chapter 13

Drugs That Affect the Central Nervous System

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Objectives

1. Describe how the central nervous system differs from the peripheral nervous system.
2. Explain the role of neurotransmitters at synaptic junctions.
3. Name the most common neurotransmitters known to affect central nervous system function and identify the two major neurotransmitters of the autonomic nervous system.
4. Explain how drugs inhibit the actions of cholinergic and adrenergic fibers.
5. Identify two broad classes of drugs used to stimulate the adrenergic nervous system.
6. Identify the neurotransmitters that are called *catecholamines* and list the neurotransmitters responsible for adrenergic activity.
7. Review the actions of adrenergic agents and the conditions that require the use of these drugs.
8. Describe the benefits of using beta-adrenergic blocking agents for hypertension, angina pectoris, cardiac dysrhythmias, and hyperthyroidism.
9. Identify disease conditions in which beta-adrenergic blocking agents should not be used, and discuss why they should not be used.
10. Describe clinical uses and the predictable adverse effects of cholinergic agents and anticholinergic agents.

Key Terms

central nervous system (SĔN-trŭl NŪR-vŭs SĪS-tĕm) (p. 201)
peripheral nervous system (pĕ-RĬF-ĕr-ăl) (p. 201)
afferent nerves (ĂF-ĕ-rĕnt NŪRVZ) (p. 201)
efferent nerves (ĔF-ĕ-rĕnt) (p. 201)
autonomic nervous system (ŏ-tŏ-NŎM-ĭk) (p. 201)
neurons (NYŪR-ŏnz) (p. 201)
synapse (sĭn-ĂPS) (p. 201)
neurotransmitters (nyū-rō-TRĂNZ-mĭ-tŭrz) (p. 202)
receptors (rē-SĒP-tŭrz) (p. 202)
norepinephrine (nōr-ĕp-ĭ-NĒF-rĭn) (p. 202)
acetylcholine (ăs-ē-tĭl-KŌ-lēn) (p. 202)
cholinergic fibers (kō-lĭn-ŪR-jĭk FĪ-bŭrz) (p. 202)
adrenergic fibers (ăd-rĭ-NŪR-jĭk) (p. 202)
cholinergic agents (kō-lĭn-ŪR-jĭk Ā-jĕnts) (p. 202)
adrenergic agents (ăd-rĭ-NŪR-jĭk) (p. 202)
anticholinergic agents (ăn-tē-kō-lĭn-ŪR-jĭk) (p. 202)
adrenergic blocking agents (ăd-rĭ-NŪR-jĭk BLŎ-kĭng Ā-jĕnts) (p. 202)
catecholamines (kăt-ĕ-KŌL-ă-mēnz) (p. 202)
alpha receptor (ĂL-fă rē-SĒP-tŭr) (p. 202)
beta receptor (BĀ-tă rē-SĒP-tŭr) (p. 202)
dopaminergic receptors (dō-pă-mĭn-ŪR-jĭk rē-SĒP-tŭrz) (p. 202)

THE CENTRAL AND AUTONOMIC NERVOUS SYSTEMS

The control of the human body as a living organism comes primarily from two major systems: the nervous system and the endocrine system. In general, the endocrine system controls the body's metabolism. The nervous system regulates the body's ongoing activities (e.g., heart and respiratory muscle contractions), its rapid response to sudden changes in the environment (e.g., skeletal muscles contracting to help an individual to avoid danger), and the rates of secretion of some glands.

The nervous system is comprised of the **central nervous system** (CNS), which is made up of the brain and the spinal cord, and the **peripheral nervous system,** which includes the peripheral nerves subdivided into the afferent and efferent nerves. The **afferent** (peripheral) **nerves** conduct signals from sensory receptors (e.g., vision, pressure, pain, cold, warmth, touch, smell) throughout the body to the central nervous system. The CNS processes these signals and controls the body's response by sending signals back through the **efferent nerves** of the peripheral nervous system. The peripheral nervous system is further subdivided into the somatic nervous system, which controls voluntary movement (e.g., skeletal muscle contractions), and the **autonomic nervous system,** which, as suggested by the name, works automatically and is not under voluntary control.

Each nerve of the central and peripheral nervous systems is actually composed of a series of segments called *neurons.* The junction between one neuron and the next is called a *synapse.* The transmission of nerve

signals or impulses occurs because of the activity of chemical substances called *neurotransmitters* (e.g., transmitters of nerve impulses). A neurotransmitter is released into the synapse at the end of one neuron, thereby activating **receptors** on the next neuron in the chain or at the end of the nerve chain and stimulating receptors on the end organ (e.g., the heart, smooth muscle, or gland). Neurotransmitters can be excitatory, which means that they stimulate the next neuron, or inhibitory, which means that they inhibit the neuron. Because a single neuron releases only one type of neurotransmitter, the CNS is composed of different types of neurons that secrete separate neurotransmitters. Research indicates that there are more than 30 different types of neurotransmitters; the more common ones throughout the CNS are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, gamma-aminobutyric acid (GABA), and glutamic acid. Substance P and the enkephalins and endorphins regulate the sensation of pain, and serotonin regulates mood. Other neurotransmitters include prostaglandins, histamine, cyclic adenosine monophosphate(cAMP), and amino acids and peptides. Neurotransmitter regulation by pharmacologic agents (e.g., medicines) is a major mechanism that allows for the control of disease processes caused by an excess or deficiency of these neurotransmitters. The use of inhibitory and excitatory neurotransmitters to control illnesses is explained in the rest of the chapters in this unit.

THE AUTONOMIC NERVOUS SYSTEM

With the exception of skeletal muscle, the autonomic nervous system controls most tissue function. This nervous system helps to control blood pressure, gastrointestinal (GI) secretion and motility, urinary bladder function, sweating, and body temperature. In general, it maintains a constant internal environment (homeostasis) and responds to emergency situations.

There are two main branches of the autonomic nervous system: the sympathetic branch and the parasympathetic branch. The sympathetic and parasympathetic branches typically function in opposition with each other. However, this can be considered complimentary in nature rather than antagonistic. The sympathetic branch speeds up normal processes, and the parasympathetic branch slows down these processes. The sympathetic division typically functions in actions that require quick responses during the "fight-or-flight" response. The parasympathetic division functions as part of actions that do not require immediate reaction during the "rest-and-digest" response.

