

Drugs Affecting the Autonomic and Central Nervous System

CHAPTER OUTLINE

- 46** Physiology of the Autonomic and Central Nervous Systems and Indications for the Use of Drug Therapy
- 47** Drug Therapy for Myasthenia Gravis, Alzheimer's Disease, and Other Conditions Treated with Cholinergic Agents
- 48** Drug Therapy for Parkinson's Disease
- 49** Drug Therapy with Opioids
- 50** Drug Therapy with Local Anesthetics
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- 52** Drug Therapy for Migraines and Other Headaches
- 53** Drug Therapy for Seizure Disorders and Skeletal Muscle Relaxants
- 54** Drug Therapy for Anxiety and Insomnia
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Physiology of the Autonomic and Central Nervous Systems and Indications for the Use of Drug Therapy

LEARNING OBJECTIVES

After studying this chapter, you should be able to:

1. Identify the physiologic effects of the sympathetic nervous system.
2. Differentiate subtypes and functions of sympathetic nervous system receptors.
3. Identify the physiologic effects of the parasympathetic nervous system.
4. Differentiate subtypes and functions of parasympathetic nervous system receptors.
5. Describe signal transduction and the intracellular events that occur when receptors of the autonomic nervous system are stimulated.
6. Recognize the terminology and general characteristics of drugs affecting the autonomic nervous system.

CLINICAL APPLICATION CASE STUDY

Jennifer Johnson is a 35-year-old woman who runs 5 miles daily before work. One morning while running, she encounters a bear on the jogging trail. She begins to hyperventilate and can feel her heart racing. She also begins to sweat profusely, and her pupils begin to dilate. The bear runs into the woods when a car approaches.

KEY TERMS

Affinity: rate of binding of ligands that demonstrates a tendency or strength of the effect

Agonist: a ligand that can bind to a receptor, alter the function of the receptor, and trigger a physiologic response for that receptor

Antagonist: a ligand that binds to a receptor but fails to activate the physiologic response for that receptor

Down-regulation: process by which a cell decreases the quantity of a cellular component in response to an external variable; also called desensitization

First messenger: extracellular ligand that binds to a cell surface receptor and initiates intracellular activity

Ligands: substances, such as neurotransmitters, medications, and hormones, that bind to receptors in the autonomic nervous system

Second messenger: molecule inside the cell that is the link between events occurring outside the cell and resulting events that will occur inside the cell

Signal transduction: cascade of intracellular events that occur when receptors located on target tissues are stimulated by a ligand

Up-regulation: process by which a cell increases the quantity of a cellular component in response to an external variable; also called hypersensitization

INTRODUCTION

The nervous system has two main divisions: the central nervous system (CNS) and the peripheral nervous system (PNS) (Fig. 46.1). The CNS includes the brain and spinal cord. It receives and processes incoming sensory information and responds by sending out signals that initiate or modify body processes. The PNS includes all the neurons and ganglia found outside the CNS. Afferent neurons carry sensory input from the periphery to the CNS and modify motor output through the action of reflex arcs. Efferent neurons carry motor signals from the CNS to the peripheral areas of the body. Ganglia are nerve cell clusters that house the cell bodies of the afferent nerves.

The efferent portion of the PNS has two subdivisions: the somatic nervous system and the autonomic nervous system

(ANS). The somatic nervous system innervates skeletal muscles and controls voluntary movement. The ANS, without conscious thought or effort, controls involuntary activities in smooth muscle, in secretory glands, and in the visceral organs of the body such as the heart.

STRUCTURE AND FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM

Structural centers in the CNS, including the hypothalamus, brainstem, and spinal cord, regulate the ANS. There are two parts of the ANS: the sympathetic nervous system (SNS) and the parasympathetic nervous system. The functions of the ANS can be broadly described as activities designed to maintain a constant internal environment (homeostasis), to respond to stress or emergencies, and to repair body tissues.

