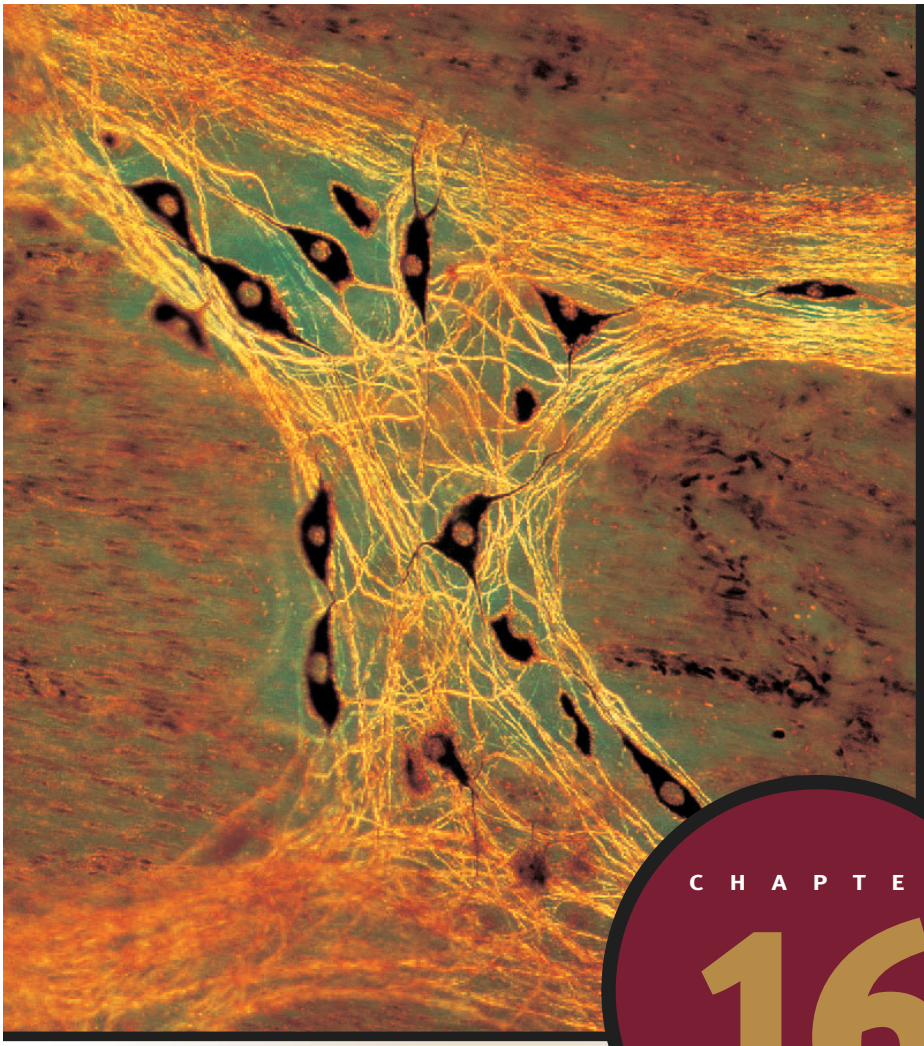

Light photomicrograph from a section of the small intestine, showing the nerve cells of the enteric plexus. These nerve cells regulate the contraction of smooth muscle and the secretion of glands within the intestinal wall.

CHAPTER 16

Autonomic Nervous System

During a picnic on a sunny spring day, it is easy to concentrate on the delicious food and the pleasant surroundings. Maintenance of homeostasis, however, requires no conscious thought. The autonomic nervous system (ANS) helps to keep body temperature at a constant level by controlling the activity of sweat glands and the amount of blood flowing through the skin. The ANS helps to regulate the complex activities necessary for the digestion of food. The movement of absorbed nutrients to tissues is possible because the ANS controls heart rate, which helps to maintain the blood pressure necessary to deliver blood to tissues. Without the ANS, all of the activities necessary to maintain homeostasis would be overwhelming.

A functional knowledge of the ANS enables you to predict general responses to a variety of stimuli, explain responses to changes in environmental conditions, comprehend symptoms that result from abnormal autonomic functions, and understand how drugs affect the ANS. This chapter examines the autonomic nervous system by *contrasting the somatic and autonomic nervous systems* (548); describing the *anatomy of the autonomic nervous system* (549), the *physiology of the autonomic nervous system* (555), and the *regulation of the autonomic nervous system* (559); and examining *functional generalizations about the autonomic nervous system* (562).

Contrasting the Somatic and Autonomic Nervous Systems

Objective

- ***Compare the structural and functional differences between the somatic and autonomic nervous systems.***

The peripheral nervous system (PNS) is composed of sensory and motor neurons. Sensory neurons carry action potentials from the periphery to the central nervous system (CNS), and motor neurons carry action potentials from the CNS to the periphery. Motor neurons are either somatic motor neurons, which innervate skeletal muscle, or autonomic motor neurons, which innervate smooth muscle, cardiac muscle, and glands.

Although axons of autonomic, somatic, and sensory neurons are in the same nerves, the proportion varies from nerve to nerve. For example, nerves innervating smooth muscle, cardiac muscle, and glands consist primarily of autonomic neurons; and nerves innervating skeletal muscles consist primarily of somatic neurons. Some cranial nerves such as the olfactory, optic, and vestibulocochlear nerves are composed entirely of sensory neurons.

The cell bodies of somatic motor neurons are in the CNS, and their axons extend from the CNS to skeletal muscle (figure 16.1*a*). The ANS, on the other hand, has two neurons in a series extending between the CNS and the organs innervated (figure 16.1*b*). The first neurons of the series are called **preganglionic neurons.** Their cell bodies are located within either the brainstem or the spinal cord, and their axons extend to autonomic ganglia located outside the CNS. The **autonomic ganglia** contain the cell bodies of the second neurons of the series, which are called **postganglionic neurons.** The preganglionic neurons synapse with the postganglionic neurons in the autonomic ganglia. The axons of the postganglionic neurons extend to effector organs, where they synapse with their target tissues.

Many movements controlled by the somatic nervous system are conscious, whereas ANS functions are unconsciously controlled. The effect of somatic motor neurons on skeletal muscle is always excitatory, but the effect of the ANS on target tissues can be excitatory or inhibitory. For example, after a meal, the ANS can stimulate stomach activities, but during exercise, the ANS can inhibit those activities. Table 16.1 summarizes the differences between the somatic nervous system and the ANS.

Sensory neurons are not classified as somatic or autonomic. These neurons propagate action potentials from sensory receptors to the CNS and can provide information for reflexes mediated through the somatic nervous system or the ANS. For example, stimulation of pain receptors can initiate somatic reflexes such as the withdrawal reflex and autonomic reflexes such as an increase in heart rate. Although some sensory neurons primarily affect somatic functions and others primarily influence autonomic functions, functional overlap makes attempts to classify sensory neurons as either somatic or autonomic meaningless.

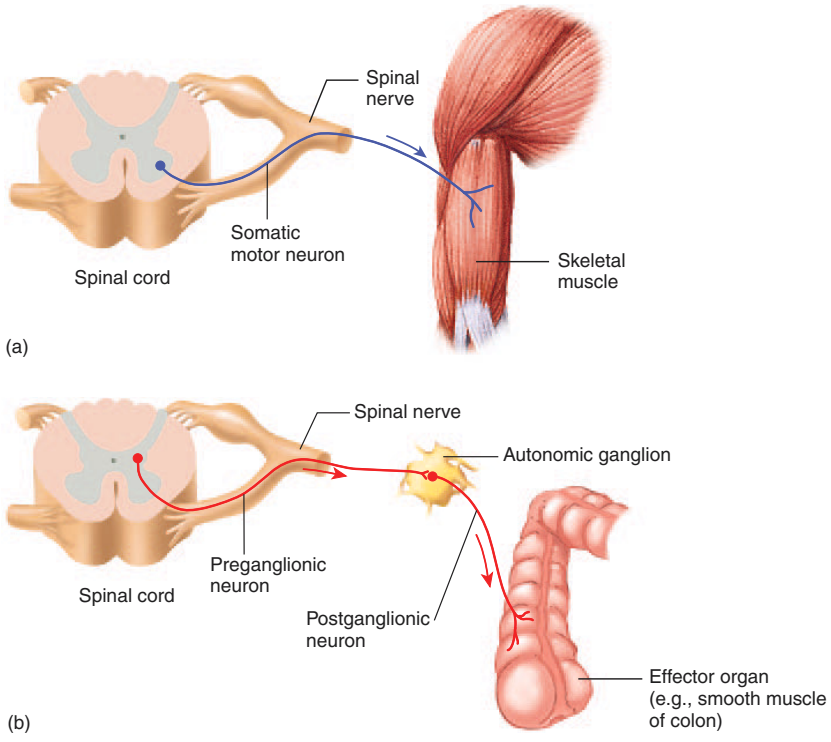

Figure 16.1 Organization of Somatic and Autonomic Nervous System Neurons

(*a*) The cell body of the somatic neuron is in the CNS, and its axon extends to the skeletal muscle. (*b*) The cell body of the preganglionic neuron is in the CNS, and its axon extends to the autonomic ganglion and synapses with the postganglionic neuron. The postganglionic neuron extends to and synapses with its effector organ.

Table 16.1 Comparison of the Somatic and Autonomic Nervous Systems

Features	Somatic Nervous System	Autonomic Nervous System
Target tissues	Skeletal muscle	Smooth muscle, cardiac muscle, and glands
Regulation	Controls all conscious and unconscious movements of skeletal muscle	Unconscious regulation, although influenced by conscious mental functions
Response to stimulation	Skeletal muscle contracts	Target tissues are stimulated or inhibited
Neuron arrangement	One neuron extends from the central nervous system (CNS) to skeletal muscle	Two neurons in series; the preganglionic neuron extends from the CNS to an autonomic ganglion, and the postganglionic neuron extends from the autonomic ganglion to the target tissue
Neuron cell body location	Neuron cell bodies are in motor nuclei of the cranial nerves and in the ventral horn of the spinal cord	Preganglionic neuron cell bodies are in autonomic nuclei of the cranial nerves and in the lateral part of the spinal cord; postganglionic neuron cell bodies are in autonomic ganglia
Number of synapses	One synapse between the somatic motor neuron and the skeletal muscle	Two synapses; first is in the autonomic ganglia; second is at the target tissue
Axon sheaths	Myelinated	Preganglionic axons are myelinated; postganglionic axons are unmyelinated
Neurotransmitter substance	Acetylcholine	Acetylcholine is released by preganglionic neurons; either acetylcholine or norepinephrine is released by postganglionic neurons
Receptor molecules	Receptor molecules for acetylcholine are nicotinic	In autonomic ganglia, receptor molecules for acetylcholine are nicotinic; in target tissues, receptor molecules for acetylcholine are muscarinic, whereas receptor molecules for norepinephrine are either α- or β-adrenergic

1. *Contrast the somatic nervous system with the ANS for each of the following:*
   a. *the number of neurons between the CNS and effector organ*
   b. *the location of neuron cell bodies*
   c. *the structures each innervates*
   d. *inhibitory or excitatory effects*
   e. *conscious or unconscious control*
2. *Why are sensory neurons not classified as somatic or autonomic?*
3. *Define the terms preganglionic neuron, postganglionic neuron, and autonomic ganglia.*

Anatomy of the Autonomic Nervous System

Objectives

- *Compare the structural differences between the sympathetic and parasympathetic divisions.*
- *Describe the structure of the enteric nervous system.*
- *Describe how sympathetic and parasympathetic axons are distributed to organs.*

The ANS is subdivided into the **sympathetic** and the **parasympathetic divisions** and the **enteric** (en-ter′ik; bowels) **nervous system (ENS).** The sympathetic and parasympathetic divisions differ structurally in (1) the location of their preganglionic neuron cell bodies within the CNS and (2) the location of their autonomic ganglia.

The enteric nervous system is a complex network of neuron cell bodies and axons within the wall of the digestive tract. An important part of this network is sympathetic and parasympathetic neurons. For this reason, the enteric nervous system is considered to be part of the ANS.

Sympathetic Division

Cell bodies of sympathetic preganglionic neurons are in the lateral horns of the spinal cord gray matter between the first thoracic (T1) and the second lumbar (L2) segments (figure 16.2). Because of the location of the preganglionic cell bodies, the sympathetic division is sometimes called the **thoracolumbar division.** The axons of the preganglionic neurons pass through the ventral roots of spinal nerves T1–L2, course through the spinal nerves for a short distance, leave these nerves, and project to autonomic ganglia on either side of the vertebral column behind the parietal pleura. These ganglia are called **sympathetic chain ganglia,** because they are connected to one another and form a chain, or **paravertebral ganglia,** because they are located along both sides of the vertebral column. Only the ganglia from T1–L2 receive preganglionic axons from the spinal cord, although the sympathetic chain extends into the cervical and sacral regions so that one pair of ganglia is associated with nearly every pair of spinal nerves. The cervical ganglia usually fuse during fetal development so only two or three pairs exist in the adult.

