

14

Autonomic Nervous System

CHAPTER OBJECTIVES

- To understand the structure and physiology of the autonomic nervous system
- To understand the pharmacologic differences between the sympathetic and parasympathetic nervous systems

A 46-year-old man underwent a right-sided pneumonectomy for carcinoma of the bronchus and is seen by his thoracic surgeon for follow-up. The patient says that he feels surprisingly fit and is gaining some of the weight that he had lost prior to the operation. His wife comments that the upper lid of his right eye tends to droop slightly when he gets tired at the end of the day.

During a careful physical examination, the surgeon notices that in addition to the ptosis of the right eye, the patient's right pupil is constricted and that his face is slightly flushed on the right side. Further examination reveals that the skin on the right side of the face appears to be warmer and drier than normal. Palpation of the deep

cervical group of lymph nodes reveals a large, hard, fixed node just above the right clavicle.

Based on his clinical findings, the surgeon makes the diagnosis of a right-sided Horner syndrome. These findings were not present before the operation. The presence of the enlarged right-sided deep cervical lymph node indicates that the bronchial carcinoma has metastasized to the lymph node in the neck and is spreading to involve the cervical part of the sympathetic trunk on the right side. This observation explains the abnormal eye and facial skin findings.

Knowledge of the sympathetic innervation of the structures of the head and neck enables the surgeon to make an accurate diagnosis in this patient.

The autonomic nervous system (ANS) and the endocrine system control the internal environment of the body. The ANS provides a fine discrete control over the functions of many organs and tissues, including heart muscle, smooth muscle, and the exocrine glands. The endocrine system, by means of its blood-borne hormones, exerts a slower more diffuse control.

The ANS, like the somatic nervous system, has afferent, connector, and efferent neurons. The afferent impulses originate in visceral receptors and travel via afferent pathways to the central nervous system (CNS), where they are integrated through connector neurons at different levels and then leave via efferent pathways to visceral effector organs. The majority of the activities of the autonomic system do not impinge on consciousness.

The efferent pathways of the autonomic system are made up of preganglionic and postganglionic neurons. The cell bodies of the preganglionic neurons are situated in the lateral gray column of the spinal cord and in the motor nuclei of the 3rd, 7th, 9th, and 10th cranial nerves. The axons of these cell bodies synapse on the cell bodies of the postganglionic neurons that are collected together to form **ganglia** outside the CNS.

The control exerted by the autonomic system is extremely rapid; it is also widespread, since one preganglionic axon may synapse with several postganglionic neurons. Large collections of afferent and efferent fibers and their associated ganglia form **autonomic plexuses** in the thorax, abdomen, and pelvis.

The visceral receptors include chemoreceptors, baroreceptors, and osmoreceptors. Pain receptors are present in viscera and certain types of stimuli, such as lack of oxygen or stretch, can cause extreme pain.

The information provided in this chapter is extensively used in clinical practice. The examples of autonomic innervations given are important and are commonly used by examiners to construct good questions.

ORGANIZATION

The ANS is distributed throughout the central and peripheral nervous systems. It is divided into two parts, the **sympathetic** and the **parasympathetic** and, as emphasized earlier, consists of both afferent and efferent fibers. This division between sympathetic and parasympathetic

is made on the basis of anatomic differences, differences in the neurotransmitters, and differences in the physiologic effects.

Both the sympathetic and parasympathetic divisions produce opposite effects in most organs and are thus considered as physiologic antagonists. However, both divisions operate in conjunction with one another and the balance in the activities maintains a stable internal environment.

Sympathetic Part

The sympathetic system is the larger of the two parts of the autonomic system and is widely distributed throughout the body, innervating the heart and lungs, the muscle in the walls of many blood vessels, the hair follicles and the sweat glands, and many abdominopelvic viscera.

The function of the sympathetic system is to prepare the body for an emergency. The heart rate is increased, arterioles of the skin and intestine are constricted, arterioles of skeletal muscle are dilated, and the blood pressure is raised. Blood is redistributed; thus, it leaves the skin and gastrointestinal tract and passes to the brain, heart, and skeletal muscle. In addition, the sympathetic nerves dilate the pupils; inhibit smooth muscle of the bronchi, intestine, and bladder wall; and close the sphincters. The hair is made to stand on end, and sweating occurs.

The sympathetic system consists of the efferent outflow from the spinal cord, two ganglionated sympathetic trunks, important branches, plexuses, and regional ganglia.

Efferent Nerve Fibers (Sympathetic Outflow)

The lateral gray columns (horns) of the spinal cord from the first thoracic segment to the second lumbar segment (sometimes third lumbar segment) possess the cell bodies of the sympathetic connector neurons (Fig. 14-1). The myelinated axons of these cells leave the cord in the anterior nerve roots and pass via the **white rami communicantes** (the white rami are white because the nerve fibers are covered with white myelin) to the **paravertebral ganglia** of the **sympathetic trunk**. Once these fibers (preganglionic) reach the ganglia in the sympathetic trunk, they are distributed as follows:

1. They synapse with an excitator neuron in the ganglion. The gap between the two neurons is bridged by the neurotransmitter **acetylcholine (ACh)**. The postganglionic nonmyelinated axons leave the ganglion and pass to the thoracic spinal nerves as **gray rami communicantes** (the gray rami are gray because the nerve fibers are devoid of myelin). They are distributed in branches of the spinal nerves to smooth muscle in the blood vessel walls, sweat glands, and arrector pili muscle of the hairs of the skin.
2. They travel cephalad in the sympathetic trunk to synapse in ganglia in the cervical region (Fig. 14-2). The postganglionic nerve fibers pass via gray rami communicantes to join the cervical spinal nerves. Many of the preganglionic fibers entering the lower part of the sympathetic trunk from the lower thoracic and upper two lumbar segments of the spinal cord travel caudad to synapse in ganglia in the lower lumbar and sacral regions. Here again, the postganglionic nerve

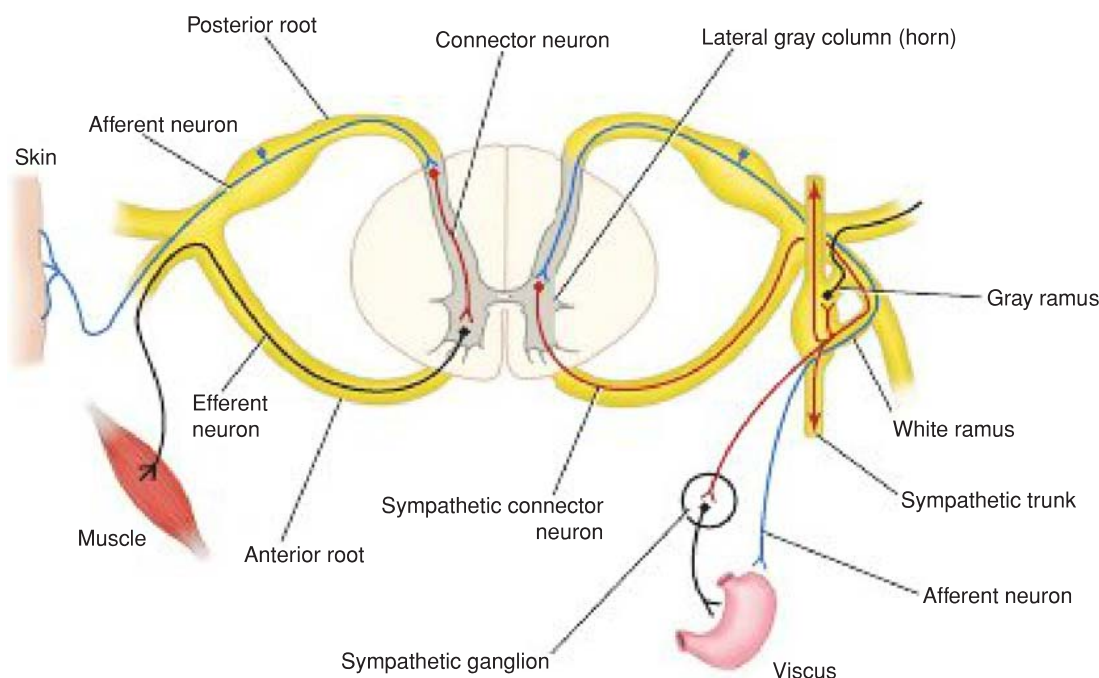


Figure 14-1 General arrangement of the somatic part of the nervous system (on **left**) compared with the autonomic part of the nervous system (on **right**).

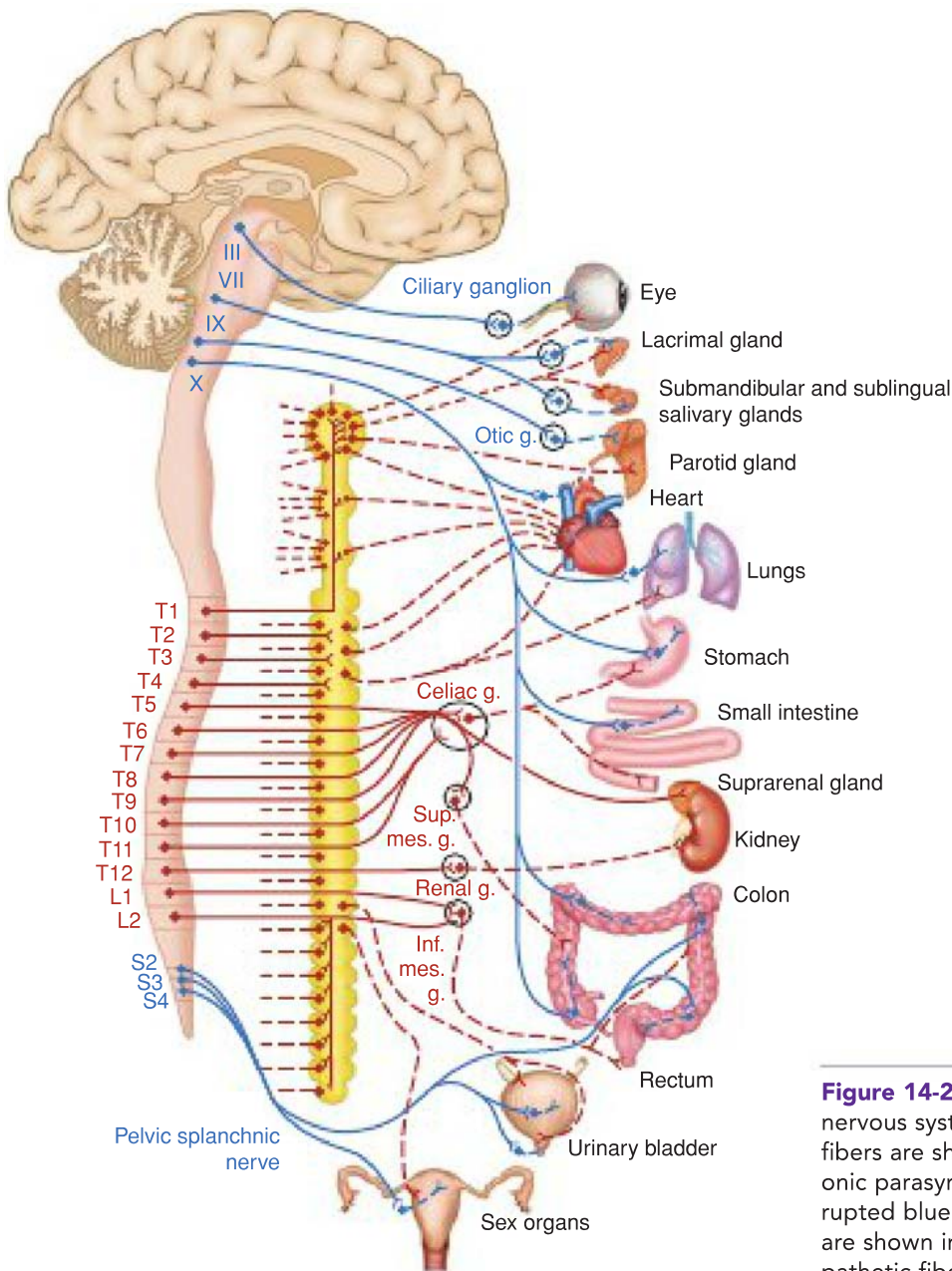


Figure 14-2 Efferent part of the autonomic nervous system. Preganglionic parasympathetic fibers are shown in solid blue and postganglionic parasympathetic fibers are shown in interrupted blue. Preganglionic sympathetic fibers are shown in solid red and postganglionic sympathetic fibers are shown in interrupted red.

fibers pass via gray rami communicantes to join the lumbar, sacral, and coccygeal spinal nerves.

3. They may pass through the ganglia of the sympathetic trunk without synapsing. These myelinated fibers leave the sympathetic trunk as the **greater splanchnic**, **lesser splanchnic**, and **lowest** or **least splanchnic nerves**. The greater splanchnic nerve is formed from branches from the fifth to the ninth thoracic ganglia. It descends obliquely on the sides of the bodies of the thoracic vertebrae and pierces the crus of the diaphragm to synapse with excitor cells in the ganglia of the **celiac plexus**, the **renal plexus**, and the suprarenal medulla. The lesser splanchnic nerve is formed from branches of the 10th and 11th thoracic ganglia. It descends with the greater splanchnic

nerve and pierces the diaphragm to join excitor cells in ganglia in the lower part of the **celiac plexus**. The lowest splanchnic nerve (when present) arises from the 12th thoracic ganglion, pierces the diaphragm, and synapses with excitor neurons in the ganglia of the **renal plexus**. The splanchnic nerves, therefore, are formed of preganglionic fibers. The postganglionic fibers arise from the excitor cells in the peripheral plexuses and are distributed to the smooth muscle and glands of the viscera. A few preganglionic fibers, traveling in the greater splanchnic nerve, end directly on the cells of the **suprarenal medulla**. These medullary cells, which may be regarded as modified sympathetic excitor neurons, are responsible for the secretion of epinephrine and norepinephrine.

The ratio of preganglionic to postganglionic sympathetic fibers is about 1:10, permitting a wide control of involuntary structures.

Afferent Nerve Fibers

Afferent myelinated nerve fibers travel from the viscera through the sympathetic ganglia without synapsing. They pass to the spinal nerve via white rami communicantes and reach their cell bodies in the posterior root ganglion of the corresponding spinal nerve (see Fig. 14-1). The central axons then enter the spinal cord and may form the afferent component of a local reflex arc or ascend to higher centers, such as the hypothalamus.