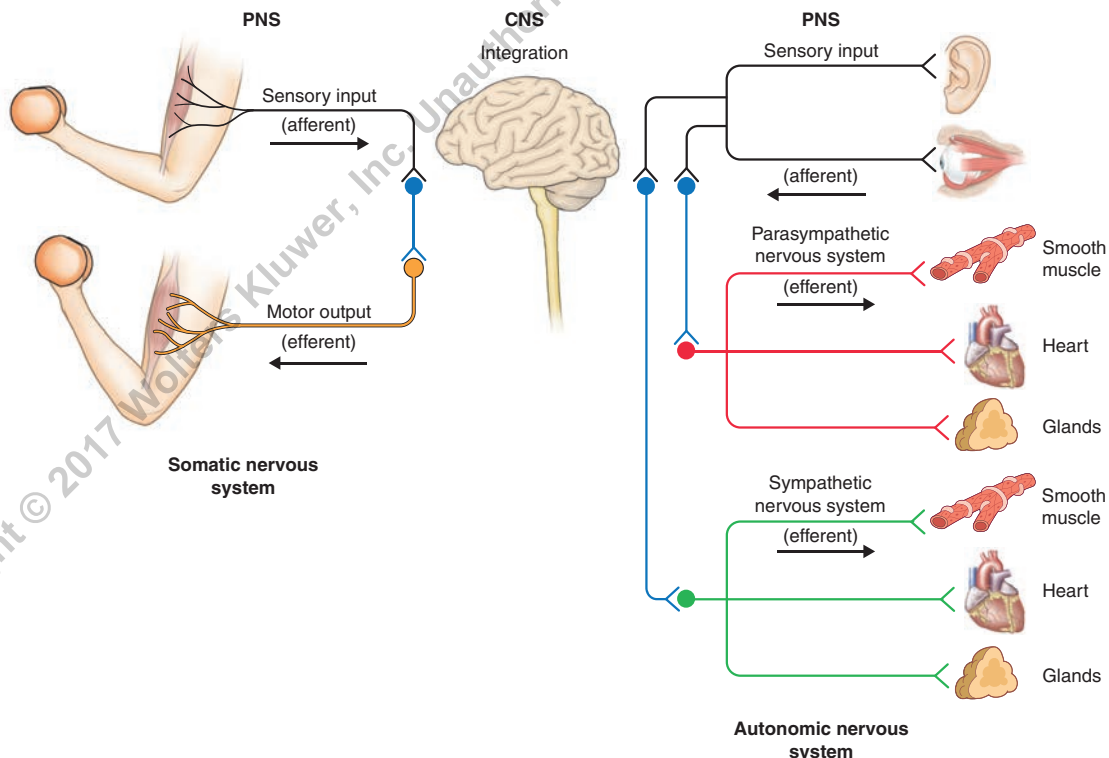


Figure 46.1. Divisions of the human nervous system. The nervous system can be divided anatomically into the central (brain and spinal cord) nervous system [CNS] and the peripheral [sensory organs and nerves] nervous system [PNS]. The nervous system can be functionally divided into the somatic nervous system and the autonomic nervous system [ANS]. The somatic nervous system leads to contraction of muscle fibers through efferent [motor] neurons. The autonomic nervous system controls the heart, glands, and hollow organs and is essential in maintaining homeostasis. [From Plowman, S. A., & Smith, D. L. (2017). *Exercise physiology for health, fitness, and performance* (5th ed.). Philadelphia, PA: Wolters Kluwer.]

Nerve impulses are generated and transmitted to body tissues in the SNS and the parasympathetic nervous system, as they are in the CNS. Preganglionic nerve impulses travel from the CNS along the presynaptic nerves to ganglia. Ganglia are bundles of nerve tissue composed of the terminal end of the presynaptic neuron and clusters of postsynaptic neuron cell bodies. A neurotransmitter is released from the terminal end of the presynaptic neuron, allowing the nervous impulse to bridge the synapse between the presynaptic and postsynaptic nerve. The postganglionic impulses travel from the ganglia to target or effector tissues of the heart, blood vessels, glands, other visceral organs, and smooth muscle. A neurotransmitter is released from the terminal end of the postsynaptic neuron, allowing the impulse to reach the effector tissue, stimulate a receptor, and bring about a response (Fig. 46.2).

The primary neurotransmitters of the ANS are acetylcholine and norepinephrine. Acetylcholine is synthesized from acetyl-coenzyme A and choline. It is released at preganglionic fibers of both the SNS and parasympathetic nervous system and at postganglionic fibers of the parasympathetic nervous system. Acetylcholine is also released from postganglionic sympathetic neurons that innervate the sweat glands and from motor neurons of the somatic nervous system that innervate the skeletal muscles. The nerve fibers that secrete acetylcholine are called cholinergic fibers. Acetylcholine acts

on receptors in body organs and tissues to cause parasympathetic effects.

Norepinephrine is synthesized from the amino acid tyrosine by a series of enzymatic conversions that also produce dopamine and epinephrine (i.e., tyrosine → dopamine → norepinephrine → epinephrine). Except in the adrenal medulla, where most of the norepinephrine is converted to epinephrine, the chemical reaction stops with norepinephrine. This neurotransmitter is released at most postganglionic fibers of the SNS. Norepinephrine-secreting nerve fibers are called adrenergic fibers. Norepinephrine acts on receptors in body organs and tissues to cause sympathetic effects.

Neurotransmitters, such as acetylcholine and norepinephrine, as well as medications and hormones, that can bind to receptors in the ANS, are collectively called **ligands**. The rate of binding is called **affinity**, and this rate typifies a tendency or strength of the effect. A ligand that can bind to a receptor, alter the function of the receptor, and trigger a physiologic response is called an **agonist** for that receptor. Ligands that bind to a receptor but fail to activate the physiologic response are receptor **antagonists**. When receptors located on target tissues are stimulated by a ligand, a cascade of intracellular events known as **signal transduction** is initiated.

The extracellular ligand that binds to the receptor to initiate the intracellular activity is the **first messenger**. In most cases,