The axons of preganglionic neurons are small in diameter and myelinated. The short connection between a spinal nerve and a sympathetic chain ganglion through which the preganglionic

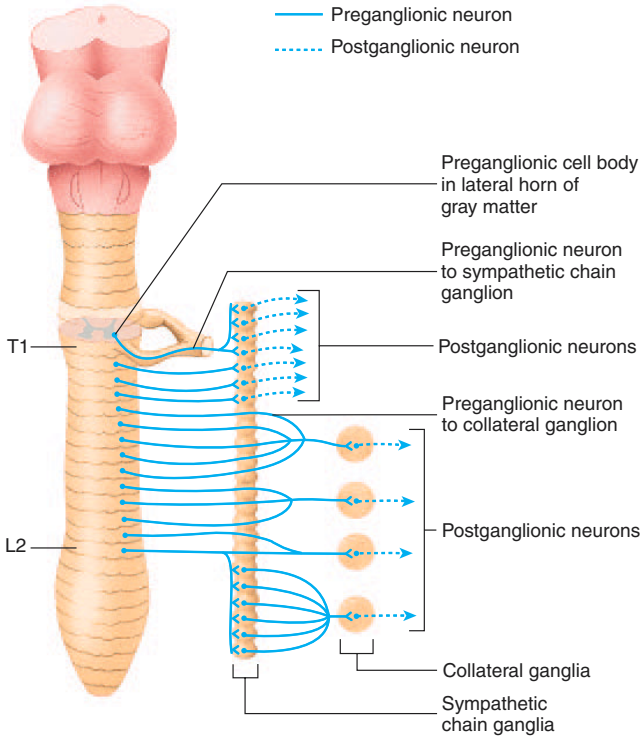

Figure 16.2 Sympathetic Division

The location of sympathetic preganglionic (*solid blue*) and postganglionic (*dotted blue*) neurons. The preganglionic cell bodies are in the lateral gray matter of the thoracic and lumbar parts of the spinal cord. The cell bodies of the postganglionic neurons are within the sympathetic chain ganglia or within collateral ganglia.

axons pass is called a **white ramus communicans** (rā′mĭs kŏ-mū′ni-kans; pl., rami communicantes, rā′mī kŏ-mū-ni-kan′tēz) because of the whitish color of the myelinated axons (figure 16.3).

Sympathetic axons exit the sympathetic chain ganglia by the following four routes:

1. *Spinal nerves* (figure 16.3*a*). Preganglionic axons synapse with postganglionic neurons in sympathetic chain ganglia at the same level that the preganglionic axons enter the sympathetic chain. Alternatively, preganglionic axons pass either superiorly or inferiorly through one or more ganglia and synapse with postganglionic neurons in a sympathetic chain ganglion at a different level. Axons of the postganglionic neurons pass through a **gray ramus communicans** and reenter a spinal nerve. Postganglionic axons are not myelinated, thereby giving the gray ramus communicans its grayish color. The postganglionic axons then project through the spinal nerve to the organs they innervate.
2. *Sympathetic nerves* (figure 16.3*b*). Preganglionic axons enter the sympathetic chain and synapse in a sympathetic chain ganglion at the same or a different level with postganglionic neurons. The postganglionic axons leaving the sympathetic chain ganglion form **sympathetic nerves.**
3. *Splanchnic* (splangk′nik) *nerves* (figure 16.3*c*). Some preganglionic axons enter sympathetic chain ganglia and, without synapsing, exit at the same or a different level to form **splanchnic nerves.** Those preganglionic axons extend to **collateral,** or **prevertebral, ganglia,** where they synapse with postganglionic neurons. Axons of the postganglionic neurons leave the collateral ganglia through small nerves that extend to target organs.
4. *Innervation to the adrenal gland* (figure 16.3*d*). The splanchnic nerve innervation to the adrenal glands is different from other ANS nerves because it consists of only preganglionic neurons. Axons of the preganglionic neurons do not synapse in sympathetic chain ganglia or in collateral ganglia. Instead, the axons pass through those ganglia and synapse with cells in the adrenal medulla. The **adrenal medulla** (me-dool′ă) is the inner portion of the adrenal gland and consists of specialized cells derived during embryonic development from neural crest cells (see figure 13.13), which are the same population of cells that give rise to the postganglionic cells of the ANS. Adrenal medullary cells are round in shape, have no axons or dendrites, and are divided into two groups. About 80% of the cells secrete **epinephrine** (ep′i-nef′rin), also called **adrenaline** (ă-dren′ă-lin), and about 20% secrete **norepinephrine** (nōr′ep-i-nef′rin), also called **noradrenaline** (nōr-ă-dren′ă-lin). Stimulation of these cells by preganglionic axons causes the release of epinephrine and norepinephrine. These substances circulate in the blood and affect all tissues having receptors to which they can bind. The general response to epinephrine and norepinephrine released from the adrenal medulla is to prepare the individual for physical activity. Secretions of the adrenal medulla are considered hormones because they are released into the general circulation and travel some distance to the tissues in which they have their effect (see chapters 17 and 18).

Parasympathetic Division

Parasympathetic preganglionic neurons are located both superior and inferior to the thoracic and lumbar regions of the spinal cord where sympathetic preganglionic neurons are found. The cell bodies of parasympathetic preganglionic neurons are either within cranial nerve nuclei in the brainstem or within the lateral parts of the gray matter in the sacral region of the spinal cord from S2–S4 (figure 16.4). For that reason, the parasympathetic division is sometimes called the **craniosacral** (krā′nē-ō-sā′krăl) **division.**

Axons of the parasympathetic preganglionic neurons from the brain are in **cranial nerves** III, VII, IX, and X; and from the spinal cord in **pelvic nerves.** The preganglionic axons course through these nerves to **terminal ganglia** where they synapse with postganglionic neurons. The axons of the postganglionic neurons extend relatively short distances from the terminal ganglia to the target organs. The terminal ganglia are either near or embedded

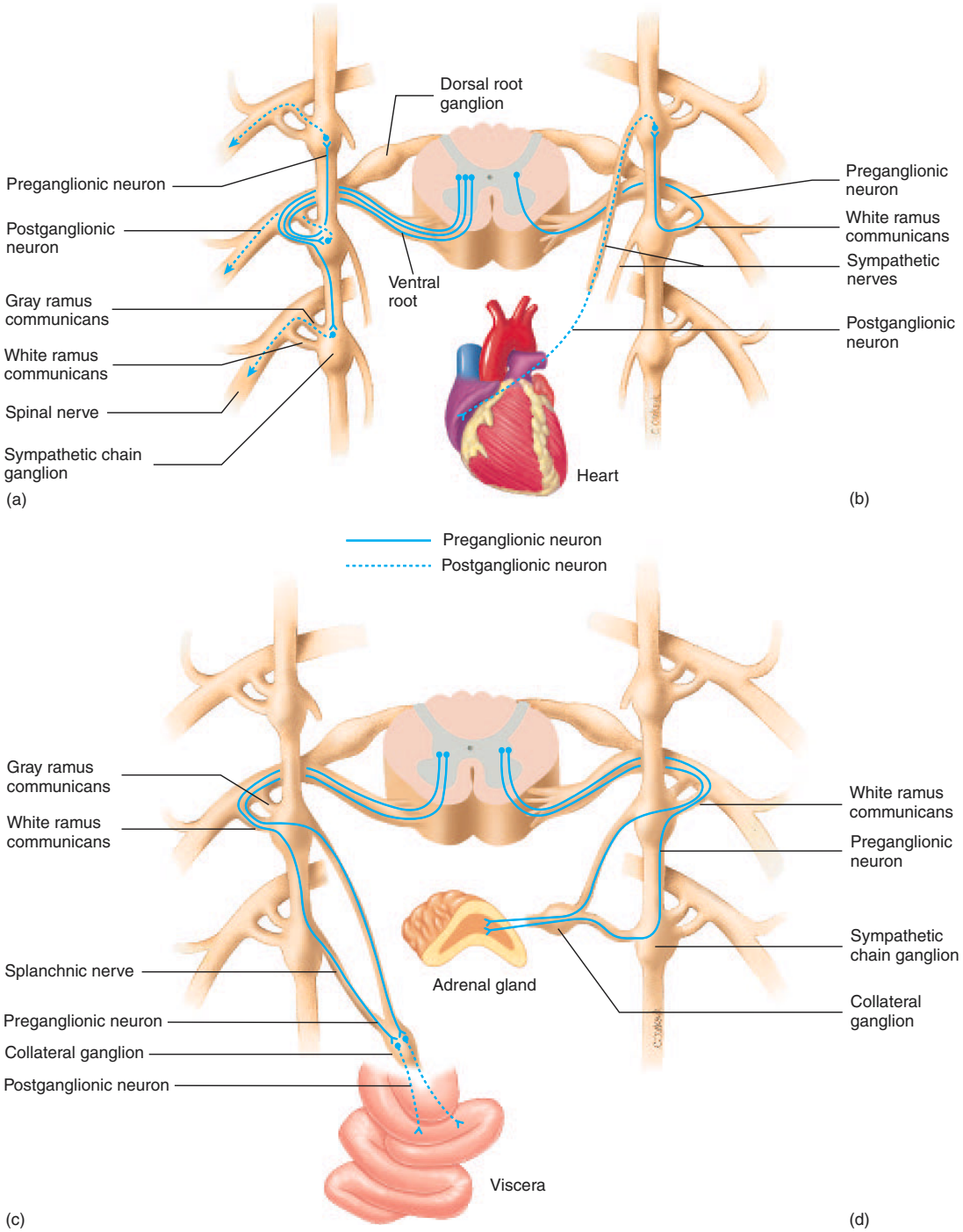

Figure 16.3 Routes Taken by Sympathetic Axons

(*a*) Preganglionic axons enter a sympathetic chain ganglion through a white ramus communicans. Some axons synapse with a postganglionic neuron at the level of entry; others ascend or descend to other levels before synapsing. Postganglionic axons exit the sympathetic chain ganglia through gray rami communicantes and enter spinal nerves. (*b*) Like part (*a*), except that postganglionic axons exit through a sympathetic nerve (only an ascending axon is illustrated). (*c*) Preganglionic neurons do not synapse in the sympathetic chain ganglia but exit in splanchnic nerves and extend to collateral ganglia, where they synapse with postganglionic neurons. (*d*) Like part (*c*), except that preganglionic axons extend to the adrenal medulla, where they synapse. There are no postganglionic neurons.

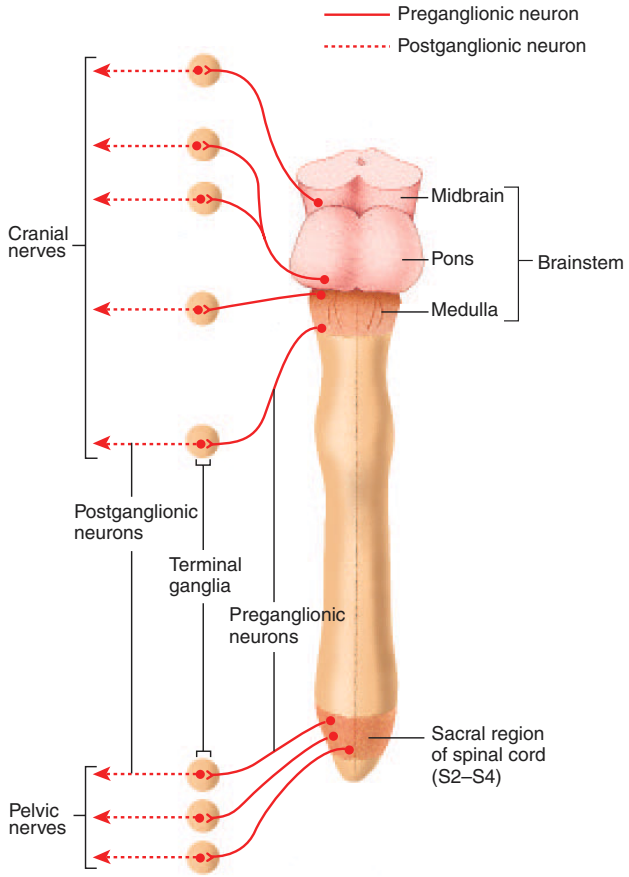

Figure 16.4 Parasympathetic Division

The location of parasympathetic preganglionic (*solid red*) and postganglionic (*dotted red*) neurons. The preganglionic neuron cell bodies are in the brainstem and the lateral gray matter of the sacral part of the spinal cord, and the postganglionic neuron cell bodies are within terminal ganglia.

within the walls of the organs innervated by the parasympathetic neurons. Many of the parasympathetic ganglia are small in size, but some, such as those in the wall of the digestive tract, are large.

