult: PO: 10-40 mg/day as a single dose or in 2 equal doses PO: 20-50 mg/day as a single dose with digoxin and diuretic IV: 1.25 mg q6h over a 5-min period</td>
<td>Heart failure</td>
</tr>
<tr>
<td>losartan (Cozaar) (C, first trimester; D, second and third trimesters)</td>
<td>Angiotensin II receptor blocker</td>
<td>Adult: PO: 25-100 mg in 1-2 doses</td>
<td>Hypertension, heart failure</td>
</tr>
</tbody>
</table>

ACE, Angiotensin-converting enzyme; IV, intravenous; PO, oral.
*Fixed-combination tablet with hydrochlorothiazide.

**Mechanism of Action and Drug Effects**

ARBs block the binding of AII to type 1 AII receptors. ACE inhibitors such as enalapril block conversion of AI to AII, but AII also may be formed by other enzymes that are not blocked by ACE inhibitors. For comparison, recall that ACE inhibitors block the breakdown of bradykinins and substance P, which accumulate and may cause adverse effects such as cough but might also contribute to the drugs’ antihypertensive and cardiac and nephroprotective effects. Bradykinins are potent vasodilators and help to reduce blood pressure by dilating arteries and decreasing SVR.

In contrast to ACE inhibitors, ARBs affect primarily vascular smooth muscle and the adrenal gland. By selectively blocking the binding of AII to the type 1 AII receptors in these tissues, ARBs block vasoconstriction and the secretion of aldosterone. All receptors have been found in other tissues throughout the body, but the effects of ARB blocking of these receptors is unknown.

Clinically, ACE inhibitors and ARBs appear to be equally effective for the treatment of hypertension. Both are well tolerated, but ARBs do not cause cough. There is evidence that ARBs are better tolerated and are associated with lower mortality after MI than ACE inhibitors. It is not yet clear whether ARBs are as effective as ACE inhibitors in treating heart failure (cardioprotective effects) or in protecting the kidneys, as in diabetes. Both types of drugs are contraindicated for use in the second or third trimester of pregnancy. Whether one or more of these drugs, particularly the newer drugs, could prove to have unique adverse effects with long-term use is unknown.

**Indications**

The therapeutic effects of ARBs are related to their potent vasodilating properties. They are excellent antihypertensives and adjunctive drugs for the treatment of heart failure. They may be used alone or in combination with other drugs such as diuretics in the treatment of hypertension or heart failure. The beneficial
hemodynamic effect of ARBs is their ability to decrease SVR (a measure of afterload). Their use is rapidly growing, and more and more studies are verifying their beneficial effects. Currently these drugs are used primarily in patients who have been intolerant of ACE inhibitors.

**Contraindications**

The only usual contraindications to the use of ARBs are known drug allergy, pregnancy, and lactation. They should be used very cautiously in elderly patients and in patients with renal dysfunction because of increased sensitivity to its effects and risk for more adverse effects in these patients. As with other antihypertensives, blood pressure and apical pulse rate should be assessed before and during drug therapy.

**Adverse Effects**

The most common adverse effects of ARBs are upper respiratory infections and headache. Occasionally dizziness, inability to sleep, diarrhea, dyspepsia, heartburn, nasal congestion, back pain, and fatigue can occur. Rarely, anxiety, muscle pain, sinusitis, weight gain, dyspepsia, chest pain, cough, and insomnia can also occur. Hyperkalemia is much less likely to occur than with the ACE inhibitors.

**Toxicity and Management of Overdose**

Overdose may manifest as hypotension and tachycardia; bradycardia occurs less often. Treatment is symptomatic and supportive, and includes the administration of intravenous fluids to expand the blood volume.

**Interactions**

The drugs that interact with ARBs, the mechanism responsible, and the result of the interaction are summarized in Table 25-4. In addition, as is the case with ACE inhibitors, ARBs can promote hyperkalemia, especially when taken concurrently with potassium supplements (although this occurs much less frequently than with ACE inhibitors). Patients’ individual chemistries vary widely, however, so monitoring of the serum potassium level is necessary for all patients. Potassium supplements may still be indicated for those patients with a tendency toward hypokalemia (whether acute or chronic).

**Dosages**

For information on the dosages for selected ARBs, see the table on page 000.

---

TABLE 25-4  **Angiotensin II Receptor Blockers: Drug Interactions**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cimetidine</td>
<td>Competes for metabolism</td>
<td>Increased ARB effect</td>
</tr>
<tr>
<td>Lithium</td>
<td>Inhibits lithium elimination</td>
<td>Increased lithium concentrations</td>
</tr>
<tr>
<td>Phenobarbital, rifampin</td>
<td>Increase metabolism</td>
<td>Decreased ARB effect</td>
</tr>
</tbody>
</table>

*ARB, Angiotensin II receptor blocker.

---

**DRUG PROFILE**

- **Losartan**

  Losartan (Cozaar) has been shown to be beneficial in patients with hypertension and heart failure. Studies indicate that ARBs are better tolerated and produce a marginally lower mortality rate after MI than treatment with ACE inhibitors.

  The use of losartan is contraindicated in patients who are hypersensitive to any component of this product. It should be used with caution in patients with renal or hepatic dysfunction and in patients with renal artery stenosis. Breast-feeding women should not take losartan, because it can cause serious adverse effects on the nursing infant. Recommended dosages are given in the table on page 000.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>1 hr</td>
<td>6 hr</td>
<td>6-9 hr</td>
<td>24 hr</td>
</tr>
</tbody>
</table>

---

**CALCIUM CHANNEL BLOCKERS**

CCBs have been discussed in some detail in the two previous chapters on antidyssrhythmic drugs (Chapter 23) and antianginal drugs (Chapter 24). As a class, they are used for several indications and have many beneficial effects and relatively few adverse effects. Their primary use is for the treatment of hypertension and angina. Their effectiveness in treating hypertension is related to their ability to cause smooth muscle relaxation by blocking the binding of calcium to its receptors, which thereby prevents contraction. Because of their effectiveness and safety, they have been added to the list of first-line drugs for the treatment of hypertension. Amlodipine (Norvasc) is the CCB most commonly used for hypertension. They are effective antidyssrhythmics and they can prevent the cerebral artery spasms that can occur after a subarachnoid hemorrhage (nimodipine). They are also sometimes used in the treatment of Raynaud disease and migraine headache. They are also used in combination with other drugs. Some examples are amlodipine/atorvastatin (Caduet), which is both an antihypertensive and a cholesterol-lowering drug (Chapter 29); amloidipine/benazepril (Lotrel); amlodipine/olmesartan (Azar); and amlodipine/valsartan (Exforge).

**DIURETICS**

The diuretics are a highly effective class of antihypertensive drugs. They are listed as the current first-line antihypertensives in the JNC 7 guidelines for the treatment of hypertension. They may be used as monotherapy (single-drug therapy) or in combination with drugs of other antihypertensive classes. Their primary therapeutic effect is decreasing the plasma and extracellular fluid volumes, which results in decreased preload. This leads to a decrease in cardiac output and total peripheral resistance, all of which decrease the workload of the heart. This large group of antihypertensives is discussed in detail in Chapter 26. The thiazide diuretics (e.g., hydrochlorothiazide) are the most commonly used diuretics for treatment of hypertension.