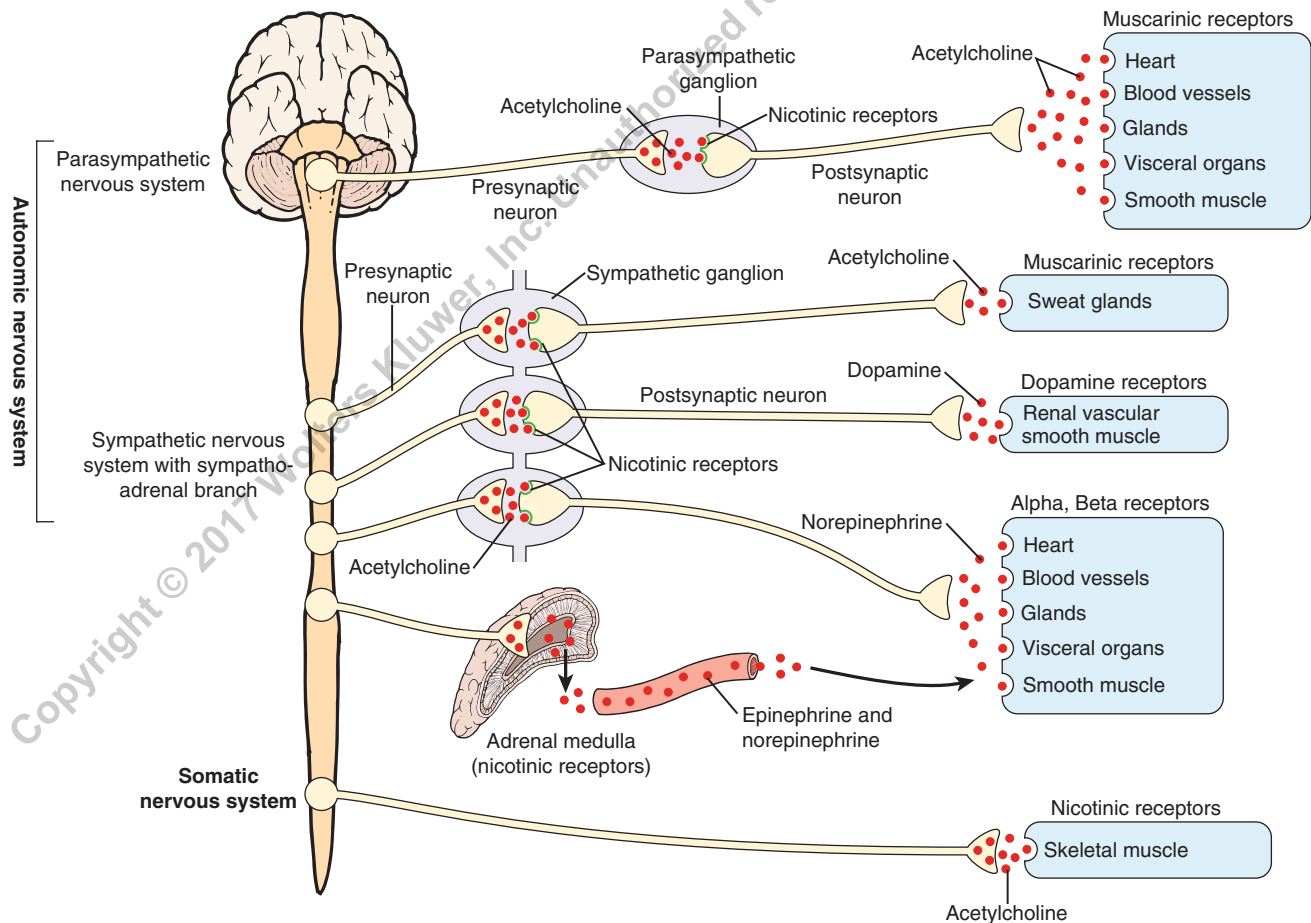


Figure 46.2. Organization of the autonomic and somatic nervous systems. [From Brophy, K., Scarlett-Ferguson, H., Webber, K. S., Abrams, A. C., Pennington, S. S., & Lammon, C. B. [2011]. *Clinical drug therapy for Canadian practice* [2nd ed.]. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins.]

this ligand–receptor interaction activates a cell membrane-bound G protein and an effector enzyme, which then activate a molecule inside the cell called a **second messenger**. This messenger is the link between events that are occurring outside the cell (i.e., receptor activation by the ligand) and resulting events that will occur inside the cell, such as opening ion channels, stimulating other enzymes, and increasing intracellular calcium levels. These intracellular events ultimately produce the physiologic responses to neurotransmitter and hormone release or drug administration. Figure 46.3 illustrates the intracellular events of signal transduction that occur when an adrenergic beta receptor is stimulated by epinephrine.

Involuntary muscles in organs and tissues in the body are innervated by both divisions of the ANS. However, most organs are predominantly controlled by one system. For example, in the gastrointestinal tract, the parasympathetic nervous system predominates, and stimulation of the parasympathetic nervous system regulates the routine activities of digestion and elimination.

The two divisions of the ANS are usually antagonistic in their actions on a particular organ. When the sympathetic system excites a particular organ, the parasympathetic system often inhibits it and vice versa. Stimulation of the ANS causes excitatory effects in some organs but inhibitory effects in others. For example, sympathetic stimulation of the heart causes an increased rate and force of myocardial contraction, and parasympathetic stimulation decreases rate and force of contraction, thereby resting the heart. In the gastrointestinal tract, stimulation of the parasympathetic nervous system promotes digestion, and sympathetic stimulation decreases blood flow and impairs digestion. Exceptions to this antagonistic action include sweating and regulation of arteriolar blood vessel diameter, which is controlled by the SNS.

