CHAPTER 6

The Autonomic Nervous System

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CHAPTER OUTLINE

- **AN OVERVIEW OF THE AUTONOMIC NERVOUS SYSTEM**
- **THE SYMPATHETIC NERVOUS SYSTEM**
- **THE PARASYMPATHETIC NERVOUS SYSTEM**

- **SPECIFIC ORGAN RESPONSES TO AUTONOMIC ACTIVITY**
- **CONTROL OF THE AUTONOMIC NERVOUS SYSTEM**

KEY CONCEPTS

1. The autonomic nervous system regulates the involuntary functions of the body.
2. The autonomic nervous system has three divisions: sympathetic, parasympathetic, and enteric.
3. A two-neuron efferent path is utilized by the autonomic nervous system.
4. The three divisions have neurochemical differences.
5. The sympathetic and parasympathetic divisions differ in anatomic origin and function.
6. The central nervous system controls autonomic function through a hierarchy of reflexes and integrative centers.

The sweating sunbather lying quietly in the summer sun or the racing heart and "hair-standing-on-end" sensations experienced by a person suddenly frightened by a horror movie are familiar examples of the body responding automatically to changes in the physical or emotional environment. These responses occur as a result of the actions of the autonomic portion of the nervous system and take place without conscious action on the part of the individual. The term *autonomic* is derived from the root *auto* (meaning "self") and *nomos* (meaning "law"). Our concept of the autonomic part of the nervous system has evolved during several centuries. The recognition of anatomic differences between the spinal cord and peripheral nerve pathways that control visceral functions from those that control skeletal muscles was a major step. Observations on the effects of the substance released by the vagus nerve on heart rate helped define unique biochemical features.

The functions of the **autonomic nervous system (ANS)** fall into three major categories:
- Maintaining homeostatic conditions within the body
- Coordinating the body's responses to exercise and stress
- Assisting the endocrine system to regulate reproduction

The ANS regulates the functions of the involuntary organs, which include the heart, the blood vessels, the exocrine glands, and the visceral organs. In some organs, the actions of the ANS are joined by circulating endocrine hormones and by locally produced chemical mediators to complete the control process.

AN OVERVIEW OF THE AUTONOMIC NERVOUS SYSTEM

On the basis of anatomic, functional, and neurochemical differences, the ANS is usually subdivided into three divisions: sympathetic, parasympathetic, and enteric. The enteric nervous system is concerned with the regulation of gastrointestinal function and covered in more detail in Chapter 26. The sympathetic and parasympathetic divisions are the primary focus of this chapter.

Coordination of the body's activities by the nervous system was the process of **sympathy** in classical anatomic and physiological thinking. Regulation of the involuntary organs came to be associated with the portions of the nervous system that were located, at least in part, outside the standard spinal cord and peripheral nerve pathways. The ganglia, located along either side of the spine in the thorax and abdominal regions and somewhat detached from the nerve trunks destined for the limbs, were found to be associated with involuntary bodily functions and, therefore, desig-

nated the **sympathetic division**. This collection of structures was also termed the **thoracolumbar division** of the ANS because of the location of the ganglia and the neuron cell bodies that supply axons to the ganglia. Nuclei and their axons that controlled internal functions were also found in the brainstem and associated cranial nerves, as well as in the most caudal part of the spinal cord. Those pathways were somewhat distinct from the sympathetic system and were designated the **parasympathetic division**. The term **craniosacral** was applied to this portion of the ANS because of the origin of cell bodies and axons.

Neurochemical differences were recognized between these two divisions, leading to the designation of the sympathetic system as **adrenergic**, for the adrenaline-like actions resulting from sympathetic nerve activation; and the parasympathetic system as **cholinergic**, for the acetylcholine-like actions of nerve stimulation.

The functions of the sympathetic and parasympathetic divisions are often simplified into a two-part scheme. The sympathetic division is said to preside over the utilization of metabolic resources and emergency responses of the body. The parasympathetic division presides over the restoration and buildup of the body's reserves and the elimination of waste products. In reality, most of the organs supplied by the ANS receive both sympathetic and parasympathetic innervation. In many instances, the two divisions are activated in a reciprocal fashion, so that if the firing rate in one division is increased, the rate is decreased in the other. An example is controlling the heart rate: Increased firing in the sympathetic nerves and simultaneous decreased firing in the parasympathetic nerves result in increased heart rate.

In some organs, the two divisions work synergistically. For example, during secretion by exocrine glands of the gastrointestinal tract, the parasympathetic nerves increase volume and enzyme content at the same time that sympathetic activation contributes mucus to the total secretory product. Some organs, such as the skin and blood vessels, receive only sympathetic innervation and are regulated by a decrease or increase in a baseline firing rate of the sympathetic nerves.

A Two-Neuron Efferent Path Is Utilized by the Autonomic Nervous System

The nervous system supplies efferent innervation to all organs via the motor system (see Chapter 5) or the ANS. In the motor system, there is an uninterrupted path from the cell body of the motor neuron, located in either the ventral horn of the spinal cord or a brainstem motor nucleus, to the skeletal muscle cells. In the ANS, the efferent path consists of a two-neuron chain with a synapse interposed between the CNS and the effector cells (Fig. 6.1). The cell bodies of the autonomic motor neurons are located in the spinal cord or specific brainstem nuclei. An efferent fiber emerges as the **preganglionic axon** and then synapses with neurons located in a peripheral ganglion. The neuron in the ganglion then projects a **postganglionic axon** to the autonomic effector cells.

The Primary Neurotransmitters of the ANS Are Acetylcholine and Norepinephrine

In the somatic nervous system, neurotransmitter is released from specialized nerve endings that make intimate contact with the target structure. The mammalian motor endplate, with one nerve terminal to one skeletal muscle fiber, illustrates this principle. This arrangement contrasts with the ANS, where postganglionic axons terminate in varicosities, swellings enriched in synaptic vesicles, which release the transmitter into the extracellular space surrounding the effector cells (see Fig. 6.1). The response to the ANS output originates in some of the effector cells and then propagates to the remainder via gap junctions.

