chapter

12 Autonomic Nervous System

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Key Terms

adrenergic fiber (p. 223)
alpha-adrenergic receptor (p. 225)
autonomic nervous system (ANS) (p. 218)
beta-adrenergic receptor (p. 225)
cholinergic fiber (p. 223)
craniosacral outflow (p. 222)
muscarinic receptors (p. 224)
nicotinic receptors (p. 224)
norepinephrine (NE) (p. 223)
parasympathetic nervous system (p. 220)
preganglionic fiber (p. 221)
postganglionic fiber (p. 221)
sympathetic nervous system (p. 219)
thoracolumbar outflow (p. 221)

Objectives

1. Describe the function and pathway of autonomic (visceral) reflexes.
2. Do the following regarding the autonomic nervous system:
   - Describe the function of the autonomic nervous system.
   - Identify the two divisions of the autonomic nervous system.
   - State the anatomical and functional differences between the sympathetic and parasympathetic nervous systems.
   - Define autonomic terminology used in pharmacology.
   - Differentiate between autonomic tone and vasomotor tone.
3. Discuss autonomic nervous system neurons, including:
   - Define *cholinergic* and *adrenergic* fibers.
   - Name the major neurotransmitters of the autonomic nervous system.
   - Name and locate the cholinergic and adrenergic receptors.
4. Explain the terms used to describe the effects of neurotransmitters and drugs on autonomic receptors.

Throughout the day, you are busy doing various things. You walk across a room, run up the stairs, write, tie your shoes, and chew your food. You perform all these activities voluntarily and consciously. Your body, however, performs many more activities automatically. For example, when you eat, you don't think, "I am eating. Therefore, I should increase the flow of my digestive enzymes and then increase the rate of contraction of my intestinal muscles in order to enhance the digestive process." Instead, your body automatically makes these decisions and carries them out for you. This automatic response is the function of the **autonomic nervous system (ANS)**. Autonomic = automatic!

AUTONOMIC (VISCERAL) REFLEXES

WHAT THEY DO

Mention the word *reflex* and what comes to mind is the knee-jerk reflex. Tap the patellar ligament and up pops the leg. The knee-jerk reflex is mediated by somatic nerves. There are also visceral reflexes. These reflexes are mediated by the ANS. As the name implies, visceral reflexes regulate organ function. Visceral reflexes control such things as heart rate, blood pressure, body temperature, digestion, air flow through respiratory passages, elimination, and pupillary (eye) responses. Note the wide variety of functions controlled by autonomic activity. It takes a load off your mind!

PATHWAY

A visceral reflex is mediated in a manner similar to the knee-jerk reflex: activation of a receptor, transmission of sensory information to the central nervous system (CNS), the processing of the information by the CNS, and the motor response sent to the effector organ(s). For example, a sudden decrease in blood pressure activates pressure receptors (baroreceptors). The information about the low blood pressure is carried to the medulla oblongata in the brain stem by sensory nerves. The

2. **According to Figure 11-2**
   a. The corticospinal tract, spinothalamic tract, and dorsal columns ascend and descend in the gray matter.
   b. The corticospinal tract runs only in the left side of the spinal cord.
   c. The ventral and posterior horns are composed of white matter.
   d. All tracts ascend and descend in white matter.

3. **According to Figure 11-5**
   a. The effector organ of the patellar tendon reflex is the patellar tendon.
   b. A sensory neuron carries information to the gray matter in the spinal cord.
   c. The response to the patellar tendon reflex is flexion of the leg at the knee.
   d. A motor neuron carries information from the patellar tendon to the spinal cord.

4. **According to Figure 11-8**
   a. The facial nerve only innervates the lower jaw.
   b. The vagus (CN X) is restricted to the thoracic cavity.
   c. CN V has two branches: vestibular and cochlear.
   d. CN VIII is the vestibulocochlear nerve.

5. **According to Figure 11-9**
   a. The sciatic and femoral nerves innervate the thoracic cavity.
   b. The phrenic nerve exits the spinal cord at the level of T6.
   c. The radial, median, and ulnar nerves exit from the lumbosacral plexus.
   d. Transection of the spinal cord at C2 causes quadriplegia.

medulla oblongata determines that the blood pressure is low and sends motor signals to the visceral effector organs (heart and blood vessels). The motor response results in changes in the heart and blood vessels that elevate blood pressure. What has been accomplished? A sudden decrease in blood pressure stimulates a visceral reflex that restores blood pressure to normal. All this has been accomplished without conscious input.

Do You Know...

What Pinocchio and Your Autonomic Nervous System Have in Common?

Although Pinocchio's nose was a dead giveaway to his lying ways, most of us do not do "the nose thing" in response to fibbing. But fibbers beware! Your ANS can act like the puppet's nose. Lying, even those little white lies, activates the sympathetic nervous system and causes physiological responses that are readily found by a polygraph machine. A modern-day Gepetto knew that we are generally unable to control the ANS and so invented the lie detector.

Why does 007 wear shades? The ANS is constantly adjusting our innards to environmental stresses. The adjustments are noticeable in our eye responses, particularly in the changes in pupil size. Bored, you say? Pupils constrict. Got your eye on a "person of interest"? Pupils dilate. James Bond certainly doesn't want to give away any of his autonomic cues and therefore wears his shades—as do poker players.

ORGANIZATION AND FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM

DIVISION OF THE AUTONOMIC NERVOUS SYSTEM

The ANS is the part of the peripheral nervous system that supplies motor activity to the visceral effector organs: glands, smooth muscles within organs and tubes, and the heart.

The two divisions of the ANS are the sympathetic (sim-pah-THET-ik) and parasympathetic (pair-ah-sim-pah-THET-ik) nervous systems. The distribution of sympathetic and parasympathetic nerves to the viscera varies. A single organ most often receives fibers from both divisions of the ANS; this is called *dual innervation*. In most instances, stimulation of one division of the ANS causes a specific effect, whereas stimulation by the other division causes an opposing effect. For example, the cells of the heart that determine heart rate receive both sympathetic and parasympathetic fibers. Stimulation of the sympathetic fibers increases heart rate, whereas stimulation of the parasympathetic fibers decreases heart rate. There are exceptions to this arrangement. In a few organs that receive dual innervation, the effects of sympathetic and parasympathetic activity are complementary rather than opposite. For example, in the male, erectile activity is regulated by the parasympathetics, whereas ejaculation is regulated by the sympathetics. The sympathetics and parasympathetics work in a complementary way to achieve the desired effect: penetration of the female and ejection of the sperm. Finally, not all organs have dual innervation. For example, the blood vessels are innervated only by the sympathetic nervous system. Regulation of blood vessel diameter is achieved through an adjustment of sympathetic activity. Increased sympathetic activity causes constriction of the blood vessels, and decreased sympathetic activity causes the blood vessels to dilate.

Table 12-1 indicates the effects of sympathetic and parasympathetic stimulation on some major organs of the body.