Sympathetic Nervous System

The SNS is stimulated by physical or emotional stress, such as strenuous exercise or work, pain, hemorrhage, intense emotions,

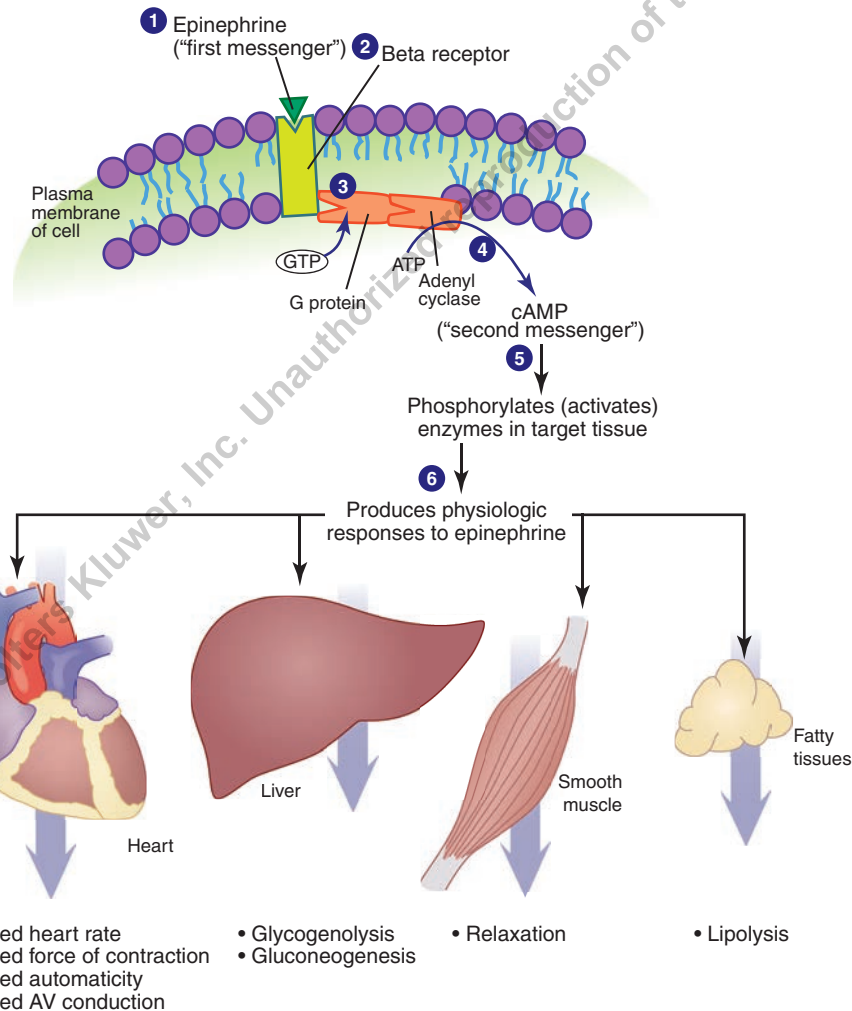


Figure 46.3. Signal transduction mechanism for an adrenergic beta receptor. Epinephrine [1], the "first messenger," interacts with a beta receptor [2]. This hormone–receptor complex activates a G protein, which reacts with a guanosine triphosphate [GTP] [3]. The activated G protein then activates the enzyme adenylyl cyclase, which [4] catalyzes the conversion of adenosine triphosphate [ATP] to cyclic adenosine monophosphate [cAMP], the "second messenger" [5]. cAMP activates enzymes, which bring about the biologic responses to epinephrine [6]. AV, atrioventricular. [From Brophy, K., Scarlett-Ferguson, H., Webber, K. S., Abrams, A. C., Pennington, S. S., & Lammon, C. B. [2011]. *Clinical drug therapy for Canadian practice* [2nd ed.]. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins.]

and temperature extremes. The reaction produced by the SNS is essentially a whole-body response and includes

- Increased arterial blood pressure and cardiac output
- Increased blood flow to the brain, heart, and skeletal muscles; decreased blood flow to viscera, skin, and other organs not needed for “fight or flight” (whether real or imaginary)
- Increased rate of cellular metabolism, with increased oxygen consumption and carbon dioxide production
- Increased breakdown of muscle glycogen for energy
- Increased blood glucose
- Increased mental activity and ability to think clearly
- Increased muscle strength
- Increased rate of blood coagulation
- Increased rate and depth of respiration
- Pupil dilation to aid vision
- Increased sweating (Note that acetylcholine is the neurotransmitter for this sympathetic response—not the normal postganglionic neurotransmitter, which is norepinephrine.)

These responses are protective mechanisms designed to help the person cope with the stress or escape from it. The intensity and duration of the sympathetic response depends on the existing amounts of the neurotransmitters norepinephrine and epinephrine.

Neurotransmitters

Norepinephrine is synthesized in adrenergic nerve endings and released into the synapse when adrenergic nerve endings are stimulated. It exerts intense but brief effects on presynaptic and postsynaptic adrenergic receptors. The effects of norepinephrine are terminated by reuptake of most of the neurotransmitter back into the nerve endings, where it is packaged into vesicles for reuse as a neurotransmitter. This reuptake and termination process can be inhibited by cocaine and tricyclic antidepressant medications and is responsible for the activation of the SNS seen with these drugs. The remainder of the norepinephrine, which was not taken back into the nerve endings, diffuses into surrounding tissue fluids and blood or is metabolized by monoamine oxidase (MAO) or catechol-*O*-methyltransferase (COMT).