**VASODILATORS**

Vasodilators act directly on arteriolar and/or venous smooth muscle to cause relaxation. They do not work through adrenergic receptors.
Mechanism of Action and Drug Effects

Direct-acting vasodilators are useful as antihypertensive drugs because of their ability to directly elicit peripheral vasodilation. This results in a reduction in SVR. In general, the most notable effect of the vasodilators is their hypotensive effect. However, in recent years minoxidil (in its topical form) has also received increasing attention because of its effectiveness in restoring hair growth. This application is described further in Chapter 56. Diazoxide, hydralazine, and minoxidil work primarily through arteriolar vasodilation, whereas nitroprusside has both arteriolar and venous effects.

Indications

All of the vasodilators can be used to treat hypertension, either alone or in combination with other antihypertensives. Sodium nitroprusside and intravenous diazoxide are reserved for the management of hypertensive emergencies, in which blood pressure is severely elevated. Minoxidil in its topical form is used to restore hair growth.

Contraindications

Contraindications include known drug allergy and may also include hypotension, cerebral edema, head injury, acute MI, and coronary artery disease.

As mentioned in Chapter 22, vasodilating drugs may also be contraindicated in cases of heart failure that is secondary to diastolic dysfunction.

Adverse Effects

Undesirable effects of diazoxide include dizziness, headache, orthostatic hypotension, dysrhythmias, sodium and water retention, nausea, vomiting, acute pancreatitis (rare), and hyperglycemia in diabetic patients. These adverse effects have dramatically reduced the use of diazoxide. The adverse effects of hydralazine include dizziness, headache, anxiety, tachycardia, edema, nasal congestion, dyspnea, anorexia, nausea, vomiting, diarrhea, anemia, agranulocytosis, hepatitis, peripheral neuritis, systemic lupus erythematosus (SLE), and rash. Minoxidil adverse effects include T-wave electrocardiographic changes, pericardial effusion or tamponade, angina, bradycardia, anemia, rashes, and thrombocytopenia. Sodium nitroprusside effects include bradycardia, decreased platelet aggregation, rash, hypothyroidism, hypotension, methemoglobinemia, and, rarely, cyanide toxicity. Cyanide ions are a by-product of nitroprusside metabolism. Cyanide and thiocyanate toxicity are seen clinically when nitroprusside is used at high dosages for long periods of time and/or in patients with renal insufficiency.

Toxicity and Management of Overdose

The main symptom of diazoxide overdose or toxicity is hypotension, which can usually be controlled by placing the patient’s bed in the Trendelenburg position. Symptomatic features such as dopamine or norepinephrine may also be required. Hydralazine toxicity or overdose produces hypotension, tachycardia, headache, and generalized skin flushing. Treatment is supportive and symptomatic and includes the administration of intravenous fluids, digitalization if needed, and the administration of beta-blockers for the control of tachycardia.

Minoxidil overdose or toxicity can precipitate excessive hypotension. Treatment is supportive and symptomatic and includes the administration of intravenous fluids. Norepinephrine and epinephrine should not be used to reverse the hypotension because of the possibility of causing excessive cardiac stimulation.

The main symptom of sodium nitroprusside overdose or toxicity is excessive hypotension. This drug is normally administered only to patients receiving intensive care. Under these conditions the infusion rate is usually carefully titrated to immediately visible results on a cardiovascular monitor that provides constant measurements of blood pressure from centrally placed venous or arterial catheters. For this reason excessive hypotension is usually avoidable. When it does occur, discontinuation of the infusion has an immediate effect, because the drug is metabolized very rapidly (half-life of 10 minutes). Treatment for the hypotension is supportive and symptomatic; if necessary, pressor drugs can be infused to quickly raise blood pressure. The chemical structure of nitroprusside does contain cyanide groups, which are released upon its metabolism in the body and can result in cyanide or thiocyanate toxicity. As noted earlier, this usually occurs clinically when the drug is used at high dosages for prolonged periods and/or in patients with renal failure. Should this occur, treatment can be administered using a standard cyanide antidote kit that includes sodium nitrite and sodium thiosulfate for injection and amyl nitrite for inhalation.

Interactions

The incidence of drug interactions is low for the direct-acting vasodilators as a class. Hydralazine can produce additive hypotensive effects when given with adrenergic or other antihypertensive drugs.

Dosages

For dosage information for selected vasodilator drugs, see the Dosages table on page 000.

<table>
<thead>
<tr>
<th>DRUG PROFILES</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydralazine</td>
</tr>
</tbody>
</table>

Hydralazine (Apresoline) is less commonly used now than when it first became available, but it is still effective for selected patients. It can be taken orally to treat routine cases of essential hypertension. It is also available in injectable form for hypertensive emergencies and is useful for patients who cannot tolerate oral therapy in the hospital. Hydralazine may be given intravenously without the need for cardiac monitoring. Contraindications, in addition to drug allergy, include coronary artery disease and mitral valve dysfunction, such as that related to childhood rheumatic fever. A new combination drug product is a tablet that contains both 37.5 mg of hydralazine and 20 mg of the antianginal drug isosorbide dinitrate (see Chapter 24). This drug combination is known as BiDil, and it is specifically indicated as an adjunct for treatment of heart failure in self-identified African American patients. This drug combination has been shown to improve patient survival and prolong time to hospitalization for heart failure in African American patient populations.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-Life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>5-20 min</td>
<td>30-45 min</td>
<td>2-8 hr</td>
<td>1-4 hr</td>
</tr>
<tr>
<td>PO</td>
<td>20-30 min</td>
<td>1-2 hr</td>
<td>2-8 hr</td>
<td>8 hr</td>
</tr>
</tbody>
</table>
Sodium nitroprusside (Nitropress), like diazoxide, is normally used in the intensive care setting for severe hypertensive emergencies and is titrated to effect by intravenous infusion. Its use is contraindicated in patients with a known hypersensitivity to the drug, severe heart failure, and known inadequate cerebral perfusion (especially during neurosurgical procedures). See the table on page 000 for dosage information.

**PHARMACOKINETICS**

<table>
<thead>
<tr>
<th>Route</th>
<th>Onset of Action</th>
<th>Peak Plasma Concentration</th>
<th>Elimination Half-life</th>
<th>Duration of Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV</td>
<td>Less than 2 min</td>
<td>2-5 min</td>
<td>2 min</td>
<td>1-10 min</td>
</tr>
</tbody>
</table>

**MISCELLANEOUS ANTIHYPERTENSIVE DRUGS**

**DRUG PROFILES**

Four newer medications exemplify some of the antihypertensive drugs most recently made available in the United States. These include eplerenone, bosentan, treprostinil, and aliskiren. All of these drugs are currently indicated for adult use only.

**eplerenone**

Eplerenone (Inspra) is currently the only drug in a new class of antihypertensive drugs called selective aldosterone blockers. It reduces blood pressure by blocking the actions of the hormone aldosterone at its corresponding receptors in the kidney, heart, blood vessels, and brain. Eplerenone is indicated for both routine treatment of hypertension and for post-MI heart failure. Its use is contraindicated in patients with known drug allergy, elevated serum potassium levels (higher than 5.5 mEq/L), or severe renal impairment and in those using a medication that inhibits the action of cytochrome P-450 enzyme 3A4. Many commonly used medications inhibit the action of this enzyme, including several antibiotic, antifungal, and antiviral drugs. The prescriber is advised to review the known drug interactions of all of the patient’s concurrently used drugs before administering this medication. Recommended dosages are given in the Dosages table on page 000.