Table 16.2 summarizes the structural differences between the sympathetic and parasympathetic divisions.

4. ***For both the sympathetic and parasympathetic divisions, state (a) the locations of their preganglionic neuron cell bodies and (b) the names and locations of their ganglia.***
5. ***What types of axon (preganglionic or postganglionic, myelinated or unmyelinated) are found in white and gray rami communicantes?***
6. ***Where do preganglionic neurons synapse with postganglionic neurons that are found in spinal and sympathetic nerves?***
7. ***Where do preganglionic axons that form splanchnic nerves (except those to the adrenal gland) synapse with postganglionic neurons?***
8. ***What is unusual about the splanchnic nerve innervation to the adrenal gland? What do the specialized cells of the adrenal medulla secrete, and what is the effect of these substances?***

Enteric Nervous System

The enteric nervous system consists of nerve plexuses within the wall of the digestive tract (see figure 24.2). The plexuses have contributions from three sources: (1) sensory neurons that connect the digestive tract to the CNS, (2) ANS motor neurons that connect the CNS to the digestive tract, and (3) enteric neurons, which are confined to the enteric plexuses. The CNS is capable of monitoring the digestive tract through sensory neurons and controlling its smooth muscle and glands through ANS motor neurons.

There are several major types of enteric neurons: (1) Enteric sensory neurons can detect changes in the chemical composition of the contents of the digestive tract or detect stretch of the digestive tract wall. (2) Enteric motor neurons can stimulate or inhibit smooth muscle contraction and gland secretion. (3) Enteric

Table 16.2 Comparison of the Sympathetic and Parasympathetic Divisions

Features	Sympathetic Division	Parasympathetic Division
Location of preganglionic cell body	Lateral horns of spinal cord gray matter (T1–L2)	Brainstem and lateral parts of spinal gray matter (S2–S4)
Outflow from the CNS	Spinal nerves Sympathetic nerves Splanchnic nerves	Cranial nerves Pelvic nerves
Ganglia	Sympathetic chain ganglia along spinal cord for spinal and sympathetic nerves; collateral ganglia for splanchnic nerves	Terminal ganglia near or on effector organ
Number of postganglionic neurons for each preganglionic neuron	Many (much divergence)	Few (less divergence)
Relative length of neurons	Short preganglionic Long postganglionic	Long preganglionic Short postganglionic

interneurons connect enteric sensory and motor neurons to each other. Although the enteric neurons are capable of controlling the activities of the digestive tract completely independently of the CNS, normally the two systems work together.

PREDICT 1

Would the ANS ganglia found in the enteric plexus be chain ganglia, collateral ganglia, or terminal ganglia? What type (preganglionic or postganglionic) of sympathetic and parasympathetic axons contribute to the enteric plexus?

The Distribution of Autonomic Nerve Fibers

Sympathetic Division

Sympathetic axons pass from the sympathetic chain ganglia to their target tissues through spinal, sympathetic, and splanchnic nerves. The sympathetic and splanchnic nerves can join **autonomic nerve plexuses,** which are complex, interconnected neural networks formed by neurons of the sympathetic and parasympathetic divisions. In addition, the axons of sensory neurons contribute to these plexuses.

The autonomic nerve plexuses typically are named according to organs they supply or to blood vessels along which they are found. For example, the cardiac plexus supplies the heart and the thoracic aortic plexus is found along the thoracic aorta. Plexuses following the route of blood vessels is a major means by which autonomic axons are distributed throughout the body.

The major means by which sympathetic axons reach organs include the following:

1. *Spinal nerves.* From all levels of the sympathetic chain, some postganglionic axons project through gray rami communicates to spinal nerves. The axons extend to the same structures innervated by the spinal nerves and supply sweat glands in the skin, smooth muscle in skeletal and skin blood vessels, and the smooth muscle of the arrector pili. See figure 12.14 for the distribution of spinal nerves to the skin.
2. *Head and neck nerve plexuses.* Most of the sympathetic nerve supply to the head and neck is derived from the superior cervical ganglion of the sympathetic chain (figure 16.5). Postganglionic axons of sympathetic nerves form plexuses that extend superiorly to the head and inferiorly to the neck. The plexuses give off branches to supply sweat glands in the skin, smooth muscle in skeletal and skin blood vessels, and the smooth muscle of the arrector pili. Axons from the plexuses also join branches of the trigeminal nerves (cranial nerve V) to supply the skin of the face, the salivary glands, the iris, and the ciliary muscles of the eye.
3. *Thoracic nerve plexuses.* The sympathetic supply for organs of the thorax is mainly derived from the cervical and upper five thoracic sympathetic chain ganglia. Postganglionic axons in sympathetic nerves contribute to the **cardiac plexus,** supplying the heart, the **pulmonary plexus,** supplying the lungs, and other thoracic plexuses (see figure 16.5).
4. *Abdominopelvic nerve plexuses.* Sympathetic chain ganglia from T5 and below mainly supply the abdominopelvic organs. The preganglionic axons of splanchnic nerves synapse with postganglionic neurons in the collateral ganglia of abdominopelvic nerve plexuses. Postganglionic axons from the collateral ganglia innervate smooth muscle and glands in the abdominopelvic organs. There are several abdominopelvic nerve plexuses (see figure 16.5). The **celiac** (sē′lē-ak) **plexus** has two large celiac ganglia and other smaller ganglia. It supplies the diaphragm, stomach, spleen, liver, gallbladder, adrenal glands, kidneys, testes, and ovaries. The **superior mesenteric** (mez-en-ter′ik) **plexus** includes the superior mesenteric ganglion and supplies the pancreas, small intestine, ascending colon, and the transverse colon. The **inferior mesenteric plexus** includes the inferior mesenteric ganglion and supplies the transverse colon to the rectum. The **hypogastric plexuses** supply the descending colon to the rectum, the urinary bladder, and reproductive organs in the pelvis.

Parasympathetic Division

Parasympathetic outflow is through cranial and sacral nerves. Branches of these nerves either supply organs or join nerve plexuses to be distributed to organs. The major means by which parasympathetic axons reach organs include the following:

1. *Cranial nerves supplying the head and neck.* Three pairs of cranial nerves have parasympathetic preganglionic axons that extend to terminal ganglia in the head. Postganglionic neurons from the terminal ganglia supply nearby structures. The parasympathetic cranial nerves, their terminal ganglia, and the structures innervated are (see figure 16.5 and table 14.1):
   a. The **oculomotor (III) nerve,** through the **ciliary** (sil′ē-ar-ē) **ganglion,** supplies the ciliary muscles and the iris of the eye.
   b. The **facial (VII) nerve,** through the **pterygopalatine** (ter′i-gō-pal′ă-tīn) **ganglion,** supplies the lacrimal gland and mucosal glands of the nasal cavity and palate. The facial nerve, through the **submandibular ganglion,** also supplies the submandibular and sublingual salivary glands.
   c. The **glossopharyngeal (IX) nerve,** through the **otic** (ō′tik) **ganglion,** supplies the parotid salivary gland.
2. *The vagus nerve and thoracic nerve plexuses.* Although cranial nerve X, the **vagus nerve,** has somatic motor and sensory functions in the head and neck, its parasympathetic distribution is to the thorax and abdomen. Preganglionic axons extend through the vagus nerves to the thorax, where they pass through branches of the vagus nerves to contribute to the cardiac plexus, which supplies the heart, and the pulmonary plexus, which supplies the lungs. The vagus nerves continue down the esophagus, and give off branches to form the **esophageal plexus.**
3. *Abdominal nerve plexuses.* After the esophageal plexus passes through the diaphragm, some of the vagal preganglionic

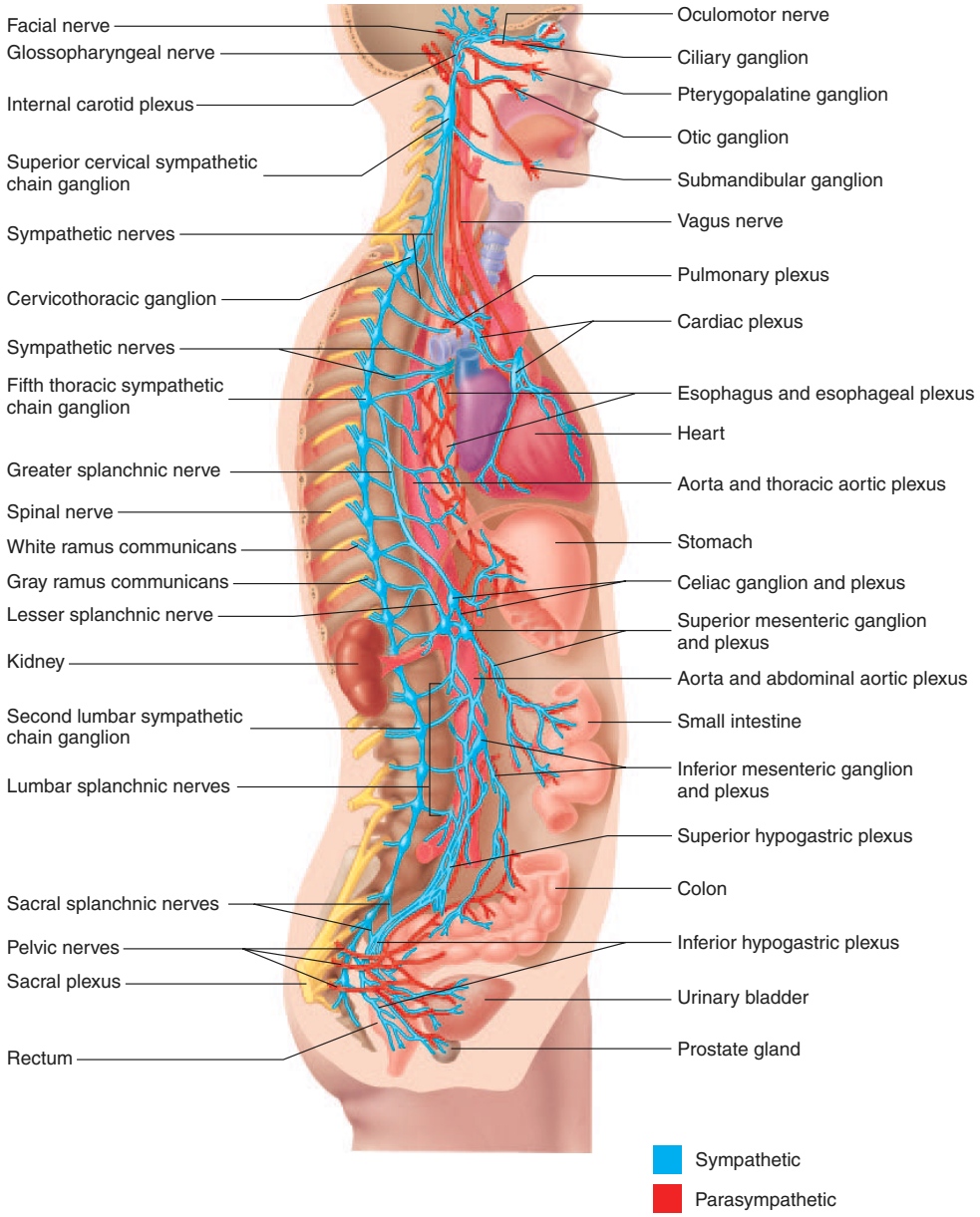

Figure 16.5 Distribution of Autonomic Nerve Fibers

Sympathetic supply: (1) spinal nerves to limbs and body, (2) head and neck by sympathetic nerves from the superior cervical chain ganglia, (3) thoracic organs by sympathetic nerves from the cervical and thoracic chain ganglia (to T5) supplying thoracic nerve plexuses, and (4) abdominopelvic nerves by splanchnic nerves from chain ganglia below T5 supplying abdominopelvic nerve plexuses. *Parasympathetic supply:* (1) head and neck by cranial nerves and their ganglia, (2) thoracic organs by vagus nerves supplying thoracic plexuses, (3) abdominal organs by vagus nerves supplying abdominal nerve plexuses, and (4) pelvic nerves from S2–S4.

axons supply terminal ganglia in the wall of the stomach, while others contribute to the celiac and superior mesenteric plexuses. Through these plexuses, the preganglionic axons supply terminal ganglia in the walls of the gallbladder, biliary ducts, pancreas, small intestine, ascending colon, and the transverse colon.

4. *Pelvic nerves and pelvic nerve plexuses.* Parasympathetic preganglionic axons whose cell bodies are in the S2–S4 region of the spinal cord pass to the ventral rami of spinal nerves and enter the pelvic nerves. The pelvic nerves supply the transverse colon to the rectum, and they also contribute to the hypogastric plexus. The hypogastric plexus and its derivatives supply the lower colon, rectum, urinary bladder, and organs of the reproductive system in the pelvis.