The two major neurotransmitters of the autonomic nervous system are **norepinephrine** and **acetylcholine.** The nerve endings that liberate acetylcholine are called *cholinergic fibers;* those that secrete norepinephrine are called *adrenergic fibers.* Most organs are innervated by both adrenergic and cholinergic fibers, but these fibers produce opposite responses. For example, in the heart, the stimulation of adrenergic fibers increases the heart rate, and the stimulation of cholinergic fibers slows the heart rate; in the eyes, the stimulation of adrenergic fibers causes pupillary dilation, and the stimulation of cholinergic fibers causes pupillary constriction (Table 13-1).

Medications that cause effects in the body similar to those produced by acetylcholine are called *cholinergic agents* or *parasympathomimetic agents,* because they mimic the action produced by the stimulation of the parasympathetic division of the autonomic nervous system. Medications that cause effects similar to those produced by the adrenergic neurotransmitter are called *adrenergic agents* or *sympathomimetic agents.* Agents that block or inhibit cholinergic activity are called *anticholinergic agents,* and those that inhibit the adrenergic system are referred to as *adrenergic blocking agents.* See Figure 13-1 for a diagram of the autonomic system and its representative stimulants and inhibitors.

DRUG CLASS: ADRENERGIC AGENTS

ACTIONS

The adrenergic nervous system may be stimulated by two broad classes of drugs: **catecholamines** and noncatecholamines. The body's naturally occurring neurotransmitter catecholamines are norepinephrine, epinephrine, and dopamine. Norepinephrine is secreted primarily from nerve terminals; epinephrine comes primarily from the adrenal medulla; and dopamine is found at selected sites in the brain, the kidneys, and the GI tract. All three agents are also synthetically manufactured and may be administered to produce the same effects as those that are naturally secreted. Noncatecholamines have actions that are somewhat similar to those of the catecholamines; however, they are more selective for certain types of receptors, they are not quite as fast acting, and they have a longer duration of action.

As illustrated in Figure 13-1, the autonomic nervous system can be subdivided into the **alpha, beta,** and **dopaminergic receptors.** When stimulated by chemicals of certain shapes, these receptors produce a specific action. In general, the stimulation of the alpha-1 receptors causes the vasoconstriction of blood vessels. The alpha-2 receptors appear to serve as mediators of negative feedback, thereby preventing the further release of norepinephrine. The stimulation of beta-1 receptors causes an increase in the heart rate, and the stimulation of beta-2 receptors causes the relaxation of smooth muscle in the bronchi (bronchodilation), the uterus (relaxation), and the peripheral arterial blood vessels (vasodilation). The stimulation of the dopaminergic receptors in the brain improves the symptoms

Table 13-1 Actions of Autonomic Nerve Impulses on Specific Tissues

TISSUE	RECEPTOR TYPE	ADRENERGIC RECEPTORS (SYMPATHETIC)	CHOLINERGIC RECEPTORS (PARASYMPATHETIC)
Blood Vessels			
Arterioles			
Coronary	α; β_2	Constriction; dilation	Dilation
Skin	α	Constriction	Dilation
Renal	α_1; β_1 and β_2	Constriction; dilation	—
Skeletal muscle	α; β_2	Constriction; dilation	Dilation
Veins (systemic)	α_1; β_2	Constriction; dilation	—
Eye			
Radial muscle, iris	α_1	Contraction (mydriasis)	—
Sphincter muscle, iris	—	—	Contraction (miosis)
Ciliary muscle	β	Relaxation for far vision	Contraction for near vision
Gastrointestinal Tract			
Smooth muscle	α; β_1 and β_2	Relaxation	Contraction
Sphincters	α	Contraction	Relaxation
Heart	β_1	Increased heart rate, force of contraction	Decreased heart rate
Kidney	Dopamine	Dilates renal vasculature, thereby increasing renal perfusion	—
Lung			
Bronchial muscle	β_2	Smooth muscle relaxation (opens airways)	Smooth muscle contraction (closes airways)
Bronchial glands	α_1; β_2	Decreased secretions; increased secretions	Stimulation
Metabolism	β_2	Glycogenolysis (increases blood glucose)	—
Urinary Bladder			
Fundus (detrusor)	β	Relaxation	Contraction
Trigone and sphincter	α	Contraction	Relaxation
Uterus	α; β_2	Pregnancy: contraction (α); relaxation (β_2)	Variable

α, Alpha receptor; α_1, alpha-1 receptor; β_1, beta-1 receptor; β_2, beta-2 receptor.

associated with Parkinson's disease. Dopamine also increases urine output as a result of the stimulation of specific receptors in the kidneys that results in better renal perfusion.

USES

As noted in Table 13-2, many drugs act on more than one type of adrenergic receptor. Fortunately, each agent can be used for a specific purpose without many adverse effects. If recommended doses are exceeded, however, certain receptors may be stimulated excessively, which can cause serious adverse effects. An example of this is terbutaline, which is primarily a beta stimulant. With normal doses, terbutaline is an effective bronchodilator. In addition to bronchodilation, higher doses of terbutaline cause central nervous system stimulation, which results in insomnia and wakefulness. See Table 13-2 for a list of the clinical uses of the adrenergic agents.

Nursing Implications for Adrenergic Agents

See Chapters 30 and 31 for more information about the nursing implications for respiratory tract disease, bronchodilators, and decongestants.

Premedication Assessment

1. Obtain baseline vital signs: heart rate and blood pressure.
2. See Chapters 30 and 31 for the premedication assessments for respiratory tract disease, bronchodilators, and decongestants.

Availability, Dosage, and Administration

See Table 13-2.