Sympathetic Trunks

The sympathetic trunks are two ganglionated nerve trunks that extend the whole length of the vertebral column (see Fig. 14-2). In the neck, each trunk has 3 ganglia; in the thorax, 11 or 12; in the lumbar region, 4 or 5; and in the pelvis, 4 or 5. In the neck, the trunks lie anterior to the transverse processes of the cervical vertebrae; in the thorax, they are anterior to the heads of the ribs or lie on the sides of the vertebral bodies; in the abdomen, they are anterolateral to the sides of the bodies of the lumbar vertebrae; and in the pelvis, they are anterior to the sacrum. Below, the two trunks terminate by joining together to form a single ganglion, the **ganglion impar**.

Parasympathetic Part

The activities of the parasympathetic part of the autonomic system are directed toward conserving and restoring energy. The heart rate is slowed, pupils are constricted, peristalsis and glandular activity is increased, sphincters are opened, and the bladder wall is contracted.

Efferent Nerve Fibers (Craniosacral Outflow)

The connector nerve cells of the parasympathetic part of the ANS are located in the brainstem and the sacral segments of the spinal cord (see Fig. 14-2).

Those nerve cells located in the brainstem form nuclei in the following cranial nerves: the **oculomotor** (parasympathetic or Edinger–Westphal nucleus), the **facial** (superior salivatory nucleus and lacrimate nucleus), the **glossopharyngeal** (inferior salivatory nucleus), and the **vagus** nerves (dorsal nucleus of the vagus). The axons of these connector nerve cells are myelinated and emerge from the brain within the cranial nerves.

The sacral connector nerve cells are found in the gray matter of the **second, third, and fourth sacral segments of the spinal cord**. These cells are not sufficiently numerous to form a lateral gray horn, as do the sympathetic connector neurons in the thoracolumbar region. The myelinated axons leave the spinal cord in the anterior nerve roots of the corresponding spinal nerves. They then leave the sacral nerves and form the **pelvic splanchnic nerves**.

The myelinated efferent fibers of the craniosacral outflow are preganglionic and synapse in peripheral ganglia located close to the viscera they innervate. Here again, acetylcholine is the neurotransmitter. The cranial parasympathetic ganglia are the **ciliary, pterygopalatine, submandibular, and otic**. In certain locations, the ganglion cells are placed in nerve plexuses, such as the **cardiac plexus, pulmonary plexus, myenteric plexus (Auerbach plexus), and submucosal plexus (Meissner plexus)**; the last two plexuses are associated with the gastrointestinal tract. The pelvic splanchnic nerves synapse in ganglia in the **hypogastric plexuses**. Characteristically, the postganglionic parasympathetic fibers are nonmyelinated and of relatively short length compared with sympathetic postganglionic fibers.

The ratio of preganglionic to postganglionic fibers is about 1:3 or less, which is much more restricted than in the sympathetic part of the system.

Afferent Nerve Fibers

Afferent myelinated fibers span from the viscera to their cell bodies, located either in the sensory ganglia of the cranial nerves or in the posterior root ganglia of the sacrospinal nerves. The central axons then enter the CNS and take part in the formation of local reflex arcs or pass to higher centers of the ANS, such as the hypothalamus.

The afferent component of the autonomic system is identical to the afferent component of somatic nerves, and it forms part of the general afferent segment of the entire nervous system. The nerve endings in the autonomic afferent component may not be activated by such sensations as heat or touch but rather by stretch or lack of oxygen. Once the afferent fibers gain entrance to the spinal cord or brain, they are thought to travel alongside, or mixed with, the somatic afferent fibers.

LARGE AUTONOMIC PLEXUSES

Large collections of sympathetic and parasympathetic efferent nerve fibers and their associated ganglia, together with visceral afferent fibers, form **autonomic nerve plexuses** (a collection of nerve fibers that form a network, possibly containing nerve cells) in the thorax, abdomen, and pelvis. Branches from these plexuses innervate the viscera. The thorax contains the cardiac, pulmonary, and esophageal plexuses. In the abdomen, the plexuses are associated with the aorta and its branches, and subdivisions of these autonomic plexuses are named according to the branch of the aorta along which they are lying: celiac, superior mesenteric, inferior mesenteric, and aortic plexuses. The pelvis contains the superior and inferior hypogastric plexuses.

AUTONOMIC GANGLIA

The **autonomic ganglion** (a knotlike mass of nerve cells found outside the CNS) is the site where preganglionic

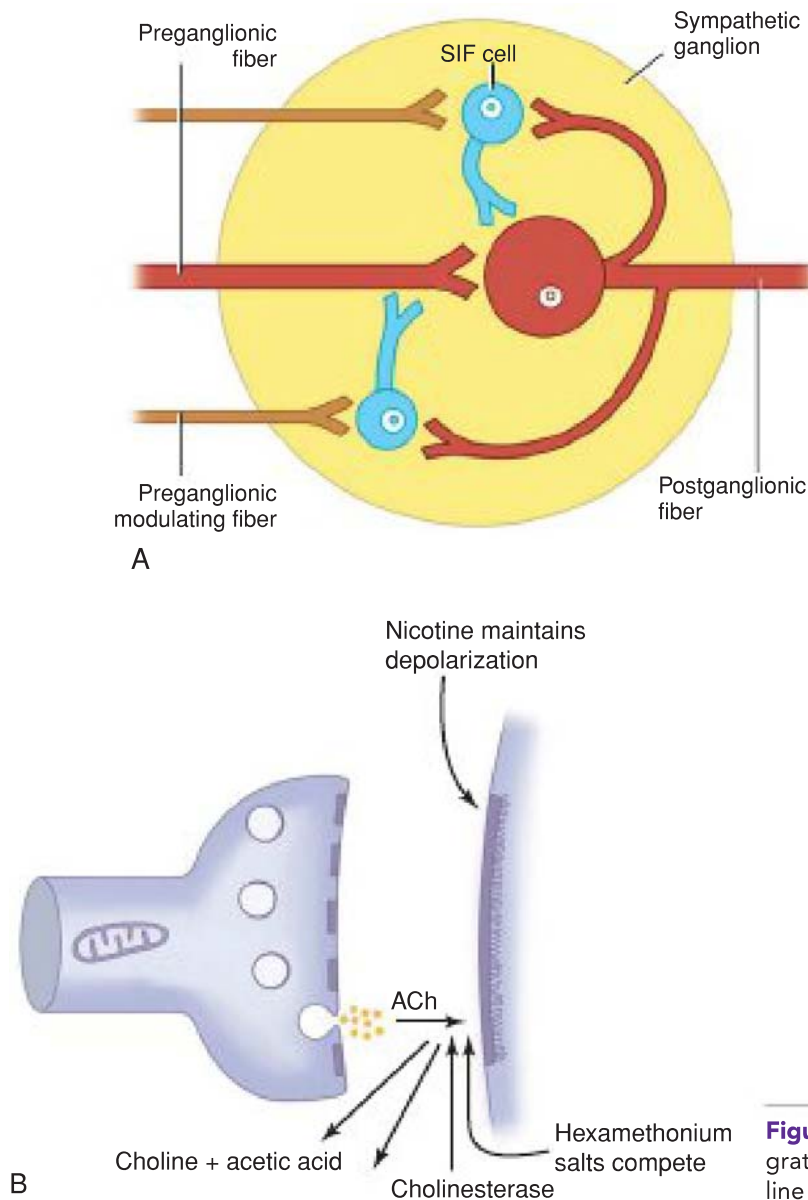


Figure 14-3 **A:** An autonomic ganglion as an integrator. Shows SIF cells. **B:** The liberation of acetylcholine (ACh) at an autonomic synapse.

nerve fibers synapse on postganglionic neurons (Fig. 14-3). Note that this term must be distinguished from the ganglion within the CNS consisting of nuclear groups (e.g., basal ganglia). Ganglia are situated along the course of efferent nerve fibers of the ANS. Sympathetic ganglia form part of the sympathetic trunk or are prevertebral in position (e.g., celiac and superior mesenteric ganglia). Parasympathetic ganglia, on the other hand, are situated close to or within the walls of the viscera.

An autonomic ganglion consists of a collection of multipolar neurons together with capsular or satellite cells and a connective tissue capsule. Nerve bundles are attached to each ganglion and consist of preganglionic nerve fibers that enter the ganglion, postganglionic nerve fibers that have arisen from neurons within the ganglion and are leaving the ganglion, and afferent and efferent nerve fibers that pass through the ganglion without synapsing. The preganglionic fibers are myelinated,

small, and relatively slow-conducting B fibers. The postganglionic fibers are unmyelinated, smaller, and slower-conducting C fibers.

The structure of synapses in autonomic ganglia shows the characteristic membrane thickening and small clear vesicles as well as some larger granular vesicles. The smaller vesicles contain ACh; the content of the granular vesicles is unknown.

Although an autonomic ganglion is the site where preganglionic fibers synapse on postganglionic neurons, the presence of small interneurons has been recognized. These cells exhibit catecholamine fluorescence and are referred to as **small intensely fluorescent (SIF)** cells. In some ganglia, these interneurons receive preganglionic cholinergic fibers and may modulate ganglionic transmission. In other ganglia, they receive collateral branches and may serve some integrative function. Many SIF cells contain **dopamine**, which is thought to be their transmitter.

PREGANGLIONIC TRANSMITTERS

As the preganglionic nerve fibers approach their termination, they wind around and between the dendritic processes of the postganglionic neuron, making multiple synaptic contacts. When the wave of excitation reaches the synaptic contacts, the synaptic transmitter is liberated, crosses the synaptic cleft to reach the receptor, and excites the postganglionic neuron (see Fig. 14-3B).

The synaptic transmitter that excites the postganglionic neurons in both sympathetic and parasympathetic ganglia is **ACh** (Fig. 14-4). The action of ACh in autonomic ganglia is quickly terminated by hydrolysis by **acetylcholinesterase (AChE)**.

Acetylcholine Receptors

ACh receptors are located on the outside of the cell membrane of postganglionic neurons. They are protein complexes that are bound to protein molecules that penetrate the cell membrane. Once the ACh molecule binds with the receptor, the structure of the protein molecule of the cell membrane changes and excitation or inhibition of the postganglionic neuron takes place. Two types of ACh receptors exist and are known as **nicotinic** and **muscarinic** receptors. These receptors are so named because nicotinic receptors respond

specifically to nicotine (from tobacco), and muscarinic receptors respond specifically to muscarine (poison from toadstools). ACh is capable of binding to both of these receptors.

In both sympathetic and parasympathetic preganglionic neurons, the release of ACh binds predominantly with the nicotinic receptors on the postganglionic neurons.

FAST, SLOW, AND INHIBITORY SYNAPTIC POTENTIALS

ACh activation of the postsynaptic nicotinic receptors on the dendrites and cell bodies of the postganglionic neurons results in a depolarization of the membrane, an influx of Na^+ and Ca^{2+} ions, and the generation of the fast excitatory postsynaptic potential (fast **EPSP**). Usually, several presynaptic axon terminals must fire simultaneously and summation has to occur for transmission along the postsynaptic axon to take place. The fast EPSP reaches a maximum within about 15 msec.

ACh is also believed to activate small numbers of postsynaptic muscarinic receptors. This results in the development of the slow excitatory postsynaptic potential (slow **EPSP**), which lasts for 2 to 5 seconds. The underlying mechanism is complicated, and the slow potential occurs when the Na^+ and Ca^{2+} channels are open and M-type K^+ channels close; this leads to membrane depolarization. Late slow **EPSP** lasting as long as 1 to 2 minutes can also be produced by neuropeptide transmitters.

The activation of postsynaptic muscarinic receptors may also result in the development of the slow inhibitory postsynaptic potential (slow **IPSP**), which lasts about 10 seconds. The IPSP results from the opening of K^+ channels, permitting K^+ ions to flow out into the synaptic space, producing hyperpolarization.

The existence of these complex postsynaptic potentials in both sympathetic and parasympathetic ganglia (see Fig. 14-4) illustrates how the postsynaptic membrane potential can be altered and ganglionic transmission modulated.

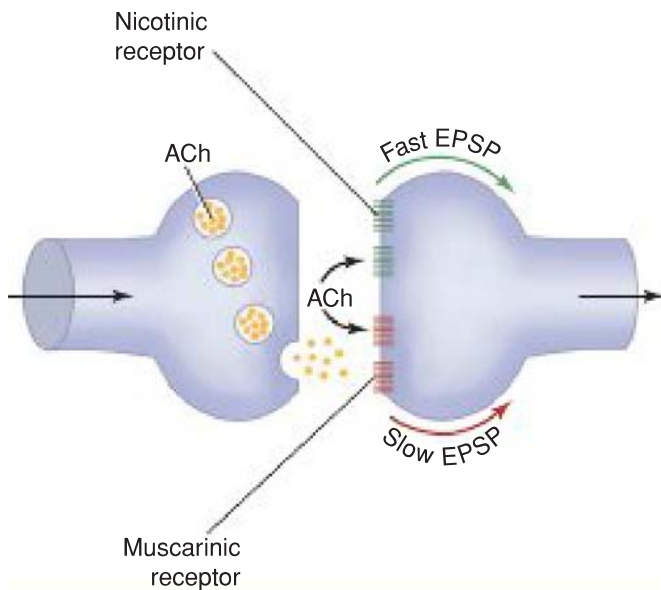


Figure 14-4 Example of the release of acetylcholine from a presynaptic terminal. A single presynaptic stimulus evokes a fast excitatory postsynaptic potential (fast **EPSP**) at a nicotinic receptor. Further stimulation may lead to a slow excitatory postsynaptic potential (slow **EPSP**) or a slow inhibitory postsynaptic potential (slow **IPSP**) at a muscarinic receptor. In preganglionic neurons, both sympathetic and parasympathetic, the release of acetylcholine binds predominantly with the nicotinic receptors on the postganglionic neurons.

GANGLION-STIMULATING AGENTS

Stimulating drugs, such as nicotine, lobeline, and dimethylphenylpiperazinium, stimulate sympathetic and parasympathetic ganglia by activating the nicotinic receptors on the postsynaptic membrane and producing a fast EPSP.