Sensory Neurons in Autonomic Nerve Plexuses

Although not strictly part of the ANS, the axons of sensory neurons run alongside ANS axons within ANS nerves and plexuses. Some of these sensory neurons are part of reflex arcs regulating organ activities. Sensory neurons also transmit pain and pressure sensations from organs to the CNS. The cell bodies of these sensory neurons are found in the dorsal root ganglia and in the sensory ganglia of certain cranial nerves, which are swellings on the nerves close to their attachment to the brain.

Effects of Spinal Cord Injury on ANS Functions

Spinal cord injury can damage nerve tracts and interrupt control of autonomic neurons by ANS centers in the brain. For the parasympathetic division, effector organs innervated through the sacral region of the spinal cord are affected, but most effector organs still have normal parasympathetic function because they are innervated by the vagus nerve. For the sympathetic division, brain control of sympathetic neurons is lost below the site of the injury. The higher the level of injury, the greater the number of body parts affected.

9. ***Where is the enteric nervous system located? Describe the types of neurons found in it.***
10. ***Define autonomic nerve plexuses. How are they typically named?***
11. ***Describe the four major ways by which sympathetic axons pass from sympathetic chain ganglia to reach organs. Name four thoracic and four abdominopelvic autonomic nerve plexuses.***
12. ***List the four major means by which parasympathetic axons reach organs. List the cranial nerves and ganglia that supply the head and neck. What cranial nerve supplies the thoracic and abdominal nerve plexuses? To what plexus do pelvic nerves contribute?***

P R E D I C T 2

Starting in the small intestine and ending with the ganglia where their cell bodies are located, trace the route for sensory axons passing alongside sympathetic axons. Name all of the plexuses, nerves, ganglia, etc. that the sensory axon passes through. Also trace the route for sensory neurons passing alongside parasympathetic axons.

Physiology of the Autonomic Nervous System

Objective

- ***Describe the major neurotransmitters and receptors of the ANS.***

Neurotransmitters

Sympathetic and parasympathetic nerve endings secrete one of two neurotransmitters. If the neuron secretes acetylcholine, it is a **cholinergic** (kol-in-er′jik) **neuron,** and if it secretes norepinephrine, it is an **adrenergic** (ad-rĕ-ner′jik) **neuron.** All preganglionic neurons of the sympathetic and parasympathetic divisions and all postganglionic neurons of the parasympathetic division are cholinergic. Almost all postganglionic neurons of the sympathetic division are adrenergic, but a few postganglionic neurons that innervate thermoregulatory sweat glands are cholinergic (figure 16.6).

In recent years, substances in addition to the regular neurotransmitters have been extracted from ANS neurons. These substances include nitric oxide; fatty acids, such as prostaglandins; peptides, such as gastrin, somatostatin, cholecystokinin, vasoactive intestinal peptide, enkephalins, and substance P; and monoamines, such as dopamine, serotonin, and histamine. The specific role that many of these compounds play in the regulation of the ANS is unclear, but they appear to function as either neurotransmitters or neuromodulator substances (see chapter 11).

Receptors

Receptors for acetylcholine and norepinephrine are located in the plasma membrane of certain cells (table 16.3). The combination of neurotransmitter and receptor functions as a signal to cells, causing them to respond. Depending on the type of cell, the response can be excitatory or inhibitory.

Cholinergic Receptors

Receptors to which acetylcholine binds are called **cholinergic receptors.** They have two major structurally different forms. **Nicotinic** (nik-ō-tin′ik) **receptors** also bind to nicotine, an alkaloid substance found in tobacco; and **muscarinic** (mŭs-kă-rin′ik) **receptors** also bind to muscarine, an alkaloid extracted from some poisonous mushrooms. Although nicotine and muscarine are not naturally in the human body, they demonstrate differences in the two classes of cholinergic receptors. Nicotine binds to nicotinic receptors but not to muscarinic receptors, whereas muscarine binds to muscarinic receptors but not to nicotinic receptors. On the other hand, nicotinic and muscarinic receptors are very similar because acetylcholine binds to and activates both types of receptors.

The membranes of all postganglionic neurons in autonomic ganglia and the membranes of skeletal muscle cells have nicotinic receptors. The membranes of effector cells that respond to acetylcholine released from postganglionic neurons have muscarinic receptors.

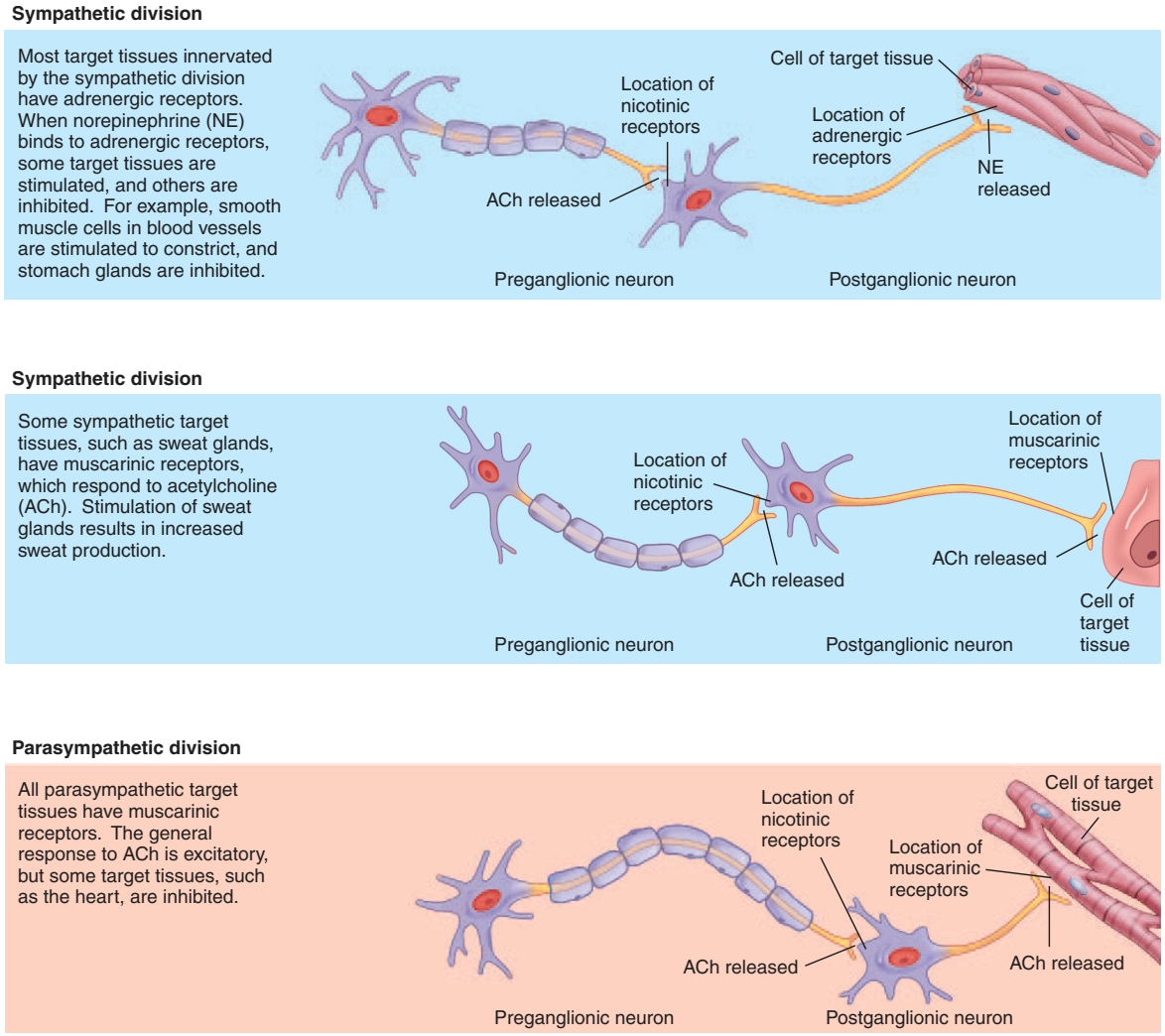

Figure 16.6 Location of ANS Receptors

Nicotinic receptors are on the cell bodies of both sympathetic and parasympathetic postganglionic cells in the autonomic ganglia. *Abbreviations: NE,* norepinephrine; *ACh,* acetylcholine.

PREDICT 3

Would structures innervated by the sympathetic division or the parasympathetic division be affected after the consumption of nicotine? After the consumption of muscarine? Explain.

Acetylcholine binding to nicotinic receptors has an excitatory effect because it results in the direct opening of Na^+ channels and the production of action potentials. When acetylcholine binds to muscarinic receptors, the cell's response is mediated through G proteins (see chapters 3 and 17). The response is either excitatory or inhibitory, depending on the target tissue in which the receptors are found. For example, acetylcholine binds to muscarinic receptors in cardiac muscle, thereby reducing heart rate; and acetylcholine binds to muscarinic receptors in smooth muscle cells of the stomach, thus increasing its rate of contraction.

Adrenergic Receptors

Norepinephrine or epinephrine can bind to **adrenergic receptors.** Norepinephrine that is released from adrenergic postganglionic neurons of the sympathetic division (see figure 16.6) diffuses across the synapse and binds to receptor molecules within the plasma membranes of effector organs. Epinephrine and norepinephrine released from the adrenal glands and carried to effector organs by the blood can also bind to adrenergic receptors. The response of cells to norepinephrine or epinephrine binding to adrenergic receptors is mediated through G proteins (see chapters 3 and 17).

Adrenergic receptors are subdivided into two major categories: **alpha (α) receptors** and **beta (β) receptors,** each of which has subtypes. The main subtypes for alpha receptors are α_1- and α_2-adrenergic receptors and for beta receptors are β_1- and

Table 16.3 Effects of the Sympathetic and Parasympathetic Divisions on Various Tissues

Organ	Sympathetic Effects and Receptor Type*	Parasympathetic Effects and Receptor Type*
Adipose tissue	Fat breakdown and release of fatty acids (α_2, β_1)	None
Arrector pili muscle	Contraction (α_1)	None
Blood (platelets)	Increases coagulation (α_2)	None
Blood vessels		
Arterioles (carry blood to tissues)		
Digestive organs	Constriction (α_1)	None
Heart	Dilation (β_2), constriction (α_1)†	None
Kidneys	Constriction (α_1, α_2); dilation (β_1, β_2)	None
Lungs	Dilation (β_2), constriction (α_1)	None
Skeletal muscle	Dilation (β_2), constriction (α_1)	None
Skin	Constriction (α_1, α_2)	None
Veins (carry blood away from tissues)	Constriction (α_1, α_2), dilation (β_2)	
Eye		
Ciliary muscle	Relaxation for far vision (β_2)	Contraction for near vision (m)
Pupil	Dilated (α_1)‡	Constricted (m)‡
Gallbladder	Relaxation (β_2)	Contraction (m)
Glands		
Adrenal	Release of epinephrine and norepinephrine (n)	None
Gastric	Decreases gastric secretion (α_2)	Increases gastric secretion (m)
Lacrimal	Slight tear production (α)	Increases tear secretion (m)
Pancreas	Decreases insulin secretion (α_2)	Increases insulin secretion (m)
	Decreases exocrine secretion (α)	Increases exocrine secretion (m)
Salivary	Constriction of blood vessels and slight production of a thick, viscous saliva (α_1)	Dilation of blood vessels and thin, copious saliva (m)
Sweat		
Apocrine	Thick, organic secretion (m)	None
Merocrine	Watery sweat from most of the skin (m); sweat from the palms and soles (α_1)	None
Heart	Increases rate and force of contraction (β_1, β_2)	Decreases rate of contraction (m)
Liver	Glucose released into blood (α_1, β_2)	None
Lungs	Dilates air passageways (β_2)	Constricts air passageways (m)
Metabolism	Increases up to 100% (α, β)	None
Sex organs	Ejaculation (α_1), erection§	Erection (m)
Skeletal muscles	Breakdown of glycogen to glucose (β_2)	None
Stomach and intestines		
Wall	Decreases tone (α_1, α_2, β_2)	Increases motility (m)
Sphincter	Increases tone (α_1)	Decreases tone (m)
Urinary bladder		
Wall (detrusor)	None	Contraction (m)
Neck of bladder	Contraction (α_1)	Relaxation (m)
Internal urinary sphincter	Contraction (α_1)	Relaxation (m)

*When known, receptor subtypes are indicated. The receptors are α_1- and α_2-adrenergic, β_1- and β_2-adrenergic, nicotinic cholinergic (n), and muscarinic cholinergic (m).
†Normally blood flow increases through coronary arteries because of increased demand by cardiac tissue for oxygen (local control of blood flow is discussed in chapter 21). In experiments that isolate the coronary arteries, sympathetic nerve stimulation, acting through α-adrenergic receptors, causes vasoconstriction. The β-adrenergic receptors are relatively insensitive to sympathetic nerve stimulation but can be activated by epinephrine released from the adrenal gland and by drugs. As a result, coronary arteries vasodilate.
‡Contraction of the radial muscles of the iris causes the pupil to dilate. Contraction of the circular muscles causes the pupil to constrict (see chapter 15).
§Decreased stimulation of alpha receptors by the sympathetic division can cause vasodilation of penile blood vessels, resulting in an erection.