Monitoring

Adverse effects associated with adrenergic agents are usually dose related and resolve when the dosage is

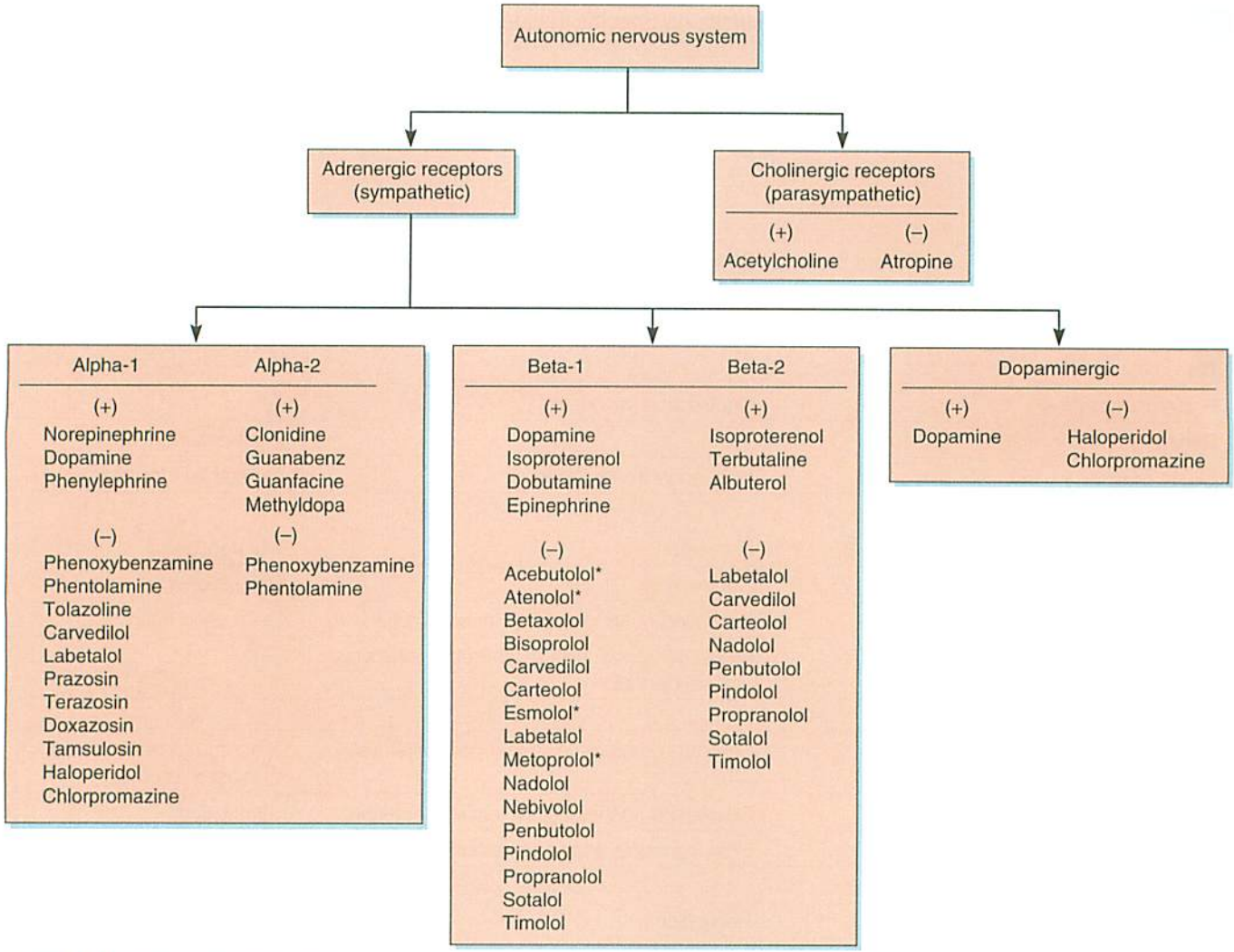

FIGURE 13-1 Receptors of the autonomic nervous system. (+) Stimulates receptors; (–) inhibits receptors; asterisks indicate representative examples of selective beta-1 antagonists only.

reduced or the medication discontinued. Patients who are potentially more sensitive to adrenergic agents are those with impaired hepatic function, thyroid disease, hypertension, and heart disease. Patients with diabetes mellitus may also have an increased frequency of episodes of hyperglycemia.

Common Adverse Effects

Cardiovascular

Palpitations, Tachycardia, Skin Flushing, Dizziness, Tremors. These adverse effects are usually mild, and they tend to resolve with continued therapy. Encourage the patient not to discontinue therapy without first consulting the physician.

Orthostatic Hypotension. Although this condition is infrequent and generally mild, adrenergic agents may cause some degree of orthostatic hypotension, which is manifested by dizziness and weakness, particularly when therapy is initiated. Monitor the blood pressure daily with the patient in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent an occurrence. Teach the patient to rise slowly from a supine or sitting position; encourage the patient to sit or lie down if he or she feels faint.

Serious Adverse Effects

Cardiovascular

Dysrhythmias, Chest Pain, Severe Hypotension, Hypertension, Anginal Pain. Discontinue therapy immediately, and notify the health care provider. Ask the patient if there has been a recent change in his or her regimen of prescription, nonprescription, or herbal medicines.

Gastrointestinal

Nausea, Vomiting. Notify the health care provider. Ask the patient if there has been a recent change in his or her regimen of prescription, nonprescription, or herbal medicines.

Drug Interactions

Agents That May Increase Therapeutic and Toxic Effects. Monoamine oxidase inhibitors (e.g., phenelzine, tranylcypromine), tricyclic antidepressants (e.g., amitriptyline, imipramine), atropine, and halothane anesthesia