SYMPATHETIC NERVOUS SYSTEM: FIGHT OR FLIGHT

In general, the **sympathetic nervous system** is activated during periods of stress or times when a person feels threatened in some way (Figure 12-1). For this reason, the sympathetic nervous system is called the *fight-or-flight* division of the ANS. In other words, the

Table 12-1 Autonomic Nervous System: Organ Responses

ORGAN	SYMPATHETIC RESPONSE	PARASYMPATHETIC RESPONSE
Heart	Increases rate and strength of contraction	Decreases rate: no direct effect on strength
Bronchial tubes	Dilates (↑ air flow)	Constricts (↓ air flow)
Iris of eye	Dilates (pupil enlarges)	Constricts (pupil becomes smaller)
Blood vessels	Constricts	No innervation
Sweat glands	Stimulates	No innervation
Intestine	Inhibits motility and secretion	Stimulates motility and secretion
Uterus	Relaxes muscle	No effect
Adrenal medulla	Stimulates secretion of epinephrine and norepinephrine	No effect
Salivary glands	Stimulates thick secretion	Stimulates watery secretion
Urinary system		
Bladder wall	Relaxes muscle	Contracts muscle
Internal sphincter	Closes sphincter	Opens sphincter

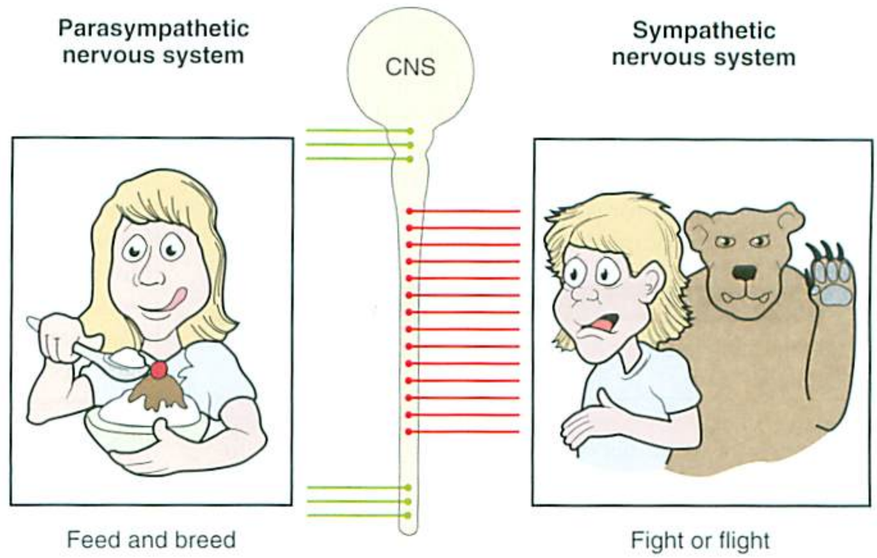

FIGURE 12-1 Autonomic nervous system: parasympathetic nervous system and sympathetic nervous system.

sympathetic nervous system causes you to be prepared either to confront (fight) or to remove yourself from the threatening situation (flight). Recall a time when you were frightened. Your heart raced and pounded in your chest. The pupils of your eyes opened wide. You breathed more quickly and more deeply. The palms of your hands became wet with perspiration, and your mouth became so dry you could hardly speak. The easiest way to remember the sympathetic responses is to recall your personal response to your own worst nightmare. You can check Table 12-1 to see if your responses matched the sympathetic column.

Although the sympathetic nervous system is activated during periods of stress, these periods are normally short-lived. If you keep yourself stressed out, however, the sympathetic nervous system keeps the body in a state of high alert. Over time, this state takes its toll on the body through stress-induced illnesses. Laughter, play, rest, and relaxation diminish sympathetic outflow and are good buffers against stress. So relax and be happy!

Do You Know...

About the Sympathetic Nervous System Gone Wild?

Several clinical conditions are caused by out-of-control sympathetic activity. One condition is called *autonomic dysreflexia*. Autonomic dysreflexia is experienced by a person who has sustained a high cervical spinal cord injury (e.g., C4 transection and quadriplegia). With this condition, the quadriplegic patient develops a distended urinary bladder, usually from a kinked urinary catheter. The distended bladder sends signals to the spinal cord, setting off massive thoracolumbar (sympathetic) discharge. The intense sympathetic activity severely elevates blood pressure, sometimes to the point of causing a cerebral hemorrhage (stroke). The sympathetic stimulation continues as long as the bladder remains distended. The ANS cannot counteract the sympathetic firing because of the spinal cord injury. Immediate treatment is to remove the stimulus (distended bladder), which then lowers the blood pressure. Out-of-control sympathetic activity is life threatening and is always taken seriously.

PARASYMPATHETIC NERVOUS SYSTEM: FEED AND BREED

The **parasympathetic nervous system** is most active during quiet, nonstressful conditions. It has a calming effect on the body. The parasympathetic nervous system plays an important role in the regulation of digestion and in reproductive function. For this reason, it is sometimes referred to as the *feed-and-breed* division of the ANS. Another descriptive term for the parasympathetic nervous system is *resting and digesting*.

What is "paradoxical fear"? Although the sympathetics are usually associated with fear reactions, the parasympathetics can be activated in situations that are perceived as hopeless and where fight or flight seems futile. The massive parasympathetic discharge can result in uncontrolled urination and defecation. It can also cause the heart rate to decrease so severely that the person faints or experiences a potentially lethal electrical disturbance of the heart. Clinically, this type of cardiac stress reaction is described as "bradying down," a reference to severe bradycardia (dangerously slow heart rate). Yes, one can die of fright!

? Re-Think

1. Explain why sympathetic activity is called *fight or flight*.
2. Explain why parasympathetic activity is called *feed and breed*.

AUTONOMIC TERMINOLOGY AND PHARMACOLOGY

Many drugs work by altering autonomic activity. Thus, many pharmacology terms refer to the autonomic nervous system. In fact, you cannot understand pharmacology without knowing ANS terminology. So get ready for some challenging words.

If a drug causes effects similar to the activation of the sympathetic nervous system, it is called a *sympathomimetic* (sim-pah-thoh-mim-ET-ik) (as in mimicking) drug. A sympathomimetic agent increases heart rate, force of cardiac contraction, and blood pressure. If the drug causes effects that are similar to a situation where the sympathetic nervous system cannot be activated, the drug is called a *sympatholytic* (sim-pah-thoh-LIT-ik) drug (*-lytic* means "inhibiting"). The administration of a sympatholytic drug prevents an increase in cardiac activity when the sympathetic nerves are fired.

If a drug causes effects similar to the activation of the parasympathetic nervous system, it is called a *parasympathomimetic* (pair-ah-sim-pah-thoh-mim-ET-ik) drug. A parasympathomimetic agent decreases heart rate and increases digestive activity. The administration of a *parasympatholytic* (pair-ah-sim-pah-thoh-LIT-ik) agent prevents activation of the parasympathetic nervous system. As if this isn't confusing enough! Most parasympathetic fibers travel with the vagus nerve (CN X). If a drug causes effects similar to parasympathetic activity, it is also called *vagomimetic*. If a drug slows parasympathetic activity, it is called *vagolytic*. The vagomimetic and vagolytic terminology is more commonly used. If an organ, such as the heart, is being driven excessively by the parasympathetic nervous system, the heart rate becomes dangerously slow (bradycardia). The administration of a parasympatholytic or vagolytic drug, such as atropine, blocks the parasympathetic effect on the heart, thereby allowing the heart rate to increase.