**bosentan**

Bosentan (Tracleer) is also currently the single drug in a new drug class and works by blocking the receptors of the hormone endothelin. Normally this hormone acts to stimulate the narrowing of blood vessels by binding to endothelin receptors (ET\(_A\) and ET\(_B\)) in the endothelial (innermost) lining of blood vessels and in vascular smooth muscle. Bosentan reduces blood pressure by blocking this...
action. However, currently it is specifically indicated only for the treatment of pulmonary artery hypertension in patients with moderate to severe heart failure. It is available only through a limited distribution program directly from the manufacturer. Its use is contraindicated in patients with known drug allergy, pregnancy, or significant liver impairment, and in patients receiving concurrent drug therapy with cyclosporine or glyburide. Recommended dosages are given in the table on page 000.

**treprostinil**

Treprostinil (Remodulin) lowers blood pressure through a combined mechanism of action by dilating both pulmonary and systemic blood vessels and by inhibiting platelet aggregation. Like bosentan, it is indicated specifically for treatment of pulmonary artery hypertension in patients with moderate to severe heart failure. Its only current contraindication is known drug allergy. It is also unique to date in being the only drug diluted to the nanogram level for administration. Recommended dosages are given in the table on page 000.

**aliskiren**

Aliskiren (Tekturna) is a member of the newest class of antihypertensives, called direct renin inhibitors. It is used for the treatment of hypertension, either alone or in combination with other antihypertensive drugs. As a direct renin inhibitor, it blocks the conversion of angiotensinogen to AI, which then decreases the level of All and activation of the renin-angiotensin-aldosterone system to further decrease the release of renin (see previous discussion on ACE inhibitors for more information on the renin-angiotensin-aldosterone system). Before aliskiren is started, hypovolemia must be corrected and volume status must be carefully monitored in patients taking concurrent diuretics. Aliskiren is a pregnancy category D drug and must be stopped immediately if pregnancy is suspected or confirmed. Recommended dosages are given in the table on page 000.

### NURSING PROCESS

Over the last several decades, the diagnosis and treatment of hypertension have changed greatly from a stepped approach to a medical regimen that is now based on guidelines from the National Institutes of Health (issued in May 2003). These guidelines apply to adults aged 18 years and older and describe evaluation, classification, diagnosis, risk factors, identifiable causes, and blood pressure measurement techniques. One of the major differences in these guidelines, contained in *JNC 7*, is the creation of a “prehypertension” category, defined as a systolic blood pressure of 120 to 139 mm Hg and/or a diastolic blood pressure of 80 to 89 mm Hg. This is a change from previous guidelines and provides a more aggressive approach to the identification and subsequent management of the disease process, instead of a later diagnosis and treatment when multiple organ damage may be present. The nursing process discussion that follows provides both general and specific information related to the pharmacologic and nonpharmacologic treatment of all stages of hypertension.

### EVIDENCE-BASED PRACTICE

**Effects of Exercise on Blood Pressure in Those 55 Years of Age and Older**

**Review**

The Senior Hypertension and Physical Exercise (SHAPE) study examined the effects of exercise on blood pressure in men and women 55 years of age or older with a diagnosis of mild hypertension. Those who participated in a 6-month exercise program showed greater reductions in diastolic (but not systolic) blood pressure than did subjects who did not exercise.

**Type of Evidence**

The participants were between 55 and 75 years of age, had systolic blood pressures (SBP) of 130 to 159 mm Hg or diastolic blood pressures (DBP) of 85 to 89 mm Hg, and were not taking any antihypertensive drugs. Fifty-three control subjects were asked to follow the standard recommendations for physical activity contained in the National Institute of Aging guidelines for exercise. They were also given dietary advice based on the American Heart Association Step 1 diet. In addition to receiving the same standard advice regarding diet and activity, the experimental group followed an exercise regimen based on the American College of Sports Medicine guidelines and participated in three supervised exercise sessions per week that included both resistance and aerobic training. Fifty-one individuals completed the exercise program between 1999 and 2003. The nonexercise group was not a true control group because these subjects may have made unreported lifestyle changes in response to the diet and exercise advice they received. SHAPE investigators were based at the Johns Hopkins School of Medicine and the National Institute on Aging.

**Results of Study**

The study reported significant mean decreases in SBP and DBP of 5.3 and 3.7 mm Hg, respectively, in the exercise group and 4.5 and 1.5 mm Hg, respectively, in the control group. The mean decrease in DBP was significantly greater in the exercisers than in the control group, but the difference in SBP in the two groups was not statistically significant. There was no difference between men and women in blood pressure reductions. The investigators pointed out that the main reason the decrease in SBP in the exercise group was smaller than anticipated was that increased arterial stiffness contributes to systolic hypertension in older patients. This age-related change may not be amenable to modification by exercise.

**Link of Evidence to Nursing Practice**

For older patients with hypertension, exercise has always been considered to be a lifestyle change that may help to decrease both SBP and DBP. Although this study did not find a larger decrease in blood pressure in the group that participated in the exercise program, as had been anticipated, other benefits were noted in this group: improvement in aerobic ability and fitness, increased strength, increase in lean body mass, and decrease in overall and abdominal obesity. Improved body composition accounted for 8% of the reduction in SBP and 17% of the reduction in DBP among the exercisers. This study may be helpful in establishing the importance of exercise training as a means of improving cardiovascular health in older men and women, as suggested by the SHAPE investigators. More research is needed to demonstrate the benefits of lifestyle changes for individuals in all age groups so that patients with hypertension can be educated regarding the importance of nonpharmacologic and pharmacologic treatment regimens for management of hypertension.

Assessment

Before any antihypertensive drug is given to a patient, a thorough health history should be obtained and a head-to-toe physical assessment should be performed. Parameters to measure and document include blood pressure, pulse rate, respirations, and pulse oximetry readings. Results of laboratory tests—especially those indicative of fluid and electrolyte imbalances, heart function, heart tissue damage, renal function, and liver function—should be monitored. These laboratory tests may include the following: (1) serum sodium, potassium, chloride, magnesium, and calcium levels; (2) serum level of troponin, which is usually elevated within 4 to 6 hours after a heart attack begins and may be a reliable indicator up to 14 days after a heart attack; (3) renal function studies, including BUN level and serum and urinary creatinine levels; and (4) hepatic function studies, including serum levels of ALT and AST. These laboratory values are important to assess because of the effect of hypertension on cardiac, vascular, renal, hepatic and retinal tissues.

Laboratory tests will most likely be complemented by more sophisticated scans and imaging studies. Noninvasive ophthalmoscopic examination of the eye structures (e.g., optic nerve, optic disk, vessels) by a professionally trained health care practitioner (e.g., nurse practitioner, physician assistant, physician, ophthalmologist, optometrist) allows easy visualization of the structures impacted by hypertension. If hypertensive retinopathy is present, the examination will reveal narrowing of blood vessels in the eye, oozing of fluid from these blood vessels, spots on the retina, swelling of the macula and optic nerve, and/or bleeding in the back of the eye. These problems may be prevented by controlling the blood pressure or treating hypertension with appropriate follow-up once it is diagnosed.