Table 13-2 Adrenergic Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	ADRENERGIC RECEPTOR	ACTION	CLINICAL USES
albuterol*	Proventil, Ventolin	Aerosol: 90 mcg/puff Tablets: 2, 4 mg Syrup: 2 mg/5 mL Tablets, extended release: 4, 8 mg	Beta-2	Bronchodilator	Asthma, emphysema
arformoterol*	Brovana	Nebulizer: 15 mcg/2 mL in 2-mL vials	Beta-2	Bronchodilator	Emphysema, chronic bronchitis
dopamine ❗	—	Intravenous: 40, 80, 160 mg/mL in 5-, 10-, 20-mL ampules	Alpha, beta-1, dopaminergic	Vasopressor	Shock, hypotension; inotropic agent
dobutamine ❗	—	Intravenous: 250 mg/20-mL vial; 500 mg/40-mL vial	Beta-1	Cardiac stimulant	Inotropic agent
ephedrine* ❗	—	Subcutaneous, intramuscular, intravenous: 50 mg/mL in 1-mL ampules Capsules: 25 mg	Alpha, beta	Bronchodilator, vasoconstrictor	Nasal decongestant, hypotension
epinephrine* ❗	Adrenalin	Intravenous: 1:1000 in 1-mL ampules; 1:10,000 in 10-mL pre-filled syringes	Alpha, beta	Allergic reactions, vasoconstrictor, bronchodilator, cardiac stimulant	Anaphylaxis, cardiac arrest; topical vasoconstrictor
formoterol*	Foradil, Perforomist, Oxeze 🍁	Capsule for inhalation: 12 mcg Nebulizer: 20 mcg/2 mL in 2-mL container	Beta-2	Bronchodilator	Asthma, emphysema, chronic bronchitis
indacaterol*	Arcapta Neohaler	Capsule for inhalation: 75 mcg	Beta-2	Bronchodilator	Emphysema, chronic bronchitis
isoproterenol ❗	Isuprel	Subcutaneous, intramuscular, intravenous: 0.2 mg/mL solution; 1-, 5-mL vials	Beta	Bronchodilator, cardiac stimulant	Shock, digitalis toxicity, bronchospasm
metaproterenol	—	Tablets: 10, 20 mg Syrup: 10 mg/5 mL	Beta-2	Bronchodilator	Bronchospasm
norepinephrine (levarterenol) ❗	Levophed	Intravenous: 1 mg/mL in 4-mL ampules	Alpha-1	Vasoconstrictor	Shock, hypotension
phenylephrine†	Neo-Synephrine	Subcutaneous, intramuscular, intravenous: 10 mg/mL in 1-mL ampules ❗ Ophthalmic drops: 0.12%, 2.5%, 10% Nasal solutions: 0.125%, 0.25%, 0.5%, 1% Tablets: 10 mg	Alpha-1	Vasoconstrictor	Shock, hypotension, nasal decongestant; ophthalmic vasoconstrictor, mydriatic
salmeterol	Serevent Diskus	Aerosol powder: 50 mcg/dose	Beta-2	Bronchodilator	Asthma, emphysema, chronic bronchitis
terbutaline*	Brethine, Bricanyl 🍁	Tablets: 2.5, 5 mg Subcutaneous: 1 mg/mL in 1-mL ampules	Beta-2	Bronchodilator, uterine relaxant	Emphysema, asthma

🍁 Available in Canada.
❗ High-alert medication.
*See also Bronchodilators (Chapter 31).
†See also Decongestants (Chapter 30).

may increase both therapeutic and toxic effects. Many over-the-counter medications (e.g., cold remedies, appetite suppressants/diet pills [e.g., pseudoephedrine, ephedrine, ma huang]) contain adrenergic medicines that can have an additive effect when they are taken with a prescribed adrenergic agent. Monitor patients for tachycardia, serious dysrhythmias, hypotension, hypertension, and chest pain.

Agents That Inhibit Therapeutic Activity. The concurrent use of beta-adrenergic blocking agents (e.g., propranolol, nadolol, timolol, pindolol, atenolol, metoprolol), alpha-adrenergic blocking agents (e.g., phenoxybenzamine, phentolamine), and reserpine with adrenergic agents is not recommended.

DRUG CLASS: ALPHA- AND BETA-ADRENERGIC BLOCKING AGENTS

ACTIONS

The alpha- and beta-adrenergic blocking agents act by plugging the alpha or beta receptors, which prevents other agents—usually the naturally occurring catecholamines—from stimulating the specific receptors.

The beta blockers can be subdivided into nonselective and selective beta antagonists. The nonselective blocking agents have an equal affinity for beta-1 and beta-2 receptors, and they inhibit both. These agents are propranolol, nadolol, pindolol, penbutolol, carteolol, sotalol, and timolol. The selective beta-1 blocking agents exhibit action against the heart's beta-1 receptors (cardioselective) and do not readily affect the beta-2 receptors of the bronchi. The selective beta-1 antagonists are esmolol, metoprolol, acebutolol, betaxolol, bisoprolol, and atenolol. This selective action is beneficial for patients in whom nonselective beta blockers may induce bronchospasm (e.g., those with asthma). However, it is important to note that the selectivity of these agents is only relative. In larger doses, these agents will also inhibit the beta-2 receptors. There are no selective beta-2 blockers available. Labetalol and carvedilol exhibit selective alpha-1 and nonselective beta-adrenergic blocking activity. The alpha and beta blockers are listed in Figure 13-1.

USES

Because one of the primary actions of the alpha-receptor stimulants is vasoconstriction, it would be expected that alpha-blocking agents are indicated for patients with diseases that are associated with vasoconstriction. In fact, phenoxybenzamine and tolazoline may be used as vasodilators for the treatment of peripheral vascular diseases such as Raynaud's disease and Buerger's disease; see Chapter 26 for more information about the clinical use of these agents. Phentolamine is used for the diagnosis and treatment of pheochromocytoma, which is a tumor that secretes epinephrine. Alpha blockers (e.g., prazosin, terazosin, doxazosin) are sometimes used to treat hypertension (see Chapter 23). Alfuzosin, doxazosin, and tamsulosin are used to relax the smooth muscle of the bladder and prostate; they are used to treat urinary obstruction caused by benign prostatic hyperplasia (see Chapter 41).

Beta-adrenergic blocking agents (e.g., beta blockers) are used extensively to treat hypertension, post–myocardial infarction, angina pectoris, cardiac dysrhythmias, symptoms of hyperthyroidism, and stage fright. Nonselective beta blockers must be used with extreme caution in patients with respiratory conditions such as bronchitis, emphysema, asthma, or allergic rhinitis. A beta blockade produces severe bronchoconstriction and may aggravate wheezing, especially during the pollen season.

Beta blockers should be used with caution in patients with diabetes and in those who are susceptible to hypoglycemia. Beta blockers further induce the hypoglycemic effects of insulin and reduce the release of insulin in response to hyperglycemia. All beta blockers mask most of the signs and symptoms of acute hypoglycemia.