AUTONOMIC TONE AND VASOMOTOR TONE

The sympathetics and parasympathetics are active at the same time, creating a background (continuous, low-level) firing of the ANS. This background autonomic activity is called *autonomic tone*. In the resting state, parasympathetic activity is generally stronger. For example, parasympathetic tone maintains the resting heart rate at around 72 beats per minute. When physical activity increases, however, the sympathetic nerves fire more intensely, whereas parasympathetic activity decreases. The shift to sympathetic discharge during exercise results in an increase in heart rate, thereby supplying more oxygen and energy to the exercising muscles. The balance between sympathetic and parasympathetic activity is maintained by the hypothalamus and parts of the brain stem.

A second example of autonomic tone involves the blood vessels. Blood vessels are innervated only by the sympathetic nerves; there is no parasympathetic innervation. Thus, the autonomic tone of the blood vessels is determined by the sympathetic nervous system. Background sympathetic firing keeps the blood vessels somewhat constricted. This sympathetically induced continuous state of blood vessel constriction is called *vasomotor tone* or *sympathetic tone*. Additional sympathetic firing causes blood vessels to constrict, thereby elevating blood pressure. A decrease in sympathetic firing causes blood vessels to dilate, thereby lowering blood pressure. A change in vasomotor tone is clinically very important. For example, loss of vasomotor tone can dangerously lower blood pressure, plunging a person into a lethal shock.

2+2 Sum It Up!

The ANS regulates visceral (organ) functions such as blood pressure. There are two divisions of the ANS: the sympathetic (fight or flight) and parasympathetic (feed and breed) nervous systems. Most organs receive dual innervation by both the sympathetic and parasympathetic nervous systems. Background firing of the sympathetic nervous system to the blood vessels is responsible for vasomotor or sympathetic tone that, in turn, plays a crucial role in the maintenance of normal blood pressure.

? Re-Think

1. What is a sympathomimetic effect? A parasympathomimetic effect?
2. What is the effect of a vagomimetic drug on heart rate? What is the effect of a vagolytic drug on heart rate?

AUTONOMIC NERVOUS SYSTEM NEURONS

NUMBERS AND GANGLIA

The numbers and arrangement of the neurons of the ANS are important. The pathways of the ANS use two neurons with a ganglion between each neuron (Figure 12-2, *A*). The cell body of neuron 1 is located in the CNS, in the brain or the spinal cord. The axon of neuron 1 leaves the CNS and extends to the ganglion where it synapses on neuron 2. The axon of neuron 1 is called the **preganglionic fiber** (because it comes before *[pre]* the ganglion). The axon of neuron 2 leaves the ganglion and extends to the effector or target organ. This axon is called the **postganglionic fiber** (because it comes after *[post]* the ganglion). Pay particular attention to the postganglionic fibers; they are key to understanding autonomic function. The postganglionic fibers of the sympathetic and parasympathetic nervous systems secrete different neurotransmitters. These different neurotransmitters account for the different effects caused by the sympathetic and parasympathetic nervous systems.

NEURONS OF THE SYMPATHETIC NERVOUS SYSTEM

The neurons of the sympathetic nervous system leave the spinal cord at the thoracic and lumbar levels (T1 to L2) (see Figure 12-2, *B*). The sympathetic nervous system is therefore called the **thoracolumbar outflow**. Most preganglionic sympathetic fibers travel a short distance and synapse within ganglia located close to the spinal cord. The sympathetic ganglia form a chain that runs parallel to the vertebral column. This chain is called the *paravertebral ganglia* or *sympathetic chain*

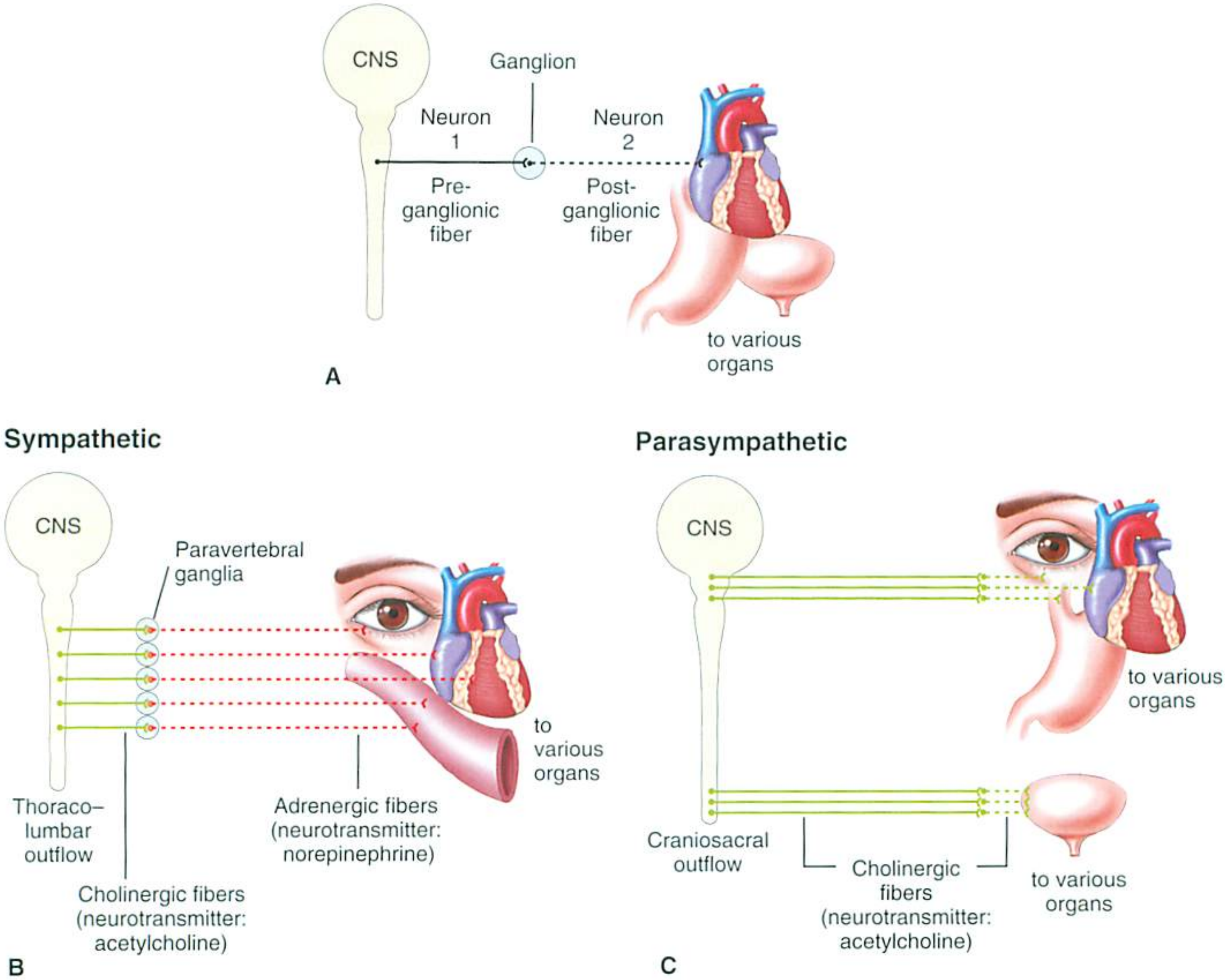

FIGURE 12-2 **A,** Arrangement of autonomic fibers. **B,** Sympathetic nervous system. **C,** Parasympathetic nervous system.

ganglia. Postganglionic fibers leave the ganglia and extend to the various target organs.