The nurse must also assess for conditions, factors, or variables that may be underlying causes of a patient’s hypertension, such as the following:

- Addison disease
- Coarctation of the aorta
- Coronary heart disease
- Culture and race or ethnicity
- Cushing disease
- Family history of hypertension
- Nicotine use
- Obesity
- Peripheral vascular disease
- Pheochromocytoma
- Renal artery stenosis
- Renal or liver insufficiency
- Stressful lifestyle

Many of these factors demand very cautious use of antihypertensive drugs. Cautions and contraindications have been discussed previously, but it should be emphasized that the use of these drugs in the elderly and those with chronic illnesses raises special concerns because of further compromise of the physical condition of these patients due to uncontrolled or untreated hypertension or the adverse effects of antihypertensives (e.g., fluid loss, dehydration, electrolyte imbalances, hypotension). For a complete listing of adverse effects as well as drug interactions associated with antihypertensives, see the pharmacology section of this chapter.

Use of alpha-adrenergic agonists demands close assessment of the patient’s blood pressure, pulse rate, and weight before and during treatment because of their strong vasodilating properties and subsequent hypotensive adverse effects. These drugs may also be associated with fluid retention and edema, and thus there is a need for assessment of heart and breath sounds as well as intake and output, and examination for dependent and peripheral edema. The alpha-adrenergic antagonists should also be used cautiously, because of the potential for hypotension-induced dizziness and syncope. The use of either of these groups of drugs requires close assessment of all parameters, especially in the elderly or other patients with preexisting dizziness or syncope, or a debilitated state. With doxazosin, first-dose orthostatic hypotension may occur within 2 to 6 hours; therefore, careful assessment of blood pressures (supine and standing) and measurement of corresponding pulse rates are needed before the first dose and 2 to 6 hours afterward, as well as with any subsequent increase in the dosage. When any antihypertensive drug is used, blood pressures and pulse rates (supine and standing) should be measured, and assessment for cautions, contraindications, and drug interactions should be performed. Centrally acting alpha-blockers require additional assessment of white blood cell counts, serum potassium and sodium levels, and level of protein in the urine (to identify proteinuria). The route of administration specified in the drug order should also be noted, because concerns differ depending on the specific route (e.g., skin sites must be assessed for readiness for transdermal application of a drug, such as clonidine).

Beta-blockers and their mechanisms of action are important to remember before these drugs are administered to a patient because of the risk for complications in certain patient populations. If a drug is a nonselective beta-blocker, it blocks both beta1 and beta2 receptors and will have both cardiac and respiratory effects, whereas if a drug is only a beta2-blocking drug, the cardiac system will be affected (pulse rate and blood pressure will decrease) but there will be no beta2 effects, which limits any concern regarding respiratory problems (e.g., bronchoconstriction). Therefore, if a patient needs a beta-blocker but has a restrictive airway problem, nonselective beta-blockers should not be used to avoid bronchoconstriction. A beta1-specific blocker should be used to avoid a negative impact on the lungs. If there is no history of respiratory illness or concerns, however, the nonselective beta-blockers may be very effective as antihypertensives. In addition, for patients with heart failure, it is important to understand that beta-blockers also have a negative inotropic effect on the heart (decreased contractility); their use would lead to worsening of heart failure, which calls for a completely different class of antihypertensive.

With the use of beta blockers, assessment should include measurement of blood pressure and apical pulse rate immediately before each dose; if the systolic blood pressure is less than 90 mm Hg or the pulse rate is less than 60 beats/min, the prescriber should be notified because of the risk of adverse effects (e.g., hypotension, bradycardia). In such cases the drug would usually be withheld, as ordered or per protocol. These blood pressure and pulse rate parameters are also applicable with use of other antihypertensives. Breath sounds and heart sounds should also be assessed before and during drug therapy.
Antihypertensive Drugs

Assessment depends on the drug’s impact on blood pressure as various groups of antihypertensives. The difference in the level of hypotension, dizziness, and syncope. See Chapters 23, 24, and 26 for discussion of other antihypertensives.

In summary, many assessment parameters are similar for the various groups of antihypertensives. The difference in the level of assessment depends on the drug’s impact on blood pressure as well as the individual’s response to the medication and any pre-existing illness or condition. Other factors to be assessed in any patient receiving these drugs, as well as most other drugs, include the patient’s cultural background, racial or ethnic group, reading level, learning needs, developmental and cognitive status, financial status, mental health status, available support systems, and overall physical health. Patients should always be encouraged to learn how to assess and monitor themselves and their individual responses to drug therapy.

Nursing Diagnoses

- Deficient knowledge related to new prescribed drug regimen and lack of familiarity with medications and lifestyle changes associated with the use of antihypertensives
- Noncompliance with drug therapy related to lack of familiarity with or acceptance of the disease process
- Sexual dysfunction related to adverse effects of some antihypertensive drugs
- Acute pain related to headache as an adverse effect of drug therapy
- Ineffective tissue cerebral and peripheral perfusion related to the impact of the hypertensive disease process and/or possible severe hypotensive adverse effects associated with antihypertensive drug therapy
- Excess fluid volume related to adverse effects of fluid retention associated with some antihypertensive drugs
- Imbalanced nutrition, less than body requirements, related to the drug’s adverse effects of impaired taste or loss of appetite
- Constipation related to the adverse effects of antihypertensive drugs
- Risk for injury (e.g., possible falls) related to possible antihypertensive drug–induced orthostatic hypotension with dizziness and syncope
- Risk for injury (e.g., possible falls) related to possibly antihypertensive drug–induced CNS adverse effects such as pares thesis, sedation, tremors, weakness, and seizures
- Risk for injury to mucous membranes related to the adverse effects of decreased saliva production and dry mouth associated with antihypertensive drug therapy
- Disturbed body image related to the undesired adverse effects associated with the use of antihypertensives, such as impotence, sexual dysfunction, weight gain, and fatigue

Planning

Nursing goals for antihypertensive therapy should focus on educating the patient and his or her family on the need for adequate management to prevent end-organ damage. These goals include making sure the patient understands the nature of the disease, its symptoms and treatment, and the importance of adhering to the treatment regimen. The patient must also come to terms with the disease process and/or possible severe hypotensive adverse effects. The influence of chronic illness and the importance of nonpharmacologic therapy, stress reduction, and follow-up care must also be emphasized. The nurse needs to plan for ongoing assessment of blood pressure, weight, diet, exercise, smoking habits, alcohol intake, compliance with therapy, and sexual function in the patient receiving therapy for hypertension.

The use of ACE inhibitors requires assessment of blood pressure, apical pulse rate, and respiratory status (because of the adverse effect of a dry, hacking, chronic cough). Blood pressure should be taken immediately before initial and subsequent doses of the drug so that extreme fluctuations may be identified early. Serum potassium, sodium, and chloride levels should also be assessed. Tests of baseline cardiac functioning will most likely be ordered prior to initiation of therapy. Because of the potential adverse effects of neutropenia and other blood disorders, a complete blood count should be performed before and during therapy, as ordered. Angiotensin receptor blockers (ARBs) should be used very cautiously in elderly patients and in patients with renal dysfunction, because such patients show increased sensitivity to the drug’s adverse effects of impaired taste or loss of appetite.