Acetylcholine.   **Acetylcholine** (ACh) is the transmitter released by the preganglionic nerve terminals of both the sympathetic and the parasympathetic divisions (Fig 6.2). The synapse at those sites utilizes a **nicotinic receptor** similar in structure to the receptor at the neuromuscular junction. Parasympathetic postganglionic neurons release ACh at the synapse with the effectors. The postganglionic sympathetic neurons to the sweat glands and to some blood
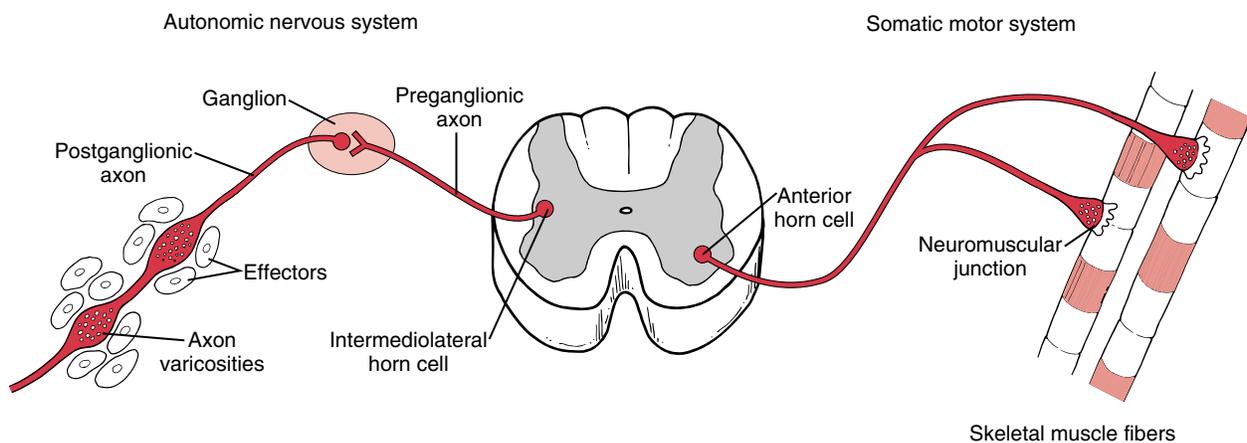

Autonomic nervous system   Somatic motor system

FIGURE 6.1   **The efferent path of the ANS as contrasted with the somatic motor system.** The ANS uses a two-neuron pathway. Note the structural differences between the synapses at autonomic effectors and skeletal muscle cells.

vessels in skeletal muscle also use ACh as the neurotransmitter. The synapse between the postganglionic neuron and the target tissues utilizes a **muscarinic receptor**. This receptor classification scheme is based on the response of the synapses to the alkaloids nicotine and muscarine, which act as agonists at their respective type of synapse. The nicotinic receptor of the ANS is blocked by the antagonist hexamethonium, in contrast to the neuromuscular junction receptor, which is blocked by curare. The muscarinic receptor is blocked by atropine.

The nicotinic receptor is of the direct ligand-gated type, meaning that the receptor and the ion channel are contained in the same structure. The muscarinic receptor is of the indirect ligand-gated type and uses a G protein to link receptor and effector functions (see Chapter 3). The action of ACh is terminated by the enzyme acetylcholinesterase. Choline released by the enzyme action is taken back into the nerve terminal and resynthesized into ACh.

Norepinephrine.   The catecholamine **norepinephrine** (**NE**) is the neurotransmitter for postganglionic synapses of the sympathetic division (see Fig. 6.2). The synapses that utilize NE receptors can also be activated by the closely related compound epinephrine (adrenaline), which is released into the general circulation by the adrenal medulla—hence, the original designation of these type receptors as adrenergic. Adrenergic receptors are classified as either α or β, based on their responses to pharmacological agents that mimic or block the actions of NE and related compounds. Alpha receptors respond best to epinephrine, less well to NE, and least well to the synthetic compound isoproterenol. Beta receptors respond best to isoproterenol, less well to epinephrine, and least well to NE. Propranolol

is a drug that acts as an antagonist at β receptors but has no action on α receptors. Each class of receptors is further classified as α_1 or α_2, and β_1, β_2, or β_3 on the basis of responses to additional pharmacological agents.

The adrenergic receptors are of the indirect, ligand-gated, G protein-linked type. They share a general structural similarity with the muscarinic type of ACh receptor. The α_1 receptors activate phospholipase C and increase the intracellular concentrations of diacylglycerol and inositol trisphosphate. The α_2 receptors inhibit adenylyl cyclase, while the β types stimulate it. The action of NE and epinephrine at a synapse is terminated by diffusion of the molecule away from the synapse and reuptake into the nerve terminal.

Other Neurotransmitters.   Neurally active peptides are often colocalized with small molecule transmitters and are released simultaneously during nerve stimulation in the CNS. This is the same in the ANS, especially in the intrinsic plexuses of the gut, where amines, amino acid transmitters, and neurally active peptides are widely distributed. In the ANS, examples of a colocalized amine and peptide are seen in the sympathetic division, where NE and neuropeptide Y are coreleased by vasoconstrictor nerves. Vasoactive intestinal polypeptide (VIP) and calcitonin-gene-related peptide (CGRP) are released along with ACh from nerve terminals innervating the sweat glands.