The location of the paravertebral ganglia is important. The paravertebral ganglia provide a site where each preganglionic fiber synapses with multiple postganglionic fibers. Why is this important? The firing of a single sympathetic neuron is capable of providing a generalized, widespread sympathetic response; many organs respond to sympathetic firing. This makes sense—if you are confronted with an emergency situation, you want the entire body to respond immediately!

The adrenal gland (adrenal medulla) acts as a modified sympathetic ganglion. Preganglionic sympathetic fibers supply the adrenal medulla, causing it to secrete hormones (epinephrine and norepinephrine) that resemble the neurotransmitters of the sympathetic nervous system. These hormones circulate in the blood throughout the body. Thus, the sympathetic nervous system and the adrenal medulla function together to achieve a sustained response.

NEURONS OF THE PARASYMPATHETIC NERVOUS SYSTEM

The neurons of the parasympathetic nervous system leave the CNS at the level of the brain stem and sacrum (S2 to S4; see Figure 12-2, C). The parasympathetic nervous system is therefore called the **craniosacral outflow**.

Because the ganglia of the parasympathetic nervous system are located close to or within the target organs, the parasympathetic nerves do not have a chain of ganglia running parallel to the spinal cord. The preganglionic fibers are long because the ganglia of the parasympathetic nervous system are located near the target organ. Short postganglionic fibers run from the ganglia to the smooth muscle or glands within the organ. Because of the location of the ganglia close to the target organs, parasympathetic activity generates a more localized response (as opposed to the generalized sympathetic response). Table 12-2

Table 12-2 Autonomic Nervous System: Comparison

CHARACTERISTIC	SYMPATHETIC	PARASYMPATHETIC
Origin of fibers	Thoracolumbar	Craniosacral
Functions	Fight or flight	Feed and breed
Ganglia	Paravertebral ganglia	Located near or in target organ
Effects	Generalized, widespread	Localized
Neurotransmitter	Norepinephrine (postganglionic)	Acetylcholine

compares the anatomical arrangement of the sympathetic and parasympathetic nervous systems.

? Re-Think

1. Why is the preganglionic fiber of the sympathetic nervous system shorter than that of the parasympathetic nervous system?
2. Why are the sympathetic nerves referred to as *thoracolumbar outflow?*
3. Why are the parasympathetic nerves referred to as the *craniosacral outflow?*

RUNNING WITH CRANIAL NERVES

Parasympathetic fibers travel from the brain stem with four cranial nerves (CNs): oculomotor (CN III), facial (CN VII), glossopharyngeal (CN IX), and vagus (CN X).

Oculomotor Nerve (CN III)

The oculomotor nerve innervates most of the extrinsic eye muscles (skeletal muscles) that move the eyeball. The oculomotor nerve also carries parasympathetic fibers to two intrinsic eye muscles: the constrictor muscle of the eye, which causes pupillary constriction, and the ciliary muscle, which controls the shape of the lens of the eye. Observation of pupillary reflexes is used clinically to observe for signs of increasing intracranial pressure and other neurological disorders. In addition, many drugs alter parasympathetic activity of the intrinsic eye muscles, and you will need to assess their clinical effects. You will have to do "eye checks"; pay close attention to the eye muscles and nerves of the eye (described in Chapter 13).

Facial Nerve (CN VII)

The facial nerve carries parasympathetic fibers to the tear glands (eyes), salivary glands (mouth), and nasal glands (nose).

Glossopharyngeal Nerve (CN IX)

The glossopharyngeal nerve (with the assistance of the trigeminal nerve) carries parasympathetic fibers to the salivary glands in the mouth.

Vagus Nerve (CN X)

The vagus nerve (the "wanderer" nerve) carries over 80% of the parasympathetic fibers. It travels from the brain stem to organs within the thoracic and abdominal cavities.

2+2 Sum It Up!

The sympathetic nervous system is called the *thoracolumbar outflow;* the parasympathetic nervous system is called the *craniosacral outflow*. Each system has preganglionic and postganglionic fibers. The ganglia of the sympathetic nerves are located in the paravertebral ganglia, and the ganglia of the parasympathetics are located near the target organ. Parasympathetic fibers travel from the brain stem with four cranial nerves: oculomotor, facial, glossopharyngeal, and vagus nerves.

NAMING FIBERS AND NEUROTRANSMITTERS

The key to understanding autonomic function and autonomic pharmacology is based on knowledge of the autonomic neurotransmitters and their receptors. The two major neurotransmitters of the ANS are acetylcholine (ACh) and **norepinephrine** (nor-ep-i-NEF-rin) **(NE)**.

The neurotransmitter is used to name the fibers of the ANS. For example, a fiber that secretes NE as its neurotransmitter is called an **adrenergic fiber** (NE is also called nor*adrenaline*). A fiber that secretes ACh (acetyl*choline*) as its neurotransmitter is called a **cholinergic fiber**.

Now, here's the challenging part. Remember, we are concerned with four fibers (two preganglionic and two postganglionic fibers, sympathetic and parasympathetic). All preganglionic fibers secrete ACh and are therefore cholinergic fibers. The postganglionic fibers of the parasympathetic nervous system secrete ACh and are also cholinergic. The postganglionic sympathetic nervous system fibers, however, secrete NE and are called *adrenergic fibers*. Refer to Figure 12-2, *B* and *C*, and note the color coding that differentiates the adrenergic from the cholinergic fibers. The cholinergic fibers are colored green, whereas the adrenergic fibers are colored red. You absolutely need this fiber-neurotransmitter information to learn autonomic pharmacology.

NEUROTRANSMITTERS: TERMINATION OF ACTIVITY

ACh is secreted by cholinergic fibers and diffuses to its receptor. After ACh exerts its effect on its receptor, it is quickly degraded by acetylcholinesterase (AChE), an enzyme found in the synapse.

NE is secreted by adrenergic fibers. The effects of NE are more prolonged because of the manner in which NE is terminated. Most of the NE is reabsorbed by the adrenergic nerve terminals themselves. The termination of NE is called *reuptake*. Note that its termination differs from that of ACh. The NE taken up by the nerve terminal is processed in two ways. Most of the NE is simply reused. Excess NE can be degraded by an enzyme located within the adrenergic nerve terminal and is called *monoamine oxidase* (MAO). Some of the NE is merely "washed away" from the synapse and is degraded by another enzyme found in surrounding tissue. The name of this enzyme is *catechol-O-methyltransferase* (COMT).