Vasodilators require baseline neurologic assessment, with attention to level of consciousness and cognitive ability. These drugs should be used with extreme caution with the elderly, because they are more sensitive to the drugs’ blood pressure–lowering effects and consequently experience more problems with hypotension, dizziness, and syncope. See Chapters 23, 24, and 26 for discussion of other antihypertensives.

In summary, many assessment parameters are similar for the various groups of antihypertensives. The difference in the level of assessment depends on the drug’s impact on blood pressure as well as the individual’s response to the medication and any pre-existing illness or condition. Other factors to be assessed in any patient receiving these drugs, as well as most other drugs, include the patient’s cultural background, racial or ethnic group, reading level, learning needs, developmental and cognitive status, financial status, mental health status, available support systems, and overall physical health. Patients should always be encouraged to learn how to assess and monitor themselves and their individual responses to drug therapy.

Nursing Diagnoses

- Deficient knowledge related to new prescribed drug regimen and lack of familiarity with medications and lifestyle changes associated with the use of antihypertensives
- Noncompliance with drug therapy related to lack of familiarity with or acceptance of the disease process
- Sexual dysfunction related to adverse effects of some antihypertensive drugs
- Acute pain related to headache as an adverse effect of drug therapy
- Ineffective tissue cerebral and peripheral perfusion related to the impact of the hypertensive disease process and/or possible severe hypotensive adverse effects associated with antihypertensive drug therapy
- Excess fluid volume related to adverse effects of fluid retention associated with some antihypertensive drugs
- Imbalanced nutrition, less than body requirements, related to the drug’s adverse effects of impaired taste or loss of appetite
- Constipation related to the adverse effects of antihypertensive drugs
- Risk for injury (e.g., possible falls) related to possible antihypertensive drug–induced orthostatic hypotension with dizziness and syncope
- Risk for injury (e.g., possible falls) related to possibly antihypertensive drug–induced CNS adverse effects such as pares thesis, sedation, tremors, weakness, and seizures
- Risk for injury to mucous membranes related to the adverse effects of decreased saliva production and dry mouth associated with antihypertensive drug therapy
- Disturbed body image related to the undesired adverse effects associated with the use of antihypertensives, such as impotence, sexual dysfunction, weight gain, and fatigue

Planning

Nursing goals for antihypertensive therapy should focus on educating the patient and his or her family on the need for adequate management to prevent end-organ damage. These goals include making sure the patient understands the nature of the disease, its symptoms and treatment, and the importance of adhering to the treatment regimen. The patient must also come to terms with the disease process and/or possible severe hypotensive adverse effects. The influence of chronic illness and the importance of nonpharmacologic therapy, stress reduction, and follow-up care must also be emphasized. The nurse needs to plan for ongoing assessment of blood pressure, weight, diet, exercise, smoking habits, alcohol intake, compliance with therapy, and sexual function in the patient receiving therapy for hypertension.

The Institute for Safe Medication Practices (ISMP) reports that oral nimodipine has been given intravenously, which resulted in patient death on several occasions. Oral nimodipine comes in capsule form, and the drug’s manufacturer indicates in the product labeling that the drug may be extracted from the capsule into a syringe, using an 18-gauge needle, and then administered via an enteric tube to patients who cannot swallow the drug. Using a parenteral syringe for an oral dose is potentially dangerous, however, as noted by the ISMP in a newsletter article dated August 25, 1999.

One fatal incident occurred when the pharmacy dispensed the nimodipine capsules without knowing that the patient could not swallow and thus did not provide instructions on how to prepare the capsule contents for feeding tube administration. The nurse used a parenteral syringe to draw up the medication from the capsule, and the dose was later administered into an intravenous (IV) line instead of the feeding tube. As a result, the patient died.

Many procedures can be used to prevent inadvertent IV administration of oral solutions. The pharmacy can prepare oral doses of nimodipine in amber oral syringes, labeling the syringes with a “use by” date, the notation “For Oral Use Only,” and the drug information. The pharmacy should also communicate to the nurse the potential danger of inadvertent IV injection of this drug. It is also important for the nurse to communicate to the pharmacy that a given patient is unable to swallow oral doses so that the correct dosage form is sent for administration. Most importantly, parenteral syringes should never be used to prepare and administer oral medications.

For more information, see Institute for Safe Medication Practices: ISMP medication safety alert: take steps to avoid inadvertent IV administration of nimodipine, 2005, available at http://www.ismp.org/Newsletters/acute/ Care/articles/20050728_1.asp.

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Goals

- Patient takes the drug exactly as prescribed.
- Patient experiences relief of symptoms for which the medication was prescribed (e.g., a decrease in blood pressure).
- Patient demonstrates adequate knowledge about the use of the specific medication, its adverse effects, and the appropriate dosing at home.
- Patient is free of self-injury resulting from adverse effects of drug therapy.
- Patient states the rationale for and importance of antihypertensive therapy.
- Patient describes measures to implement to decrease the impact of the adverse effects of antihypertensive therapy.
- Patient reports any change in sexual patterns and function, bowel pattern changes, and activity intolerance.
- Patient remains compliant with the therapy regimen.

Outcome Criteria

- Patient states the risks and complications of potent antihypertensive drugs, such as tremors, decreased sweating, tachycardia, and hypotension.
- Patient states conditions to report to the prescriber, such as syncope and chest pain.
- Patient states the importance of lifelong adherence to the drug regimen for hypertension to decrease end-organ damage and complications.
- Patient follows instructions to change position slowly, monitor blood pressure, keep follow-up appointments with the prescriber, and maintain a journal to help monitor the effects of therapy.
- Patient communicates openly with nurses and other members of the health care team regarding the disease, its treatment, and any concerns related to changes in body image.
- Patient reports to the prescriber immediately any pitting edema of the feet, hands, or sacral area or a weight gain of 2 pounds or more within 24 hours or 5 pounds or more in 1 week.
- Patient maintains normal nutritional status through adherence to a prescribed diet high in fiber and fluids and avoidance of alcohol.

Implementation

Nursing interventions may help patients achieve stable blood pressure while minimizing adverse effects during treatment with antihypertensives. Many patients have problems complying with treatment because the disease itself is silent or without symptoms. Because of this, patients are unaware of their blood pressure or think that if they do not feel bad there is nothing wrong with them, which poses many problems for treatment. Also, the antihypertensives are often associated with multiple adverse effects that may impact patients’ self-concept and/or sexual integrity. These adverse effects may lead patients to abruptly stop taking the medication. It is important to inform patients that any abrupt withdrawal is a serious concern because of the risk of developing rebound hypertension. Rebound hypertension is characterized by a sudden and very high elevation of blood pressure. This places the patient at risk for a cerebrovascular accident or other cerebral or cardiac adverse event. It is important to understand that with all antihypertensives there is a risk of rebound hypertension, and prevention of this through patient education is critical to patient safety. Other interventions related to each major group of drugs are discussed in the following paragraphs. See the Patient Teaching Tips for more information.