Beta-adrenergic blocking agents should be used only in patients with controlled heart failure. Further hypotension, bradycardia, or heart failure may develop.

Nursing Implications for Beta-Adrenergic Blocking Agents

See also the nursing implications for patients with antidysrhythmic therapy (pp. 388-390) and for those with hypertension (pp. 362-366).

Premedication Assessment

1. Obtain baseline vital signs: heart rate and blood pressure.
2. See also the premedication assessments for patients with antidysrhythmic therapy (Chapter 24) and for those with hypertension (Chapter 23).

Availability, Dosage, and Administration

See Table 13-3.

Individualization of Dosage. Although the onset of activity is fairly rapid, it may take several days to weeks for a patient to show optimal improvement and to become stabilized on an adequate maintenance dosage. Patients must be periodically reevaluated to determine the lowest effective dosage that is necessary to control the disorder.

Sudden Discontinuation. Patients must be counseled against poor adherence or the sudden discontinuation of therapy without a health care provider's advice. Sudden discontinuation has resulted in an exacerbation of anginal symptoms, and this has been followed in some cases by myocardial infarction. When discontinuing chronically administered beta blockers, the

Table 13-3 Beta-Adrenergic Blocking Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	CLINICAL USES	DOSAGE RANGE
acebutolol	Sectral, *Monitan*	Capsules: 200, 400 mg	Hypertension, ventricular dysrhythmias	PO: initial, 400 mg daily; maintenance, 600-1200 mg daily
atenolol	Tenormin, Nu-Atenol	Tablets: 25, 50, 100 mg	Hypertension, angina pectoris, after myocardial infarction	PO: initial, 50 mg daily; maintenance, ≤200 mg daily
betaxolol	Kerlone	Tablets: 10, 20 mg	Hypertension	PO: initial, 10 mg daily; maintenance, 20 mg daily
bisoprolol	Zebeta, Novo-Bisoprolol	Tablets: 5, 10 mg	Hypertension	PO: initial, 5 mg daily; maintenance, 10-20 mg daily
carteolol	Cartrol	Tablets: 2.5, 5 mg	Hypertension	PO: initial, 2.5 mg daily; maintenance, 2.5-10 mg daily
carvedilol	Coreg, Coreg CR, Apo-Carvedilol	Tablets: 3.125, 6.25, 12.5, 25 mg Capsules, extended release: 10, 20, 40, 80 mg	Hypertension, heart failure, myocardial infarction	PO: initial, 6.25 mg twice daily; maintenance, ≤50 mg daily
esmolol !	Brevibloc	Injection: 10 mg/mL in 10-mL ampules	Supraventricular tachycardia, hypertension	IV: initial, 500 mcg/kg/min for 1 min followed by 50 mcg/kg/min for 4 min and then adjusted to patient's needs
labetalol !	Trandate	Tablets: 100, 200, 300 mg Injection: 5 mg/mL in 4-, 20-, 40-mL vials	Hypertension	PO: initial, 100 mg twice daily; maintenance, ≤2400 mg daily
metoprolol !	Lopressor, Toprol XL, Betaloc	Tablets: 25, 50, 100 mg Tablets, extended release: 25, 50, 100, 200 mg Injection: 1 mg/mL in 5-mL ampules	Hypertension, myocardial infarction, angina pectoris, heart failure	PO, extended release: initial, 50 mg daily; maintenance, 100-450 mg daily PO, not extended release: 50 mg twice daily
nadolol	Corgard, Apo-Nadol	Tablets: 20, 40, 80, mg	Angina pectoris, hypertension	PO: initial, 40 mg daily; maintenance, 80-320 mg daily; maximum, 320 mg daily
nebivolol	Bystolic	Tablets: 2.5, 5, 10, 20 mg	Hypertension	PO: initial, 5 mg daily; maintenance, ≤40 mg daily
penbutolol	Levatol	Tablets: 20 mg	Hypertension	PO: initial, 20 mg daily; maintenance, 20 mg daily
pindolol	Apo-Pindol	Tablets: 5, 10 mg	Hypertension	PO: initial, 5 mg twice daily; maximum, 60 mg daily
propranolol !	Inderal, Inderal LA, Detensol	Tablets: 10, 20, 40, 60, 80 mg Solution: 20, 40 mg/5 mL Capsules, sustained release: 60, 80, 120, 160 mg IV: 1 mg/mL in 1-mL ampules	Dysrhythmias, hypertension, angina pectoris, myocardial infarction, migraine, tremor, hypertrophic subaortic stenosis	PO, immediate release: initial, 40 mg twice daily; maintenance, 120-640 mg daily in two to four divided doses PO, sustained release: 80-160 mg daily IV: 1-3 mg with close electrocardiographic monitoring
sotalol	Betapace, Sotacor	Tablets: 80, 120, 160, 240 mg	Dysrhythmias	PO: initial, 80 mg twice daily; maintenance, ≤320 mg daily
timolol	Blocadren	Tablets: 5, 10, 20 mg	Hypertension, myocardial infarction, migraine	PO: initial, 10 mg twice daily; maintenance, ≤30 mg twice daily

IV, Intravenous; *PO*, by mouth.
Available in Canada.
! High-alert medication.

dosage should be gradually reduced over 1 to 2 weeks, with careful patient monitoring. If anginal symptoms develop or become more frequent, beta-blocker therapy should be restarted temporarily.

Monitoring Considerations

Most of the adverse effects associated with beta-adrenergic blocking agents are dose related. Response by individual patients is highly variable. Many of these adverse effects may occur, but they may be transient. Strongly encourage patients to see their health care providers before discontinuing therapy. Minor dosage adjustment may be all that is required to eliminate most adverse effects.

Common Adverse Effects

Endocrine

Patients With Diabetes. Monitor for symptoms of hypoglycemia, including headache, weakness, decreased coordination, general apprehension, diaphoresis, hunger, or blurred or double vision. Many of these symptoms may be masked by beta-adrenergic blocking agents. Notify the health care provider if any of the symptoms described appear intermittently.

Serious Adverse Effects

Cardiovascular

Bradycardia, Peripheral Vasoconstriction (e.g., Purple, Mottled Skin). Discontinue further doses until the patient is evaluated by a health care provider.