Do You Know...

Why You Might Have to "Hold the Beer and Sausage" If You Are Taking an MAO Inhibitor?

Monoamine oxidase (MAO) is an enzyme that breaks down norepinephrine in the CNS. An MAO-inhibitor drug prevents the breakdown of NE and is used in the treatment of depression. Although the drug relieves the depression by increasing NE in the CNS, it can also cause serious adverse effects such as a dangerously elevated blood pressure. Certain foods (e.g., beer, cheese, sausage) contain an amino acid that is used in the synthesis of NE. The combination of the drugs and food increases NE and blood pressure and the possibility of a stroke. Some herbals such as St. John's wort have MAO inhibitor activity and may also dangerously elevate blood pressure. Taking an MAO inhibitor? Hold the beer and sausage!

2+2 Sum It Up!

The two major neurotransmitters of the ANS are acetylcholine (ACh) and norepinephrine (NE). ACh is secreted by cholinergic fibers. The effects of ACh are short lived; the ACh is degraded by acetylcholinesterase located in the synapse. NE is secreted by adrenergic fibers. The effects of the sympathetic nervous system are primarily caused by NE. The effects of NE are more prolonged because of how NE is terminated (through reuptake). Excess NE is degraded by monoamine oxidase (MAO). Some NE is simply washed away and degraded at distal sites by another enzyme.

? Re-Think

1. What is the difference between a cholinergic and adrenergic fiber?
2. Explain how neurotransmitter activity is ended.

RECEPTORS OF THE AUTONOMIC NERVOUS SYSTEM

The neurotransmitters of the ANS—ACh and NE—bind to receptors on target cells (cardiac muscle, smooth muscle, and glands). A receptor is any site on the cell to which a neurotransmitter binds, causing an alteration in cellular function. For example, ACh binds to a receptor on a heart cell and causes the heart rate to decrease. NE binds to a different receptor on the heart cell and causes the heart rate to increase. The ANS has two receptor types: cholinergic and adrenergic receptors.

CHOLINERGIC RECEPTORS

Cholinergic receptors are activated by ACh. There are two types of cholinergic receptors: **muscarinic** (mus-kar-IN-ik) **receptors** and **nicotinic receptors**. The different types of cholinergic receptors explain the variety of effects of cholinergic receptor activation by ACh.

Where are these receptors located? Muscarinic receptors are located on the effector or target organs (cardiac muscle, smooth muscle, and glands) of the parasympathetic nerves (Figure 12-3, *A*). Thus, activation of the parasympathetic nervous system releases ACh and stimulates muscarinic receptors. Refer to Table 12-3 and note several of the effects of muscarinic activation. For example, activation of the muscarinic receptors on the constrictor muscle of the iris causes pupil size to decrease. Activation of the muscarinic receptors in the heart (sinoatrial node) causes the heart rate to decrease. Muscarinic activation of the urinary bladder causes the bladder muscle to contract and the outlet sphincter muscle of the urinary bladder to relax; these coordinated muscarinic responses of the bladder promote urination.

There are two types of nicotinic receptors in the peripheral nervous system. The nicotinic neural (N_N) receptors are located within the ganglia of the ANS (see Figure 12-3, *A* and *B*). Because these nicotinic receptors are located in both the sympathetic nervous system and parasympathetic nervous system, the responses to N_N activation are difficult to predict. Nicotinic receptors are also located outside the ANS. For example, the receptors located on skeletal muscles in the neuromuscular junction are nicotinic muscle

Table 12-3 Cholinergic Receptors and Responses*

ORGAN	RECEPTOR	ACTIVATION RESPONSE
Heart	Muscarinic	Decreases heart rate
Bronchial tubes	Muscarinic	Constricts (↓ air flow)
Iris of eye	Muscarinic	Constricts (pupil becomes smaller)
Urinary system		
Bladder wall	Muscarinic	Contracts
Internal sphincter	Muscarinic	Relaxes and opens sphincter

*Muscarinic receptors that are commonly targeted by pharmacological agents are listed in this table.

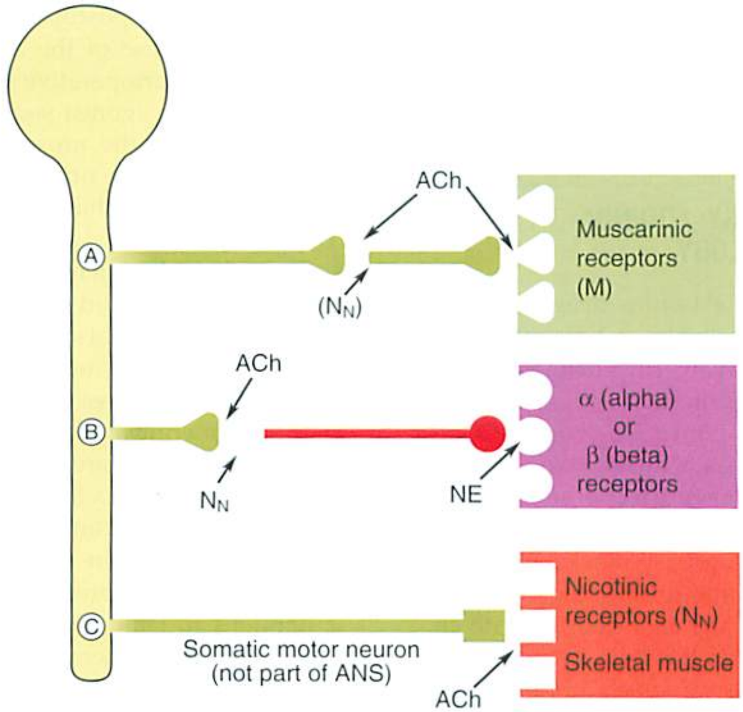

FIGURE 12-3 Receptors: adrenergic and cholinergic.

receptors (N_M; see Figure 12-3, *C*). Activation of the N_M receptors in the neuromuscular junction causes skeletal muscle contraction. Remember, the N_N receptors are part of the ANS; the N_M receptors are part of the somatic motor nervous system and skeletal muscle. The cholinergic receptor subtypes are important in pharmacology and are worthwhile learning. However, in this chapter we will refer only to the muscarinic receptors.