Because of the potential for drug-related orthostatic hypotensive effects, patients taking alpha-adrenergic agonists will need to monitor their blood pressure and pulse rate at home or else have these parameters measured for them by a family member who has received instructions or by local fire department or rescue or emergency medical personnel. The blood pressure machines found in grocery stores do not provide as accurate readings as measurement in the aforementioned ways. Alpha-adrenergic antagonist drugs are associated with first-dose syncope, so to avoid injury, patients must be told to remain supine for the first dose of the drug. More than likely, these drugs will be prescribed to be given at bedtime to allow the patient to sleep through the drug’s first-dose syncope. It may take 4 to 6 weeks for the drug to achieve its full therapeutic effects, so education about delayed onset of action and bedtime dosing is important to avoid injury. The patient should also receive continued monitoring for dizziness, syncope, edema, and other adverse effects (e.g., shortness of breath, exacerbation of preexisting cardiac disorders). Diuretics may be ordered as adjunctive therapy to minimize the adverse effects of edema, but they may lead to more dizziness and electrolyte problems. Centraly acting alpha-blockers require the same type of nursing interventions as other alpha-blockers; however, as their name indicates, the mechanism of action of these drugs is central, so adverse effects are often more pronounced (e.g., hypotension, sedation, bradycardia, edema). See the Patient Teaching Tips for more information.

CASE STUDY

Aliskiren for Hypertension

Hypertension was diagnosed in Gina S., who is 30 years old. Both her mother and her sister have hypertension, and both were also in their thirties when it was diagnosed. Gina’s most current blood pressure reading is 150/96 mm Hg, and for this reason the nurse practitioner has recommended therapy with aliskiren (Tekturna), light exercise in the form of walking, and relaxation therapy. After 1 month of therapy, Gina’s blood pressure is 145/86 mm Hg. Stress reduction has been the biggest obstacle in her treatment, because she is a lawyer with a prominent law firm and has found that her blood pressure is consistently elevated (160/100 mm Hg) whenever she measures it at work. At this follow-up visit, she is also given a prescription for a diuretic to help with her blood pressure control.

1. How does aliskiren reduce blood pressure?
2. What precautions should Gina be aware of while taking this drug?
3. Gina states that she and her husband are planning to start a family in a year. What should you, as her nurse, tell her about pregnancy and therapy with aliskiren?
4. What lifestyle changes would you, as her nurse, recommend that she make and, even more important, what information would you give her to help her change her lifestyle and more effectively reduce the stress in her life?

For answers, see http://evolve.elsevier.com/Lilley.
The beta-blockers are either nonselective (block both beta_1 and beta_2 receptors; e.g., propranolol) or cardioselective (block mainly beta_1 receptors; e.g., atenolol). With any beta-blocker, careful adherence to the drug regimen is critical to patient safety. Patients taking beta-blockers may experience an exacerbation of respiratory diseases such as asthma, bronchospasm, and chronic obstructive pulmonary disease (because of increased bronchoconstriction due to beta_2 blocking) or an exacerbation of heart failure because of the drug’s negative inotropic effects (decreased contractility due to beta_1 blocking). Instructions about reporting adverse effects and instructions for taking blood pressure and pulse rates must be clear and concise. If a beta_1-blocker causes shortness of breath, it is most likely due to edema and/or exacerbation of congestive heart failure. Any dizziness, depression, confusion, or unusual bleeding or bruising should also be reported to the prescriber immediately. See the Patient Teaching Tips for more information.

ACE inhibitors must also be taken exactly as prescribed. If angioedema occurs, the prescriber should be contacted immediately. If the drug must be discontinued, weaning is recommended (as with all antihypertensives) to avoid rebound hypertension. Serum sodium and potassium levels should be monitored during therapy. Serum potassium levels increase as an adverse effect of these drugs, and this may lead to hyperkalemia with more complications. Impaired taste may occur as an adverse effect and last up to 2 to 3 months after the drug has been discontinued. It is also important to educate the patient that it takes several weeks to see the full therapeutic effects and that potassium supplements should not be used with these drugs (due to the adverse effect of hyperkalemia).

Angiotensin Receptor Blockers must also be taken exactly as prescribed. They are often tolerated best with meals, as with many antihypertensives. The dosage should not be changed nor the medication discontinued except on the order of the prescriber. With ARBs, if the patient has hypovolemia or hepatic dysfunction, the dosage may need to be reduced. A diuretic such as hydrochlorothiazide may be ordered in combination with an ARB for patients who have hypertension with left ventricular hypertrophy. Losartan is also an option for patients at risk for stroke and for those who are hypertensive and have left ventricular hypertrophy. Most importantly, with ARBs, any unusual shortness of breath, dyspnea, weight gain, chest pain, or palpitations should be reported to the prescriber immediately.

Some nursing considerations for vasodilators are similar to those for other antihypertensives; however, the impact of the vasodilators on blood pressure may be more drastic, depending on the specific drug and dosage. Hydralazine given by injection may result in reduced blood pressure within 10 to 80 minutes after administration and requires very close monitoring of the patient. With hydralazine, SLE may be an adverse effect if the patient is taking more than 200 mg/day orally. If signs and symptoms of SLE occur, such as glomerulonephritis, photosensitivity, characteristic skin rashes, CNS changes, or various blood dyscrasias (hemolytic anemia, leucopenia, thrombocytopenia), the drug should be discontinued, the prescriber should be contacted immediately, and the patient should be closely monitored. Electrocardiographic changes, cardiovascular inadequacies, and hypotension may have pronounced effects on the patient’s cardiac status, and therefore the drug should never be given without adequate monitoring and frequent assessment. Pyridoxine may help to diminish the adverse effect of peripheral neuritis.

Sodium nitroprusside must always be diluted per manufacturer’s guidelines. Because this drug is a potent vasodilator, it may lead to extreme decreases in the patient’s blood pressure. Close monitoring is therefore important to prevent further complications. Severe drops in blood pressure may lead to irreversible ischemic injury and even death. The nurse must remember that sodium nitroprusside should never be infused at the maximum dose rate for more than 10 minutes. If this drug does not control a patient’s blood pressure after 10 minutes, it will most likely be ordered to be discontinued. To help prevent complications of cyanide and thiocyanate toxicity, the nurse should (1) dilute the medication properly and avoid use of any solution that has turned blue, green, or red; (2) infuse only using a volumetric infusion pump, not through ordinary intravenous sets; (3) continuously monitor blood pressure during the infusion (often by invasive measures); and (4) when more than 500 mcg/kg of sodium nitroprusside is administered at a rate faster than 2 mcg/kg/min, be aware that this may result in production of cyanide at a faster rate than it can be eliminated by the patient unaided. (See the Laboratory Values Related to Drug Therapy box on p. 000 for more information.)

Calcium channel blockers and related nursing interventions are discussed only briefly here, because these drugs are covered in other chapters. Drugs like enalapril are to be taken exactly as prescribed with a warning to the patient not to puncture, open, or crush the extended-release or sustained-release tablets or capsules. The nurse must be aware that CCBs are negative inotropic drugs (decrease cardiac contractility), because this action may induce more signs of heart failure if these drugs are given with drugs that are used to increase cardiac contractility, such as digitals glycosides. Monitoring of blood pressure and pulse rate before and during therapy will aid in prevention or early detection of any problems related to the negative inotropic effects, negative chronotropic effects (decreased heart rate), and negative dromotropic effects (decreased conduction).