GANGLION-BLOCKING AGENTS

The two types of ganglion-blocking agents are depolarizing and nonpolarizing. **Nicotine** in high concentrations acts as a blocking agent by first stimulating the postganglionic neuron and causing depolarization and then by maintaining depolarization of the excitable membrane. During this latter phase, the postganglionic

neuron will fail to respond to the administration of any stimulant, regardless of the type of receptor it activates.

Hexamethonium and **tetraethylammonium** block ganglia by competing with ACh at the nicotinic receptor sites.

POSTGANGLIONIC NERVE ENDINGS

The postganglionic fibers terminate on the effector cells without special discrete endings. The axons run between the gland cells and the smooth and cardiac muscle fibers and lose their covering of Schwann cells. At sites where transmission occurs, clusters of vesicles are present within the axoplasm (see Fig. 3-35). The site on the axon may lie at some distance from the effector cell; thus, the transmission time may be slow at these endings. The diffusion of the transmitter through the large extracellular distance also permits a given nerve to have an action on a large number of effector cells.

POSTGANGLIONIC TRANSMITTERS

Parasympathetic postganglionic nerve endings liberate **ACh** as their transmitter substance (Fig. 14-5). All neurons that release ACh at their endings are called **cholinergic** (work like ACh). The ACh traverses the synaptic cleft and binds reversibly with the cholinergic

(**muscarinic**) receptor on the postsynaptic membrane. Within 2 to 3 msec, ACh is hydrolyzed into acetic acid and choline by the enzyme **AChE**, which is located on the surface of the nerve and receptor membranes. The choline is reabsorbed into the nerve ending and used again for synthesis of ACh.

Most sympathetic postganglionic nerve endings liberate **norepinephrine** as their transmitter substance. In addition, some sympathetic postganglionic nerve endings, particularly those that end on cells of sweat glands and the blood vessels in skeletal muscle, release **ACh**, which binds with muscarinic receptors on the postsynaptic membrane.

Sympathetic endings that use norepinephrine are called **adrenergic endings**. The two major kinds of receptors in the effector organs are called α and β **receptors**.

Two subgroups of α receptors (α_1 and α_2 receptors) and two subgroups of β receptors (β_1 and β_2 receptors) have been described. Norepinephrine has a greater effect on α receptors than on β receptors. **Phenylephrine** is a pure α stimulator. The bronchodilating drugs, such as **metaproterenol** and **albuterol**, mainly act on β_2 receptors. As a general rule, α receptor sites are associated with most of the excitatory functions of the sympathetic system (e.g., smooth muscle contraction, vasoconstriction, diaphoresis), whereas the β receptor sites are associated with most of the inhibitory functions (e.g., smooth muscle relaxation). β_2 Receptors are mainly in the lung, and stimulation results in

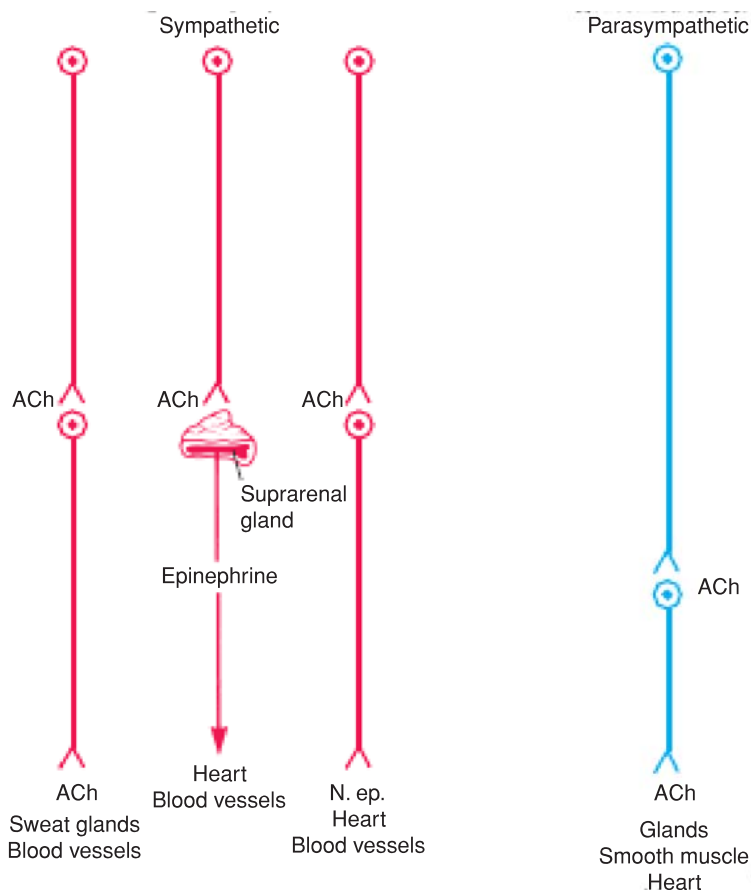


Figure 14-5 Efferent parts of the autonomic nervous system and the chemical transmitter substances released at the nerve endings. (ACh, acetylcholine; N. ep., norepinephrine.)

bronchodilation. β_1 Receptors are in the myocardium, where they are associated with excitation.

The action of norepinephrine on the receptor site of the effector cell is terminated by reuptake into the nerve terminal, where it is stored in presynaptic vesicles for reuse. Some of the norepinephrine escapes from the synaptic cleft into the general circulation and is subsequently metabolized in the liver.

OTHER POSTGANGLIONIC TRANSMITTERS

Sympathetic and parasympathetic postganglionic neurons have been shown to liberate substances other than ACh or norepinephrine at their endings; these include adenosine triphosphate (ATP), neuropeptide **Y**, and substance **P**. These substances may be released alone or from neurons that release ACh or norepinephrine; they have their own specific receptors. The function of these transmitters is probably to modulate the effects of the primary transmitter.

CHOLINERGIC RECEPTOR BLOCKADE

In the case of the parasympathetic and the sympathetic postganglionic nerve endings that liberate ACh as the transmitter substance, the receptors on the effector cells are **muscarinic**. This means that the action can be blocked by **atropine**. Atropine competitively antagonizes the muscarinic action by occupying the cholinergic receptor sites on the effector cells.

ADRENERGIC RECEPTOR BLOCKADE

The α -adrenergic receptors can be blocked by agents such as **phenoxybenzamine**, and the β -adrenergic receptors can be blocked by agents such as **propranolol**. The synthesis and storage of norepinephrine at sympathetic endings can be inhibited by **reserpine**.

HIGHER CONTROL

The hypothalamus has a controlling influence on the ANS and appears to integrate the autonomic and neuroendocrine systems, thus preserving body homeostasis (Fig. 14-6). Essentially, the hypothalamus should be

regarded as a higher nervous center for the control of lower autonomic centers in the brainstem and spinal cord.

Stimulation of the anterior region of the hypothalamus can influence parasympathetic responses, whereas stimulation of the posterior part of the hypothalamus gives rise to sympathetic responses. In addition, lower brainstem centers such as **vasopressor**, **vasodilator**, **cardioaccelerator**, **cardiodecelerator**, and **respiratory centers** have been found in the reticular formation as the result of experimental stimulation in more primitive animals. The various levels of control are believed to be exerted as the result of interconnections of the different regions by ascending and descending pathways. The neurons of the thoracolumbar outflow of the sympathetic part of the system and the neurons of the craniosacral outflow of the parasympathetic part of the system receive their control through the descending tracts of the reticular formation.

Stimulation of different parts of the cerebral cortex and the limbic system produces autonomic effects, and this is presumably brought about through the hypothalamus. The ANS can be brought under voluntary control to some extent. This is seen, for example, in young individuals who may blush easily when embarrassed. As they mature, they are usually able to consciously train themselves to control this response. Also note that the higher centers of the brain can abnormally influence the activities of the ANS and induce diseases such as cardiac palpitations (arrhythmias) and even myocardial infarction.

ENTERIC NERVOUS SYSTEM

Two important plexuses of nerve cells and fibers extend continuously along and around the length of the gastrointestinal tract from the esophagus to the anal canal. The submucous or Meissner plexus lies between the mucous membrane and the circular muscle layer, and the myenteric or Auerbach plexus lies between the circular and longitudinal muscle layers. The submucous plexus is mainly concerned with the control of the glands of the mucous membrane, whereas the myenteric plexus controls the muscle and movements of the gut wall.

Different types of neurons have been recognized in the plexuses. Some neurons are bipolar or unipolar and are thought to be sensory and involved in local reflex activity; other neurons send axons to the celiac

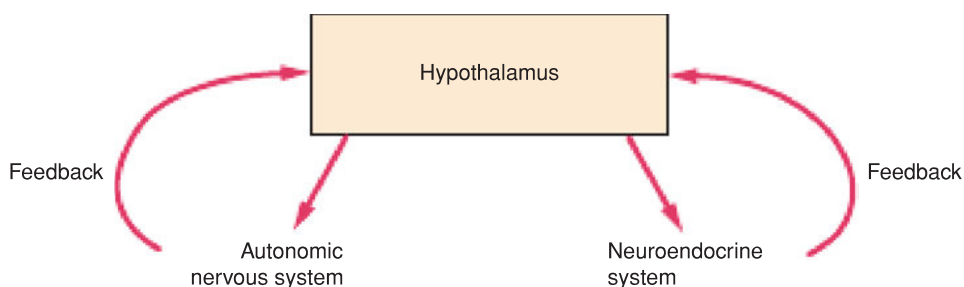


Figure 14-6 Hypothalamus as the control center for the autonomic nervous system and the neuroendocrine system.

and mesenteric plexuses. Preganglionic parasympathetic fibers synapse on nerve cells that give rise to postganglionic fibers that innervate the smooth muscle and glands. Postganglionic sympathetic fibers have been seen to terminate on parasympathetic nerve cells and probably exert an inhibitory role in parasympathetic activity. Internuncial neurons are also present. Interestingly, the nerve cells and their processes are surrounded by neuroglialike cells that closely resemble astrocytes in the CNS. It has been suggested that while the enteric plexuses can coordinate the activities of the gut wall, the parasympathetic and sympathetic inputs modulate these activities.

FUNCTIONS

The ANS, along with the endocrine system, maintains body homeostasis. The endocrine control is slower and exerts its influence by means of blood-borne hormones.

The ANS functions for the most part at the subconscious level. We are not aware, for example, that our pupils are dilating or that our arteries are constricting. The system should not be regarded as an isolated portion of the nervous system; it can play a role with somatic activity in expressing emotion and certain autonomic activities, such as micturition, can be brought under voluntary control. The various activities of the autonomic and endocrine systems are integrated within the hypothalamus.

The sympathetic and parasympathetic components of the ANS cooperate in maintaining the stability of the internal environment. The sympathetic part prepares and mobilizes the body in an emergency when sudden severe exercise, fear, or rage occurs. The parasympathetic part aims at conserving and storing energy, for example, in the promotion of digestion and the absorption of food by increasing the secretions of the glands of the gastrointestinal tract and stimulating peristalsis.

The sympathetic and parasympathetic parts of the ANS usually have antagonistic control over a viscus. For example, the sympathetic activity will increase the heart rate, whereas the parasympathetic activity will slow the heart rate. The sympathetic activity will make the bronchial smooth muscle relax, but the muscle is contracted by parasympathetic activity.

However, many viscera do not possess this fine dual control from the ANS. For example, the smooth muscle of the hair follicles (the arrector pili muscle) is made to contract by the sympathetic activity without parasympathetic control.

The activities of some viscera are kept under a constant state of inhibition by one or the other components of the ANS. The heart in a trained athlete is maintained at a slow rate by the activities of the parasympathetic system. This is of considerable importance because the heart is a more efficient pump when contracting slowly than when contracting very quickly, thus permitting adequate diastolic filling of the ventricles.

DIFFERENCES BETWEEN SYMPATHETIC AND PARASYMPATHETIC SYSTEMS

Important anatomic, physiologic, and pharmacologic differences between the sympathetic and parasympathetic parts of the ANS are shown in Table 14-1.

1. The sympathetic efferent nerve fibers originate (see Fig. 14-2) from nerve cells in the lateral gray column of the spinal cord between the first thoracic and second lumbar segments (the **thoracic outflow**). The parasympathetic efferent nerve fibers originate from nerve cells in the 3rd, 7th, 9th, and 10th cranial nerves and in the gray matter of the 2nd, 3rd, and 4th sacral segments of the cord (the **craniosacral outflow**).
2. The sympathetic ganglia are located either in the paravertebral sympathetic trunks or in the prevertebral ganglia, such as the celiac ganglion. The parasympathetic ganglion cells are located as small ganglia close to the viscera or within plexuses within the viscera.
3. The sympathetic part of the autonomic system has long postganglionic fibers, whereas the parasympathetic system has short fibers (see Fig. 14-5).
4. The sympathetic part of the system has a widespread action on the body as the result of the preganglionic fibers synapsing on many postganglionic neurons and the suprarenal medulla releasing the sympathetic transmitters epinephrine and norepinephrine, which are distributed throughout the body through the bloodstream. The parasympathetic part of the autonomic system has a more discrete control, since the preganglionic fibers synapse on only a few postganglionic neurons with no comparable organ to the suprarenal medulla.
5. The sympathetic postganglionic endings liberate norepinephrine at most endings and ACh at a few endings (e.g., sweat glands). The parasympathetic postganglionic endings liberate ACh.
6. The sympathetic part of the autonomic system prepares the body for emergencies and severe muscular activity, whereas the parasympathetic part conserves and stores energy.