Norepinephrine also functions as a circulating neurohormone, along with epinephrine. In response to adrenergic nerve stimulation, norepinephrine and epinephrine are secreted into the bloodstream by the adrenal medullae and transported to all body tissues. They are continually present in arterial blood in amounts that vary according to the degree of stress present and the ability of the adrenal medullae to respond to stimuli. The larger proportion of the circulating hormones (~80%) is epinephrine.

Norepinephrine and epinephrine exert the same effects on target tissues as those caused by direct stimulation of the SNS. However, the effects last longer because the hormones are removed from the blood more slowly. The enzymes MAO and COMT metabolize these hormones, mainly in the liver. Box 46.1 outlines the strength and type of response to activation of alpha and beta receptors.

Dopamine is also an adrenergic neurotransmitter and a catecholamine. In the brain, dopamine is essential for normal function. In peripheral tissues, its main effects are on the heart and blood vessels of the renal system and viscera, where it produces vasodilation.

BOX 46.1

Response to Activation of Alpha and Beta Receptors

Activation of alpha₁ and beta₁ receptors causes stimulatory responses.

- When activating alpha₁ receptors, norepinephrine causes a greater response than does epinephrine.
- When activating beta₁ receptors, epinephrine and norepinephrine cause equal responses.

Activation of alpha₂, beta₂, and beta₃ receptors causes inhibitory responses.

- When activating alpha₂ receptors, epinephrine causes a greater or equal response than does norepinephrine.
- When activating beta₂ receptors, epinephrine causes a significantly greater response than does norepinephrine.

Clinical Application 46.1

- When Mrs. Johnson returns home, she tells her husband about the experience and states “I have never been so scared in my whole life.” She tells her husband that even though she was afraid, she remembers being able to think clearly and feeling physically stronger after she spotted the bear.
- Explain Mrs. Johnson’s physiologic response to the experience. What additional symptoms does this physiologic response trigger?

Adrenergic Receptors

When norepinephrine and epinephrine act on body cells that respond to sympathetic nerve or catecholamine stimulation, they interact with two distinct adrenergic receptors, alpha and beta. Norepinephrine acts mainly on alpha receptors, and epinephrine acts on both alpha and beta receptors. These receptors have been further subdivided into alpha₁, alpha₂, beta₁, beta₂, and beta₃ receptors.



QSEN Alert: Evidence-Based Practice

Although the roles of beta₁ and beta₂ adrenergic receptors are well established, the activity of beta₃ receptors seems to differ from that of the classic beta₁ and beta₂ receptors and continues to be defined. Research has found that beta₃ receptors augment heat production, produce lipolysis, increase energy expenditure, and manage bladder dysfunction and type 2 diabetes mellitus. Niu et al. [2012] explored in vivo the cardioprotective potential of activation of beta₃ receptors. Beta₃ receptors produced a negative inotropic action on the ventricles, action mediated through the activation of G proteins. Findings suggest that beta₃ receptors may play an important role in modulation of cardiovascular function and reduce cardiac remodeling in heart failure.

When dopamine acts on body cells that respond to adrenergic stimulation, it can activate alpha₁ and beta₁ receptors as well as dopaminergic receptors. Only dopamine can activate dopaminergic receptors. Dopamine receptors are located in the brain, in blood vessels of the kidneys and other viscera, and probably in presynaptic sympathetic nerve terminals. Activation

(agonism) of these receptors may result in stimulation or inhibition of cellular function. Like alpha and beta receptors, dopamine receptors are divided into several subtypes (D_1 to D_5), and specific effects depend on which subtype of receptor is activated. Additional discussion about the adrenergic receptors is found in Table 29.1, which describes the locations of adrenergic receptors in the body and the response that occurs when each receptor is stimulated.

Q1

The intracellular events resulting from signal transduction after stimulation of adrenergic receptors are thought to include the following mechanisms:

- **Alpha₁ receptors:** Activation of alpha₁ receptors in smooth muscle cells is thought to open ion channels, allow calcium ions to move into the cell, and produce muscle contraction (e.g., vasoconstriction, gastrointestinal and bladder sphincter contraction).
- **Alpha₂ receptors:** In the brain, some of the norepinephrine released into the synaptic cleft between neurons returns to the nerve endings from which it was released and stimulates presynaptic alpha₂ receptors. This negative feedback prevents calcium-mediated release of norepinephrine from storage vesicles into the synapse, resulting in decreased sympathetic outflow and an antiadrenergic effect. In addition, alpha₂ receptors cause a decrease in cyclic adenosine monophosphate (cAMP), resulting in smooth muscle contraction.
- **Beta₁, beta₂, and beta₃ receptors:** Activation of these receptors stimulates activity of adenylyl cyclase (an enzyme in cell membranes), which increases intracellular cAMP activity. cAMP serves as a second messenger and can initiate several different intracellular actions, such as cardiac contraction, smooth muscle relaxation, and glycogenolysis. An enzyme called phosphodiesterase rapidly degrades cAMP to 5'-adenosine monophosphate. Drugs such as theophylline inhibit phosphodiesterase and increase cAMP concentrations, resulting in bronchodilation (see Chap. 33).
- **Dopaminergic receptors D₁ and D₅:** Activation of these receptors is thought to stimulate the production of cAMP, as does activation of beta₁ and beta₂ receptors.
- **Dopaminergic receptors D₂, D₃, and D₄:** Activation of this receptor is thought to inhibit formation of cAMP and to alter calcium and potassium ion currents. D₃ and D₄ receptors are grouped with D₂ receptors, but the effects of their activation have not been clearly delineated.