ADRENERGIC RECEPTORS

There are two main types of adrenergic receptors: **alpha- (α) adrenergic** and **beta- (β) adrenergic receptors** (see Figure 12-3, *B*). There are subtypes of the adrenergic receptors: $alpha_1$-, $alpha_2$-, $beta_1$-, and $beta_2$-adrenergic receptors. Adrenergic receptors are located on the target organs of the sympathetic nerves, so that stimulation of the sympathetic nervous system causes activation of adrenergic receptors. See Table 12-4 for the effects of adrenergic receptor activation. Note that activation of the $alpha_1$ receptors of the blood vessels of the mucous membrane causes constriction, thereby decreasing blood flow and shrinking swollen membranes to relieve the discomfort of a stuffy nose. Activation of the $alpha_1$ receptors on blood vessels causes vasoconstriction, thereby elevating blood pressure. These drugs are used in the treatment of conditions that involve low blood pressure, such as shock. Activation of the $beta_1$ receptors in the heart increases heart rate and the strength of cardiac muscle contraction. Activation of the $beta_2$ receptors dilates the breathing tubes, thereby increasing air flow; this action is the basis of the bronchodilators used in the treatment of asthma. Activation of the $alpha_1$ receptors in the iris (eye) causes the radial muscle to contract and the pupil to dilate. Finally, activation of the $beta_2$ receptors in the pregnant uterus causes the uterine muscles to relax, thereby preventing the premature delivery of the fetus. The adrenergic receptors are activated by NE and other natural catecholamines, such as epinephrine and dopamine.

There are a small number of dopamine receptors (also classified as adrenergic receptors) located in the blood vessels of the kidney. Activation of the dopamine receptors causes the blood vessels in the kidney to dilate, thereby increasing blood flow to the kidneys. Dopamine is often administered clinically to maintain blood flow to the kidneys during shocklike episodes that would normally diminish blood flow to the kidneys.

Table 12-4 Adrenergic Receptors and Responses*

ORGAN	RECEPTOR†	ACTIVATION RESPONSE
Heart	β_1	Increases heart rate and strength of contraction
Bronchial tubes	β_2	Dilates (↑ air flow)
Iris of eye	α_1	Dilates (pupil enlarges)
Blood vessels	α_1	Constricts
Uterus	β_2	Relaxes

*Adrenergic receptors commonly targeted by pharmacological agents are listed in this table.
†α, Alpha; β, beta.

Re-Think

1. Name and locate the cholinergic receptors. Name the neurotransmitter that activates cholinergic receptors.
2. Name and locate the adrenergic receptors. Name a neurotransmitter that activates adrenergic receptors.

AUTONOMIC TERMINOLOGY: "DOING" AUTONOMIC PHARMACOLOGY

Autonomic pharmacology classifies drugs according to their receptors. For example, a beta$_1$-adrenergic agonist is a drug that activates the beta$_1$-adrenergic receptors. (An agonist is a drug that activates a receptor.) A beta$_1$-adrenergic antagonist is a drug that blocks the effect of beta$_1$-adrenergic activation. (An antagonist or blocker is a drug that prevents receptor activation.) A muscarinic agonist activates the muscarinic receptor, whereas a muscarinic antagonist blocks muscarinic receptor activation. The same terminology (agonist/antagonist) is applied to drugs that interact with cholinergic and adrenergic receptors.

Let's see if you can figure out some autonomic physiology and pharmacology.

- *Question 1.* Mr. T was admitted to the ER experiencing respiratory distress caused by asthma. Why was he given a beta$_2$-adrenergic agonist (albuterol)? Check Table 12-4 for the respiratory effects of beta$_2$-adrenergic activation. *Answer.* Activation of the beta$_2$-adrenergic receptors on the bronchioles (airways) causes the airways to dilate (open up), thereby improving the flow of air and relieving the respiratory distress of asthma.
- *Question 2.* A very anxious Mr. Q was admitted with a rapid heart rate. Why was he given a beta$_1$-adrenergic blocker (propranolol)? Check Table 12-4 for the cardiac (heart) effects of beta$_1$-adrenergic response. *Answer.* Mr. Q's heart rate was elevated because of excess sympathetic stimulation (an anxiety effect). A beta$_1$-adrenergic blocker prevents activation of the beta$_1$-adrenergic receptors on the heart, thereby reducing heart rate.
- *Question 3.* A patient has had a heart attack and is experiencing a very slow heart rate caused by excessive parasympathetic (vagal) activity. Why was he given a muscarinic antagonist (atropine)? Check Table 12-3 for the effects of muscarinic activation on heart rate. *Answer.* Muscarinic activation (caused by excess parasympathetic activity) slows heart rate. By blocking muscarinic receptors with atropine, heart rate increases.
- *Question 4.* Ms. S is diagnosed with hypertension (high blood pressure). Why did her physician prescribe an alpha$_1$-adrenergic blocker? Check Table 12-4 for the effect of an alpha$_1$-adrenergic response on blood vessels. *Answer.* The alpha$_1$-adrenergic antagonist blocks the alpha$_1$ receptors in the blood vessels, causing them to dilate. Blood vessel dilation decreases blood pressure.
- *Question 5.* A postoperative patient is unable to urinate because of the anticholinergic drugs used during the perioperative period. Why was she given a muscarinic agonist such as bethanechol? *Answer.* Activation of the muscarinic receptors stimulates contraction of the urinary bladder and relaxation of the bladder sphincter. Both actions facilitate urination.
- *Question 6.* A patient goes to his eye doctor for an eye exam. Why did the physician put anticholinergic eyedrops in his eyes (see Table 12-3)? *Answer.* Activation of the muscarinic receptor on the pupillary muscles causes pupillary constriction. By using anticholinergic (antimuscarinic) eyedrops, the muscarinic receptors are blocked, and the pupil dilates. The dilated pupils facilitate the eye exam.
- *Question 7.* A canine friend (Dillon) routinely "bradys down" in response to general anesthesia and is therefore premedicated with atropine. What happens to Dillon without and with the atropine? *Answer.* The general anesthesia causes sustained vagal discharge to the heart and a significant decrease in heart rate (bradycardia). By premedicating with a vagolytic or antimuscarinic drug (see Table 12-3), atropine, the decline in heart rate is prevented.

This is how to analyze autonomic function and "do" autonomic pharmacology. Learn the receptors and the consequences of receptor activation (agonist) and blockade (antagonist).

Do You Know...

About the Parasympathetics, Nitric Oxide, Erections … and, By the Way, Viagra?

In response to sexual stimulation, parasympathetic fibers stimulate the endothelial cells of the blood vessels of the penis to secrete nitric oxide, a gas that triggers a series of reactions that produce cyclic guanosine monophosphate (cGMP). cGMP relaxes the smooth muscle of the blood vessels, thereby increasing blood flow to the penis. Hence, the erection. Having done its job, the cGMP is degraded by an enzyme called *phosphodiesterase*. Most men with erectile dysfunction have difficulty in sustaining their erections. Enter Viagra (sildenafil)! Viagra inhibits the activity of phosphodiesterase, thereby prolonging the life of cGMP and sustaining the erection.

2+2 Sum It Up!

The neurotransmitters, ACh and NE, bind to receptors. There are two types of autonomic receptors: cholinergic and adrenergic. Cholinergic receptors are activated by ACh. There are two types of cholinergic receptors: muscarinic and nicotinic. The muscarinic receptors are located on the target organs of the parasympathetic nerves. The adrenergic receptors are activated by NE. There are two types of adrenergic receptors: alpha- and beta-adrenergic receptors. The adrenergic receptors are located on the target organs of the sympathetic nervous system.