Nitric oxide is another type of neurotransmitter produced by some autonomic nerve endings. The term **nonadrenergic noncholinergic** (**NANC**) has been applied to such nerves. Nitric oxide is a highly diffusible substance important in the regulation of smooth muscle contraction, (see Chapter 1).
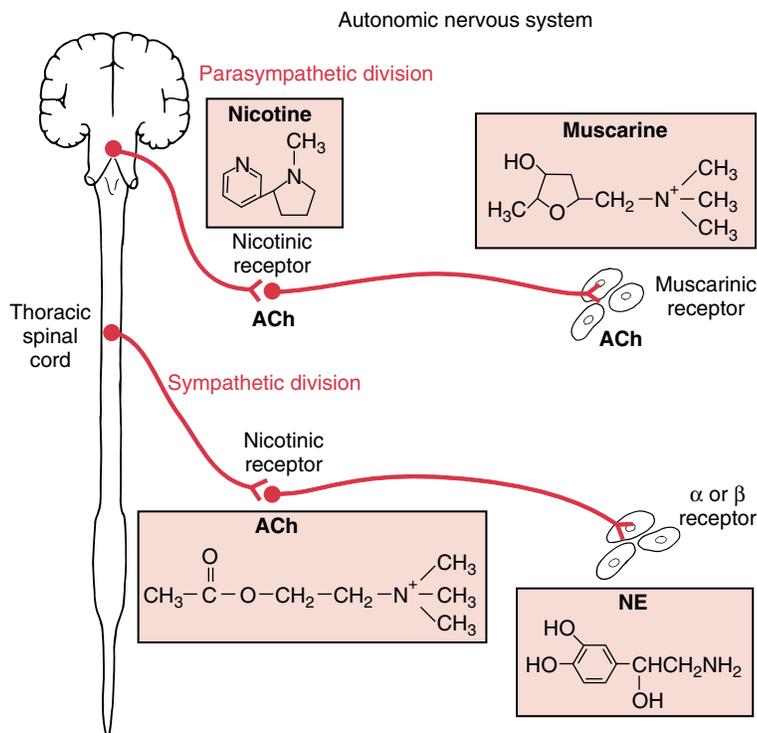

FIGURE 6.2   **The neurochemistry of the autonomic paths.** The structures of the neurotransmitters and the agonists for which the synapses were originally named are shown.
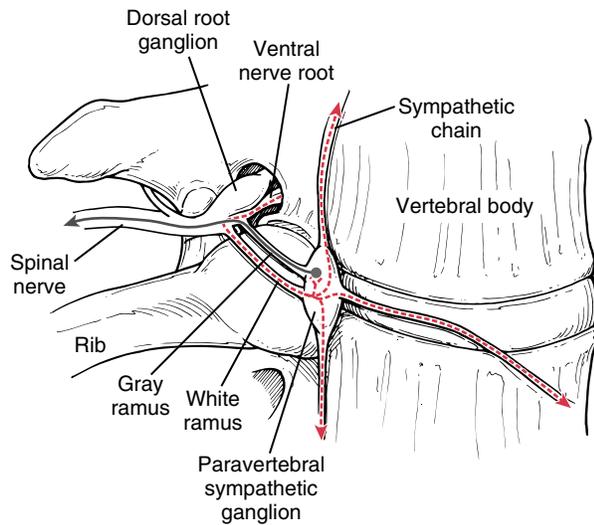
Dorsal root ganglion
Ventral nerve root
Sympathetic chain
Vertebral body
Spinal nerve
Rib
Gray ramus
White ramus
Paravertebral sympathetic ganglion

FIGURE 6.3 **Peripheral sympathetic anatomy.** The preganglionic axons course through the spinal nerve and white ramus to the paravertebral ganglion. Synapse with the postganglionic neuron may occur at the same spinal level, or at levels above or below. Postganglionic axons rejoin the spinal nerve through the gray ramus to innervate structures in the limbs or proceed to organs, such as the lungs or heart, in discrete nerves. Preganglionic axons may also pass to a prevertebral ganglion without synapsing in a paravertebral ganglion.

THE SYMPATHETIC NERVOUS SYSTEM

Preganglionic neurons of the sympathetic division originate in the intermediolateral horn of the thoracic (T1 to T12) and upper lumbar (L1 to L3) spinal cord. The preganglionic axons exit the spinal cord in the ventral nerve roots. Immediately after the ventral and dorsal roots merge to form the spinal nerve, the sympathetic axons leave the spinal nerve via the **white ramus** and enter the **paravertebral sympathetic ganglia** (Fig. 6.3). The paravertebral ganglia form an interconnected chain located on either side of the vertebral column. These ganglia extend above and below the thoracic and lumbar spinal levels, where preganglionic fibers emerge, to provide postganglionic sympathetic axons to the cervical and lumbosacral spinal nerves (Fig. 6.4). The preganglionic axons that ascend to the cervical levels arise from T1 to T5 and form three major ganglia: the **superior**, the **middle**, and the **inferior cervical ganglia**. Preganglionic axons descend below L3, forming two additional lumbar and at least four sacral ganglia. The preganglionic axons may synapse with postganglionic neurons in the paravertebral ganglion at the same level, ascend or descend up to several spinal levels and then synapse, or pass through the paravertebral ganglia en route to a **prevertebral ganglion**.

Postganglionic axons that are destined for somatic structures—such as sweat glands, pilomotor muscles, or blood vessels of the skin and skeletal muscles—leave the paravertebral ganglion in the **gray ramus** and rejoin the spinal nerve for distribution to the target tissues. Postganglionic axons to the head, heart, and lungs originate in the cervical or upper thoracic paravertebral ganglia and make their way to the specific organs as identifiable, separate nerves (e.g., the cardiac nerves), as small-caliber individual nerves that may group together, or as perivascular plexuses of axons that accompany arteries.

The superior cervical ganglion supplies sympathetic axons that innervate the structures of the head. These axons travel superiorly in the perivascular plexus along the carotid arteries. Structures innervated include the radial muscle of the iris, responsible for dilation of the pupil; Müller's muscle, which assists in elevating the eyelid; the lacrimal gland; and the salivary glands. Lesions that interrupt this pathway produce easily detectable clinical signs (see Clinical Focus Box 6.1). The middle and inferior cervical ganglia innervate organs of the chest, including the trachea, esophagus, heart, and lungs.

Postsynaptic axons destined for the abdominal and pelvic visceral organs arise from the prevertebral ganglia (see Fig. 6.4). The three major prevertebral ganglia, also called **collateral ganglia**, overlie the celiac, superior mesenteric, and inferior mesenteric arteries at their origin from the aorta and are named accordingly. The **celiac ganglion** provides sympathetic innervation to the stomach, liver, pancreas, gallbladder, small intestine, spleen, and kidneys. Preganglionic axons originate in the T5 to T12 spinal levels. The

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CLINICAL FOCUS BOX 6.1

Horner's Syndrome

Lesions of the sympathetic pathway to the head produce abnormalities that are easily detectable on physical examination. The deficits of function occur ipsilateral to the lesion and include:
- Partial constriction of the pupil as a result of loss of sympathetic pupillodilator action
- Drooping of the eyelid, termed *ptosis*, as a result of loss of sympathetic activation of Müller's muscle of the eyelid
- Dryness of the face as a result of the lack of sympathetic activation of the facial sweat glands.