To assist with the learning of the different actions of these two components of the autonomic system, imagine that sympathetic activity would be maximal in a man who finds himself suddenly alone in a field with a bull that is about to charge. His hair will stand on end with fear; his skin will be pale as the result of vasoconstriction, which causes a redistribution of blood away from the skin and viscera to the heart muscle and skeletal muscle. His upper eyelids will be raised and his pupils will be widely dilated so that he can see where to run. His heart rate will rise and the peripheral resistance of the arterioles will be increased, causing a rise in blood pressure. His bronchi will dilate to permit maximum respiratory flow of air. His peristaltic activity will be inhibited and his gut sphincters will be contracted. His vesical sphincter will also be contracted (this is certainly not the time to be thinking of defecation or

Table 14-1 Anatomic, Physiologic, and Pharmacologic Characteristics of Sympathetic Versus Parasympathetic Systems

	Sympathetic	Parasympathetic
Action	Prepares body for emergency	Conserves and restores energy
Outflow	T1–L2 (3)	Cranial nerves III, VII, IX, and X; S2–S4
Preganglionic fibers	Myelinated	Myelinated
Ganglia	Paravertebral (sympathetic trunks), prevertebral (e.g., celiac, superior mesenteric, inferior mesenteric)	Small ganglia close to viscera (e.g., otic, ciliary) or ganglion cells in plexuses (e.g., cardiac, pulmonary)
Neurotransmitter within ganglia	Acetylcholine	Acetylcholine
Ganglion-blocking agents	Hexamethonium and tetraethylammonium by competing with acetylcholine	Hexamethonium and tetraethylammonium by competing with acetylcholine
Postganglionic fibers	Long, nonmyelinated	Short, nonmyelinated
Characteristic activity	Widespread due to many postganglionic fibers and liberation of epinephrine and norepinephrine from suprarenal medulla	Discrete action with few postganglionic fibers
Neurotransmitter at postganglionic endings	Norepinephrine at most endings and acetylcholine at few endings (sweat glands)	Acetylcholine at all endings
Blocking agents on receptors of effector cells	α -Adrenergic receptors—phenoxybenzamine β -Adrenergic receptors—propranolol	Atropine, scopolamine
Agents inhibiting synthesis and storage of neurotransmitter at postganglionic endings	Reserpine	
Agents inhibiting hydrolysis of neurotransmitter at site of effector cells		Acetylcholinesterase blockers (e.g., neostigmine)
Drugs mimicking autonomic activity	Sympathomimetic drugs Phenylephrine: α receptors; Isoproterenol: β receptors	Parasympathomimetic drugs Pilocarpine Methacholine
Higher control	Hypothalamus	Hypothalamus

micturition). Glycogen will be converted into glucose for energy and he will sweat to lose body heat.

On the other hand, the parasympathetic activity will be great in a woman who has fallen asleep in an armchair after a satisfying meal. Her heart rate will be slow and her blood pressure will not be high. Her upper eyelids will droop or be closed and her pupils will be constricted. Her breathing will be noisy owing to bronchial constriction. Her abdomen may rumble owing to excessive peristaltic activity. She may feel the inclination to defecate or micturate.

AUTONOMIC INNERVATIONS

Some important ANS innervations are shown in Table 14-2.

Eye

Both sympathetic and parasympathetic nervous systems control involuntary function in the iris and

lacrimal glands, whereas the eyelids are only affected by the sympathetic nervous system.

Upper Lid

The upper lid is raised by the levator palpebrae superioris muscle. The major part of this muscle is formed by skeletal muscle innervated by the oculomotor nerve. A small part is composed of smooth muscle fibers innervated by sympathetic postganglionic fibers from the superior cervical sympathetic ganglion (Fig. 14-7).

Iris

The smooth muscle fibers of the iris consist of circular and radiating fibers. The circular fibers form the sphincter pupillae and the radial fibers form the dilator pupillae.

The sphincter pupillae is supplied by parasympathetic fibers from the parasympathetic nucleus (Edinger–Westphal nucleus) of the oculomotor nerve.

Table 14-2 Autonomic Nervous System Effects on Body Organs

Organ		Sympathetic Action	Parasympathetic Action
Eye	Pupil	Dilates	Constricts
	Ciliary muscle	Relaxes	Contracts
Glands	Lacrimal, parotid, submandibular, sublingual, nasal	Reduce secretion by causing vasoconstriction of blood vessels	Increase secretion
	Sweat	Increases secretion	
Heart	Cardiac muscle	Increases force of contraction	Decreases force of contraction
	Coronary arteries (mainly controlled by local metabolic factors)	Dilates (β receptors), constricts (α receptors)	
Lung	Bronchial muscle	Relaxes (dilates bronchi)	Contracts (constricts bronchi)
	Bronchial secretion		Increases secretion
	Bronchial arteries	Constricts	Dilates
Gastrointestinal tract	Muscle in walls	Decreases peristalsis	Increases peristalsis
	Muscle in sphincters	Contracts	Relaxes
	Glands	Reduces secretion by vasoconstriction of blood vessels	Increases secretion
Liver		Breaks down glycogen into glucose	
Gallbladder		Relaxes	Contracts
Kidney		Decreases output due to constriction of arteries	
Urinary bladder	Bladder wall (detrusor)	Relaxes	Contracts
	Sphincter vesicae	Contracts	Relaxes
Erectile tissue of penis and clitoris			Relaxes, causes erection
Ejaculation		Contracts smooth muscle of vas deferens, seminal vesicles, and prostate	
Systemic arteries			
Skin		Constrict	
Abdominal		Constrict	
Muscle		Constrict (α receptors), dilate (β receptors), dilate (cholinergic)	
erector pili muscle		Contract	
prerenal			
Cortex		Stimulates	
Medulla		Liberates epinephrine and norepinephrine	

After synapsing in the **ciliary ganglion**, the postganglionic fibers pass forward to the eyeball in the **short ciliary nerves**. (The ciliary muscle of the eye is also supplied by the short ciliary nerves; see p. 406.)

The dilator pupillae is supplied by postganglionic fibers from the superior cervical sympathetic ganglion. The postganglionic fibers reach the orbit along the internal carotid and ophthalmic arteries. They pass unin-

terrupted through the ciliary ganglion and reach the eyeball in the **short ciliary nerves**. Other sympathetic fibers reach the eyeball in the **long ciliary nerves**.

Lacrimal Gland

The parasympathetic secretomotor nerve supply to the lacrimal gland originates in the **lacrimal nucleus**

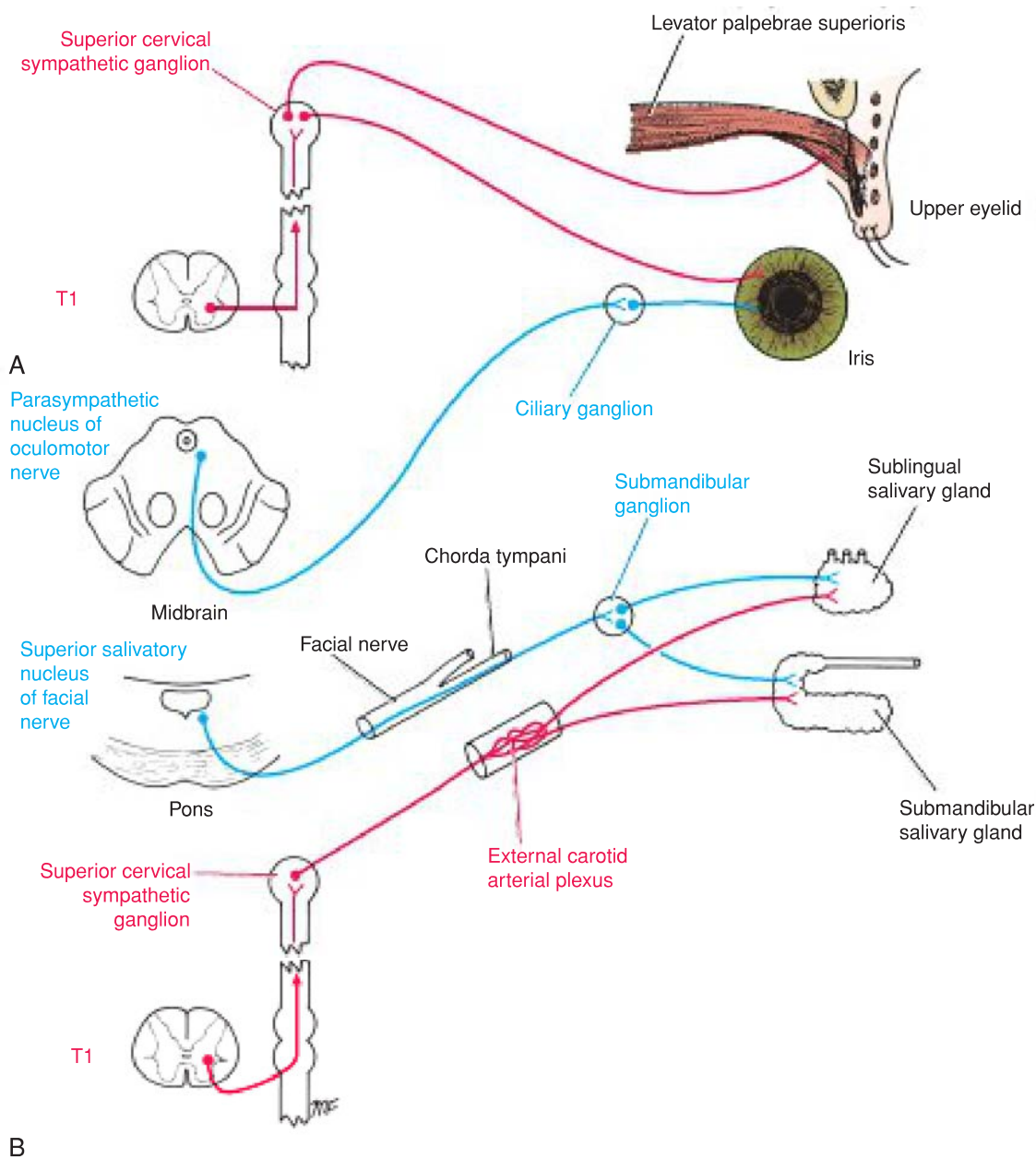


Figure 14-7 Autonomic innervation of the upper eyelid and iris (**A**) and the sublingual and submandibular salivary glands (**B**).

of the facial nerve (Fig. 14-8). The preganglionic fibers reach the **pterygopalatine ganglion** through the **nervus intermedius** and its **great petrosal branch** and through the **nerve of the pterygoid canal**. The postganglionic fibers leave the ganglion and join the maxillary nerve. They then pass into its **zygomatic branch** and the **zygomaticotemporal nerve**. They reach the lacrimal gland within the **lacrimal nerve**.

The sympathetic postganglionic fibers arise from the superior cervical sympathetic ganglion and travel in the plexus of nerves around the internal carotid artery. They join the **deep petrosal nerve**, the **nerve of the pterygoid canal**, the **maxillary nerve**, the **zygomatic nerve**, **zygomaticotemporal nerve**, and finally the lacrimal nerve. They function as vasoconstrictor fibers.

Salivary Glands

The involuntary action of the salivary glands is controlled by the ANS. These three, paired glands have similar sympathetic nerve origination but have unique parasympathetic origins.

Submandibular and Sublingual Glands

The parasympathetic secretomotor supply originates in the **superior salivatory nucleus** of the facial nerve (see Fig. 14-7). The preganglionic fibers pass to the **submandibular ganglion** and other small ganglia close to the duct through the **chorda tympani nerve** and the **lingual nerve**. Postganglionic fibers reach the submandibular gland either directly or along the duct. Postganglionic

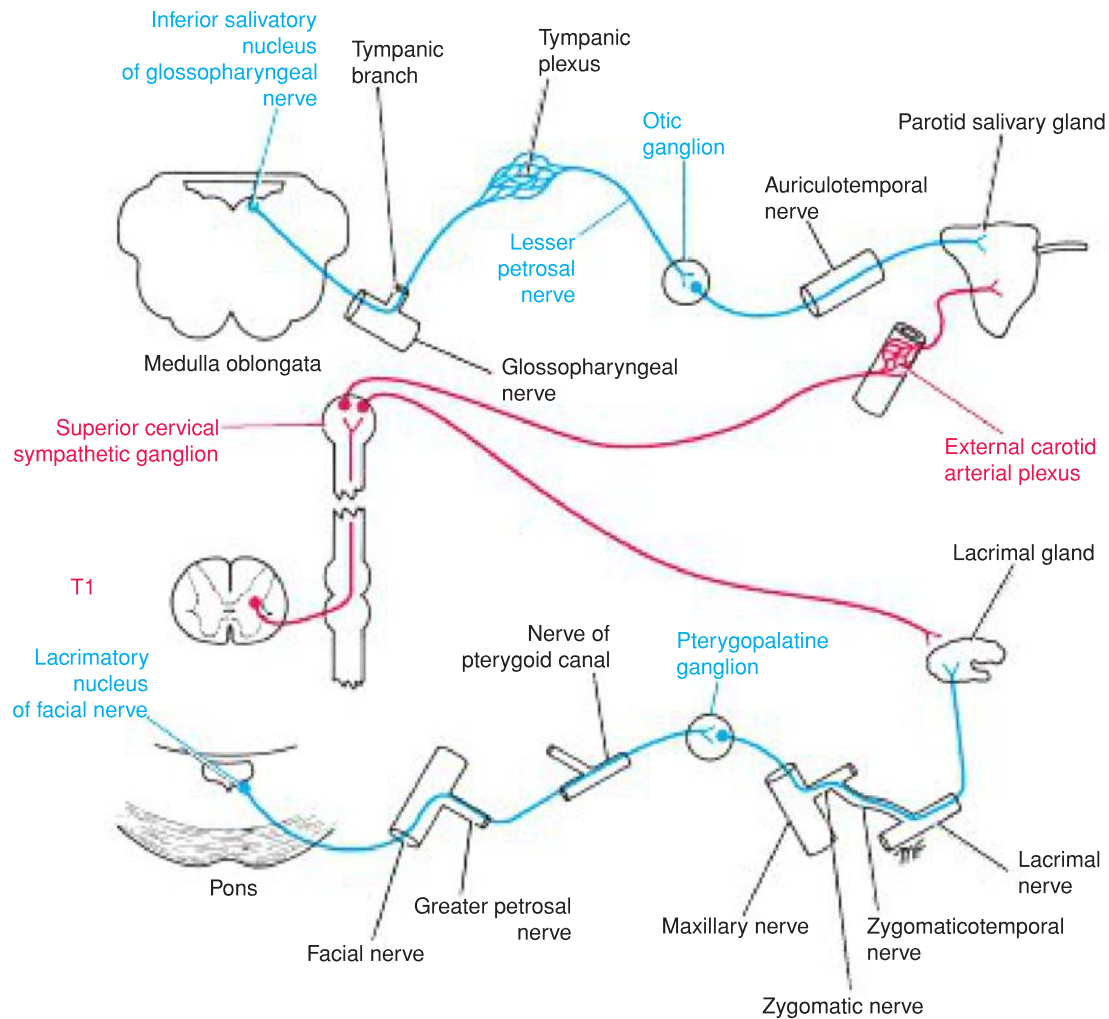


Figure 14-8 Autonomic innervation of the parotid salivary gland and lacrimal gland.

fibers to the sublingual gland travel through the lingual nerve.