Heart Failure. Monitor patients for an increase in edema, dyspnea, crackles, bradycardia, and orthopnea. Notify the health care provider if these symptoms develop.

Respiratory

Bronchospasm, Wheezing. Withhold additional doses until the patient has been evaluated by a health care provider.

Drug Interactions

Antihypertensive Agents. All beta-blocking agents have hypotensive properties that are additive with antihypertensive agents (e.g., angiotensin-converting enzyme inhibitors, calcium channel blockers, diuretics, angiotensin-receptor blockers, methyldopa, hydralazine, clonidine, reserpine). If it is decided to discontinue therapy in patients who are receiving beta blockers and clonidine concurrently, the beta blocker should be withdrawn gradually and discontinued several days before gradually withdrawing the clonidine.

Beta-Adrenergic Agents. Depending on the dosage, the beta stimulants (e.g., isoproterenol, metaproterenol, terbutaline, albuterol) may inhibit the action of beta-blocking agents and vice versa.

Lidocaine, Procainamide, Phenytoin, Disopyramide, Digoxin. When these drugs are occasionally used concurrently, the patient must be monitored carefully for additional arrhythmias, bradycardia, and signs of heart failure.

Enzyme-Inducing Agents. Enzyme-inducing agents (e.g., cimetidine, phenobarbital, pentobarbital, rifampin, phenytoin) enhance the metabolism of propranolol, metoprolol, pindolol, and timolol. This reaction probably does not occur with nadolol or atenolol because they are not metabolized but rather are excreted unchanged. The dosage of the beta blocker may have to be increased to provide therapeutic activity. If the enzyme-inducing agent is discontinued, the dosage of the beta blocker will also require reduction.

Nonsteroidal Anti-Inflammatory Agents. Indomethacin, salicylates, and possibly other prostaglandin inhibitors reduce the antihypertensive activity of propranolol and pindolol. This results in a loss of hypertensive control. The dose of the beta blocker may have to be increased to compensate for the antihypertensive inhibitory effect of indomethacin and perhaps other prostaglandin inhibitors.

DRUG CLASS: CHOLINERGIC AGENTS

ACTIONS

Cholinergic agents, which are also known as *parasympathomimetic agents*, produce effects that are similar to those of acetylcholine. Some cholinergic agents act by directly stimulating the parasympathetic nervous system, whereas others inhibit acetylcholinesterase, which is the enzyme that metabolizes acetylcholine after it has been released by the nerve ending. These latter agents are known as *indirect-acting cholinergic agents*. Some of the cholinergic actions are slow heartbeat; increased GI motility and secretions; increased contractions of the urinary bladder, with relaxation of the muscle sphincter; increased secretions and contractility of the bronchial smooth muscle; sweating; miosis of the eyes, which reduces intraocular pressure; increased force of the contraction of skeletal muscle; and, sometimes, decreased blood pressure.

USES

See Table 13-4.

Nursing Implications for Cholinergic Agents

See also the nursing implications for patients with disorders of the eyes (Chapter 43), glaucoma (Chapter 43), urinary system disease (Chapter 42), and respiratory tract disease (Chapters 30 and 31).

Premedication Assessment

1. Obtain baseline vital signs: heart rate and blood pressure.
2. See also the premedication assessments for patients with disorders of the eyes (Chapter 43), glaucoma (Chapter 43), urinary system disease (Chapter 42), and respiratory tract disease (Chapters 30 and 31).

Table 13-4 Cholinergic Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	CLINICAL USES
ambenonium	Mytelase	Tablets: 10 mg	Treatment of myasthenia gravis
bethanechol	Urecholine	—	See Chapter 42
edrophonium	Enlon	Injection: 10 mg/mL in 15-mL vial	Diagnosis of myasthenia gravis; reverse nondepolarizing muscle relaxants (e.g., tubocurarine)
guanidine	Guanidine	Tablets: 125 mg	Treatment of myasthenia gravis
neostigmine	Prostigmin	Tablets: 15 mg Injection: 0.5, 1 mg/mL	Treatment of myasthenia gravis; reverse nondepolarizing muscle relaxants (e.g., tubocurarine)
physostigmine	—	Injection: 1 mg/mL in 2-mL ampules	Reverse toxicity of overdoses of anticholinergic agents (e.g., pesticides, insecticides)
pilocarpine	Isopto Carpine, Pilopine HS	—	See Chapter 43
pyridostigmine	Mestinon	Tablets: 60 mg Syrup: 60 mg/5 mL Tablets, sustained release, 180 mg	Treatment of myasthenia gravis

Dosage and Administration

See Table 13-4.

Monitoring Considerations

Because cholinergic fibers innervate the entire body, effects in most body systems can be expected. Fortunately, because all receptors do not respond to the same dosage, adverse effects are not always seen. The higher the dosage, however, the greater the likelihood of adverse effects.

Common Adverse Effects

Gastrointestinal

Nausea, Vomiting, Diarrhea, Abdominal Cramping. These symptoms are extensions of the pharmacologic effects of the medication, and they are dose related. Reducing the dosage may be effective for controlling adverse effects without eliminating the desired pharmacologic effect.

Cardiovascular

Dizziness, Hypotension. Monitor the patient's blood pressure and pulse. To minimize hypotensive episodes, instruct the patient to rise slowly from a supine or sitting position, and have him or her perform exercises to prevent blood from pooling while he or she is standing or sitting in one position for a prolonged period. Teach the patient to sit or lie down if he or she feels faint.

Serious Adverse Effects

Respiratory

Bronchospasm, Wheezing. Withhold the next dose until the patient is evaluated by a health care provider.

Cardiovascular

Bradycardia. Withhold the next dose until the patient is evaluated by a health care provider.

Drug Interactions

Atropine, Antihistamines. Atropine, other anticholinergic agents, and most antihistamines antagonize the effects of cholinergic agents.