A pattern of historical or physical examination findings that is consistent from patient to patient is often termed a ***syndrome***. Johann Horner, a 19th century Swiss ophthal-mologist, described this pattern of eye and facial abnormalities in patients, and these are referred to as Horner's syndrome. Etiologies for Horner's syndrome include:
- Brainstem lesions, such as produced by strokes, which interrupt the tracts that descend to the sympathetic neurons in the spinal cord
- Upper thoracic nerve root lesions, such as those produced by excessive traction on the arm or from infiltration of the nerve roots by cancer spreading from the lung
- Cervical paravertebral ganglia lesions from accidental or surgical trauma, or metastatic cancer
- Arterial injury in the neck, from neck hyperextension, or direct trauma, which interrupt the postganglionic axons traveling in the carotid periarterial plexus.

Sympathetic Division

Parasympathetic Division

Paravertebral ganglia
A = Superior cervical ganglion
B = Middle cervical ganglion
C = Inferior cervical ganglion

To skin and musculoskeletal system

Eye

Lacrimal gland

Submandibular and
sublingual glands

Parotid gland

Heart

Trachea

Lung

Liver

Gallbladder

Stomach

Small intestine

Adrenal gland

Kidney

Large intestine

Bladder

Genitalia

Ciliary
ganglion

Pterygopalatine
ganglion

Submandibular
ganglion

Otic
ganglion

III

Midbrain

VII

IX

X

Medulla

Cervical

Thoracic

Lumbar

Sacral

A

B

C

Greater
splanchnic
nerve

1

Lesser
splanchnic
nerve

2

3

Prevertebral ganglia
1 = Celiac ganglion
2 = Superior mesenteric ganglion
3 = Inferior mesenteric ganglion

FIGURE 6.4 **The organ-specific arrangement of the ANS.** Preganglionic axons are indicated by solid lines, postganglionic axons by dashed lines. Sympathetic ax- ons destined for the skin and musculoskeletal system are shown on the left side of the spinal cord. Note the named paravertebral and prevertebral ganglia.

superior mesenteric ganglion innervates the small and large intestines. Preganglionic axons originate primarily in T10 to T12. The inferior mesenteric ganglion innervates the lower colon and rectum, urinary bladder, and reproductive organs. Preganglionic axons originate in L1 to L3.

The Sympathetic Division Can Produce Local or Widespread Responses

The sympathetic division exerts a continuous influence on the organs it innervates. This continuous level of control is called sympathetic tone, and it is accomplished by a persistent, low rate of discharge of the sympathetic nerves. When the situation dictates, the rate of firing to a particular organ can be increased or decreased, such as an increased firing rate of the sympathetic neurons supplying the iris to produce pupillary dilation in dim light or a decreased firing rate and pupillary constriction during drowsiness.

The number of postganglionic axons emerging from the paravertebral ganglia is greater than the number of preganglionic neurons that originate in the spinal cord. It is estimated that postganglionic sympathetic neurons outnumber preganglionic neurons by 100:1 or more. This spread of influence, termed divergence, is accomplished by collateral branching of the presynaptic sympathetic axons, which then make synaptic connections with postganglionic neurons both above and below their original level of emergence from the spinal cord. Divergence enables the sympathetic division to produce widespread responses of many effectors when physiologically necessary.

The Adrenal Medulla Is a Mediator of Sympathetic Function

In addition to divergence, the sympathetic division has a hormonal mechanism to activate target tissues endowed with adrenergic receptors, including those innervated by the sympathetic nerves. The hormone is the catecholamine epinephrine, which is secreted with much lesser amounts of norepinephrine by the adrenal medulla during generalized response to stress.

The adrenal medulla, a neuroendocrine gland, forms the inner core of the adrenal gland situated on top of each kidney. Cells of the adrenal medulla are innervated by the lesser splanchnic nerve, which contains preganglionic sympathetic axons originating in the lower thoracic spinal cord (see Fig. 6.4). These axons pass through the paravertebral ganglia and the celiac ganglion without synapsing and terminate on the chromaffin cells of the adrenal medulla (Fig. 6.5). The chromaffin cells are modified ganglion cells that synthesize both epinephrine and norepinephrine in a ratio of about 8:1 and store them in secretory vesicles. Unlike neurons, these cells possess neither axons nor dendrites but function as neuroendocrine cells that release hormone directly into the bloodstream in response to preganglionic axon activation.

Circulating epinephrine mimics the actions of sympathetic nerve stimulation but with greater efficacy because epinephrine is usually more potent than norepinephrine in stimulating both α-adrenergic and β-adrenergic receptors. Epinephrine can also stimulate adrenergic receptors on
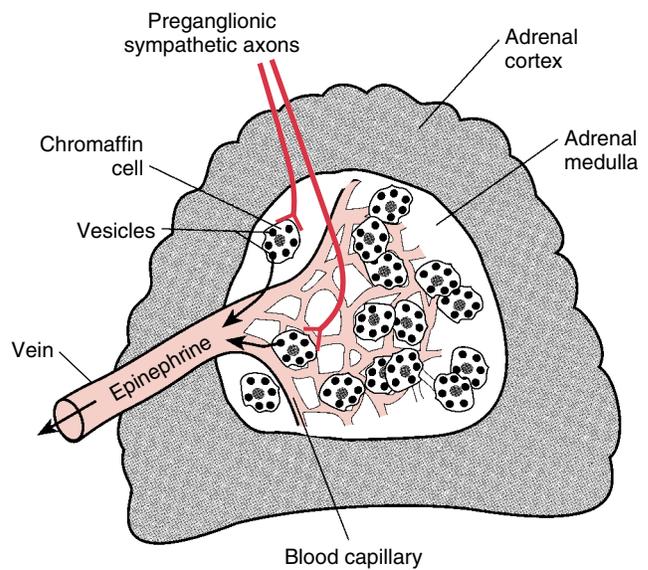

FIGURE 6.5 Sympathetic innervation of the adrenal medulla. Preganglionic sympathetic axons terminate on the chromaffin cells. When stimulated, the chromaffin cells release epinephrine into the circulation.

cells that receive little or no direct sympathetic innervation, such as liver and adipose cells for mobilizing glucose and fatty acids, and blood cells which participate in the clotting and immune responses.