Sympathetic postganglionic fibers arise from the superior cervical sympathetic ganglion and reach the glands as a plexus of nerves around the external carotid, facial, and lingual arteries. They function as vasoconstrictor fibers.

Parotid Gland

Parasympathetic secretomotor fibers from the **inferior salivatory nucleus** of the glossopharyngeal nerve supply the gland (see Fig. 14-8). The preganglionic nerve fibers pass to the otic ganglion through the **tympanic branch of the glossopharyngeal nerve** and the **lesser petrosal nerve**. Postganglionic fibers reach the gland through the auriculotemporal nerve.

Sympathetic postganglionic fibers arise from the superior cervical sympathetic ganglion and reach the gland as a plexus of nerves around the external carotid artery. They function as vasoconstrictor fibers.

Heart

The sympathetic postganglionic fibers arise from the cervical and upper thoracic portions of the sympathetic

trunks (Fig. 14-9). Postganglionic fibers reach the heart by way of the **superior, middle, and inferior cardiac branches** of the cervical portion of the sympathetic trunk and a number of **cardiac branches** from the thoracic portion of the sympathetic trunk. The fibers pass through the **cardiac plexuses** and terminate on the **sinoatrial** and **atrioventricular nodes**, on cardiac muscle fibers, and on coronary arteries. Activation of these nerves results in cardiac acceleration, increased force of contraction of the cardiac muscle, and dilatation of the coronary arteries. The coronary dilatation is mainly produced in response to local metabolic needs rather than by direct nerve stimulation of the coronary arteries.

The parasympathetic preganglionic fibers originate in the **dorsal nucleus of the vagus nerve** and descend into the thorax in the vagus nerves. The fibers terminate by synapsing with postganglionic neurons in the **cardiac plexuses**. Postganglionic fibers terminate on the **sinoatrial** and **atrioventricular nodes** and on the coronary arteries. Activation of these nerves results in a reduction in the rate and force of contraction of the myocardium and a constriction of the coronary arteries. Here again, the coronary constriction is mainly produced by the reduction in local metabolic needs rather than by neural effects.

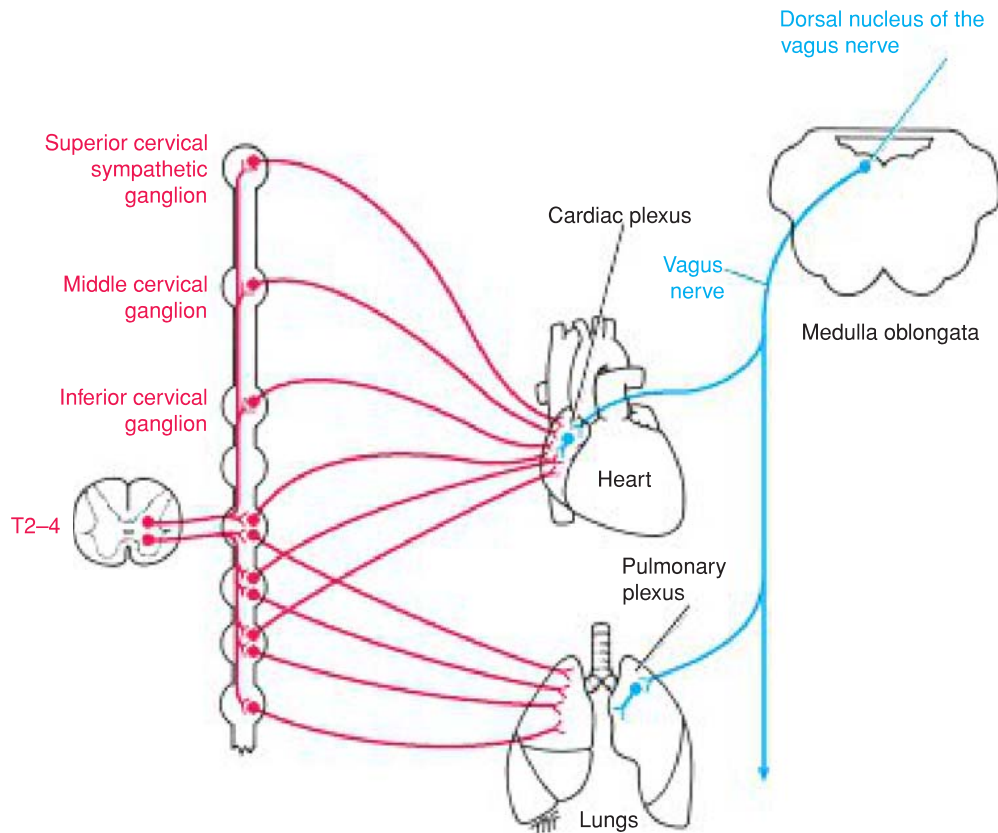


Figure 14-9 Autonomic innervation of the heart and lungs.

Lungs

The sympathetic postganglionic fibers arise from the second to the fifth thoracic ganglia of the sympathetic trunk (see Fig. 14-9). The fibers pass through the pulmonary plexuses and enter the lung, where they form networks around the bronchi and blood vessels. The sympathetic fibers produce bronchodilation and slight vasoconstriction.

The parasympathetic preganglionic fibers arise from the **dorsal nucleus of the vagus** and descend to the thorax within the vagus nerves. The fibers terminate by synapsing with postganglionic neurons in the pulmonary plexuses. The postganglionic fibers enter the lung, where they form networks around the bronchi and blood vessels. The parasympathetic fibers produce bronchoconstriction and slight vasodilation and increase glandular secretion.

Gastrointestinal Tract

Stomach and Intestine (to Splenic Flexure)

Preganglionic parasympathetic fibers enter the abdomen in the **anterior (left)** and **posterior (right) vagal trunks** (Fig. 14-10). The fibers are distributed to many abdominal viscera and to the gastrointestinal tract from the stomach to the splenic flexure of the colon. The fibers that pass to the gastrointestinal tract terminate on postganglionic neurons in the **myenteric (Auerbach)**

and **submucosal (Meissner) plexuses**. The postganglionic fibers supply the smooth muscle and glands. The parasympathetic nerves stimulate peristalsis and relax the sphincters; they also stimulate secretion.

Sympathetic preganglionic nerve fibers pass through the thoracic part of the sympathetic trunk and enter the **greater** and **lesser splanchnic nerves**. These descend into the abdomen and synapse with postganglionic neurons in the **celiac** and **superior mesenteric ganglia**. The postganglionic nerve fibers are distributed to the stomach and intestine as nerve plexuses around the branches of the celiac and superior mesenteric arteries. The sympathetic nerves inhibit peristalsis and cause contraction of the sphincters; they also inhibit secretion (see the enteric nervous system, p. 394).

Descending Colon, Pelvic Colon, and Rectum

The preganglionic parasympathetic fibers originate in the gray matter of the spinal cord from the second to the fourth sacral segments (see Fig. 14-10). The fibers pass through the **pelvic splanchnic nerves** and the nerve plexuses around the branches of the inferior mesenteric artery. They terminate on postganglionic neurons in the myenteric (Auerbach) and submucosal (Meissner) plexuses. The postganglionic fibers supply the smooth muscle and glands. The parasympathetic nerves stimulate peristalsis and secretion.

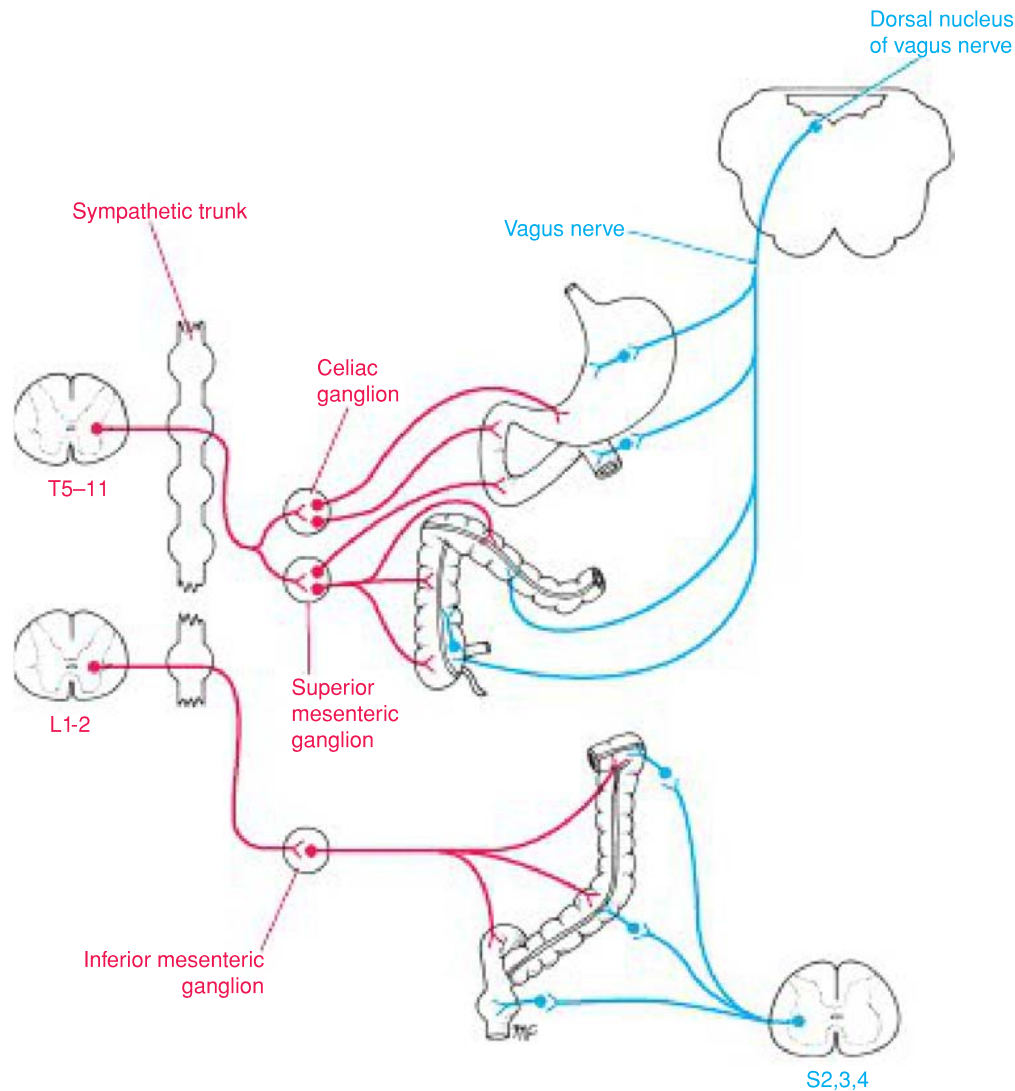


Figure 14-10 Autonomic innervation of the gastrointestinal tract.

The sympathetic preganglionic nerve fibers pass through the lumbar part of the sympathetic trunk and synapse with postganglionic neurons in the **inferior mesenteric plexus**. Postganglionic fibers are distributed to the bowel as nerve plexuses around the branches of the inferior mesenteric arteries. The sympathetic nerves inhibit peristalsis and secretion.

Gallbladder and Biliary Ducts

The gallbladder and biliary ducts receive postganglionic parasympathetic and sympathetic fibers from the hepatic plexus. Parasympathetic fibers derived from the vagus are thought to be motor fibers to the smooth muscle of the gallbladder and bile ducts and inhibitory to the sphincter of Oddi.

Autonomic afferent fibers are also present. Some of the fibers are believed to leave the hepatic plexus and join the right phrenic nerve, thus partially explaining the phenomenon of referred shoulder pain in the presence of gallbladder disease (see p. 410).

Kidney

Preganglionic sympathetic fibers pass through the lower thoracic part of the sympathetic trunk and the lowest thoracic splanchnic nerve to join the **renal plexus** around the renal artery (Fig. 14-11). The preganglionic fibers synapse with postganglionic neurons in the renal plexus. The postganglionic fibers are distributed to the branches of the renal artery. The sympathetic nerves are vasoconstrictor in action to the renal arteries within the kidney.

Preganglionic parasympathetic fibers enter the renal plexus from the vagus. Here, they synapse with postganglionic neurons whose fibers are distributed to the kidney along the branches of the renal artery. The parasympathetic nerves are thought to be vasodilator in action.

Suprarenal Gland Medulla

Preganglionic sympathetic fibers descend to the gland in the **greater splanchnic nerve**, a branch of the thoracic

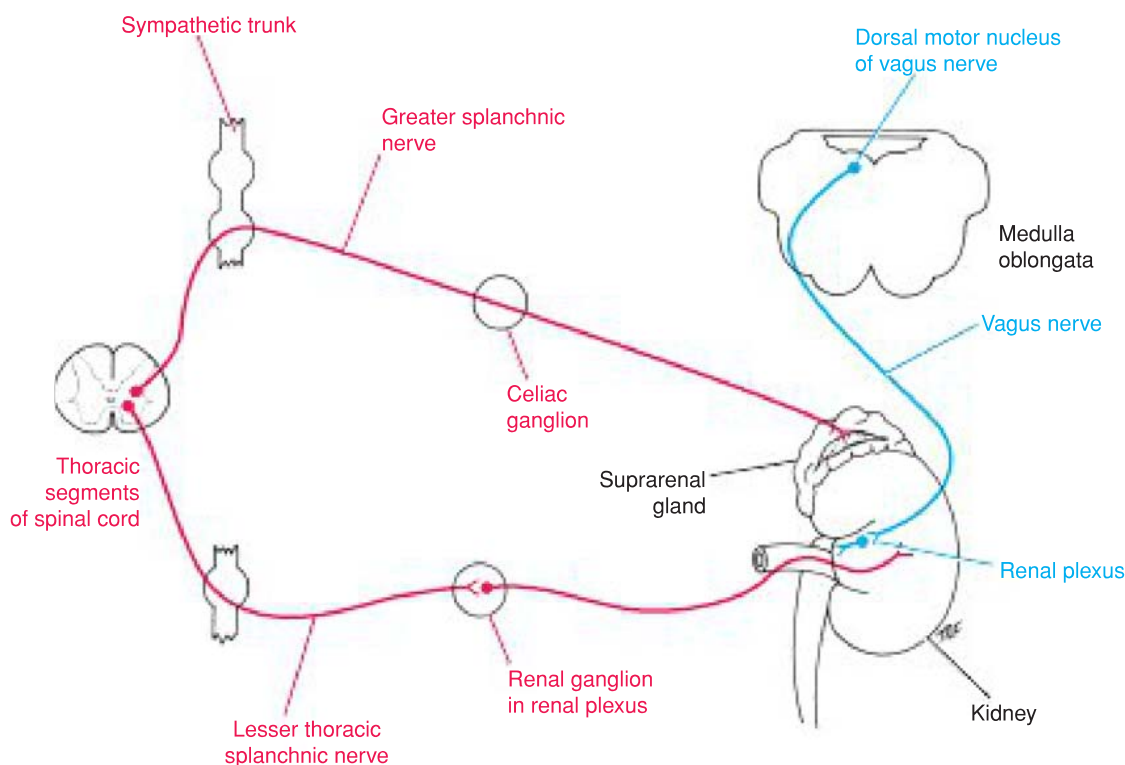


Figure 14-11 Autonomic innervation of the kidney and suprarenal gland.

part of the sympathetic trunk (see Fig. 14-11). The nerve fibers terminate on the secretory cells of the medulla, which are comparable to postganglionic neurons. ACh is the transmitter substance between the nerve endings and the secretory cells, as at any other preganglionic endings. The sympathetic nerves stimulate the secretory cells of the medulla to increase the output of epinephrine and norepinephrine. The medulla of the suprarenal gland lacks parasympathetic innervation.