The nurse must remember always to base nursing interventions on a thorough assessment and plan of care that also includes consideration of the patient’s cultural and ethnic group. This is particularly important with antihypertensives, because research studies have documented differences in responses to antihypertensives among different racial and ethnic groups. Some ethnic groups respond less favorably to certain drugs than to others. As for patients with any disease, patients with hypertension must be treated with respect and with an appreciation for a holistic approach to health care in which all physical, psychosocial, and spiritual needs are taken into consideration (see Cultural Implications box on p. 000). In summary, some educational information to be conveyed to the patient has been mentioned for particular groups of drugs or specific drugs. The nurse must remember that patient education is of critical importance and plays an important role in ensuring adherence to the drug regimen and in decreasing the incidence of problems related to these medications.

Evaluation
Because patients with hypertension are at high risk for cardiovascular injury, it is critical for them to adhere to both their pharmacologic and nonpharmacologic treatment regimens. Monitoring patients for the adverse effects (e.g., orthostatic hypotension, dizziness,
The evaluation process helps the nurse to identify potentially life-threatening complications. The most important aspect of the evaluation process is collecting data and monitoring patients for evidence of controlled blood pressure. Blood pressure should be maintained at values lower than the parameters established by the Joint National Committee or below the levels set by the Joint National Committee for "prehypertension," namely, a systolic blood pressure of 120 to 139 mm Hg and/or a diastolic blood pressure of 80 to 89 mm Hg. If compelling indications are present, such as diabetes mellitus or kidney disease, then the blood pressure goal is often lower. Blood pressure should be monitored at periodic intervals, and patient education about self-monitoring is very important to the safe use of these drugs. Updated information on hypertension and its diagnosis, treatment, and evaluation is available at the National Heart, Lung, and Blood Institute website at [http://www.nhlbi.nih.gov/guidelines/hypertension](http://www.nhlbi.nih.gov/guidelines/hypertension).

In addition, sodium nitroprusside may lead to toxic reactions, even at dosages that are within the recommended ranges. Toxic reactions are manifested by extreme hypotension, cyanide toxicity, or thiocyanate toxicity. Cyanide assays are performed to detect cyanide in body fluids, but the results of this test are difficult to interpret and so it is not the most reliable method of monitoring. Other laboratory tests that may be helpful in diagnosing cyanide toxicity are alterations of acid-base balance and venous oxygen concentrations. Actual cyanide levels in the blood may lag behind peak cyanide levels by an hour or longer. Signs of thiocyanate toxicity include ringing of the ears (tinnitus), miosis, and hyper-reflexia as well as methemoglobinemia.

### Laboratory Values Related to Drug Therapy

<table>
<thead>
<tr>
<th>Sodium Nitroprusside</th>
<th>Normal Ranges</th>
<th>Rationale for Assessment</th>
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<tbody>
<tr>
<td>Serum methemoglobin and serum cyanide levels</td>
<td>Normally there are no detectable amounts with appropriate drug levels of sodium nitroprusside</td>
<td>Use of sodium nitroprusside may be associated with sequestration of hemoglobin as methemoglobin. The appearance of this clinically significant adverse effect of methemoglobin is rare (less than 10% of cases). For a patient receiving this drug at the maximum rate of 10 mcg/kg/min, 16 or more hours would be required for the patient to reach a total accumulated dose of 10 mg/kg, so serum laboratory testing is used to measure the amount of methemoglobin. One significant clinical sign of this adverse effect is impaired oxygen delivery despite adequate cardiac output. When the sequestration is diagnosed, the treatment of choice is 1 to 2 mg/kg of methylene blue given intravenously over several minutes to allow binding of the metabolic by-product of cyanide to methemoglobin as cyanmethemoglobin, but this should be given only as ordered and with extreme caution. In addition, sodium nitroprusside may lead to toxic reactions, even at dosages that are within the recommended ranges. Toxic reactions are manifested by extreme hypotension, cyanide toxicity, or thiocyanate toxicity. Cyanide assays are performed to detect cyanide in body fluids, but the results of this test are difficult to interpret and so it is not the most reliable method of monitoring. Other laboratory tests that may be helpful in diagnosing cyanide toxicity are alterations of acid-base balance and venous oxygen concentrations. Actual cyanide levels in the blood may lag behind peak cyanide levels by an hour or longer. Signs of thiocyanate toxicity include ringing of the ears (tinnitus), miosis, and hyper-reflexia as well as methemoglobinemia.</td>
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Antihypertensive Drugs

CHAPTER 25

Antihypertensives in General

- Medications should be taken exactly as ordered with avoidance of doubling up or omitting doses.
- Successful therapy requires adherence to the medication regimen as well as to any dietary restrictions (e.g., decreasing consumption of fatty or high-cholesterol foods).
- The patient should always monitor stress levels and use biofeedback, imagery, and/or relaxation techniques or massage, as needed. Exercise, if approved by the prescriber, may also help in the management of hypertension and serves to relieve stress; supervised, prescribed exercise is usually included.
- The importance of safety and the need to avoid smoking and excessive alcohol intake as well as excessive exercise, hot climates, saunas, hot tubs, and hot environments should be emphasized. Heat may precipitate vasodilation and lead to worsening of hypotension with the risk of fainting and injury to self.
- Frequent laboratory tests may be needed for the duration of therapy, so the importance of keeping follow-up appointments must be emphasized to the patient.
- All medications should be kept out of the reach of children because of the potential for extreme toxicity. If a transdermal patch is used, the patient should be taught to check periodically to make sure the patch is in place and intact. There have been cases in which a patch that was placed on an adult later dropped off and was accidentally picked up on the skin of a crawling infant, with severe consequences.
- Encourage the wearing of a medical alert bracelet or necklace and to carry a medical identification card specifying the patient’s diagnosis, listing allergies, and listing all medications taken (e.g., prescribed drugs, over-the-counter medications, herbas, vitamins, and supplements). The same information should be kept in a visible location in the patient’s car as well as in the patient’s home on the refrigerator for emergency medical personnel.
- It is recommended that the patient’s weight be measured daily each morning before breakfast, at the same time and with the same amount of clothing worn. This information should be recorded in a daily journal along with blood pressure readings. The patient should be instructed to report to the prescriber an increase in weight by 2 pounds or more over a 24-hour period or 5 pounds or more in 1 week.
- Blood pressure should be recorded, including postural blood pressures. The patient should be sure he or she feels comfortable in taking his or her own blood pressure and pulse rate. The patient should practice as needed and should never hesitate to ask for assistance.
- The patient should inform all health care providers (e.g., dentist, surgeon) that he or she is taking an antihypertensive drug.
- Encourage careful, purposeful and cautious changing of positions because of the possible adverse effect of postural hypotension and associated risk for dizziness, lightheadedness, and possible fainting and falls.
- Adequate supply of antihypertensive medications should be kept on hand, especially while traveling.
- Scheduling of periodic eye examinations (e.g., every 6 months) should be emphasized because of the need to evaluate treatment effectiveness and the impact of hypertension on the vascularature of the eyes.