Clinical Focus The Influence of Drugs on the Autonomic Nervous System

Some drugs that affect the ANS have important therapeutic value in treating certain diseases because they can increase or decrease activities normally controlled by the ANS. Chemicals that affect the ANS are also found in medically hazardous substances such as tobacco and insecticides.

Direct-acting and indirect-acting drugs influence the ANS. Direct-acting drugs bind to ANS receptors to produce their effects. For example, **stimulating agents** bind to specific receptors and activate them, and **blocking agents** bind to specific receptors and prevent them from being activated. The main topic of this Clinical Focus is direct-acting drugs. It should be noted, however, that some indirect-acting drugs produce a stimulatory effect by causing the release of neurotransmitters or by preventing the metabolic breakdown of neurotransmitters. Other indirect-acting drugs produce an inhibitory effect by preventing the biosynthesis or release of neurotransmitters.

Drugs That Bind to Nicotinic Receptors

Drugs that bind to nicotinic receptors and activate them are **nicotinic agents.** Although these agents have little therapeutic value and are mainly of interest to researchers, nicotine is medically important because of its presence in tobacco. Nicotinic agents bind to the nicotinic receptors on all postganglionic neurons within autonomic ganglia and produce stimulation. Responses to nicotine are variable and depend on the amount taken into the body. Because nicotine stimulates the postganglionic neurons of both the sympathetic and parasympathetic divisions, much of the variability of its effects results from the opposing actions of these divisions. For example, in response to the nicotine contained in a cigarette, the heart rate may either increase or decrease. Heart rate rhythm tends to become less regular as a result of the simultaneous actions on the sympathetic division, which increases the heart rate, and the parasympathetic division, which decreases the heart rate. Blood pressure tends to increase because of the constriction of blood vessels, which are almost exclusively innervated by sympathetic neurons. In addition to its influence on the ANS, nicotine also affects the CNS; therefore, not all of its effects can be explained on the basis of action on the ANS. Nicotine is extremely toxic, and small amounts can be lethal.

Drugs that bind to and block nicotinic receptors are called **ganglionic blocking agents** because they block the effect of acetylcholine on both parasympathetic and sympathetic postganglionic neurons. The effect of these substances on the sympathetic division, however, overshadows the effect on the parasympathetic division. For example, trimethaphan camsylate (trī-meth′ă-fan kam′sil-āt), used to treat high blood pressure, blocks sympathetic stimulation of blood vessels, causing the blood vessels to dilate, which decreases blood pressure. Ganglionic blocking agents have limited uses because they affect both sympathetic and parasympathetic ganglia. Whenever possible, more selective drugs, which affect receptors of target tissues, are now used.

Drugs That Bind to Muscarinic Receptors

Drugs that bind to and activate muscarinic receptors are **muscarinic,** or **parasympathomimetic** (par-ă-sim′pă-thō-mi-met′ik), **agents.** These drugs activate the muscarinic receptors of target tissues of the parasympathetic division and the muscarinic receptors of sweat glands, which

β_2-adrenergic receptors. Activation of α_1 and β_1 receptors generally produces a stimulatory response. For example, stimulation of α_1 receptors in most smooth muscle and β_1 receptors in cardiac muscle results in contraction. The response to the activation of α_2 and β_2 receptors varies so much with different target cells that no simple generalization about their effects is appropriate. Activation of α_2 receptors on platelets promotes blood clotting but decreases insulin secretion by the pancreas; activation of β_2 receptors stimulates the liver to release glucose but causes smooth muscle relaxation.

The α_1 and β_1 receptors are typically found in the membranes of target cells in the vicinity of sympathetic nerve terminals. Thus, the sympathetic division controls target cells with α_1 and β_1 receptors through sympathetic nerves. For example, at rest, stimulation of α_1 receptors at sympathetic nerve terminals in smooth muscle cells of blood vessels results in partial constriction of the vessels. The sympathetic division regulates blood flow by slightly increasing or decreasing stimulation of the blood vessels. Increased stimulation causes further constriction and reduces blood flow, whereas decreased stimulation results in dilation and increases blood flow. Control of blood vessel diameter plays an important role in the regulation of blood flow and blood pressure (see chapter 20).

The α_2 and β_2 receptors are typically found in parts of the membrane that are not near nerve terminals releasing norepinephrine. These receptors respond to epinephrine and norepinephrine released from the adrenal glands into the blood. During exercise, epinephrine and norepinephrine bind to β_2 receptors and causes blood vessel dilation in skeletal muscles.

Dopamine and the Treatment of Shock

Norepinephrine is produced from a precursor molecule called dopamine. Certain sympathetic neurons release dopamine, which binds to dopamine receptors. Dopamine is structurally similar to norepinephrine and also binds to beta receptors. Dopamine hydrochloride has been used successfully to treat circulatory shock because it can bind to dopamine receptors in kidney blood vessels. The resulting vasodilation increases blood flow to the kidneys and prevents kidney damage. At the same time, dopamine can bind to beta receptors in the heart, causing stronger contractions.

are innervated by the sympathetic division. Muscarine causes increased sweating, increased secretion of glands in the digestive system, decreased heart rate, constriction of the pupils, and contraction of respiratory, digestive, and urinary system smooth muscles. Bethanechol (be-than′ĕ-kol) chloride is a parasympathomimetic agent used to stimulate the urinary bladder following surgery, because the general anesthetics used for surgery can temporarily inhibit a person's ability to urinate.

Drugs such as atropine that bind to and block the action of muscarinic receptors are **muscarinic,** or **parasympathetic, blocking agents.** These drugs dilate the pupil of the eye and are used during eye examinations to help the examiner see the retina through the pupil. They also decrease salivary secretion and are used during surgery to prevent patients from choking on excess saliva while they are anesthetized.

Drugs That Bind to Alpha and Beta Receptors

Drugs that activate adrenergic receptors are **adrenergic,** or **sympathomimetic** (sim′-pă-thō-mi-met′ik) **agents.** Drugs such as phenylephrine (fen-il-ef′rin) stimulate alpha receptors, which are numerous in the smooth muscle cells of certain blood vessels, especially in the digestive tract and the skin. These drugs increase blood pressure by causing vasoconstriction. On the other hand, albuterol (al-bū′ter-ol) is a drug that selectively activates beta receptors in cardiac muscle and bronchiolar smooth muscle. β-adrenergic-stimulating agents are sometimes used to dilate bronchioles in respiratory disorders such as asthma and are occasionally used as cardiac stimulants.

Drugs that bind to and block the action of alpha receptors are **α-adrenergic-blocking agents.** For example, prazosin (prā′zō-sin) hydrochloride is used to treat hypertension. By binding to alpha receptors in the smooth muscle of blood vessel walls, prazosin hydrochloride blocks the normal effects of norepinephrine released from sympathetic postganglionic neurons. Thus, the blood vessels relax, and blood pressure decreases.

Propranolol (prō-pran′ō-lōl) is an example of a **β-adrenergic-blocking agent.** These drugs are sometimes used to treat high blood pressure, some types of cardiac arrhythmias, and patients recovering from heart attacks. Blockage of the beta receptors within the heart prevents sudden increases in heart rate and thus decreases the probability of arrhythmic contractions.

Future Research

Our present knowledge of the ANS is more complicated than the broad outline presented here. In fact, each of the major receptor types has subtype receptors. For example, α-adrenergic receptors are subdivided into the following subgroups: α_{1A}-, α_{1B}-, α_{2A}-, and α_{2B}-adrenergic receptors. The exact number of subtypes in humans is not yet known; however, their existence suggests the possibility of designing drugs that affect only one subtype. For example, a drug that affects the blood vessels of the heart but not other blood vessels might be developed. Such drugs could produce specific effects yet would not produce undesirable side effects because they would act only on specific target tissues.

13. *Define cholinergic and adrenergic neurons. Which neurons of the ANS are cholinergic and adrenergic?*
14. *Name the two major subtypes of cholinergic receptors. Where are they located? When acetylcholine binds to each subtype, does it result in an excitatory or inhibitory cell response?*
15. *Name the two major subtypes of adrenergic receptors. Where are they located?*
16. *On what part of a cell are α_1- and β_1-adrenergic receptors typically found? How are they typically stimulated? What type of response is generally produced when they are stimulated?*
17. *On what part of a cell are α_2- and β_2-adrenergic receptors typically found? How are they typically stimulated? What type of responses are produced when they are stimulated?*

PREDICT 4

Injection of a small dose of epinephrine causes vasodilation of skeletal muscle blood vessels. An injection of a large dose, however, causes vasoconstriction. Explain.

Regulation of the Autonomic Nervous System

Objectives

- *Explain how autonomic and local reflexes help to maintain homeostasis.*
- *Describe the role of the hypothalamus in controlling the ANS.*

Much of the regulation of structures by the ANS occurs through autonomic reflexes, but input from the cerebrum, hypothalamus, and other areas of the brain allows conscious thoughts and actions, emotions, and other CNS activities to influence autonomic functions. Without the regulatory activity of the ANS, an individual has limited ability to maintain homeostasis.

Autonomic reflexes, like other reflexes, involve sensory receptors; sensory, association, and motor neurons; and effector cells (figure 16.7; see chapter 12). For example, **baroreceptors** (stretch receptors) in the walls of large arteries near the heart detect

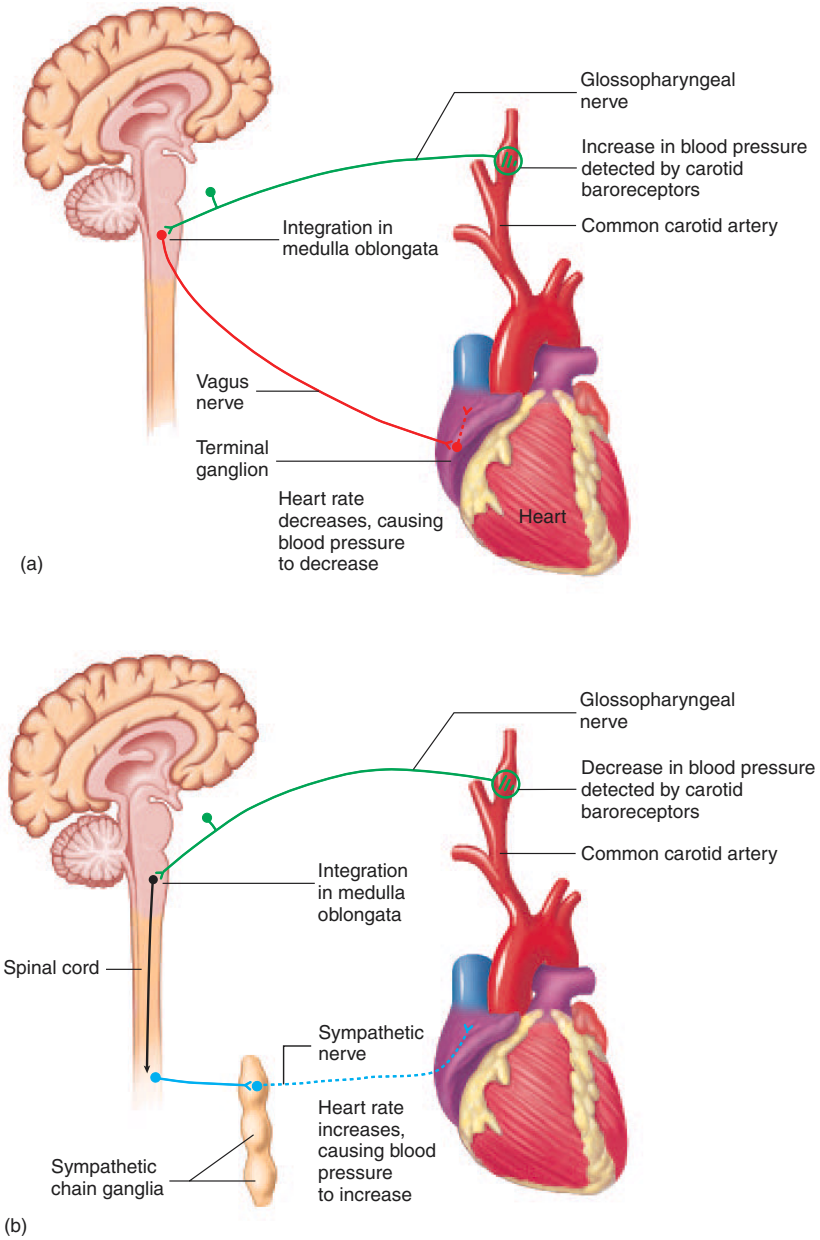

Figure 16.7 Autonomic Reflexes

Sensory input from the carotid baroreceptors is sent along the glossopharyngeal nerves to the medulla oblongata. The input is integrated in the medulla, and motor output is sent to the heart. (*a*) **Parasympathetic reflex.** Increased blood pressure results in increased stimulation of the heart by the vagus nerves, which increases inhibition of the heart and lowers heart rate. (*b*) **Sympathetic reflex.** Decreased blood pressure results in increased stimulation of the heart by sympathetic nerves, which, in turn, increases stimulation of the heart and increases heart rate and the force of contraction.

changes in blood pressure, and sensory neurons transmit information from the baroreceptors through the glossopharyngeal and vagus nerves to the medulla oblongata. Interneurons in the medulla oblongata integrate the information, and action potentials are produced in autonomic neurons that extend to the heart. If baroreceptors detect a change in blood pressure, autonomic reflexes change heart rate, which returns blood pressure to normal. A sudden increase in blood pressure initiates a parasympathetic reflex that inhibits cardiac muscle cells and reduces heart rate, thus bringing blood pressure down toward its normal value. Conversely, a sudden decrease in blood pressure initiates a sympathetic reflex, which stimulates the heart to increase its rate and force of contraction, thus increasing blood pressure.