Anal Canal Involuntary Internal Sphincter

The circular smooth muscle coat is thickened at the upper end of the anal canal to form the involuntary internal sphincter. The sphincter is innervated by postganglionic sympathetic fibers from the **hypogastric plexuses** (Fig. 14-12). Each hypogastric plexus receives sympathetic fibers from the **aortic plexus** and from the lumbar and pelvic parts of the sympathetic trunks. The sympathetic nerves cause the internal anal sphincter to contract.

Urinary Bladder

The muscular coat of the bladder is composed of smooth muscle, which at the bladder neck is thickened to form the **sphincter vesicae**. The nerve supply of the smooth muscle is from the hypogastric plexuses (see Fig. 14-12). The sympathetic postganglionic fibers originate in the first and second lumbar ganglia of the sympathetic trunk and travel to the hypogastric plexuses.

The parasympathetic preganglionic fibers arise as the pelvic splanchnic nerves from the second, third, and fourth sacral nerves; they pass through the hypogastric plexuses to reach the bladder wall, where they synapse with postganglionic neurons.

The sympathetic nerves to the detrusor muscle have little or no action on the smooth muscle of the bladder wall and are distributed mainly to the blood vessels. The sympathetic nerves to the sphincter vesicae play only a minor role in causing contraction of the sphincter in maintaining urinary continence. However, in the male, the sympathetic innervation of the sphincter causes active contraction of the bladder neck during ejaculation (brought about by sympathetic action), thus preventing seminal fluid from entering the bladder. The parasympathetic nerves stimulate the contraction of the smooth muscle of the bladder wall and, in some way, inhibit the contraction of the sphincter vesicae.

Penile and Clitoral Erection

In erection, the genital **erectile tissue** becomes engorged with blood. The initial vascular engorgement is controlled by the parasympathetic part of the ANS. The parasympathetic preganglionic fibers originate in the gray matter of the second, third, and fourth sacral segments of the spinal cord (Fig. 14-13). The fibers enter the hypogastric plexuses and synapse on the postganglionic neurons. The postganglionic fibers join the internal pudendal arteries and are distributed along their branches, which enter the erectile tissue. The parasympathetic nerves

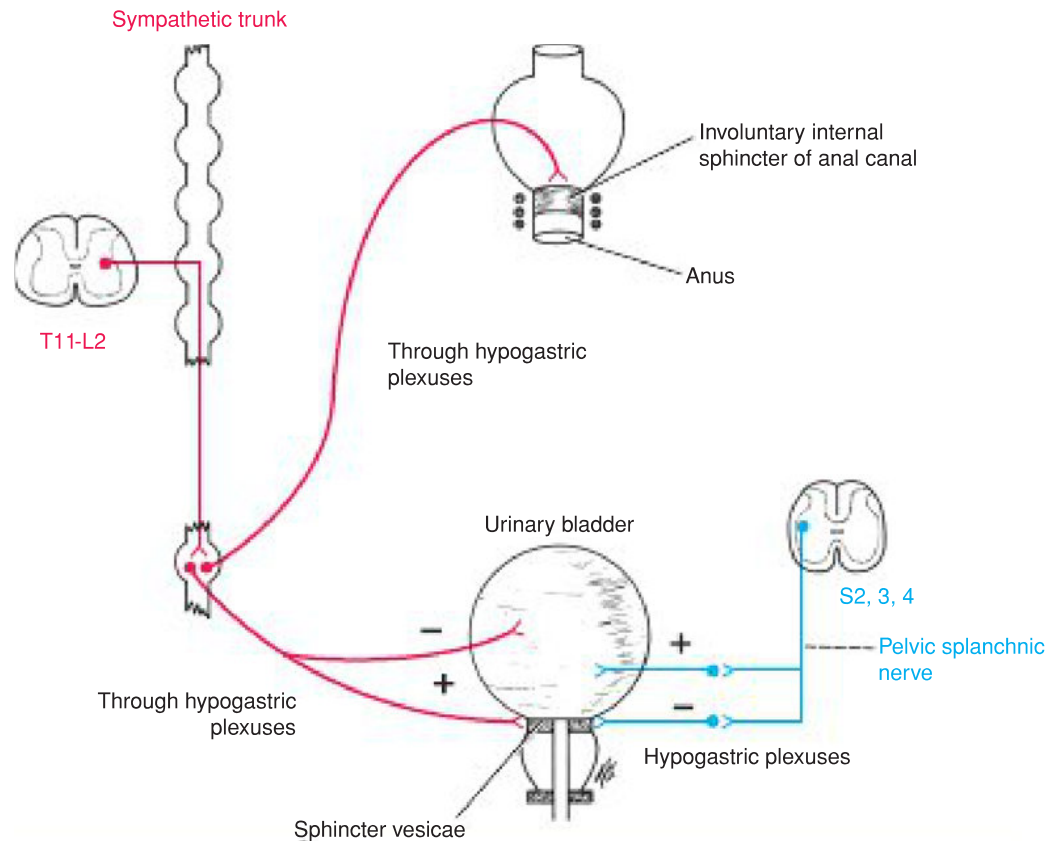


Figure 14-12 Autonomic innervation of the sphincters of the anal canal and urinary bladder.

cause vasodilatation of the arteries and greatly increase the blood flow to the erectile tissue.

Ejaculation

During the increasing sexual excitement that occurs during sex play, the external urinary meatus of the glans penis becomes moist as a result of the secretions of the bulbourethral glands. Friction on the glans penis, reinforced by other afferent nervous impulses, results in a discharge along the sympathetic nerve fibers to the smooth muscle of the duct of the epididymis and the vas deferens on each side, the seminal vesicles, and the prostate. The smooth muscle contracts and the spermatozoa, together with the secretions of the seminal vesicles and prostate, are discharged into the prostatic urethra. The fluid now joins the secretions of the bulbourethral glands and penile urethral glands and is then ejected from the penile urethra as a result of the rhythmic contractions of the bulbospongiosus muscles, which compress the urethra. Meanwhile, the sphincter of the bladder contracts and prevents a reflux of the spermatozoa into the bladder. The spermatozoa and the secretions of the several accessory glands constitute the **seminal fluid**, or **semen**. At the climax of male sexual excitement, a mass discharge of nervous impulses takes place in the CNS. Impulses pass down the spinal cord to the sympathetic outflow (T1–L2). The nervous impulses that pass to the

genital organs are thought to leave the cord at the first and second lumbar segments in the preganglionic sympathetic fibers (see Fig. 14-13). Many of these fibers synapse with postganglionic neurons in the first and second lumbar ganglia. Other fibers may synapse in ganglia in the lower lumbar or pelvic parts of the sympathetic trunks. The postganglionic fibers are then distributed to the **vas deferens**, the **seminal vesicles**, and the **prostate** through the **hypogastric plexuses**. The sympathetic nerves stimulate the contractions of the smooth muscle in the walls of these structures and cause the spermatozoa, together with the secretions of the seminal vesicles and prostate, to be discharged into the urethra.

Uterus

Preganglionic sympathetic nerve fibers leave the spinal cord at segmental levels T12 and L1 and are believed to synapse with ganglion cells in the sympathetic trunk or possibly in the inferior hypogastric plexuses (Fig. 14-14). The postganglionic fibers supply the smooth muscle of the uterus. Parasympathetic preganglionic fibers leave the spinal cord at levels S2–S4 and synapse with ganglion cells in the inferior hypogastric plexuses. Although the uterine muscle is largely under hormonal control, sympathetic innervation may cause uterine contraction and vasoconstriction, whereas parasympathetic fibers have the opposite effect.

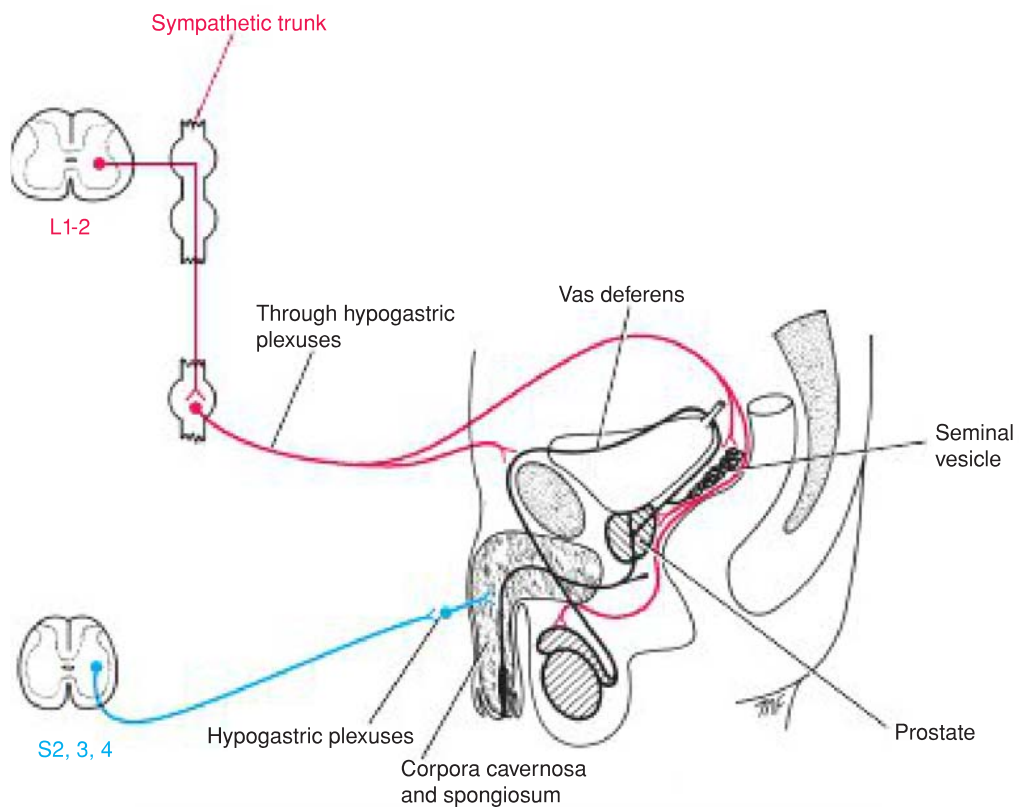


Figure 14-13 Autonomic innervation of the male reproductive tract.

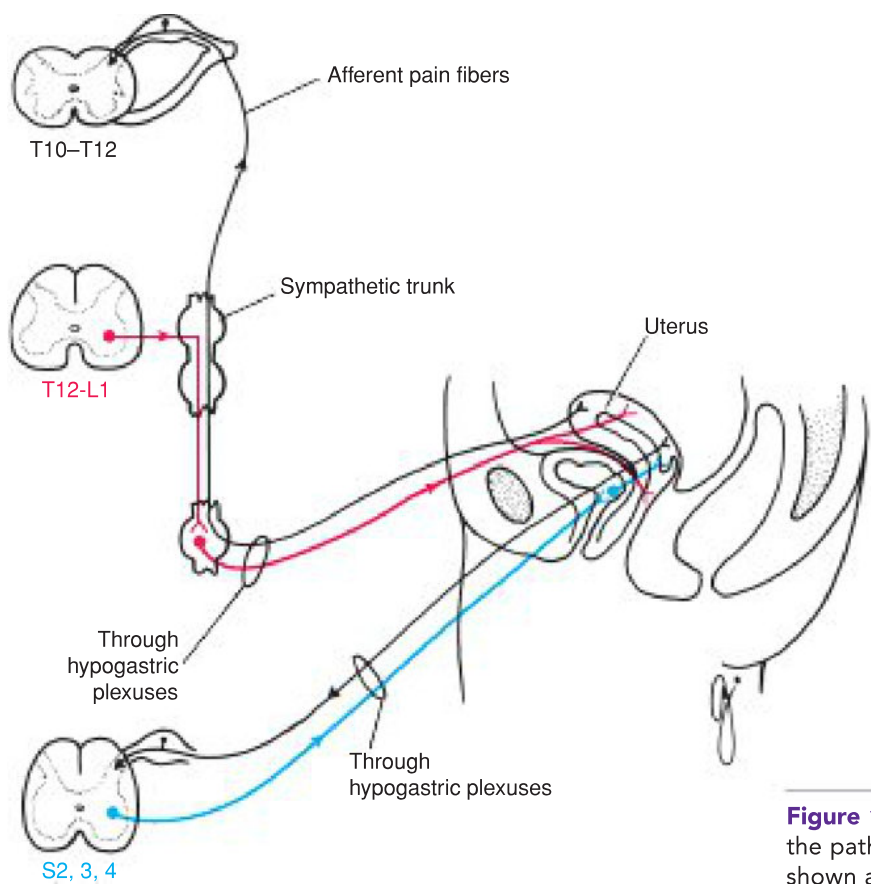


Figure 14-14 Autonomic innervation of the uterus; the pathway taken by the afferent sensory fibers is shown as well.