The Fight-or-Flight Response Is a Result of Widespread Sympathetic Activation

This response is the classic example of the sympathetic nervous system's ability to produce widespread activation of its effectors; it is activated when an organism's survival is in jeopardy and the animal may have to fight or flee. Some components of the response result from the direct effects of sympathetic activation, while the secretion of epinephrine by the adrenal medulla also contributes.

Sympathetic stimulation of the heart and blood vessels results in a rise in blood pressure because of increased cardiac output and increased total peripheral resistance. There is also a redistribution of the blood flow so that the muscles and heart receive more blood, while the splanchnic territory and the skin receive less. The need for an increased exchange of blood gases is met by acceleration of the respiratory rate and dilation of the bronchiolar tree. The volume of salivary secretion is reduced but the relative proportion of mucus increases, permitting lubrication of the mouth despite increased ventilation. The potential demand for an enhanced supply of metabolic substrates, like glucose and fatty acids, is met by the actions of the sympathetic nerves and circulating epinephrine on hepatocytes and adipose cells. Glycogenolysis mobilizes stored liver glycogen, increasing plasma levels of glucose. Lipolysis in fat cells converts stored triglycerides to free fatty acids that enter the bloodstream.

The skin plays an important role in maintaining body temperature in the face of increased heat production from contracting muscles. The sympathetic innervation of the

skin vasculature can adjust blood flow and heat exchange by vasodilation to dissipate heat or by vasoconstriction to protect blood volume. The eccrine sweat glands are important structures that also can be activated to enhance heat loss. Sympathetic nerve stimulation of the sweat glands results in the secretion of a watery fluid, and evaporation then dissipates body heat. Constriction of the skin vasculature, concurrent with sweat gland activation, produces the cold, clammy skin of a frightened individual. Hair-standing-on-end sensations result from activation of the piloerector muscles associated with hair follicles. In humans, this action is likely a phylogenetic remnant from animals that use hair erection for body temperature preservation or to enhance the appearance of body size or ferocity.

THE PARASYMPATHETIC NERVOUS SYSTEM

The parasympathetic division is comprised of a cranial portion, emanating from the brainstem, and a sacral portion, originating in the intermediate gray zone of the sacral spinal cord (see Fig. 6.4). In contrast to the widespread activation pattern of the sympathetic division, the neurons of the parasympathetic division are activated in a more localized fashion. There is also much less tendency for divergence of the presynaptic influence to multiple postsynaptic neurons—on average, one presynaptic parasympathetic neuron synapses with 15 to 20 postsynaptic neurons. An example of localized activation is seen in the vagus nerve, where one portion of its outflow can be activated to slow the heart rate without altering the vagal control to the stomach.

Ganglia in the parasympathetic division are located either close to the organ innervated or embedded within its walls. The organs of the gastrointestinal system demonstrate the latter pattern. Because of this arrangement, preganglionic axons are much longer than postganglionic axons.

Brainstem Parasympathetic Neurons Innervate Structures in the Head, Chest, and Abdomen

Four of the twelve cranial nerves—numbers III, VII, IX, and X—contain parasympathetic axons. The nuclei of these nerves, which occupy areas of the tectum in the midbrain, pons, and medulla, are the centers for the initiation and integration of autonomic reflexes for the organ systems they innervate. Parasympathetic and sympathetic activities are coordinated by these nuclei.

Cranial Nerve III.   The **oculomotor nerve** originates from nuclei in the tectum of the midbrain, where synaptic connections with the axons of the optic nerves provide input for ocular reflexes. The parasympathetic neurons are located in the **Edinger-Westphal nucleus**. The presynaptic axons travel in the superficial aspect of cranial nerve III to the **ciliary ganglion,** located inside the orbit where the synapse occurs. The postganglionic axons enter the eyeball near the optic nerve and travel between the sclera and the choroid. These axons supply the sphincter muscle of the iris; the ciliary muscle, which focuses the lens; and the choroidal blood vessels. About 90% of the axons are destined for the ciliary muscle, while only about 3 to 4% innervate the iris sphincter.

Cranial Nerve VII.   The parasympathetic presynaptic axons of the **facial nerve** arise from the **superior salivatory nuclei** in the rostral medulla. Presynaptic axons pass from the facial nerve into the greater superficial petrosal nerve and synapse in the **pterygopalatine ganglion**. The postsynaptic axons from that ganglion innervate the lacrimal gland and the glands of the nasal and palatal mucosa. Other facial nerve presynaptic axons travel via the chorda tympani and synapse in the **submandibular ganglion.** These postsynaptic axons stimulate the production of saliva by the submandibular and sublingual glands. Parasympathetic activation can also produce dilation of the vasculature within the areas supplied by the facial nerve.

Cranial Nerve IX.   The parasympathetic presynaptic axons of the **glossopharyngeal nerve** arise from the **inferior salivatory nuclei** of the medulla. The axons follow a circuitous course through the lesser petrosal nerve to reach the **otic ganglion**, where they synapse. From the otic ganglion, the postsynaptic axons join the auriculotemporal branch of cranial nerve V and arrive at the parotid gland, where they stimulate secretion of saliva.

Sensory axons that are important for autonomic function are also conveyed in cranial nerve IX. The carotid bodies sense the concentrations of oxygen and carbon dioxide in blood flowing in the carotid arteries and transmit that chemosensory information to the medulla via glossopharyngeal afferents. The carotid sinus, which is located in the proximal internal carotid artery, monitors blood pressure and transmits this baroreceptor information to the **tractus solitarius** in the medulla.

Cranial Nerve X.   The **vagus nerve** has an extensive autonomic component, which arises from the **nucleus ambiguus** and the **dorsal motor nuclei** in the medulla. It has been estimated that vagal output comprises up to 75% of total parasympathetic activity. Long preganglionic axons travel in the vagus trunks to ganglia in the heart and lungs and to the intrinsic plexuses of the gastrointestinal tract. Sympathetic postsynaptic axons also intermingle with the parasympathetic presynaptic axons in these plexuses and travel together to the target tissues.