Q2

The number of receptors and the binding activity of receptors to target organs and tissues are dynamic and may be altered. These phenomena are most clearly understood with beta receptors. For example, when chronically exposed to high concentrations of substances that stimulate their function, the beta receptors decrease in number and become less efficient in stimulating adenylyl cyclase. The resulting decrease in beta-adrenergic responsiveness is called desensitization or **down-regulation** of receptors. Conversely, when chronically exposed to substances that block their function, the receptors may increase in number and become more efficient in stimulating adenylyl cyclase. The resulting increase in beta-adrenergic responsiveness, called hypersensitization or **up-regulation**, may lead to an exaggerated response when the blocking substance is withdrawn.

NCLEX Success

1. Activation of the sympathetic nervous system will result in which of the following? (Check all that apply.)
 - A. increased rate and depth of respiration
 - B. pupil dilation to aid vision
 - C. increased blood pressure and heart rate
 - D. increased urine output
2. Which of the following statements is correct regarding the sympathetic and the parasympathetic nervous systems?
 - A. Acetylcholine activates muscarinic receptors.
 - B. Activation of the sympathetic nervous system causes a decrease in blood pressure.
 - C. Acetylcholine activates adrenergic receptors.
 - D. Norepinephrine activates cholinergic receptors.
3. The sympathetic nervous system is also called the
 - A. fight-or-flight system
 - B. eat-drink-and-rest system
 - C. autonomic nervous system
 - D. somatic nervous system
4. A drug that has the same effects on the human body as stimulation of the sympathetic nervous system is called which of the following? (Check all that apply.)
 - A. sympathomimetic agent
 - B. adrenergic drug
 - C. beta-adrenergic agonist drug
 - D. alpha-adrenergic blocking agent
5. When the body is exposed to high concentrations of substances that stimulate their function, the resulting decrease in beta-adrenergic responsiveness is called which of the following? (Check all that apply.)
 - A. desensitization
 - B. down-regulation
 - C. fight-or-flight
 - D. norepinephrine reuptake

Parasympathetic Nervous System

Experts often describe processes stimulated by the parasympathetic nervous system as “rest and digest” because of their resting, reparative, or vegetative functions. They include digestion, excretion, cardiac deceleration, anabolism, and near vision.

Approximately 75% of all parasympathetic nerve fibers are in the vagus nerves. These nerves supply the thoracic and abdominal organs; their branches go to the heart, lungs, esophagus, stomach, small intestine, proximal half of the colon, the liver, gallbladder, pancreas, and the upper portions of the ureters. Other parasympathetic fibers supply pupillary sphincters and circular muscles of the eye; lacrimal, nasal, submaxillary, and parotid glands; descending colon and rectum; lower portions of the ureters and bladder; and genitalia.

Specific body responses to parasympathetic stimulation include

- Dilation of blood vessels in the skin
- Decreased heart rate, possibly bradycardia
- Increased secretion of digestive enzymes and motility of the gastrointestinal tract
- Constriction of smooth muscle of bronchi
- Increased secretions from glands in the lungs, stomach, intestines, and skin (sweat glands)
- Constricted pupils (from contraction of the circular muscle of the iris) and accommodation to near vision (from contraction of the ciliary muscle of the eye)
- Contraction of smooth muscle in the urinary bladder
- Contraction of skeletal muscle
- Release of nitrous oxide from the endothelium of blood vessels, resulting in decreased platelet aggregation, decreased inflammation, relaxation of vascular smooth muscle, and dilation of blood vessels

Neurotransmitters

Parasympathetic responses are regulated by acetylcholine, a neurotransmitter in the brain, ANS, and neuromuscular junctions. Acetylcholine is formed in cholinergic nerve endings from choline and acetyl-coenzyme A, in a chemical reaction catalyzed by choline acetyltransferase. After its release from the nerve ending, the effect of acetylcholine on receptors of the parasympathetic nervous system is brief and measured in milliseconds. The action of acetylcholine on receptors is terminated because of rapid metabolism by acetylcholinesterase, an enzyme present in the nerve ending and on the surface of the receptor organ. Acetylcholinesterase splits the active acetylcholine into inactive acetate and choline. The choline is taken up again by the presynaptic nerve terminal and reused to form more acetylcholine. Acetylcholine exerts excitatory effects at nerve synapses and neuromuscular junctions and inhibitory effects at some peripheral sites such as the heart.

Cholinergic Receptors

When acetylcholine acts on body cells that respond to parasympathetic nerve stimulation, it interacts with two types of *cholinergic* receptors: *nicotinic* and *muscarinic*. Nicotinic receptors are located in motor nerves and skeletal muscle. When they are activated by acetylcholine, the cell membrane depolarizes and produces muscle contraction. Muscarinic receptors are located in most internal organs, including the cardiovascular, respiratory, gastrointestinal, and genitourinary systems. When muscarinic receptors are activated by acetylcholine, the affected cells may be excited or inhibited in their functions.