Afferent pain fibers from the fundus and the body of the uterus ascend to the spinal cord through the hypogastric plexuses, entering it through the posterior roots of the 10th, 11th, and 12th thoracic spinal nerves. Fibers from the cervix run in the pelvic splanchnic nerves and enter the spinal cord through the posterior roots of the second, third, and fourth sacral nerves.

Upper Limb Arteries

The arteries of the upper limb are innervated by sympathetic nerves. The preganglionic fibers originate from cell bodies in the second to the eighth thoracic segments of the spinal cord (Fig. 14-15). They pass to the sympathetic trunk through white rami and ascend in the trunk to synapse in the middle cervical, inferior cervical, first thoracic, or stellate ganglia. The

postganglionic fibers join the nerves that form the brachial plexus and are distributed to the arteries within the branches of the plexus. The sympathetic nerves cause vasoconstriction of cutaneous arteries and vasodilatation of arteries that supply skeletal muscle.

Lower Limb Arteries

The arteries of the lower limb are also innervated by sympathetic nerves (see Fig. 14-15). The preganglionic fibers originate from cell bodies in the lower three thoracic and upper two or three lumbar segments of the spinal cord. The preganglionic fibers pass to the lower thoracic and upper lumbar ganglia of the sympathetic trunk through white rami. The fibers synapse in the lumbar and sacral ganglia and the postganglionic fibers reach the arteries through branches of the lumbar and sacral plexuses.

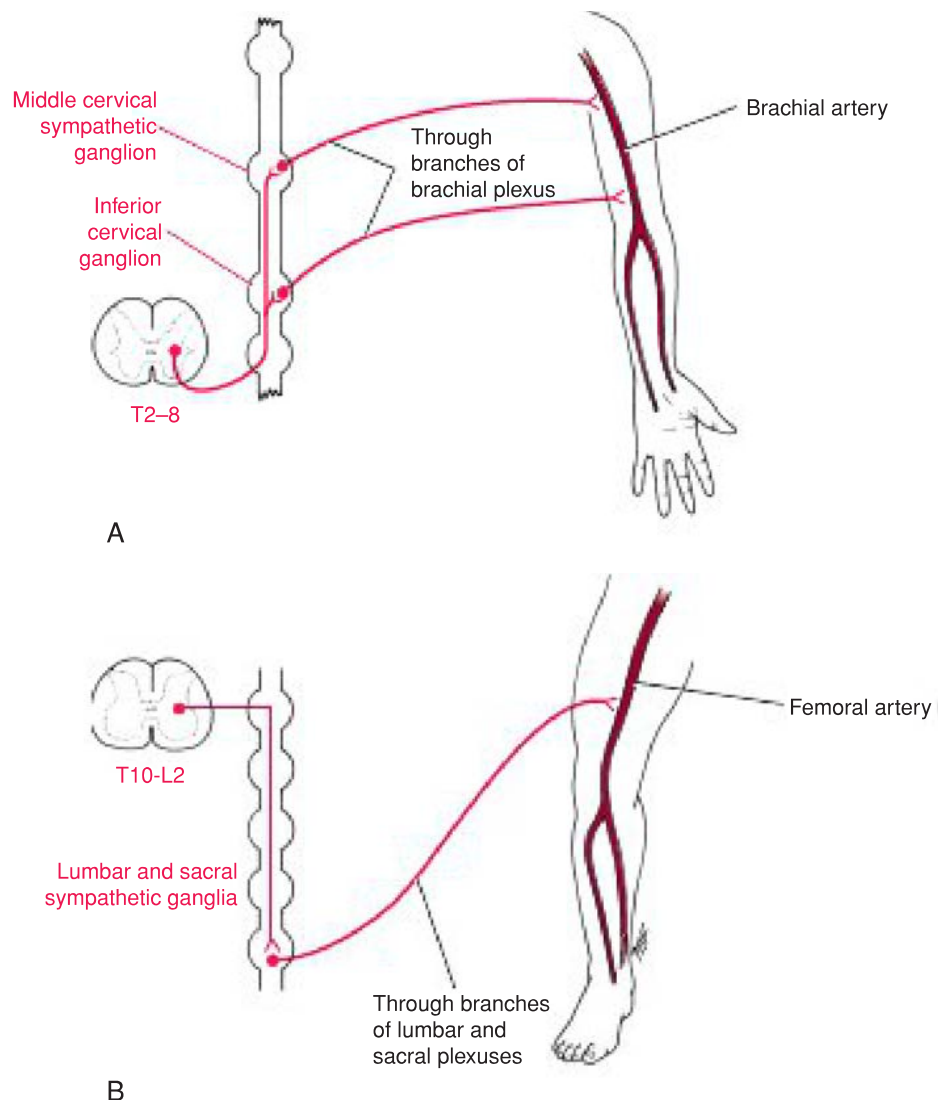


Figure 14-15 Sympathetic innervation of the arteries of the upper limb (A) and lower limb (B).

ANS PHYSIOLOGIC REFLEXES

The ANS is involved in important visual and cardiovascular reflexes.

Direct and Consensual Light Reflexes

Afferent nervous impulses travel from the retina through the optic nerve, optic chiasma, and optic tract (see Fig. 11-3). A small number of fibers leave the optic tract and synapse on nerve cells in the **pretectal nucleus**, which lies close to the superior colliculus. The impulses are passed by axons of the pretectal nerve cells to the parasympathetic nuclei (Edinger–Westphal nuclei) of the oculomotor nerve on both sides. Here, the fibers synapse and the parasympathetic nerves travel through the oculomotor nerve to the **ciliary ganglion** in the orbit. Finally, postganglionic parasympathetic fibers pass through the **short ciliary nerves** to the eyeball and to the constrictor pupillae muscle of the iris. Both pupils constrict in the consensual light reflex because the pretectal nucleus sends fibers to the parasympathetic nuclei on both sides of the midbrain.

Accommodation Reflex

When the eyes are directed from a distant to a near object, contraction of the medial recti brings about convergence of the ocular axes, the lenses thicken to increase their refractive power by contraction of the ciliary muscle, and the pupils constrict to restrict the light waves to the thickest central part of the lenses. The afferent impulses travel through the optic nerve, the optic chiasma, the optic tract, the lateral geniculate body, and the optic radiation to the visual cortex (see Fig. 11-3). The visual cortex is connected to the eye field of the frontal cortex. From here, cortical fibers descend through the internal capsule to the oculomotor nuclei in the midbrain. The oculomotor nerve travels to the medial recti muscles. Some of the descending cortical fibers synapse with the parasympathetic nuclei (Edinger–Westphal nuclei) of the oculomotor nerve on both sides. The parasympathetic preganglionic fibers

then travel through the oculomotor nerve to the **ciliary ganglion** in the orbit where they synapse. Finally, postganglionic parasympathetic fibers pass through the **short ciliary nerves** to the ciliary muscle and the constrictor pupillae muscle of the iris.

Carotid Sinus and Aortic Arch Reflexes

The carotid sinus, located in the bifurcation of the common carotid artery, and the aortic arch serve as baroreceptors. As the blood pressure rises, nerve endings situated in the walls of these vessels are stimulated. The afferent fibers from the carotid sinus ascend in the glossopharyngeal nerve and terminate in the **nucleus solitarius** (see Figs. 11-16 and 11-17). The afferent fibers from the aortic arch ascend in the vagus nerve. Connector neurons in the medulla oblongata activate the parasympathetic nucleus (dorsal nucleus) of the vagus, which slows the heart rate. At the same time, reticulospinal fibers descend to the spinal cord and inhibit the preganglionic sympathetic outflow to the heart and cutaneous arterioles. The combined effect of stimulation of the parasympathetic action on the heart and inhibition of the sympathetic action on the heart and peripheral blood vessels reduces the rate and force of contraction of the heart and reduces the peripheral resistance of the blood vessels. Consequently, the blood pressure falls. The blood pressure of the individual is thus modified by the afferent information received from the baroreceptors. The modulator of the ANS, namely, the hypothalamus, in turn, can be influenced by other, higher centers in the CNS.

Bainbridge Right Atrial Reflex

This reflex is initiated when the nerve endings in the wall of the right atrium and in the walls of the venae cavae are stimulated by a rise of venous pressure. The afferent fibers ascend in the vagus to the medulla oblongata and terminate on the **nucleus of the tractus solitarius** (see Fig. 11-18). Connector neurons inhibit the parasympathetic nucleus (dorsal) of the vagus, and reticulospinal fibers stimulate the thoracic sympathetic outflow to the heart, resulting in cardiac acceleration.



CLINICAL NOTES

General Considerations

Clearly, the ANS is not an isolated part of the nervous system. It should be regarded as the part of the nervous system that, with the endocrine system, is particularly involved in maintaining the stability of the internal environment of the body. Its activities are modified by the hypothalamus, whose function is to integrate vast amounts of afferent information received from other areas of the nervous system and to translate changing hormonal levels of the bloodstream into appropriate nervous and hormonal activities.

Because the ANS is so important in maintaining normal body homeostasis, not surprisingly, the system is subject to many pharmacologic interventions. Propranolol and atenolol,

for example, are β -adrenergic antagonists that can be used in the treatment of hypertension and ischemic heart disease.

Autonomic Nervous System Injury

Trauma to the ANS is usually limited to either sympathetic or parasympathetic components, rarely both at the same time, due to their relative locations in the thorax or cranial cavity, respectively.

Sympathetic Injuries

The sympathetic trunk in the neck can be injured by stab and bullet wounds. Traction injuries to the first thoracic root of the brachial plexus can damage sympathetic nerves

destined for the stellate ganglion. All these conditions can produce a preganglionic type of Horner syndrome. Injuries to the spinal cord or cauda equina can disrupt the sympathetic control of the bladder (see p. 402).

Parasympathetic Injuries

The oculomotor nerve is vulnerable in head injuries (herniated disc) and can be damaged by compression by aneurysms in the junction between the posterior cerebral artery and posterior communicating artery. The preganglionic parasympathetic fibers traveling in this nerve are situated in the periphery of the nerve and can be damaged. Surface aneurysmal compression characteristically causes dilation of the pupil and loss of the visual light reflexes.

The autonomic fibers in the facial nerve can be damaged by fractures of the skull involving the temporal bone. The vestibulocochlear nerve is closely related to the facial nerve in the internal acoustic meatus, so clinical findings involving both nerves are common. Involvement of the parasympathetic fibers in the facial nerve may produce impaired lacrimation in addition to paralysis of the facial muscles.

The glossopharyngeal and vagus nerves are at risk in stab and bullet wounds of the neck. The parasympathetic secretomotor fibers to the parotid salivary gland leave the glossopharyngeal nerve just below the skull; therefore, they are rarely damaged.

The parasympathetic outflow in the sacral region of the spinal cord (S2–S4) may be damaged by spinal cord and cauda equina injuries, leading to disruption of bladder, rectal, and sexual functions.

Degeneration and Regeneration of Autonomic Nerves

The structural changes are identical to those found in other areas of the peripheral and central parts of the nervous system. Functional recoveries following sympathectomy operations can be explained only by the assumption either that the operative procedure was inadequate and nerve fibers were left intact or regenerated or that alternative nervous pathways existed and were left undisturbed.

The denervation of viscera supplied by autonomic nerves is followed by their increased sensitivity to the agent that was previously the transmitter substance. One explanation is that following nerve section, there may be an increase in the number of receptor sites on the postsynaptic membrane. Another possibility, which applies to endings where norepinephrine is the transmitter, is that the reuptake of the transmitter by the nerve terminal is interfered with in some way.

Urinary Bladder Dysfunction

Injuries to the spinal cord are followed by disruption of the nervous control of micturition. The normal bladder is innervated as follows:

Sympathetic innervation is from the first and second lumbar segments of the spinal cord.

Parasympathetic innervation is from the second, third, and fourth sacral segments of the spinal cord.

Sensory nerve fibers enter the spinal cord at the above segments.

The **atonic bladder** occurs during the phase of spinal shock immediately following the injury and may last from a few days to several weeks. The bladder wall muscle is relaxed, the sphincter vesicae is tightly contracted (loss of inhibition from higher levels), and the sphincter urethrae is

relaxed. The bladder becomes greatly distended and finally overflows. Depending on the level of the cord injury, the patient may or may not be aware that the bladder is full but has no voluntary control.

The **automatic reflex bladder** occurs after the patient has recovered from spinal shock, provided that the cord lesion lies above the level of the parasympathetic outflow (S2–S4). This is the type of bladder normally found in infancy. The descending fibers in the spinal cord are sectioned, so voluntary control is not possible. The bladder fills and empties reflexly. Stretch receptors in the bladder wall are stimulated as the bladder fills and the afferent impulses pass to the spinal cord (S2–S4). Efferent impulses pass down to the bladder muscle, which contracts; the sphincter vesicae and the urethral sphincter both relax. This simple reflex occurs every 1 to 4 hours.

The **autonomous bladder** is the condition that occurs if the sacral segment of the spinal cord is destroyed or if the cauda equina is severed. The bladder has no reflex control or voluntary control. The bladder wall is flaccid and the capacity of the bladder is greatly increased. It fills to capacity and overflows, which results in continual dribbling. The bladder may be partially emptied by manual compression of the lower part of the anterior abdominal wall, but infection of the urine and back pressure effects on the ureters and kidneys are inevitable.

Defecation

The act of defecation involves a coordinated reflex that results in the emptying of the descending colon, pelvic colon, rectum, and anal canal. It is assisted by a rise in the intra-abdominal pressure brought about by contraction of the muscles of the anterior abdominal wall. The involuntary internal sphincter of the anal canal normally is innervated by postganglionic sympathetic fibers from the hypogastric plexuses, and the voluntary external sphincter of the anal canal is innervated by the inferior rectal nerve. The desire to defecate is initiated by stimulation of the stretch receptors in the wall of the rectum.