PATIENT TEACHING TIPS

- With successful therapy, the patient’s condition will improve; however, the patient should be cautioned not to stop taking the medication just because he or she is feeling better. Lifelong therapy is usually required.
- Saliva substitutes, use of sugar-free hard candy/gum and forcing fluids (unless contraindicated) may help with dry mouth. Forcing fluids and increasing dietary fiber and roughage may help with preventing constipation and if remains a problem, the prescriber should be contacted.
- Sexual dysfunction may occur with antihypertensives, so the patient should be encouraged to be open in reporting and discussing any problems or concerns. The patient should be told that, should this adverse effect occur, options are available to help alleviate the problem, such as combination therapy that allows lower dosages of drugs to be used, as well as a change to other types of antihypertensives. The patient should always report any problems to the prescriber, because solutions are usually available.
- Medications should never be stopped abruptly for any reason, including sexual problems, because of the risk of severe hypertensive rebound. Avoiding abrupt withdrawal of any of the antihypertensives is critical to patient safety.
- The patient should be aware that antihypertensives may lead to depression, so any change in emotional status should be reported to the prescriber.

Alpha-Adrenergic Agonists

- First-dose syncope is related to the alpha adrenergic agonists and so patients should avoid conditions/situations/drugs that would exacerbate this.
- The patient should be cautioned to be careful at first with driving and other activities requiring alertness. The patient may have to postpone driving and other activities until the drug-related drowsiness subsides.
- The patient should report any jaundice, unexplained fever, or flu-like symptoms to the prescriber immediately.
- Because centrally acting blockers may also affect the patient’s sexual functioning (e.g., causing impotence or decreased libido), the patient should be informed of these possible adverse effects and should be told to contact the prescriber if these effects are problematic for them. Other treatment options may be indicated.
- Transdermal patches of clonidine should be applied to nonhairy areas of the skin as ordered, and application sites should be rotated. All residual drug on the skin should be cleansed with a cloth soaked in lukewarm water before applying a new patch.

Beta-Blockers

- The patient should be cautioned to move and change positions slowly to avoid possible dizziness, fainting, and falls and should be instructed to report a pulse rate lower than 60 beats/min, any peripheral numbness, dizziness, weight gain (see earlier), or a systolic blood pressure of 90 mm Hg or lower to the prescriber.
- Prolonged sitting or standing and excessive physical exercise may also lead to exacerbation of hypotensive effects, so the patient should be encouraged to avoid these activities or counteract them with healthy practices such as pumping the feet up and down while sitting.
CRITICAL THINKING ACTIVITIES: BEST ACTION

1 Primary hypertension has been diagnosed in a 53-year-old woman who has a history of hypothyroidism and asthma. The nurse is reviewing the new orders and notes an order for carvedilol (Coreg) as part of the treatment for hypertension. Considering the patient’s history, what is the nurse’s best action at this time?

2 A 79-year-old woman has been admitted to the emergency department after experiencing severe headaches and “feeling faint.” Upon admission, her blood pressure is measured as 286/190 mm Hg. A sodium nitroprusside infusion is started, and the nurse is monitoring the patient closely. After 8 minutes of infusion, the nurse notes that the patient’s blood pressure suddenly drops to 100/60. What is the best action of the nurse at this time?

3 During a follow-up appointment, a 58-year-old man is pleased to hear that his blood pressure is 118/64 mm Hg. He says, “I’ve been hoping to hear this good news! Now I can stop the medications.” What would be the nurse’s best answer?

For answers, see http://evolve.elsevier.com/Lilley.

POINTS TO REMEMBER

• All antihypertensives in some way affect cardiac output. Cardiac output is the amount of blood ejected from the left ventricle and is measured in liters per minute.
• The major groups of antihypertensives are diuretics (see Chapter 26), alpha-blockers, centrally active alpha-blockers, beta-blockers, ACE inhibitors, vasodilators, CCBs, and ARBs.
• ACE inhibitors work by blocking a critical enzyme system responsible for the production of All (a potent vasoconstrictor). They (1) prevent vasoconstriction caused by All, (2) prevent aldosterone secretion and therefore sodium and water resorption, and (3) prevent the breakdown of bradykinin (a potent vasodilator) by All.
• ARBs work by blocking the binding of angiotensin at the receptors; the end result is a decrease in blood pressure.
• Calcium channel blockers may be used to treat angina, dysrhythmias, and hypertension and help to reduce blood pressure by causing smooth muscle relaxation and dilatation of blood vessels. If calcium is not present, then the smooth muscle of the blood vessels cannot contract.

A thorough nursing assessment should include finding out whether the patient has any underlying causes of hypertension, such as renal or liver dysfunction, a stressful lifestyle, Cushing disease, Addison disease, renal artery stenosis, peripheral vascular disease, or pheochromocytoma.

The nurse should always assess for the presence of contraindications, cautions, and potential drug interactions before administering any of the antihypertensive drugs. Contraindications include a history of MI or chronic renal disease. Cautious use is recommended in patients with renal insufficiency or glaucoma. Drugs that interact with antihypertensive drugs include other antihypertensive drugs, anesthetics, and diuretics.

Patients’ hypertension should be managed by both pharmacologic and nonpharmacologic means. Patients should be encouraged to consume a diet low in fat, make any other necessary modifications in their diet (such as possibly decrease the intake of sodium and increase fiber intake), engage in regular supervised exercise, and reduce the amount of stress in their lives.

NCLEX EXAMINATION REVIEW QUESTIONS

1 The nurse is administering antihypertensive drugs to older adult patients. The nurse knows that which adverse effect is of most concern for these patients?

a) Dry mouth
b) Hypotension
c) Restlessness
d) Constipation

2 When giving antihypertensive drugs, the nurse must consider giving the first dose at bedtime for which class of drugs?

a) Alpha-blockers such as doxazosin (Cardura)
b) Diuretics such as furosemide (Lasix)
c) ACE inhibitors such as captopril (Capoten)
d) Vasodilators such as hydralazine (Apresoline)

3 A 56-year-old man started antihypertensive drug therapy 3 months earlier and is in the office for a follow-up visit. While the nurse is taking his blood pressure, he informs the nurse that he has had some problems with sexual intercourse. Which would be the most appropriate response by the nurse?

a) “Not to worry. Eventually, tolerance will develop.”
b) “The physician can work with you on changing the dose and/or drugs.”
c) “Sexual dysfunction happens with this therapy, and you must learn to accept it.”
d) “This is an unusual occurrence, but it is important to stay on your medications.”

4 When a patient is being taught about the potential adverse effects of an ACE inhibitor, which of the following should the nurse mention as possibly occurring when this drug is taken to treat hypertension?

a) Hypokalemia
b) Nausea
c) Dry, nonproductive cough
d) Sedation

e) An NSAID taken as needed for headaches.

5 A patient has a new prescription for a beta-blocker. During a review of the patient’s list of current medications, which would cause concern for a possible interaction with this new prescription? (Select all that apply.)

a) A benzodiazepine taken as needed for allergies
b) A multivitamin with iron taken daily
c) An oral anticoagulant taken daily
d) An opioid used for occasional severe pain
e) An NSAID taken as needed for headaches.