The right vagus nerve supplies axons to the sinoatrial node of the heart, and the left vagus nerve supplies the atrioventricular node. Vagal activation slows the heart rate and reduces the force of contraction. The vagal efferents to the lung control smooth muscle that constricts bronchioles, and also regulate the action of secretory cells. Vagal input to the esophagus and stomach regulates motility and influences secretory function in the stomach. Acetylcholine plus vasoactive intestinal peptide (VIP) are the transmitters of the postsynaptic neurons.

There is also vagal innervation to the kidneys, liver, spleen, and pancreas, but the role of these inputs is not yet fully established.

Sacral Spinal Cord Parasympathetic Neurons Innervate Structures in the Pelvis

Preganglionic fibers of the sacral division originate in the intermediate gray matter of the sacral spinal cord, emerging from segments S2, S3, and S4 (see Fig. 6.4). These preganglionic fibers synapse in ganglia in or near the pelvic organs, including the lower portion of the gastrointestinal

tract (the sigmoid colon, rectum, and internal anal sphincter), the urinary bladder, and the reproductive organs.

SPECIFIC ORGAN RESPONSES TO AUTONOMIC ACTIVITY

As noted earlier, most involuntary organs are dually innervated by the sympathetic and parasympathetic divisions, often with opposing actions. A list of these organs and a summary of their responses to sympathetic and parasympathetic stimulation is given in Table 6.1. The type of receptor at the

TABLE 6.1	Responses of Effectors to Parasympathetic and Sympathetic Stimulation	
Effector	**Parasympathetic**	**Sympathetic**
Eye		
Pupil	Constriction	Dilation (α_1)
Ciliary muscle	Contraction	Relaxation (β_2)
Müller's muscle	None	Contraction (α_1)
Lacrimal gland	Secretion	None
Nasal glands	Secretion	Inhibition (α_1)
Salivary glands	Secretion	Amylase secretion (β)
Skin		
Sweat glands	None	Secretion (cholinergic muscarinic)
Piloerector muscles	None	Contraction (α_1)
Blood vessels		
Skin	None	Constriction (α)
Skeletal muscle	None	Dilation (β_2), Constriction (α)
Viscera	None	Constriction (α_1)
Heart		
Rate	Decrease	Increase (β_1, β_2)
Force	Decrease	Increase (β_1, β_2)
Lungs		
Bronchioles	Constriction	Dilation (β_2)
Glands	Secretion	Decreased (α_1), incr. (β_2) secretion
Gastrointestinal tract		
Wall muscles	Contraction	Relaxation (α, β_2)
Sphincters	Relaxation	Contraction (α_1)
Glands	Secretion	Inhibition
Liver	None	Glycogenolysis and Gluconeogenesis (α_1, β_2)
Pancreas (insulin)	None	Decreased secretion (α_2)
Adrenal medulla	None	Secretion of epinephrine (cholinergic nicotinic)
Urinary system		
Ureter	Relaxation	Contraction (α_1)
Detrusor	Contraction	Relaxation (β_2)
Sphincter	Relaxation	Contraction (α_1)
Reproductive system		
Uterus	Variable	Contraction (α_1)
Genitalia	Erection	Ejaculation/vaginal contraction (α)
Adipose cells	None	Lipolysis (β)

synapse with the effectors is also indicated. More detailed discussions of the effects of autonomic nerve activation are found in the chapters on the specific organ systems.

CONTROL OF THE AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system utilizes a hierarchy of reflexes to control the function of autonomic target organs. These reflexes range from local, involving only a part of one neuron, to regional, requiring mediation by the spinal cord and associated autonomic ganglia, to the most complex, requiring action by the brainstem and cerebral centers. In general, the higher the level of complexity, the more likely the reflex will require coordination of both sympathetic and parasympathetic responses. Somatic motor neurons and the endocrine system may also be involved.

Sensory Input Contributes to Autonomic Function

The ANS is traditionally regarded as an efferent system, and the sensory neurons innervating the involuntary organs are not considered part of the ANS. Sensory input, however, is important for autonomic functioning. The sensory innervation to the visceral organs, blood vessels, and skin forms the afferent limb of autonomic reflexes (Fig. 6.6). Most of the sensory axons from ANS-innervated structures are unmyelinated C fibers.

Sensory information from these pathways may not reach the level of consciousness. Sensations that are perceived may be vaguely localized or may be felt in a somatic structure rather than the organ from which the afferent action potentials originated. The perception of pain in the left arm during a myocardial infarction is an example of pain being referred from a visceral organ.

Local Axon Reflexes Are Paths for Autonomic Activation

A sensory neuron may have several terminal branches peripherally that enlarge the receptive area and innervate multiple receptors. As a sensory action potential which originated in one of the terminal branches propagates afferently, or **orthodromically,** it may also enter some other branches of that same axon and then conduct efferently, or **antidromically**, for short distances. The distal ends of the sensory axons may release neurotransmitters in response to the antidromic action potentials. The process of action potential spread can result in a more wide-ranging reaction than that produced by the initial stimulus. If the sensory neuron innervates blood vessels or sweat glands, the response can produce reddening of the skin as a result of vasodilation, local sweating as a result of sweat gland activation, or pain as a result of the action of the released neurotransmitter. This process is called a **local axon reflex** (see Fig. 6.6). It differs from the usual reflex pathway in that a synapse with an efferent neuron in the spinal cord or peripheral ganglion is not required to produce a response. The neurotransmitter producing this local reflex is likely the same as that released
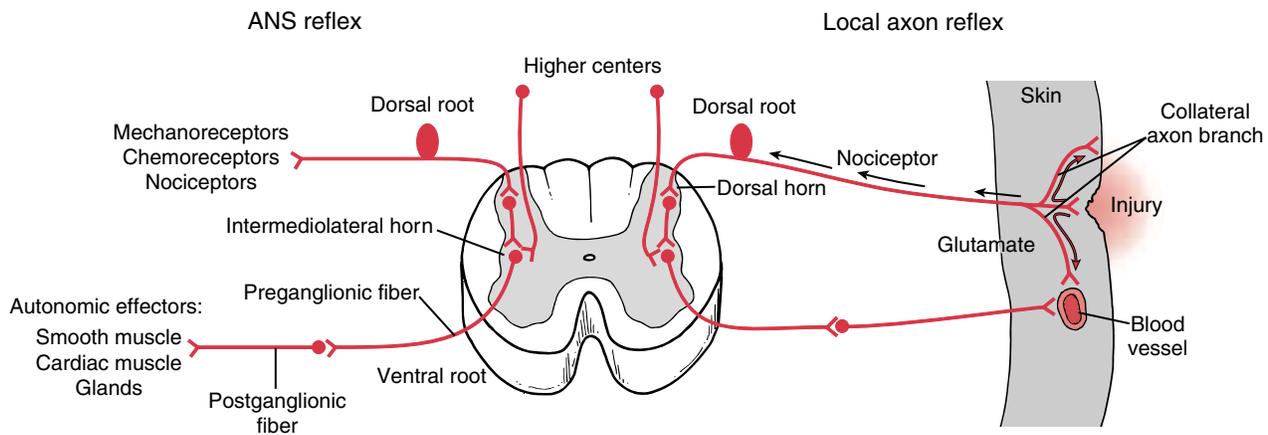
ANS reflex   Local axon reflex