DRUG CLASS: ANTICHOLINERGIC AGENTS

ACTIONS

Anticholinergic agents, which are also known as *cholinergic blocking agents* or *parasympatholytic agents*, block the action of acetylcholine in the parasympathetic nervous system. These drugs act by occupying receptor sites at parasympathetic nerve endings, which prevents the action of acetylcholine. The parasympathetic response is reduced, depending on the amount of anticholinergic drug that is blocking the receptors. The inhibition of cholinergic activity (e.g., anticholinergic effects) includes the following: mydriasis of the pupil with increased intraocular pressure in patients with glaucoma; dry, tenacious secretions of the mouth, nose, throat, and bronchi; decreased secretions and motility of the GI tract; increased heart rate; and decreased sweating.

USES

The anticholinergic agents are used clinically for the treatment of GI and ophthalmic disorders, bradycardia, Parkinson's disease, and genitourinary disorders; as a preoperative drying agent; and to prevent vagal stimulation from skeletal muscle relaxants or from the placement of an endotracheal tube (Table 13-5).

Table 13-5 Anticholinergic Agents

GENERIC NAME	BRAND NAME	AVAILABILITY	CLINICAL USES
atropine	Atropine Sulfate	Injection: 0.05, 0.1, 0.4, 0.5, 0.8, 1, 2 mg/mL Tablets: 0.4 mg	Presurgery: to reduce salivation and bronchial secretions; to minimize bradycardia during intubation; for the treatment of pylorospasm and spastic conditions of the gastrointestinal tract; for the treatment of urethral and biliary colic
dicyclomine	Bentyl, Bentylol 🍁	Tablets: 20 mg Capsules: 10 mg Syrup: 10 mg/5 mL Injection: 10 mg/mL Solution: 1 mg/5 mL	Irritable bowel syndrome; infant colic
glycopyrrolate	Robinul	Tablets: 1, 2 mg Injection: 0.2 mg/mL	Peptic ulcer disease; presurgery: to reduce salivation and bronchial secretions and to minimize bradycardia during intubation
mepenzolate	Cantil	Tablets: 25 mg	Peptic ulcer disease
propantheline	—	Tablets: 15 mg	Peptic ulcer disease

🍁 Available in Canada.

Nursing Implications for Anticholinergic Agents

See also the nursing implications for patients with Parkinson's disease (Chapter 15), disorders of the eyes (Chapter 43), and for antihistamines (Chapter 30).

Premedication Assessments

1. All patients should be screened for closed-angle glaucoma, because anticholinergic agents may precipitate an acute attack. Patients with open-angle glaucoma can safely use anticholinergic agents in conjunction with miotic therapy.
2. Check for the patient's history for an enlarged prostate. If this condition is present, anticholinergic agents may cause the patient to have the temporary inability to void.
3. Obtain baseline vital signs: heart rate and blood pressure. See also the premedication assessments for patients with Parkinson's disease (Chapter 15), disorders of the eyes (Chapter 43), and antihistamines (Chapter 30).

Availability

See Table 13-5.

Monitoring Considerations

Because cholinergic fibers enervate the entire body, effects from blocking this system occur throughout most systems. Fortunately, because all receptors do not respond to the same dose, all adverse effects are not seen to the same degree with all cholinergic blocking agents. The higher the dosage, however, the greater the likelihood of more adverse effects.

Common Adverse Effects. These symptoms are the anticholinergic effects that are produced by these agents. Patients who are taking these medications should be monitored for the development of these adverse effects.

Sensory

Blurred Vision. Warn the patient that blurred vision may occur, and make appropriate suggestions for the patient's personal safety.

Gastrointestinal

Constipation; Dryness of the Mucosa of the Mouth, Nose, and Throat. Mucosa dryness may be alleviated by sucking hard candy or ice chips or by chewing gum. Give the patient stool softeners as prescribed. Encourage adequate fluid intake and the eating of foods that provide sufficient bulk.

Genitourinary

Urinary Retention. If the patient develops urinary hesitancy, assess him or her for bladder distention. Contact the health care provider for further evaluation.

Serious Adverse Effects

Sensory

Glaucoma. All patients should be screened for closed-angle glaucoma before the initiation of therapy. Patients with open-angle glaucoma can safely use anticholinergic agents. Monitor the patient's intraocular pressures regularly.

Psychological

Confusion, Depression, Nightmares, Hallucinations. Perform a baseline assessment of the patient's degree of alertness and orientation to name, place, and time before initiating therapy. Make regularly scheduled subsequent evaluations of the patient's mental status, and compare findings. Report the development of alterations, and provide for patient safety during these episodes. A reduction in the daily medication dosage may control these adverse effects.

Cardiovascular

Orthostatic Hypotension. Although orthostatic hypotension occurs infrequently and is generally mild, all anticholinergic agents may cause some degree of this condition, which is manifested by dizziness and weakness, particularly when therapy is initiated. Monitor the patient's blood pressure daily in both the supine and standing positions. Anticipate the development of postural hypotension, and take measures to prevent it. Teach the patient to rise slowly from a supine or sitting position, and encourage the patient to sit or lie down if he or she feels faint.

Palpitations, Dysrhythmias. Contact the health care provider for further evaluation.

Drug Interactions

Amantadine, Tricyclic Antidepressants, Phenothiazines. These agents may potentiate anticholinergic adverse effects. Confusion and hallucinations are characteristic of excessive anticholinergic activity.

Get Ready for the NCLEX® Examination!

Key Points

- The nervous system is one of two primary regulators of body homeostasis and defense. The CNS is composed of the brain and the spinal cord.
- The efferent nervous system is subdivided into the motor nervous system, which controls skeletal muscle, and the autonomic nervous system, which regulates smooth muscle and heart muscle and which controls secretions from certain glands.
- Nerve impulses are passed between neurons and from neurons to end organs by neurotransmitters. The main neurotransmitters of the autonomic nervous system are acetylcholine and norepinephrine. Nerve endings that liberate acetylcholine are called *cholinergic fibers;* those that secrete norepinephrine are called *adrenergic fibers.*
- The CNS is composed of systems of different types of neurons that secrete separate neurotransmitters, such as acetylcholine, norepinephrine, epinephrine, dopamine, serotonin, and gamma-aminobutyric acid.
- The control of neurotransmitters is a primary way to alleviate the symptoms that are associated with many diseases. As shown in Table 13-1, the administration of one type of autonomic nervous system drug can affect several organ systems, and adverse effects can be numerous. Therefore, the use of these drugs requires the monitoring of more than just the symptoms for which the medicine was prescribed.