Nicotinic and muscarinic receptors have been further subdivided; two types of nicotinic and five types of muscarinic receptors have been identified. Although the subtypes of cholinergic receptors have not been as well characterized as those of the adrenergic receptors, the intracellular events resulting from signal transduction after receptor stimulation are thought to include the following mechanisms:

- *Muscarinic₁ receptors*: Muscarinic₁ receptors are expressed primarily in the CNS, autonomic ganglia, and the gastric and salivary glands. Activation of these receptors results in a series of processes during which phospholipids in the cell

membrane and inside the cell are broken down. One of the products of phospholipid metabolism is inositol phosphate. Inositol phosphate acts as a second messenger to increase the intracellular concentration of calcium. Calcium also acts as a second messenger and functions to activate several intracellular enzymes, initiate contraction of smooth muscle cells, increase secretions of exocrine glands, increase cognitive function, and decrease dopamine release.

- *Muscarinic₂ receptors*: Receptor activation results in inhibition of adenylyl cyclase in the heart, smooth muscle, and brain. As a result, less cAMP is formed to act as a second messenger and stimulate intracellular activity. Receptor stimulation also results in activation of potassium channels in cell membranes of the heart. The overall consequences of M₂ activation are inhibition of cardiac function, increased contraction of smooth muscle, and inhibition of neuronal transmission.
- *Muscarinic₃ receptors*: Muscarinic₃ receptors are expressed primarily in the CNS, smooth muscle, glands, and heart. Activation apparently causes the same cascade of intracellular processes as with activation of the M₁ receptors, resulting in decreased dopamine release, increased smooth muscle contraction, and increased glandular secretion. In addition, nitrous oxide is generated from vascular endothelial cells, resulting in dilation of vessels.
- *Muscarinic₄ receptors*: Activation of these receptors in the CNS results in a molecular response similar to M₂ receptor activation. Muscarinic₄ activation results in inhibition of acetylcholine release in the striatum, a subcortical portion of the forebrain. These receptors have a regulatory effect on dopaminergic neurotransmission, and activation facilitates dopamine release. Alterations in M₄ receptors may contribute to disorders such as Parkinson's disease.
- *Muscarinic₅ receptors*: Receptor activation results in a molecular response similar to M₁ receptor activation. The receptor has been identified in CNS tissues (especially the substantia nigra); its activation results in dilation of cerebral arteries and arterioles and facilitation of dopamine release. In addition, stimulation of M₅ receptors decreases cAMP levels.



QSEN Alert: Safety

Muscarinic₅ activation also plays a role in augmentation of drug-seeking behavior and reward.

Although five muscarinic receptor subtypes have been identified, currently available drug therapies do not selectively differentiate among the various receptor subtypes.

- *Nicotinic_n receptors*: These receptors are located on autonomic ganglia and the adrenal medulla. Activation results in enhanced transmission of nerve impulses at all parasympathetic and sympathetic ganglia and release of epinephrine from the adrenal medullae.
- *Nicotinic_m receptors*: These are located at neuromuscular junctions in skeletal muscle. Their activation causes muscle contraction.
- *Nicotinic_{CNS} receptors*: These receptors are located on presynaptic nerve fibers in the brain and spinal cord. Their activation promotes the release of acetylcholine in the cerebral cortex.

Nicotinic receptors are composed of five different protein subunits. The protein subunits that make up a nicotinic_n receptor vary from those that make up a nicotinic_m receptor, thus allowing the development of medications that are more selective in their actions.

QSEN Alert: Safety

Neuromuscular-blocking medications such as pancuronium, which act selectively at nicotinic_m receptors, can paralyze skeletal muscles in patients when limiting movement is therapeutic (such as in the ventilated patient or during surgery), without adversely affecting the other functions of the ANS.

CHARACTERISTICS OF AUTONOMIC DRUGS

Many drugs are used clinically because of their ability to stimulate or block activity of the SNS or parasympathetic nervous system. Drugs that stimulate activity act like endogenous neurotransmitter substances; drugs that block activity prevent the actions of both endogenous substances and stimulating drugs. Specific drugs that either stimulate or block the SNS are well described in the cardiac section of this text. Chapters 47 and 48 discuss the influence of drugs on the PNS.

Because ANS receptors are widespread throughout the body, drugs that act on the ANS usually affect the entire body rather than certain organs and tissues. Drug effects depend on which branch of the ANS is involved and whether it is stimulated or inhibited by drug therapy. Thus, knowledge of the physiology of the ANS is required if drug effects are to be understood and predicted. In addition, it is becoming increasingly important to understand receptor activity and the consequences of stimulation or inhibition. More drugs are being developed to stimulate or inhibit particular subtypes of receptors. This is part of the continuing effort to design drugs that act more selectively on particular body tissues and decrease adverse effects on other body tissues. For example, drugs such as terbutaline (see Chap. 33) have been developed to stimulate beta₂ receptors in the respiratory tract and produce bronchodilation (a desired effect) with decreased stimulation of beta₁ receptors in the heart (an adverse effect).

The terminology used to describe autonomic drugs is often confusing because different terms are used to refer to the same phenomenon. Thus, sympathomimetic, adrenergic, and alpha- and beta-adrenergic agonists are used to describe a drug that has the same effects on the human body as stimulation of the SNS. Parasympathomimetic, cholinomimetic, and cholinergic

are used to describe a drug that has the same effects on the body as stimulation of the parasympathetic nervous system. There are also drugs that oppose or block stimulation of these systems. Sympatholytic, antiadrenergic, and alpha- and beta-adrenergic blocking drugs inhibit sympathetic stimulation. Parasympatholytic, anticholinergic, and cholinergic blocking drugs inhibit parasympathetic stimulation. This text uses the terms adrenergic, antiadrenergic, cholinergic, and anticholinergic when describing medications.