FIGURE 6.6   **Sensory components of autonomic function.** Left, Sensory action potentials from mechanical, chemical, and nociceptive receptors that propagate to the spinal cord can trigger ANS reflexes. Right, Local axon reflexes occur when an orthodromic action potential from a sensory nerve ending propagates antidromically into collateral branches of the same neuron. The antidromic action potentials may provoke release of the same neurotransmitters, like substance P or glutamate, from the nerve endings as would be released at the synapse in the spinal cord. Local axon reflexes may perpetuate pain, activate sweat glands, or cause vasomotor actions.

at the synapse in the spinal cord—substance P or glutamate for sensory neurons or ACh and NE at the target tissues for autonomic neurons. Local axon reflexes in nociceptive nerve endings that become persistently activated after local trauma can produce dramatic clinical manifestations (see Clinical Focus Box 6.2).

The Autonomic Ganglia Can Modify Reflexes

Although the paravertebral ganglia may serve merely as relay stations for synapse of preganglionic and postganglionic sympathetic neurons, evidence suggests that synaptic activity in these ganglia may modify efferent activity. Input from other preganglionic neurons provides the modifying influence. Prevertebral ganglia also serve as integrative centers for reflexes in the gastrointestinal tract. Chemoreceptors and mechanoreceptors located in the gut produce afferent action potentials that pass to the spinal cord and then to the celiac or mesenteric ganglia where changes in motility and secretion may be instituted during digestion. The integrative actions of these ganglia are also responsible for halting motility and secretion in the gas-

trointestinal tract during a generalized stress reaction (the fight-or-flight response).

The intrinsic plexuses of the gastrointestinal visceral wall are reflex integrative centers where input from presynaptic parasympathetic axons, postganglionic sympathetic axons, and the action of intrinsic neurons may all participate in reflexes that influence motility and secretion. The intrinsic plexuses also participate in centrally mediated gastrointestinal reflexes (see Chapter 26).

The Spinal Cord Coordinates Many Autonomic Reflexes

Reflexes coordinated by centers in the lumbar and sacral spinal cord include micturition (emptying the urinary bladder), defecation (emptying the rectum), and sexual response (engorgement of erectile tissue, vaginal lubrication, and ejaculation of semen). Sensory action potentials from receptors in the wall of the bladder or bowel report about degrees of distenion. Sympathetic, parasympathetic, and somatic efferent actions require coordination to produce many of these responses.

CLINICAL FOCUS BOX 6.2

Reflex Sympathetic Dystrophy (RSD)

RSD is a clinical syndrome that includes spontaneous pain, painful hypersensitivity to nonnoxious stimuli such as light touch or moving air, and evidence of ANS dysfunction in the form of excessive coldness and sweating of the involved body part. The foot, knee, hand, and forearm are the more common sites of involvement. Local trauma, which may be minor in degree, and surgical procedures on joints or bones are common precipitating events. The term *dystrophy* applies to atrophic changes that may occur in the skin, soft tissue, and bone in the

painful areas if the condition goes untreated for many months. A full explanation of the pathogenetic mechanisms is still lacking. Local axon reflexes in traumatized nociceptive neurons and reflex activation of the sympathetic nervous system are thought to be contributors. Repeated blockade of sympathetic neuron action by local anesthetic injection into the paravertebral ganglia serving the involved body part, followed by mobilization of the body part in a physical therapy program, are the mainstays of treatment. RSD is now termed *Complex Regional Pain Syndrome Type I.*

Higher centers provide facilitating or inhibiting influences to the spinal cord reflex centers. The ability to voluntarily suppress the urge to urinate when the sensation of bladder fullness is perceived is an example of higher CNS centers inhibiting a spinal cord reflex. Following injury to the cervical or upper thoracic spinal cord, micturition may occur involuntarily or be provoked at much lower than normal bladder volumes. Episodes of hypertension and piloerection in spinal cord injury patients are another example of uninhibited autonomic reflexes arising from the spinal cord.

The Brainstem Is a Major Control Center for Autonomic Reflexes

Areas within all three levels of the brainstem are important in autonomic function (Fig. 6.7). The **periaqueductal gray matter** of the midbrain coordinates autonomic responses to painful stimuli and can modulate the activity of the sensory tracts that transmit pain. The **parabrachial nucleus** of the pons participates in respiratory and cardiovascular control. The **locus ceruleus** may have a role in micturition reflexes. The medulla contains several key autonomic areas. The **nucleus of the tractus solitarius** receives afferent input from cardiac, respiratory, and gastrointestinal receptors. The **ventrolateral medullary area** is the major center for control of the preganglionic sympathetic neurons in the spinal cord. Vagal efferents arise from this area also. Neurons that control specific functions like blood pressure and heart rate are clustered within this general region. The descending paths for regulation of the preganglionic sympathetic and spinal parasympathetic neurons are not yet fully delineated. The reticulospinal tracts may carry some of these axons. Autonomic reflexes coordinated in the brainstem include pupillary reaction to light, lens accommodation, salivation, tearing, swallowing, vomiting, blood pressure regulation, and cardiac rhythm modulation.