P R E D I C T 5

Sympathetic neurons stimulate sweat glands in the skin. Predict how they function to control body temperature during exercise and during exposure to cold temperatures.

Other autonomic reflexes participate in the regulation of blood pressure (see chapter 21). For example, numerous sympathetic neurons transmit a low but relatively constant frequency of action potentials that stimulate blood vessels throughout the body, keeping them partially constricted. If the vessels constrict further, blood pressure increases; and if they dilate, blood pressure decreases. Thus, altering the frequency of action potentials delivered to blood vessels along sympathetic neurons can either raise or lower blood pressure.

P R E D I C T 6

How would sympathetic reflexes that control blood vessels respond to a sudden decrease and a sudden increase in blood pressure?

The brainstem and the spinal cord contain important autonomic reflex centers responsible for maintaining homeostasis (figure 16.8). The hypothalamus, however, is in overall control of the ANS. Almost any type of autonomic response can be evoked by stimulating some part of the hypothalamus, which, in turn, stimulates ANS centers in the brainstem or spinal cord. Although there is overlap, stimulation of the posterior hypothalamus produces sympathetic responses, whereas stimulation of the anterior hypothalamus produces parasympathetic responses. In addition, the hypothalamus monitors and controls body temperature.

The hypothalamus has connections with the cerebrum and is an important part of the limbic system, which plays an important role in emotions. The hypothalamus integrates thoughts and emotions to produce ANS responses. Pleasant thoughts of a delicious banquet initiate increased secretion by salivary glands and by

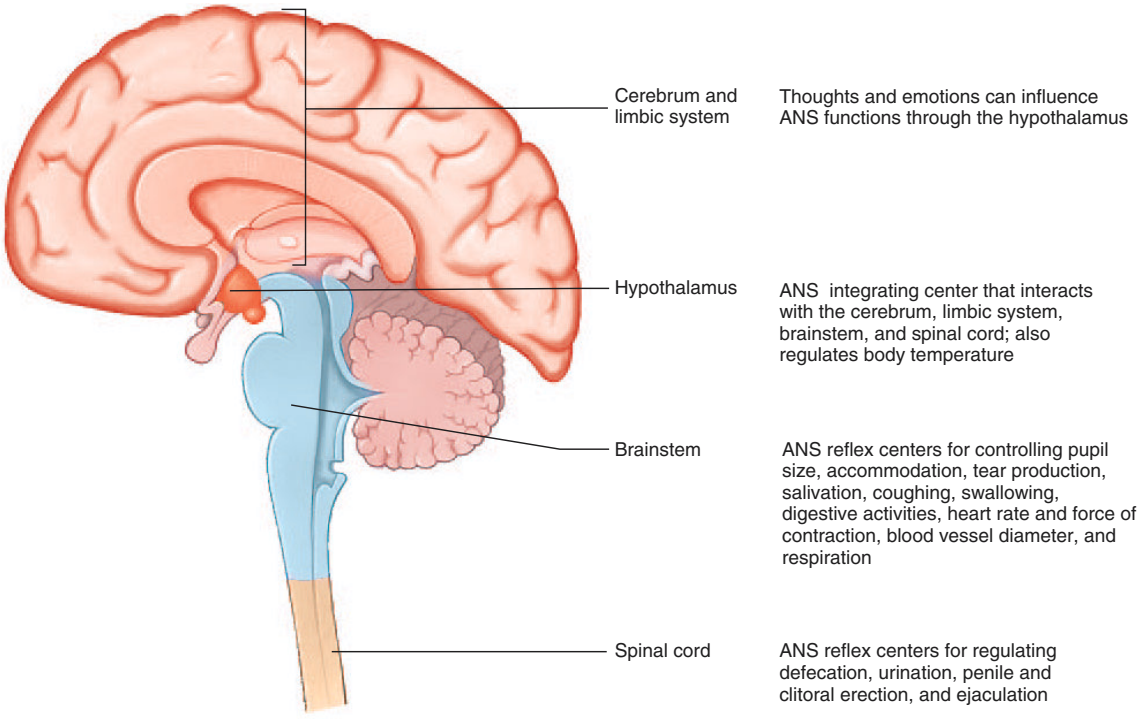

Figure 16.8 Influence of Higher Parts of the Brain on Autonomic Functions

The hypothalamus and the cerebrum influence the ANS. Neural pathways extend from the cerebrum to the hypothalamus and from the hypothalamus to neurons of the ANS.

Clinical Focus Biofeedback, Meditation, and the Fight-or-Flight Response

Biofeedback takes advantage of electronic instruments or other techniques to monitor and change subconscious activities, many of which are regulated by the ANS. Skin temperature, heart rate, and brain waves are monitored electronically. By watching the monitor and using biofeedback techniques, a person can learn how consciously to reduce heart rate and blood pressure and regulate blood flow in the limbs. For example, people claim that they can prevent the onset of migraine headaches or reduce their intensity by learning to dilate blood vessels in the skin of their forearms and hands. Increased blood vessel dilation increases skin temperature, which is correlated with a decrease in the severity of the migraine. Some people use biofeedback methods to relax by learning to reduce their heart rate or change the pattern of their brain waves. The severity of some stomach ulcers, high blood pressure, anxiety, and depression may be reduced by using biofeedback techniques.

Meditation is another technique that influences autonomic functions. Although numerous claims about the value of meditation include improving one's spiritual well-being, consciousness, and holistic view of the universe, it has been established that meditation does influence autonomic functions. Meditation techniques are useful in some people in reducing heart rate, blood pressure, severity of ulcers, and other symptoms that are frequently associated with stress.

The fight-or-flight response occurs when an individual is subjected to stress, such as a threatening, frightening, embarrasing, or exciting situation. Whether a person confronts or avoids a stressful situation, the nervous system and the endocrine system are involved either consciously or unconsciously. The autonomic part of the fight-or-flight response results in a general increase in sympathetic activity, including heart rate, blood pressure, sweating, and other responses, that prepare the individual for physical activity. The fight-or-flight response is adaptive because it also enables the individual to resist or move away from a threatening situation.

glands within the stomach and increased smooth muscle contractions within the digestive system. These responses are controlled by parasympathetic neurons. Emotions like anger increase blood pressure by increasing heart rate and constricting blood vessels through sympathetic stimulation.

The enteric nervous system is involved with autonomic and local reflexes that regulate the activity of the digestive tract. Autonomic reflexes help control the digestive tract because sensory neurons of the enteric plexuses supply the CNS with information about intestinal contents and ANS neurons to the enteric plexuses affect the responses of smooth muscle and glands within the digestive tract wall. For example, sensory neurons detecting stretch of the digestive tract wall send action potentials to the CNS. In response, the CNS sends action potentials out the ANS, causing smooth muscle in the digestive tract wall to contract.

The neurons of the enteric nervous system also operate independently of the CNS to produce local reflexes. A **local reflex** does not involve the CNS, but it does produce an involuntary, unconscious, stereotypic response to a stimulus. For example, sensory neurons not connected to the CNS detect stretch of the digestive tract wall. These sensory neurons send action potentials through the enteric plexuses to motor neurons, causing smooth muscle contraction or relaxation. See chapter 24 for more information on local reflexes.

18. *Name the components of an autonomic reflex. Describe the autonomic reflex that maintains blood pressure by altering heart rate or the diameter of blood vessels.*
19. *What part of the CNS stimulates ANS reflexes and integrates thoughts and emotions to produce ANS responses?*
20. *Define a local reflex. Explain how the enteric nervous system operates to produce local reflexes.*

Functional Generalizations About the Autonomic Nervous System

Objective

- ***Describe the generalizations that can be made about the ANS, and explain the limitations of these generalizations.***

Generalizations can be made about the function of the ANS on effector organs, but most of the generalizations have exceptions.

Stimulatory Versus Inhibitory Effects

Both divisions of the ANS produce stimulatory and inhibitory effects. For example, the parasympathetic division stimulates contraction of the urinary bladder and inhibits the heart, causing a decrease in heart rate. The sympathetic division causes vasoconstriction by stimulating smooth muscle contraction in blood vessel walls and produces dilation of lung air passageways by inhibiting smooth muscle contraction in the walls of the passageways. Thus, it is *not* true that one division of the ANS is always stimulatory and the other is always inhibitory.

Dual Innervation

Most organs that receive autonomic neurons are innervated by both the parasympathetic and the sympathetic divisions (figure 16.9). The gastrointestinal tract, heart, urinary bladder, and reproductive tract are examples (see table 16.3). Dual innervation of organs by both divisions of the ANS is not universal, however. Sweat glands and blood vessels, for example, are innervated by sympathetic neurons almost exclusively. In addition, most structures receiving dual innervation are not regulated equally by both

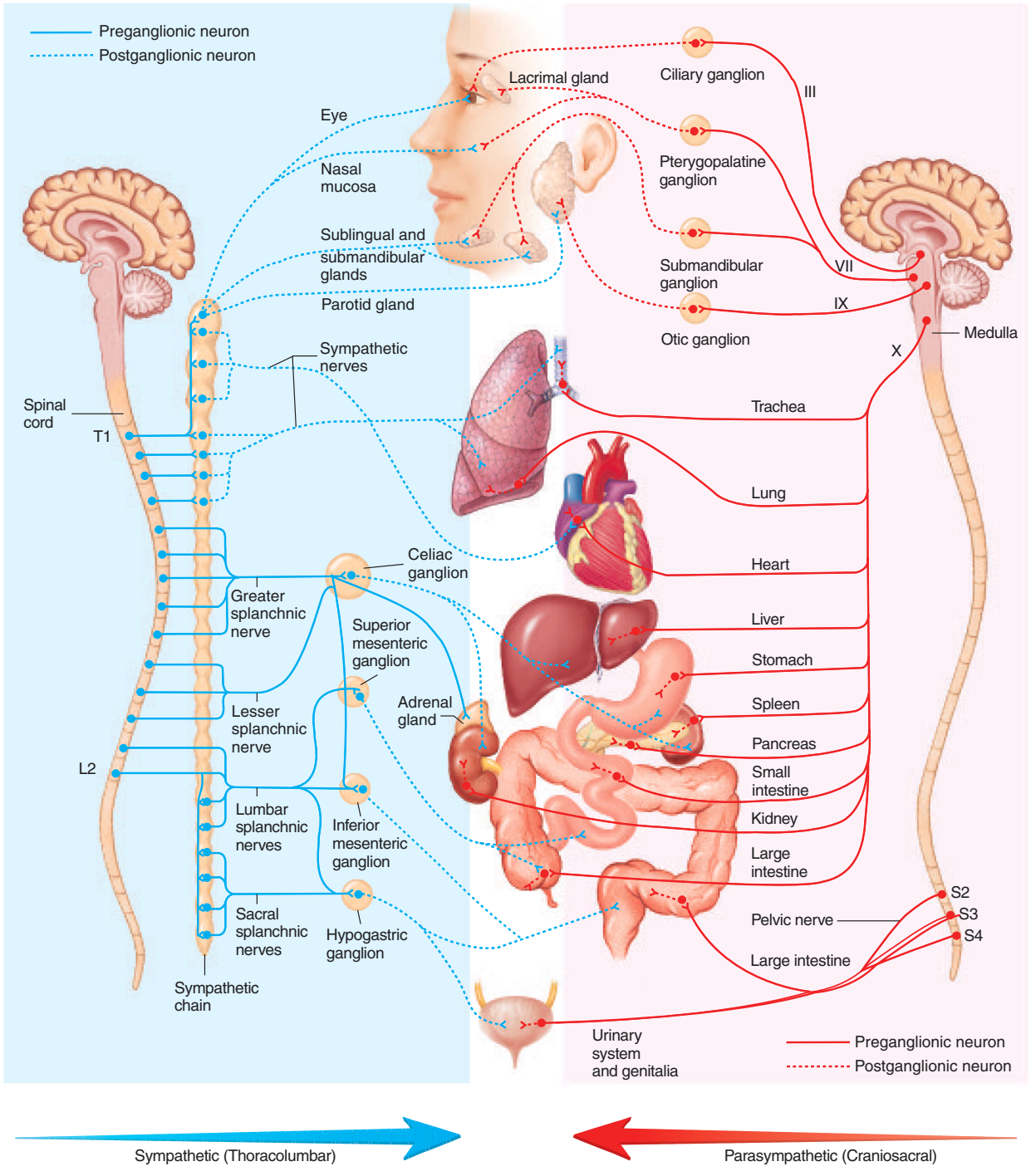

Figure 16.9 Innervation of Organs by the ANS

Preganglionic fibers are indicated by *solid lines*, and postganglionic fibers are indicated by *dashed lines*.

divisions. For example, parasympathetic innervation of the gastrointestinal tract is more extensive and exhibits a greater influence than does sympathetic innervation.