NCLEX Success

6. During a teaching session for a patient who is receiving a respiratory inhaler that stimulates beta₂ receptors in the respiratory tract, the patient asks why he needs to take the inhaler. The best response by the nurse is that the effect of a beta₂ receptor is
 - A. prevention of bronchospasm
 - B. reduction of sputum production
 - C. maintenance of respiratory rate
 - D. suppression of cough
7. Functions stimulated by the parasympathetic nervous system include which of the following? [Check all that apply.]
 - A. digestion
 - B. excretion
 - C. catabolism
 - D. anabolism
8. A drug that has the same effects on the body as stimulation of the parasympathetic nervous system is described as
 - A. cholinergic
 - B. sympatholytic
 - C. antiadrenergic
 - D. parasympatholytic
9. Activation of the parasympathetic system will result in which of the following? [Check all that apply.]
 - A. dilation of blood vessels in the skin
 - B. decreased heart rate
 - C. increased motility of the gastrointestinal tract
 - D. constriction of smooth muscle of bronchi

THE NURSING PROCESS

A concept map outlines the nursing process related to drug therapy considerations in this chapter. Additional nursing implications related to the disease process should also be considered in care decisions.



KEY CONCEPTS

- The ANS controls involuntary activities in smooth muscle, secretory glands, and in the visceral organs of the body such as the heart.
- The ANS functions to maintain homeostasis, to respond to stress, and to repair body tissues.
- The ANS is composed of the sympathetic and parasympathetic nervous systems; these two divisions are usually antagonistic in their actions on a particular organ. Exceptions to this antagonism are sweating and regulation of arteriolar diameter, which are controlled by the sympathetic nervous system.
- Release of neurotransmitters allows nerve impulses in the ANS to bridge synapses and travel from presynaptic to post-synaptic nerves, eventually stimulating receptors located on effector organs.
- Stimulation of receptors in the SNS produces adrenergic effects. Blockade of receptors produces antiadrenergic effects.
- Stimulation of receptors in the parasympathetic nervous system produces cholinergic effects. Blockade of receptors produces anticholinergic effects.
- Drugs that activate ANS receptors stimulate the ANS; these medications function like endogenous neurotransmitters.
- Drugs that block activity of ANS receptors prevent the actions of both endogenous neurotransmitters and ANS agonists.
- Adrenergic receptors include alpha and beta receptors as well as dopamine receptors; there are several subtypes.
- Cholinergic receptors include muscarinic and nicotinic receptors; there are several subtypes.
- The number of receptors in the ANS is dynamic and can be up-regulated or down-regulated as needed.

CLINICAL REASONING CASE STUDY

Meet the Patient

Michele Washington, a 65-year-old woman with a history of asthma, presents to the emergency department (ED) with significant wheezing on auscultation. Her vital signs are temperature 99°F orally, pulse 112 beats/min, respiratory rate 32 per minute, and blood pressure 146/88 mm Hg. She is having moderate difficulty breathing. She has been using an albuterol inhaler but has not been able to afford to purchase the inhaler for the last month. She is provided an albuterol inhaler in the ED, which is effective in causing bronchodilation. A nursing student asks the nurse taking care of Ms. Washington why Ms. Washington did not receive a drug such as epinephrine.

- What would be the best response by the nurse?
- What signs and symptoms may indicate worsening of the patient's condition?

Assessing Drug Information

- Epinephrine is effective in producing bronchodilation and can be administered nasally, subcutaneously, or intravenously. Because epinephrine affects both β_1 and β_2 adrenergic receptors, untoward adverse effects could result from β_1 stimulation, particularly because her pulse and blood pressure are already elevated.
- Albuterol is a β_2 -selective drug that is equally effective in causing bronchodilation with a much lower risk of adverse cardiovascular effects.

Nursing Actions

- Observe Ms. Washington for signs of worsening respiratory status (e.g., rate below 12 or above 24 per minute, dyspnea, cough, orthopnea, wheezing, “noisy” respirations).
 - Severe respiratory distress is characterized by tachypnea, dyspnea, use of accessory muscles of respiration, and hypoxia.
 - Early signs of hypoxia include mental confusion, restlessness, anxiety, and increased blood pressure and pulse rate. Late signs include cyanosis and decreased blood pressure and pulse rate. Hypoxemia is confirmed if arterial blood gas analysis shows decreased PO_2 .
- Assess for improvement in Ms. Washington's pulmonary function. General assessment factors include rate and character of respiration, skin color, arterial blood gas analysis, and pulmonary function tests. Assess for the return of stable vital signs.
- Once acute event has resolved, try to determine the frequency and severity of acute attacks; factors that precipitate or relieve acute attacks; allergies; and condition between acute attacks, such as restrictions in activities of daily living due to asthma.
- Consult to social services to determine what options are available for financial assistance in obtaining the prescribed inhaler and other essentials.

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Q3

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Queries

[Q1] Please verify the cross reference of Table 29.1.

[Q2] Please verify the cross reference of other chapters.

[Q3] Please update the reference "UpToDate".

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