The Hypothalamus and Cerebral Hemispheres Provide the Highest Levels of Autonomic Control

The **periventricular**, **medial**, and **lateral areas** of the **hypothalamus** in the diencephalon control circadian rhythms, and homeostatic functions such as thermoregulation, appetite, and thirst. Because of the major role of the hypothalamus in autonomic function, it has at times been labeled the "head ganglion of the ANS." The **insular** and **medial prefrontal areas** of the cerebral cortex are the respective sensory and motor areas involved with the regulation of autonomic function. The **amygdala** in the temporal lobe coordinates the autonomic components of emotional responses.

The areas of the cerebral hemispheres, diencephalon, brainstem, and central path to the spinal cord that are involved with the control of autonomic functions are collectively termed the **central autonomic network** (see Fig. 6.7).
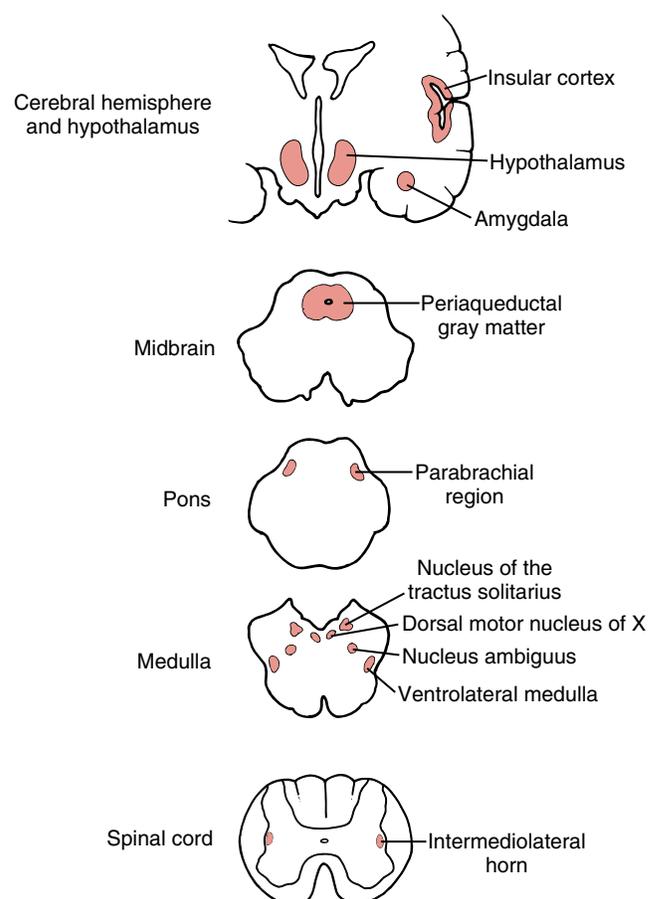

FIGURE 6.7 **The central autonomic network.** Note the cerebral, hypothalamic, brainstem, and spinal cord components. A hierarchy of reflexes initiated from these different levels regulates autonomic function.

REVIEW QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE lettered answer or completion that is BEST in each case.

1. Impaired dilation of the pupil when entering a dark room is due to deficient functioning of

(A) Presynaptic axons that travel in the oculomotor nerve
(B) Postsynaptic axons that travel in the facial nerve
(C) Acetylcholine delivered by the circulatory system
(D) Postsynaptic axons arising from paravertebral ganglia
(E) Postsynaptic axons arising from prevertebral ganglia

2. Which effects would destruction of the lumbar paravertebral ganglia by a gunshot cause in the ipsilateral leg?
(A) It would be cold and clammy
(B) It would be weak
(C) There would be decreased sensation for painful stimuli
(D) It would be warm and dry
(E) There would be no detectable change

(continued)

3. Which of these is not a neurotransmitter in the autonomic nervous system?
   (A) Acetylcholine
   (B) Norepinephrine
   (C) Epinephrine
   (D) Muscarine
   (E) Neuropeptide Y
4. With which other entity do the receptors of the parasympathetic postganglionic target tissue synapse share general structural similarity?
   (A) The receptor of the sympathetic postganglionic target tissue synapse
   (B) The receptor of the sympathetic preganglionic synapse
   (C) The receptor of the parasympathetic preganglionic synapse
   (D) The voltage-gated calcium channel
   (E) The receptor at the neuromuscular junction
5. By which route are the sweat glands supplied with parasympathetic innervation?
   (A) Vagal preganglionics to paravertebral ganglion to cutaneous nerve
   (B) Vagal preganglionics to prevertebral ganglion to cutaneous nerve
   (C) Spinal preganglionics to para-vertebral ganglion to cutaneous nerve
   (D) Spinal gray ramus to cutaneous nerve

   (E) There is no parasympathetic innervation to the sweat glands
6. Which statement correctly describes the relationship between preganglionic and postganglionic sympathetic axons?
   (A) The number of presynaptic axons is much greater than the number of postsynaptic axons
   (B) The number of postsynaptic axons is much greater than the number of presynaptic axons
   (C) The number of presynaptic and postsynaptic axons is equal
   (D) Convergence of presynaptic influence onto the postsynaptic neurons is the rule
   (E) Presynaptic and postsynaptic neurons are joined by gap junctions
7. A patient who is being treated with a medication complains of the adverse effect of difficulty adjusting his eyes to bright lights. How is the medication modifying autonomic function?
   (A) Enhancing cholinergic activity
   (B) Enhancing adrenergic activity
   (C) Mimicking the action of epinephrine
   (D) Inhibiting cholinergic activity
   (E) Inhibiting adrenergic activity
8. The activation of which type of synapse could alter cyclic AMP levels in the postsynaptic cell?
   (A) Preganglionic to postganglionic sympathetic

   (B) Preganglionic to postganglionic parasympathetic
   (C) Postganglionic axon-target tissue nicotinic
   (D) Postganglionic axon-target tissue muscarinic
   (E) Postganglionic-target tissue curare-sensitive
9. A concurrent increase in parasympathetic and decrease in sympathetic outflow to the heart would be coordinated at which level of the nervous system?
   (A) Insular cortex
   (B) Axon reflexes in cardiac sensory nerves
   (C) Periaqueductal gray matter of the mesencephalon
   (D) Gray matter of the upper thoracic spinal cord
   (E) Reticular formation of the medulla

SUGGESTED READING

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