Opposite Effects

When a *single* structure is innervated by both autonomic divisions, the two divisions usually produce opposite effects on the structure. As a consequence, the ANS is capable of both increasing and decreasing the activity of the structure. In the gastrointestinal tract, for example, parasympathetic stimulation increases secretion from glands, whereas sympathetic stimulation decreases secretion. In a few instances, however, the effect of the two divisions is not clearly opposite. For example, both divisions of the ANS increase salivary secretion: the parasympathetic division initiates the production of a large volume of thin, watery saliva, and the sympathetic division causes the secretion of a small volume of viscous saliva.

Cooperative Effects

One autonomic division can coordinate the activities of *different* structures. For example, the parasympathetic division stimulates the pancreas to release digestive enzymes into the small intestine and stimulates contractions to mix the digestive enzymes with food within the small intestine. These responses enhance the digestion and absorption of the food.

Both divisions of the ANS can act together to coordinate the activity of *different* structures. In the male, the parasympathetic division initiates erection of the penis, and the sympathetic division stimulates the release of secretions from male reproductive glands and helps initiate ejaculation in the male reproductive tract.

General Versus Localized Effects

The sympathetic division has a more general effect than the parasympathetic division because activation of the sympathetic division often causes secretion of both epinephrine and norepinephrine from the adrenal medulla. These hormones circulate in the blood and stimulate effector organs throughout the body. Because circulating epinephrine and norepinephrine can persist for a few minutes before being broken down, they can also produce an effect for a longer time than the direct stimulation of effector organs by postganglionic sympathetic axons.

The sympathetic division diverges more than the parasympathetic division. Each sympathetic preganglionic neuron synapses with many postganglionic neurons, whereas each parasympathetic preganglionic neuron synapses with about two postganglionic neurons. Consequently, stimulation of sympathetic preganglionic neurons can result in greater stimulation of an effector organ.

Sympathetic stimulation often activates many different kinds of effector organs at the same time as a result of CNS stimulation or epinephrine and norepinephrine release from the adrenal medulla. It's possible, however, for the CNS to selectively activate effector organs. For example, vasoconstriction of cutaneous blood vessels in a cold hand is not always associated with an increased heart rate or other responses controlled by the sympathetic division.

Functions at Rest Versus Activity

In cases in which both sympathetic and parasympathetic neurons innervate a single organ, the sympathetic division has a major influence under conditions of physical activity or stress, whereas the parasympathetic division tends to have a greater influence under resting conditions. The sympathetic division does play a major role during resting conditions, however, by maintaining blood pressure and body temperature.

In general, the sympathetic division decreases the activity of organs not essential for the maintenance of physical activity and shunts blood and nutrients to structures that are active during physical exercise. This is sometimes referred to as the **fight-or-flight response** (see preceding Clinical Focus on "Biofeedback, Meditation, and the Fight-or-Flight Response"). Typical responses produced by the sympathetic division during exercise include:

1. Increased heart rate and force of contraction increase blood pressure and the movement of blood.
2. As skeletal or cardiac muscle contracts, oxygen and nutrients are used and waste products are produced. During exercise, a decrease in oxygen and nutrients and an accumulation of waste products are stimuli that cause vasodilation of muscle blood vessels (see local control of blood vessels in chapter 21). Vasodilation is beneficial because it increases blood flow, bringing needed oxygen and nutrients and removing waste products. Too much vasodilation, however, can cause a decrease in blood pressure that decreases blood flow. Increased stimulation of skeletal muscle blood vessels by sympathetic nerves during exercise causes vasoconstriction that prevents a drop in blood pressure (see chapter 21).
3. Increased heart rate and force of contraction potentially increases blood flow through tissues. Vasoconstriction of blood vessels in tissues not involved in exercise, such as abdominopelvic organs, reduces blood flow through them, thus making more blood available for the exercising tissues.
4. Dilation of air passageways increases air flow into and out of the lungs.
5. The availability of energy sources increases. Skeletal muscle cells and liver cells (hepatocytes) are stimulated to break down glycogen to glucose. Skeletal muscle cells use the glucose and liver cells release it into the blood for use by other tissues. Fat cells (adipocytes) break down triglycerides and release fatty acids into the blood, which are used as an energy source by skeletal and cardiac muscle.
6. As exercising muscles generate heat, body temperature increases. Vasodilation of blood vessels in the skin brings warm blood close to the surface, where heat is lost to the environment. Sweat gland activity increases, resulting in increased sweat production, and evaporation of the sweat removes additional heat.

Clinical Focus Disorders of the Autonomic Nervous System

Normal function of all components of the ANS is not required to maintain life, as long as environmental conditions are constant and optimal. Abnormal autonomic functions, however, markedly affect an individual's ability to respond to changing conditions. **Sympathectomy,** the removal of sympathetic ganglia, demonstrates this. The normal regulation of body temperature is lost following sympathectomy. In a hot environment, the ability to lose heat by increasing blood flow to the skin and by sweating is decreased. When exposed to the cold, the ability to reduce blood flow to the skin and conserve heat is decreased. Sympathectomy also results in low blood pressure caused by dilation of peripheral blood vessels and in the inability to increase blood pressure during periods of physical activity.

Orthostatic hypotension is a drop in blood pressure that occurs when a person who was sitting or lying down suddenly stands up. It is sometimes caused by disorders, such as diabetes mellitus, that decrease the frequency of action potentials in sympathetic nerves innervating blood vessels. Consequently, on standing, blood pools in dilated blood vessels in the lower extremities, less blood returns to the heart, and the amount of blood the heart pumps decreases. Blood pressure decreases, resulting in reduced blood flow to the brain, which causes fainting because of a lack of oxygen.

Raynaud's disease involves the spasmodic contraction of blood vessels in the periphery of the body, especially in the digits, and results in pale, cold hands that are prone to ulcerations and gangrene because of poor circulation. This condition can be caused by exaggerated sensitivity of blood vessels to sympathetic innervation. Preganglionic denervation (cutting the preganglionic neurons) is occasionally performed to alleviate the condition.

Hyperhidrosis (hī′per-hī-drō′sis), or excessive sweating, is caused by exaggerated sympathetic innervation of the sweat glands.

Achalasia (ak-ă-lā′zē-ă) is characterized by difficulty in swallowing and in controlling contraction of the esophagus where it enters the stomach, therefore interrupting normal peristaltic contractions of the esophagus. The swallowing reflex is controlled partly by somatic reflexes and partly by parasympathetic reflexes. The cause of achalasia can be abnormal parasympathetic regulation of the swallowing reflex. The condition is aggravated by emotions.

Dysautonomia (dis′aw-tō-nō′mē-ă), an inherited condition involving an autosomal-recessive gene, causes reduced tear gland secretion, poor vasomotor control, trouble in swallowing, and other symptoms. It is the result of poorly controlled autonomic reflexes.

Hirschsprung's disease, or **megacolon,** is caused by a functional obstruction in the lower colon and rectum. Ineffective parasympathetic stimulation and a predominance of sympathetic stimulation of the colon inhibit peristaltic contractions, causing feces to accumulate above the inhibited area. The resulting dilation of the colon can be so great that surgery is required to alleviate the condition.

7. The activities of organs not essential for exercise decrease. For example, the process of digesting food slows as digestive glands decrease their secretions and the contractions of smooth muscle that mix and move food through the gastrointestinal tract decrease.

Increased activity of the parasympathetic division is generally consistent with resting conditions. The acronym SLUDD can be used to remember activities that increase as a result of parasympathetic activity. SLUDD stands for *s*alivation, *l*acrimation (tear production), *u*rination, *d*igestion, and *d*efecation. Activities that decrease as a result of increased parasympathetic activity are heart rate, diameter of air passageways, and diameter of the pupils.

21. *What kinds of effects, excitatory or inhibitory, are produced by the sympathetic and parasympathetic divisions?*
22. *Give two exceptions to the generalization that organs are innervated by both divisions of the ANS.*
23. *When a single organ is innervated by both ANS divisions, do they usually produce opposite effects?*
24. *Explain how the ANS coordinates the activities of different organs.*
25. *Which ANS division produces the most general effects? How does this happen?*
26. *Use the fight-or-flight response and the acronym SLUDD to describe the responses produced by the ANS.*

PREDICT 7

Bethanechol (be-than′ĕ-kol) chloride is a drug that binds to muscarinic receptors. Explain why this drug can be used to promote emptying of the urinary bladder. Which of the following side effects would you predict: abdominal cramps, asthmatic attack, decreased tear production, decreased salivation, dilation of the pupils, or sweating.

S U M M A R Y

Contrasting the Somatic and Autonomic Nervous Systems (p. 548)

1. The cell bodies of somatic neurons are located in the CNS, and their axons extend to skeletal muscles, where they have an excitatory effect that usually is controlled consciously.
2. The cell bodies of the preganglionic neurons of the ANS are located in the CNS and extend to ganglia, where they synapse with postganglionic neurons. The postganglionic axons extend to smooth muscle, cardiac muscle, or glands and have an excitatory or inhibitory effect that usually is controlled unconsciously.

Anatomy of the Autonomic Nervous System (p. 549)

Sympathetic Division

1. Preganglionic cell bodies are in the lateral horns of the spinal cord gray matter from T1–L2.
2. Preganglionic axons pass through the ventral roots to the white rami communicantes to the sympathetic chain ganglia. From there, four courses are possible.
   - Preganglionic axons synapse (at the same or a different level) with postganglionic neurons, which exit the ganglia through the gray rami communicantes and enter spinal nerves.
   - Preganglionic axons synapse (at the same or a different level) with postganglionic neurons, which exit the ganglia through sympathetic nerves.
   - Preganglionic axons pass through the chain ganglia without synapsing to form splanchnic nerves. Preganglionic axons then synapse with postganglionic neurons in collateral ganglia.
   - Preganglionic axons synapse with the cells of the adrenal medulla.

Parasympathetic Division

1. Preganglionic cell bodies are in nuclei in the brainstem or the lateral parts of the spinal cord gray matter from S2–S4.
   - Preganglionic axons from the brain pass to ganglia through cranial nerves.
   - Preganglionic axons from the sacral region pass through the pelvic nerves to the ganglia.
2. Preganglionic axons pass to terminal ganglia within the wall of or near the organ that is innervated.

Enteric Nervous System

1. The enteric nerve plexus is within the wall of the digestive tract.
2. The enteric plexus consists of sensory neurons, ANS motor neurons, and enteric neurons.

The Distribution of Autonomic Nerve Fibers

1. Sympathetic axons reach organs through spinal nerves, head and neck nerve plexuses, thoracic nerve plexuses, and abdominopelvic nerve plexuses.
2. Parasympathetic axons reach organs through cranial nerves, thoracic nerve plexuses, abdominopelvic nerve plexuses, and pelvic nerves.
3. Sensory neurons run alongside sympathetic and parasympathetic neurons within nerves and nerve plexuses.

Physiology of the Autonomic Nervous System (p. 555)

Neurotransmitters

1. Acetylcholine is released by cholinergic neurons (all preganglionic neurons, all parasympathetic postganglionic neurons, and some sympathetic postganglionic neurons).
2. Norepinephrine is released by adrenergic neurons (most sympathetic postganglionic neurons).

Receptors

1. Acetylcholine binds to nicotinic receptors (found in all postganglionic neurons) and muscarinic receptors (found in all parasympathetic and some sympathetic effector organs).
2. Norepinephrine and epinephrine binds to alpha and beta receptors (found in most sympathetic effector organs).
3. Activation of nicotinic receptors is excitatory, whereas activation of the alpha and beta receptors are either excitatory or inhibitory.
4. The main subtypes for alpha receptors are α_1- and α_2-adrenergic receptors, and for beta receptors are β_1- and β_2-adrenergic receptors.