As You Age

1. Aging causes an increase in synaptic delay and a 5% to 10% decrease in the speed of nerve conduction. Consequently, nerve reflexes become slower.
2. Aging causes a loss of the sense of vibration at the ankle after the age of 65. This change is accompanied by a decrease of the ankle-jerk reflex and may affect balance, increasing the chance of falling.
3. An aging ANS causes many changes. For example, a less-efficient sympathetic nervous system may cause transient hypotension and fainting. A decreased responsiveness of the baroreceptor reflex contributes to the fainting episodes.
4. Decreased autonomic nerve activity supplying the eyes causes changes in pupil size and pupillary reactivity. There is some decline in function of the cranial nerves mediating taste and smell.

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Somatic Efferent and Autonomic Nervous Systems

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
Words			
autonomic	auto-	self	**Autonomic** means *automatic*. In response to changing body needs the autonomic nervous system (ANS) automatically helps regulate organ function, such as heart rate. The sympathetic division increases heart rate, whereas the parasympathetic division lowers heart rate.
	-nom(os)-	law	
	-ic	pertaining to	
contralateral	contra-	opposite	*A reference to the opposite side of the body.* For example, a patient suffered a brain attack on the left side of her brain and experienced hemiparalysis on the contralateral side (right) of her body.
	-later/o-	side	
	-al	pertaining to	
decussate		From a Latin word meaning "to mark with a cross"	Means *to cross over*. For example, the pyramidal tract decussates at the medulla oblongata and descends on the contralateral side of the spinal cord.
ipsilateral	ipse-	same	*A reference to the same side of the body.* For example, a patient suffered a brain attack (left brain) and suffered right-sided hemiparalysis and ipsilateral paresis (left side of the body).
	-lateral	side	
Disorders			
amyotrophic lateral sclerosis	a-	without	Also called **ALS** or **Lou Gehrig disease**. ALS refers to *progressive deterioration of motor nerve cells resulting in a progressive loss of muscle control.* Muscle atrophy is caused by hardening of nerve tissue on the lateral columns of the spinal cord. Disability increases from muscle weakness in the extremities, muscles of speech and swallowing, and muscles of respiration to total paralysis and death.
	-myo-	muscle	
	-throph/o-	nourishment	
	later/o	side	
	scler/o-	hardening	
	-osis	condition of	
autonomic dysreflexia	dys-	difficult or faulty	See the "Do You Know" feature on p. 220.
	-reflexia	reflex	
meningocele	mening/o-	meninges	*Protrusion of the meninges through a defect in the skull or vertebra (spina bifida).* A **myelomeningocele** is *a protrusion of the spinal cord and meninges through a defect in the vertebrae.* Disability is related to the location and size of the protruding spinal cord and nervous tissue.
	-cele	protrusion, hernia	
multiple sclerosis	scler/o-	hardening	**Multiple sclerosis** (MS) is *a progressive demyelination of the neurons, especially the oligodendrocytes; the demyelination produces sclerotic lesions along the neurons, thereby interfering with nerve conduction*. The most common form of MS is called *relapsing-remitting MS,* in which the symptoms appear and disappear (exacerbations and remissions). Degenerative changes affect cognitive, sensory, and motor activity. Fatigue, weakness, paresthesias, ataxia (a- = without; -tax/o- = coordination), and optic neuritis are common. Optic neuritis causes a variety of visual disturbances: diplopia, nystagmus, diminished vision, and blindness.
	-osis	condition of	

Continued

MEDICAL TERMINOLOGY AND DISORDERS Disorders of the Somatic Efferent and Autonomic Nervous Systems—cont'd

Medical Term	Word Parts	Word Part Meaning or Derivation	Description
neuralgia	neur/o- -algia	nerve pain	**Neuralgia** is *pain that involves a nerve.* Sciatica is a form of neuralgia; pain moves along the sciatic nerve and its branches through the buttocks and into the thigh and leg. Shingles or herpes zoster sometimes causes postherpetic neuralgia, a severe pain that persists long after the lesions have healed. Pain and a vesicular rash progress along the course of one or more spinal nerves, usually the intercostal nerves and sometimes the trigeminal nerve. Trigeminal neuralgia is due to inflammation of the trigeminal nerve (CN V); it causes excruciating pain in the facial area.
paralysis	para- -lysis	alongside of or abnormal breakdown	**Paralysis** refers to *the complete loss of muscle function in one or more muscle groups.* Paralysis (-plegia) may be accompanied by loss of sensation. Most episodes of paralysis in adults are due to CVA and spinal cord injury. Paralysis may be described as being flaccid or spastic. Flaccid paralysis is described as flabby or lack of muscle control and is caused by damaged nerves. With spastic paralysis there is stiff and poorly coordinated muscle control. It is due to CNS disorders such as cerebral palsy. Infantile paralysis or polio is a contagious viral infection that destroys the motor neurons in the grey matter (polio means "grey") of the brain stem and the spinal cord. Bell's palsy is a weakness or paralysis of one side of the face in response to inflammation of the facial nerve (CN VII). The word part paresis means "slight paralysis," as in hemiparesis (slight paralysis or weakness of the right or left half of the body). Gastroparesis causes weak stomach (gastr/o- = stomach) muscle contractions and delayed gastric emptying. Vocal cord paresis causes diminishment in voice quality and volume.
paresthesia	para- -esthesia	alongside of or abnormal sensation or feeling	*Refers to abnormal sensation such as burning, numbness, prickling, or tingling.* Paresthesias can be caused by lesions of both the central and peripheral nervous system and often are symptomatic of other disorders such as multiple sclerosis and diabetes mellitus. **Anesthesia** is *a lack of sensation* and hyperesthesia is *an increased sensitivity to a sensory stimulus (skin/touch).*
peripheral neuropathy	neur/o- -path/o- -y	nerve disease condition of	*A loss of normal sensation caused by peripheral nerve damage.* There are many causes of neuropathies. The pain has different intensities (severe to mild), multiple distribution patterns (hands, foot, pain), and a variety of descriptions (numbness, burning, tingling, prickly, akin to electric shock).
spinal cord injury			*Any condition or event that damages the spinal cord.* Complete transection of the cord produces quadriplegia or paraplegia, depending on the level of injury. Immediately after the injury, the person experiences spinal shock that may last from several hours to several weeks.

Get Ready for Exams!

Summary Outline

I. Autonomic or Visceral Reflexes
- A. What they do: autonomic nerves reflexively regulate organ function.
- B. Pathway: the sequence is receptor activation, sensory input (→ CNS), motor neuron response, and effector response.

II. Organization and Function of the Autonomic Nervous System
- A. Divisions of the ANS: two divisions
  1. Sympathetic nervous system, called *fight or flight*
  2. Parasympathetic nervous system, called *feed and breed*
- B. Autonomic terminology and autonomic pharmacology
  1. Drugs that affect the sympathetic nervous system are called *sympathomimetic* and *sympatholytic*.
  2. Drugs that affect the parasympathetic nervous system are called *parasympathomimetic* (vagomimetic) and *parasympatholytic* (vagolytic).
- C. Autonomic tone and vasomotor tone
  1. Background firing of the ANS causes autonomic tone.