Additional Learning Resources

SG Go to your Study Guide for additional Review Questions for the NCLEX® Examination, Critical Thinking Clinical Situations, and other learning activities to help you master this chapter's content.

evolve Go to your Evolve Web site (http://evolve.elsevier.com/Clayton) for the following FREE learning resources:

- Animations
- Appendices
- Drug Dosage Calculators
- Drugs@FDA (a catalog of FDA-approved drug products)
- Gold Standard Patient Teaching Handouts in English and Spanish
- Interactive Drug Flashcards
- Interactive Review Questions for the NCLEX® Examination and more!

Review Questions for the NCLEX® Examination

1. The prescriber orders phenytoin (Dilantin) suspension, 150 mg q8h.

   Available: Dilantin suspension, 125 mg/5 mL
   Calculate the correct dose to the nearest whole number: Give _____ mL every _____ hours.

2. Which data in the patient's history and physical examination cause the nurse to question a preoperative medication order for atropine sulfate and morphine before administration?
   1. Excessive oral secretions
   2. Bradycardia
   3. Increased gastric motility
   4. Prostatic enlargement

3. A patient who has recently been prescribed a beta-adrenergic blocking drug presents to the emergency department with a serious adverse effect. Which adverse effect is the patient likely exhibiting?
   1. Hypertension
   2. Angina pectoris
   3. Bronchoconstriction
   4. Cardiac dysrhythmias

4. A nurse was assessing a patient who presented to the clinic with complaints of dizziness and weakness after starting amitriptyline for sleep. The nurse knows that over-the-counter medications may increase therapeutic effects and even cause toxic effects. Which medication that the patient reports taking would be the most concerning?
   1. Thyroid medications
   2. Aspirin
   3. Cold remedies
   4. Vitamin supplements

5. A patient with closed-angle glaucoma can safely receive drugs from which classification? *(select all that apply.)*
   1. Beta-adrenergic receptor blockers
   2. Anticholinergic agents
   3. Cholinergic agents
   4. Alpha-adrenergic receptor blockers
   5. Dopaminergic agents

chapter

14

Drugs Used for Sleep

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Objectives

1. Differentiate among the terms *sedative* and *hypnotic; initial, intermittent,* and *terminal insomnia;* and *rebound sleep* and *paradoxical excitement.*
2. Identify alterations found in the sleep pattern when hypnotics are discontinued.
3. Cite nursing interventions that can be implemented as an alternative to administering a sedative-hypnotic medication.
4. Compare the effects of barbiturates and benzodiazepines on the central nervous system.
5. Identify the antidote drug used for the management of benzodiazepine overdose.
6. Identify laboratory tests that should be monitored when benzodiazepines or barbiturates are administered for an extended period.

Key Terms

rapid eye movement (REM) sleep (p. 212)
insomnia (ĭn-SŎM-nē-ă) (p. 213)
hypnotic (hĭp-NŎT-ĭk) (p. 213)
sedative (SĔD-ă-tĭv) (p. 213)
rebound sleep (RĒ-bŏwnd SLĒP) (p. 213)

SLEEP AND SLEEP PATTERN DISTURBANCE

Sleep is a state of unconsciousness from which a patient can be aroused by an appropriate stimulus. It is a naturally occurring phenomenon that occupies about one third of an adult's life.

Adequate sleep that progresses through the normal stages is important to maintain body function, including psychiatric equilibrium and the strengthening of the immune system to ward off disease. A normal sleep duration of 7 to 8 hours per night is thought to be optimal for good health. Studies also show that a reduced amount of sleep is associated with overweight and obesity as well as the development of metabolic syndrome (see Chapter 21). Obesity itself is also detrimental to healthy sleep patterns, and it can contribute to the development of sleep apnea. Other studies show a strong connection between a shortened duration of sleep and cardiovascular disease. Individuals who sleep less than 5 hours per night have a threefold increased risk of heart attacks. The National Health Interview Survey also demonstrates a close relationship between symptoms of insomnia and common adverse physical and mental health conditions, including obesity, diabetes mellitus, hypertension, heart failure, anxiety, and depression. *Healthy People 2020* has as one of its objectives the promotion of sleep health, which includes promoting optimal sleep durations and reducing the prevalence and impact of sleep disorders.

Natural sleep rhythmically progresses through phases that provide both physical and mental rest. On the basis of brain-wave activity, muscle activity, and eye movement, normal sleep can be divided into two phases: non–rapid eye movement (NREM) sleep and ***rapid eye movement (REM) sleep.*** The NREM phase can be further divided into four stages, each of which is characterized by a specific set of brain-wave activities. Stage 1 is a transition phase between wakefulness and sleep that lasts only a few minutes. Some people experience it as wakefulness, whereas others feel it as drowsiness. Approximately 2% to 5% of sleep is stage 1 sleep. Stage 2 sleep comprises about 50% of normal sleep time. People often experience a drifting or floating sensation, and, if they are awakened during this stage, they will often deny being asleep, responding, "I was just resting my eyes." Stages 1 and 2 are light sleep periods from which a person is easily aroused. Stage 3 is a transition from the lighter to deeper sleep state of stage 4. Stage 4 sleep is dreamless, very restful, and associated with a 10% to 30% decrease in blood pressure, respiratory rate, and basal metabolic rate. Stage 4 sleep is also referred to as *delta sleep* on the basis of the pattern of brain waves that are observed during this stage. Stage 4 sleep comprises 10% to 15% of sleep time in young, healthy adults. Stage 4 sleep diminishes in length as people age, and many people who are more than 75 years old do not demonstrate any stage 4 sleep patterns. Older adults also take longer to cycle through the relaxation stages of NREM sleep, with an increased frequency and duration of awakenings.

During a normal night of sleep, a person will rhythmically cycle from wakefulness through stages 1, 2, 3, and 4; he or she will then go back to stage 3, then to stage 2, and then to REM sleep over the course of about 90 minutes. The early episodes of REM sleep last only a few minutes. However, as sleep progresses, the