Regulation of the Autonomic Nervous System (p. 559)

1. Autonomic reflexes control most of the activity of visceral organs, glands, and blood vessels.
2. Autonomic reflex activity can be influenced by the hypothalamus and higher brain centers.
3. The sympathetic and parasympathetic divisions can influence the activities of the enteric nervous system through autonomic reflexes. The enteric nervous system can function independently of the CNS through local reflexes.

Functional Generalizations About the Autonomic Nervous System (p. 562)

1. Both divisions of the ANS produce stimulatory and inhibitory effects.
2. Most organs are innervated by both divisions. Usually each division produces an opposite effect on a given organ.
3. Either division alone or both working together can coordinate the activities of different structures.
4. The sympathetic division produces more generalized effects than the parasympathetic division.
5. Sympathetic activity generally prepares the body for physical activity, whereas parasympathetic activity is more important for vegetative functions.

REVIEW AND COMPREHENSION

1. Given these statements:
   1. neuron cell bodies in the nuclei of cranial nerves
   2. neuron cell bodies in the lateral gray matter of the spinal cord (S^2–S^4)
   3. two synapses between the CNS and effector organs
   4. regulates smooth muscle

   Which of the statements are true for the autonomic nervous system?
   a. 1,3
   b. 2,4
   c. 1,2,3
   d. 2,3,4
   e. 1,2,3,4
2. Given these structures:
   1. gray ramus communicans
   2. white ramus communicans
   3. sympathetic chain ganglion

   Choose the arrangement that lists the structures in the order an action potential passes through them from a spinal nerve to an effector organ.
   a. 1,2,3
   b. 1,3,2
   c. 2,1,3
   d. 2,3,1
   e. 3,2,1
3. Given these structures:
   1. collateral ganglion
   2. sympathetic chain ganglion
   3. white ramus communicans
   4. splanchnic nerve

   Choose the arrangement that lists the structures in the order an action potential travels through them on the way from a spinal nerve to an effector organ.
   a. 1,3,2,4
   b. 1,4,2,3
   c. 3,1,4,2
   d. 3,2,4,1
   e. 4,3,1,2
4. The white ramus communicans contains
   a. preganglionic sympathetic fibers.
   b. postganglionic sympathetic fibers.
   c. preganglionic parasympathetic fibers.
   d. postganglionic parasympathetic fibers.
5. The cell bodies of the postganglionic neurons of the sympathetic division are located in the
   a. sympathetic chain ganglia.
   b. collateral ganglia.
   c. terminal ganglia.
   d. dorsal root ganglia.
   e. both a and b.
6. Splanchnic nerves
   a. are part of the parasympathetic division.
   b. have preganglionic neurons that synapse in the collateral ganglia.
   c. exit from the cervical region of the spinal cord.
   d. travel from the spinal cord to the sympathetic chain ganglia.
   e. all of the above.
7. Which of the following statements regarding the adrenal gland is true?
   a. The parasympathetic division stimulates the adrenal gland to release acetylcholine.
   b. The parasympathetic division stimulates the adrenal gland to release epinephrine.
   c. The sympathetic division stimulates the adrenal gland to release acetylcholine.
   d. The sympathetic division stimulates the adrenal gland to release epinephrine.
8. The parasympathetic division
   a. is also called the craniosacral division.
   b. has preganglionic axons in cranial nerves.
   c. has preganglionic axons in pelvic nerves.
   d. has ganglia near or in the wall of effector organs.
   e. all of the above.
9. Which of these is *not* a part of the enteric nervous system?
   a. ANS motor neurons
   b. neurons located only in the digestive tract
   c. sensory neurons
   d. somatic neurons
10. Sympathetic axons reach organs through all of the following *except*
    a. abdominopelvic nerve plexuses.
    b. head and neck nerve plexuses.
    c. thoracic nerve plexuses.
    d. pelvic nerves.
    e. spinal nerves.
11. Which of these cranial nerves does *not* contain parasympathetic fibers?
    a. oculomotor (III)
    b. facial (VII)
    c. glossopharyngeal (IX)
    d. trigeminal (V)
    e. vagus (X)
12. Which of the following statements concerning the preganglionic neurons of the ANS is true?
    a. All parasympathetic preganglionic neurons secrete acetylcholine.
    b. Only parasympathetic preganglionic neurons secrete acetylcholine.
    c. All sympathetic preganglionic neurons secrete norepinephrine.
    d. Only sympathetic preganglionic neurons secrete norepinephrine.
13. A cholinergic neuron
    a. secretes acetylcholine.
    b. has receptors for acetylcholine.
    c. secretes norepinephrine.
    d. has receptors for norepinephrine.
    e. secretes both acetylcholine and norepinephrine.
14. When acetylcholine binds to nicotinic receptors,
    a. the cell's response is mediated by G proteins.
    b. the response can be excitatory or inhibitory.
    c. Na^+ channels open.
    d. it occurs at the effector organ.
    e. all of the above.

15. Nicotinic receptors are located in
    a. postganglionic neurons of the parasympathetic division.
    b. postganglionic neurons of the sympathetic division.
    c. membranes of skeletal muscle cells.
    d. both a and b.
    e. all of the above.
16. The activation of α_1- and β_1-adrenergic receptors
    a. generally produces a stimulatory response.
    b. generally produces an inhibitory response.
    c. most commonly occurs when epinephrine from the adrenal glands binds to them.
    d. occurs when acetylcholine binds to them.
17. The sympathetic division
    a. is always stimulatory.
    b. is always inhibitory.
    c. is usually under conscious control.
    d. generally opposes the actions of the parasympathetic division.
    e. both a and c.
18. A sudden increase in blood pressure
    a. initiates a sympathetic reflex that decreases heart rate.
    b. initiates a local reflex that decreases heart rate.
    c. initiates a parasympathetic reflex that decreases heart rate.
    d. both a and b.
    e. both b and c.
19. Which of these structures is innervated almost exclusively by the sympathetic division?
    a. gastrointestinal tract
    b. heart
    c. urinary bladder
    d. reproductive tract
    e. blood vessels
20. Which of these is expected if the sympathetic division is activated?
    a. Secretion of watery saliva increases.
    b. Tear production increases.
    c. Air passageways dilate.
    d. Glucose release from the liver decreases.
    e. All of the above.

Answers in Appendix F

CRITICAL THINKING

1. When a person is startled or sees a "pleasurable" object, the pupils of the eyes may dilate. What division of the ANS is involved in this reaction? Describe the nerve pathway involved.
2. Reduced secretion from salivary and lacrimal glands could indicate damage to what nerve?
3. In a patient with Raynaud's disease, blood vessels in the skin of the hand may become chronically constricted, thereby reducing blood flow and producing gangrene. These vessels are supplied by nerves that originate at levels T2 and T3 of the spinal cord and eventually exit through the first thoracic and inferior cervical sympathetic ganglia. Surgical treatment for Raynaud's disease severs this nerve supply. At which of the following locations would you recommend that the cut be made: white rami of T2–T3, gray rami of T2–T3, spinal nerves T2–T3, or spinal nerves C1–T1? Explain.
4. Patients with diabetes mellitus can develop autonomic neuropathy, which is damage to parts of the autonomic nerves. Given the following parts of the ANS—vagus nerve, splanchnic nerve, pelvic nerve, cranial nerve, outflow of gray ramus—match the part with the symptom it would produce if the part were damaged:
    a. impotence
    b. subnormal sweat production
    c. gastric atony and delayed emptying of the stomach
    d. diminished pupil reaction (constriction) to light
    e. bladder paralysis with urinary retention
5. Explain why methacholine, a drug that acts like acetylcholine, is effective for treating tachycardia (heart rate faster than normal). Which of the following side effects would you predict: increased salivation, dilation of the pupils, sweating, and difficulty in taking a deep breath?
6. A patient has been exposed to the organophosphate pesticide malathion, which inactivates acetylcholinesterase. Which of the following symptoms would you predict: blurring of vision, excess tear formation, frequent or involuntary urination, pallor (pale skin), muscle twitching, or cramps? Would atropine be an effective drug to treat the symptoms (see p. 559 for the action of atropine)? Explain.
7. Epinephrine is routinely mixed with local anesthetic solutions. Why?
8. A drug blocks the effect of the sympathetic division on the heart. Careful investigation reveals that after administration of the drug, normal action potentials are produced in the sympathetic preganglionic and postganglionic neurons. Also, injection of norepinephrine produces a normal response in the heart. Explain, in as many ways as you can, the mode of action of the unknown drug.
9. A drug is known to decrease heart rate. After cutting the white rami of T1–T4, the drug still causes heart rate to decline. After cutting the vagus nerves, the drug no longer affects heart rate. Which division of the ANS does the drug affect? Does the drug have its effect at the synapse between preganglionic and postganglionic neurons, at the synapse between postganglionic neurons and effector organs, or in the CNS? Is the effect of the drug excitatory or inhibitory?
10. Make a list of the responses controlled by the ANS in (a) a person who is extremely angry and (b) a person who has just finished eating and is relaxing.

Answers in Appendix G

ANSWERS TO PREDICT QUESTIONS

1. Terminal ganglia are found near or embedded within the wall of organs supplied by the parasympathetic division and contribute to the enteric nervous system. Postganglionic parasympathetic axons from the terminal ganglia also contribute to the enteric nervous system. Chain ganglia and collateral ganglia contain the cell bodies of sympathetic neurons. They are not embedded within the walls of organs supplied by the sympathetic division. Instead, postganglionic neurons extend from them to organs. Thus, postganglionic sympathetic axons are found in the enteric nervous system.
2. For a sensory axon running alongside sympathetic axons, the sensory axon leaves the wall of the small intestine, joins the superior mesenteric plexus, and passes through the superior mesenteric ganglion and from there through a splanchnic nerve to a sympathetic chain ganglion. From the sympathetic chain ganglion the sensory axon passes through a white ramus communicans, the ventral rami of a spinal nerve, a spinal nerve, the dorsal root of a spinal nerve, to a dorsal root ganglion. For a sensory axon running alongside parasympathetic axons, the sensory axon leaves the wall of the small intestine, joins the superior mesenteric plexus, and passes to the esophageal plexus. From there, the sensory axon passes through a vagus nerve to its sensory ganglion.
3. Nicotinic receptors are located within the autonomic ganglia as components of the membranes of the postganglionic neurons of the sympathetic and parasympathetic divisions. Nicotine binds to the nicotinic receptors of the postganglionic neurons, resulting in action potentials. Consequently, the postganglionic neurons stimulate their effector organs. After consumption of nicotine, structures innervated by both the sympathetic and parasympathetic divisions are affected.

   After the consumption of muscarine, only the effector organs that respond to acetylcholine are affected. This includes all the effector organs innervated by the parasympathetic division, and the sweat glands, which are innervated by the sympathetic division.
4. The low dose of epinephrine stimulates β_2 receptors and causes vasodilation. Although the large dose also stimulates β_2 receptors, it stimulates so many α_1 receptors that the vasoconstriction effect dominates the vasodilation effect.
5. The frequency of action potentials in sympathetic neurons to the sweat glands increases as the body temperature increases. The increasing body temperature is detected by the hypothalamus, which activates the sympathetic neurons. Sweating cools the body by evaporation. As the body temperature declines, the frequency of action potentials in sympathetic neurons to the sweat glands decreases. A lack of sweating helps prevent heat loss from the body.
6. In response to an increase in blood pressure, information is transmitted in the form of action potentials along sensory neurons to the medulla oblongata. From the medulla oblongata, the frequency of action potentials delivered along sympathetic nerve fibers to blood vessels decreases. As a result, blood vessels dilate, causing the blood pressure to decrease.

   In response to a decrease in blood pressure, fewer action potentials are transmitted along sensory neurons to the medulla oblongata, which responds by increasing the frequency of action potentials delivered along sympathetic nerves to blood vessels. As a result, blood vessels constrict, causing blood pressure to increase.
7. The parasympathetic division releases acetylcholine, which binds to muscarinic receptors on organs. Bethanechol chloride produces effects similar to stimulation of organs by the parasympathetic division. Thus, this drug should stimulate the urinary bladder to contract. Side effects can be produced by stimulation of muscarinic receptors elsewhere in the body. Stimulation of smooth muscle in the digestive tract can produce abdominal cramps. Stimulation of air passageways can cause an asthmatic attack. Decreased tear production, salivation, and dilation of the pupils are not expected side effects because parasympathetic stimulation causes increased tear production, salivation, and constriction of the pupils. Sweat glands are innervated by the sympathetic division but have muscarinic receptors. Bethanechol chloride can increase sweating.