2. Background sympathetic stimulation of the blood vessels causes vasomotor or sympathetic tone.

III. Autonomic Nervous System: Neurons

A. Numbers and ganglia
1. Preganglionic fibers are fibers that extend from the CNS to the ganglia.
2. Postganglionic fibers are fibers that extend from the ganglia to the effector or target organ.

B. Neurons of the sympathetic nervous system
1. The sympathetic nervous system is called the *thoracolumbar outflow*.
2. The sympathetic ganglia are located in a chain close to the spinal cord; the chain is called *paravertebral ganglia*.
3. The adrenal medulla secretes hormones that mimic the sympathetic nervous system.

C. Neurons of the parasympathetic nervous system
1. The parasympathetic nervous system is called the *craniosacral outflow*.
2. Some parasympathetic fibers travel with cranial nerves; most parasympathetics run with the vagus nerve (CN X).

D. Naming fibers and neurotransmitters
1. Cholinergic fibers secrete acetylcholine (ACh).
2. Adrenergic fibers secrete norepinephrine (NE).

E. Neurotransmitters: termination of activity
1. ACh is degraded immediately by acetylcholinesterase.
2. NE activity is ended primarily by reuptake of the NE into the nerve terminal and by MAO activity in the nerve terminal. Distally, NE is degraded by COMT.

IV. Receptors of the Autonomic Nervous System

A. Cholinergic receptors
1. Activated by ACh
2. Two types: muscarinic and nicotinic (and subtypes)

B. Adrenergic receptors
1. Activated by NE
2. Two types: alpha and beta (and subtypes)

C. Receptor activation and blockade can be determined by examining Tables 12-1, 12-3, and 12-4.

D. Autonomic receptors—doing autonomic pharmacology
1. Clinical examples where drugs target autonomic receptors

Review Your Knowledge

Matching: Sympathetic or Parasympathetic

Directions: Indicate if the following statements describe the sympathetic nervous system (S) or the parasympathetic nervous system (P).

1. ___ Paravertebral ganglia
2. ___ Feed-and-breed function
3. ___ Thoracolumbar outflow
4. ___ Postganglionic fiber is adrenergic.
5. ___ The target organs are stimulated by norepinephrine (NE).
6. ___ Fight-or-flight function
7. ___ The postganglionic fiber is cholinergic.
8. ___ The target organs are stimulated by acetylcholine (ACh).
9. ___ Craniosacral outflow
10. ___ The effects of this system are more widespread and prolonged.

Matching: Norepinephrine or Acetylcholine

Directions: Indicate if the statements are descriptive of norepinephrine (NE) or acetylcholine (ACh).

1. ___ Secreted by adrenergic fibers
2. ___ Causes activation of alpha-adrenergic receptors
3. ___ Secreted by the postganglionic fibers of the parasympathetic nervous system
4. ___ Causes activation of muscarinic receptors
5. ___ Action terminated by acetylcholinesterase, an enzyme located within the synapse
6. ___ Action terminated by reuptake of the neurotransmitter and MAO
7. ___ Causes activation of beta-adrenergic receptors
8. ___ Causes activation of nicotinic receptors, including the N_M receptors in the neuromuscular junction of skeletal muscle
9. ___ Mediates fight or flight (postganglionic)
10. ___ Mediates feed and breed

Multiple Choice

1. Which of the following is least related to the sympathetic nervous system?
- **a.** Includes the paravertebral ganglia
- **b.** Is also called the *fight-or-flight* response
- **c.** Is also called *craniosacral outflow*
- **d.** Uses norepinephrine as a transmitter

2. Which of the following is most related to the parasympathetic nervous system?
- **a.** Uses norepinephrine as a postganglionic transmitter
- **b.** Mediates feed-and-breed activities
- **c.** Is also called the *fight-or-flight* response
- **d.** Postganglionic fiber is adrenergic

3. What is the role of monoamine oxidase (MAO)?
- **a.** Destroys norepinephrine
- **b.** Activates the muscarinic receptors
- **c.** Activates the $beta_1$-adrenergic receptors
- **d.** Inactivates acetylcholine

4. Activation of the $beta_2$-adrenergic receptors
- **a.** is a response to the binding of ACh.
- **b.** causes wheezing.
- **c.** dilates the breathing passages.
- **d.** slows the heart rate.

5. Activation of the muscarinic receptors
- **a.** dilates the breathing passages.
- **b.** slows the heart rate.
- **c.** dilates the pupil.
- **d.** is a response to norepinephrine.

6. Blockade of the $alpha_1$-adrenergic receptors is the basis for what group of drugs?
- **a.** Hypoglycemic agents
- **b.** Antihypertensive drugs
- **c.** Cardiac stimulants
- **d.** Bronchodilators

7. Pupillary dilation, an increase in heart rate, and an inability to urinate are effects of
   a. alpha$_1$-adrenergic activation.
   b. beta$_2$-adrenergic activation.
   c. muscarinic blockade.
   d. vagomimetic activity.
8. A vagolytic drug exerts the same effects as
   a. a sympathomimetic agent.
   b. a beta$_1$-adrenergic agonist.
   c. a muscarinic agonist.
   d. an antimuscarinic agent.
9. Fight or flight, paravertebral ganglia, and norepinephrine are most related to
   a. cholinergic fibers.
   b. sympathetic nervous system.
   c. nicotinic and muscarinic receptors.
   d. craniosacral outflow.
10. Feed and breed, craniosacral outflow, and ACh are most related to the
    a. sympathetic nervous system.
    b. adrenergic fibers.
    c. nicotinic and muscarinic receptors.
    d. paravertebral ganglia.

Go Figure

1. **According to Figure 12-1**
   a. The sympathetic nervous system is called the *craniosacral outflow*.
   b. The parasympathetic nervous system is called the *thoracolumbar outflow*.
   c. Activation of the craniosacral outflow mediates a calming effect.
   d. Fight-or-flight best describes craniosacral outflow.
2. **According to Figure 12-2**
   a. All preganglionic fibers secrete ACh.
   b. All postganglionic fibers secrete ACh.
   c. Cholinergic fibers are restricted to the parasympathetic nervous system.
   d. Adrenergic fibers are restricted to the parasympathetic nervous system.
3. **According to Figure 12-2**
   a. The postganglionic fibers of the sympathetic nervous system are longer than those of the parasympathetic nervous system.
   b. All fibers of the sympathetic nervous system secrete norepinephrine.
   c. Paravertebral ganglia are found only within the parasympathetic nervous system.
   d. The ganglia of sympathetic fibers are found near or in the organ of innervation.
4. **According to Figure 12-3**
   a. ACh activates muscarinic receptors.
   b. Parasympathetic nervous system discharge activates muscarinic receptors.
   c. Sympathetic nervous system discharge activates alpha- and beta-adrenergic receptors.
   d. All of the above are true.
5. **According to Tables 12-3 and 12-4**
   a. Activation of the muscarinic receptors decreases heart rate.
   b. Activation of the nicotinic receptors on skeletal muscle is an autonomic effect.
   c. Activation of the adrenergic receptors decreases heart rate and dilates all blood vessels.
   d. All of the above are true.