Following severe spinal cord injuries (or cauda equina injuries), the patient is not aware of rectal distention. Moreover, the parasympathetic influence on the peristaltic activity of the descending colon, sigmoid colon, and rectum is lost. In addition, control over the abdominal musculature and sphincters of the anal canal may be severely impaired. The rectum, now an isolated structure, responds by contracting when the pressure within its lumen rises. This local reflex response is much more efficient if the sacral segments of the spinal cord and the cauda equina are intact. At best, however, the force of the contractions of the rectal wall is small and constipation and impaction are the usual outcome. The treatment of patients with spinal cord injuries is to empty the rectum with biweekly enemas; the use of suppositories also may be helpful.

Erection and Ejaculation

As described previously, erection of the penis or clitoris is controlled by the parasympathetic nerves that originate from the second, third, and fourth sacral segments of the spinal cord. Bilateral damage to the reticulospinal tracts in the spinal cord above the second sacral segment of the spinal cord will result in loss of erection. Later, when the effects of spinal shock have disappeared, spontaneous or reflex erection may occur if the sacral segments of the spinal cord are intact.

Ejaculation is controlled by sympathetic nerves that originate in the first and second lumbar segments of the spinal cord. Ejaculation brings about a flow of seminal fluid into the prostatic urethra. The final ejection of the fluid from the penis is the result of the rhythmic contractions of the bulbospongiosus muscles, which compress the urethra. The bulbospongiosus muscles are innervated by the pudendal nerve (S2–S4). Discharge of the seminal fluid into the bladder is prevented by the contraction of the sphincter vesicae, which is innervated by the sympathetic nerves (L1–L2). As in the case of erection, severe bilateral damage to the spinal cord results in loss of ejaculation. Later, reflex ejaculation may be possible in patients with spinal cord transections in the thoracic or cervical regions. Some individuals have a normal ejaculation without external emission, and the seminal fluid passes into the bladder owing to paralysis of the sphincter vesicae.

Diseases Involving the Autonomic Nervous System

The ANS can be affected by a variety of diseases that compromise the integrity of peripheral nerves containing sympathetic and parasympathetic fibers.

Diabetes Mellitus

Diabetes mellitus is a common cause of peripheral nerve neuropathy. This involves sensory and motor dysfunction and may also include autonomic dysfunction. The clinical features of autonomic dysfunction include postural hypotension, peripheral edema, pupillary abnormalities, and impaired sweating. The cause is probably associated with chronic hyperglycemia.

Horner Syndrome

Horner syndrome consists of (1) constriction of the pupil (miosis), (2) slight drooping of the eyelid (ptosis), (3) enophthalmos (which, although apparent, is not real and is caused by the ptosis; however, the orbitalis muscle is paralyzed, and involvement may be responsible), (4) vasodilation of skin arterioles, and (5) loss of sweating (anhidrosis). All these symptoms result from an interruption of the sympathetic nerve supply to the head and neck. Pathologic causes include lesions in the brainstem or cervical part of the spinal cord that interrupt the reticulospinal tracts descending from the hypothalamus to the sympathetic outflow in the lateral gray column of the first thoracic segment of the spinal cord. Such lesions include **multiple sclerosis** and **syringomyelia**. Traction on the stellate ganglion due to a **cervical rib** or involvement of the ganglion in a metastatic lesion may interrupt the peripheral part of the sympathetic pathway.

All patients with Horner syndrome have miosis and ptosis. However, a distinction should be made between lesions occurring at the first neuron (the descending reticulospinal fibers within the CNS), the second neuron (the preganglionic fibers), and the third neuron (postganglionic fibers). For example, the clinical signs suggestive of a first-neuron defect (central Horner syndrome) could include contralateral hyperesthesia of the body and loss of sweating of the entire half of the body. Signs suggesting a second-neuron involvement (preganglionic Horner syndrome) include loss of sweating limited to the face and neck and the presence of flushing or blanching of the face and neck. Signs suggesting third-neuron involvement (postganglionic Horner syndrome) include facial pain or ear, nose, or throat disease.

The presence or absence of other localizing signs and symptoms may assist in differentiating the three types of Horner syndrome.

Argyll Robertson Pupil

Argyll Robertson pupil is characterized by a small pupil, which is of fixed size and does not react to light but does contract with accommodation. It is usually caused by a neurosyphilitic lesion interrupting the fibers that run from the pretectal nucleus to the parasympathetic nuclei (Edinger–Westphal nuclei) of the oculomotor nerve on both sides. The fact that the pupil constricts with accommodation implies that the connections between the parasympathetic nuclei and the constrictor pupillae muscle of the iris are intact.

Adie Tonic Pupil Syndrome

In Adie tonic pupil syndrome, the pupil has a decreased or absent light reflex, a slow or delayed contraction to near vision, and a slow or delayed dilatation in the dark. This benign syndrome, which probably results from a disorder of the parasympathetic innervation of the constrictor pupillae muscle, must be distinguished from the Argyll Robertson pupil (see above), which is caused by neurosyphilis. Adie syndrome can be confirmed by looking for hypersensitivity to cholinergic agents. Drops commonly used for this test are 2.5% methacholine (Mecholyl) or 0.1% pilocarpine. The Adie tonic pupil should constrict when these drops are put in the eye. These cholinergic agents do not cause pupillary constriction in mydriasis caused by oculomotor lesion or in drug-related mydriasis.

Frey Syndrome

Frey syndrome is an interesting complication that sometimes follows penetrating wounds of the parotid gland. During the process of healing, the postganglionic parasympathetic secretomotor fibers traveling in the auriculotemporal nerve grow out and join the distal end of the great auricular nerve, which supplies the sweat glands of the overlying facial skin. By this means, a stimulus intended for saliva production instead produces sweat secretion.

A similar syndrome may follow injury to the facial nerve. During the process of regeneration, parasympathetic fibers normally destined for the submandibular and sublingual salivary glands are diverted to the lacrimal gland. This produces watering of the eyes associated with salivation, the so-called **crocodile tears**.

Hirschsprung Disease

Hirschsprung disease (megacolon) is a congenital condition in which the myenteric plexus (Auerbach plexus) fails to develop in the distal part of the colon. The involved part of the colon possesses no parasympathetic ganglion cells and peristalsis is absent. This effectively blocks the passage of feces and the proximal part of the colon becomes enormously distended.

Disease Caused by Botulinum Toxin

A very small amount of botulinum toxin binds irreversibly to the nerve plasma membranes and prevents the release of ACh at cholinergic synapses and neuromuscular junctions, producing an atropinelike syndrome with skeletal muscle weakness.

Disease Caused by Black Widow Spider Venom

The venom of a black widow spider causes a brief release of ACh at the nerve endings followed by a permanent blockade.

Disease Caused by Anticholinesterase Agents

AChE, which is responsible for hydrolyzing and limiting the action of ACh at nerve endings, can be blocked by certain drugs. Physostigmine, neostigmine, pyridostigmine, and carbamate and organophosphate insecticides are effective AChE inhibitors. Their use results in an excessive stimulation of the cholinergic receptors, producing the “SLUDG syndrome”—salivation, lacrimation, urination, defecation, and gastrointestinal distress.

Sympathectomy

Sympathectomy, or surgical removal of a sympathetic nerve ganglion, can be used to treat arterial disease.

Raynaud Disease

Raynaud disease is a vasospastic disorder involving the digital arteries of the upper limb. The disorder is usually bilateral and an attack is provoked by exposure to cold. Pallor or cyanosis of the fingers is seen as well as severe pain. Gangrene of the tips of the fingers may occur.

In mild cases of Raynaud disease, the treatment is the avoidance of cold and no smoking (smoking causes vasoconstriction). In more severe cases, drugs that inhibit sympathetic activity, such as reserpine, bring about arterial vasodilatation with consequent increase in blood flow to the fingers. Cervicothoracic preganglionic sympathectomy has been used, but the long-term results are disappointing.

Intermittent Claudication

Intermittent claudication, which is common in men, is due to arterial occlusive disease of the leg. Ischemia of the

muscles produces a cramplike pain on exercise. Lumbar preganglionic sympathectomy may be advocated as a form of treatment in order to bring about vasodilatation and an increase in blood flow through the collateral circulation. Preganglionic sympathectomy is performed by removing the upper three lumbar ganglia and the intervening parts of the sympathetic trunk.

Hypertension

In the past, severe essential hypertension was treated by bilateral thoracolumbar sympathectomy to reduce the vasomotor control over the peripheral resistance and thus lower the blood pressure. Today, chemical blocking agents of the sympathetic system are widely used with great success and the resulting reduction in the force of myocardial contraction reduces the arterial blood pressure.

Referred Visceral Pain

Most viscera are innervated only by autonomic nerves. Therefore, it follows that visceral pain is conducted along afferent autonomic nerves. Visceral pain is diffuse and poorly localized, whereas somatic pain is intense and discretely localized. Visceral pain frequently is referred to skin areas that are innervated by the same segments of the spinal cord as the painful viscus (Fig. 14-16). The explanation for referred pain is not known. One theory is that the nerve fibers from the viscus and the dermatome ascend in the CNS along a common pathway and the cerebral cortex is incapable of distinguishing between the sites of origin. Another theory is that under normal conditions, the viscus does not give rise to painful stimuli, whereas the skin area

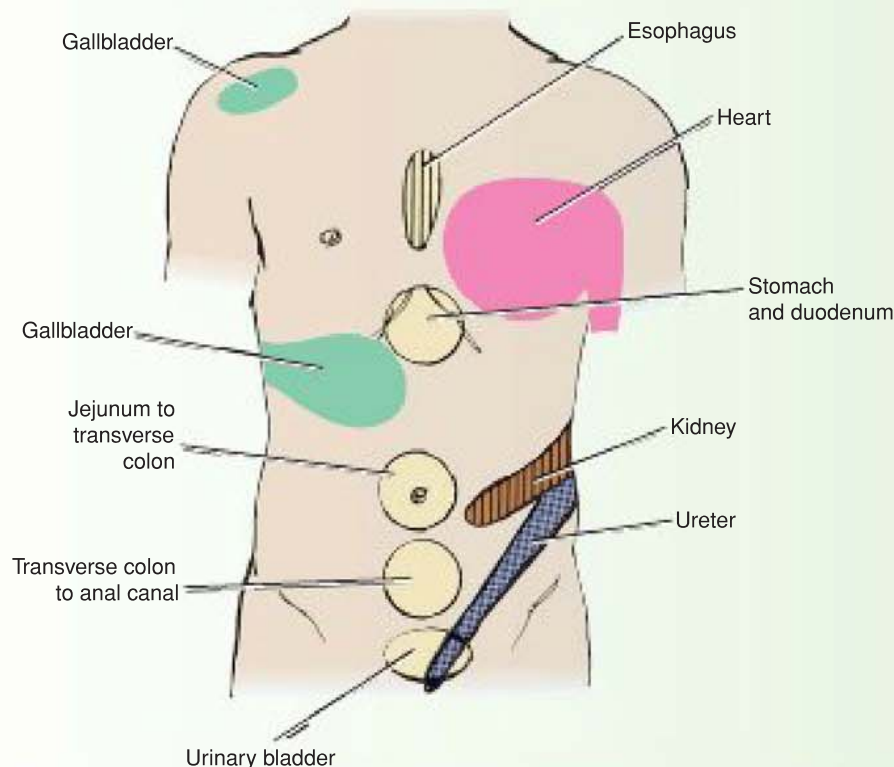


Figure 14-16 Some areas of referred pain from the viscera. In the case of the heart, the pain is usually referred to the left side of the thorax; occasionally, it is referred to both sides.

repeatedly receives noxious stimuli. Because both afferent fibers enter the spinal cord at the same segment, the brain interprets the information as coming from the skin rather than from the viscus. Pain arising from the gastrointestinal tract is referred to the midline. This can probably be explained by the fact that the tract arises embryologically as a midline structure and receives a bilateral nerve supply.

Cardiac Pain

Pain originating in the heart as the result of acute myocardial ischemia is assumed to be caused by oxygen deficiency and the accumulation of metabolites, which stimulate the sensory nerve endings in the myocardium. The afferent nerve fibers ascend to the CNS through the cardiac branches of the sympathetic trunk and enter the spinal cord through the posterior roots of the upper four thoracic nerves. The nature of the pain varies considerably, from a severe crushing pain to nothing more than a mild discomfort.

The pain is not felt in the heart but is referred to the skin areas supplied by the corresponding spinal nerves. The skin areas supplied by the upper four intercostal nerves and by the intercostobrachial nerve (T2) are therefore affected. The intercostobrachial nerve communicates with the medial cutaneous nerve of the arm and is distributed to skin on the medial side of the upper part of the arm. A certain amount of spread of nervous information must occur within the CNS, as the pain is sometimes felt in the neck and the jaw.

Myocardial infarction involving the inferior wall or diaphragmatic surface of the heart often gives rise to discomfort in the epigastrium, just below the sternum. One must assume that the afferent pain fibers from the heart ascend in the sympathetic nerves and enter the spinal cord in the posterior roots of the seventh, eighth, and ninth thoracic spinal nerves and give rise to referred pain in the T7–T9 thoracic dermatomes in the epigastrium.

Because the heart and the thoracic part of the esophagus probably have similar afferent pain pathways, pain from **acute esophagitis** can mimic the pain of myocardial infarction.

Stomach Pain

Referred pain from the stomach is commonly felt in the epigastrium. The afferent pain fibers from the stomach ascend in company with the sympathetic nerves and pass through the celiac plexus and the greater splanchnic nerves. The

sensory fibers enter the spinal cord at segments T5–T9 and give rise to referred pain in the dermatomes T5–T9 on the lower chest and abdominal walls.

Appendicular Pain

Visceral pain from the appendix is produced by distention of its lumen or spasm of its muscle. It travels in nerve fibers that accompany sympathetic nerves through the superior mesenteric plexus and the lesser splanchnic nerve to the spinal cord (T10 segment). The vague referred pain is felt in the region of the umbilicus, which is innervated by the 10th intercostal nerve (T10 dermatome). Later, when the inflammatory process involves the parietal peritoneum in the right iliac fossa, which is innervated by the 12th thoracic and 1st lumbar spinal nerves, the now somatic pain becomes severe and dominates the clinical picture. The somatic pain is localized precisely to the right lower quadrant of the anterior abdominal wall (T12–L1 dermatomes).

Gallbladder Pain

Visceral pain impulses from the gallbladder (acute cholecystitis, gallstone colic) travel in nerve fibers that accompany sympathetic fibers through the celiac plexus and the greater splanchnic nerves to the spinal cord (segments T5–T9). The vague referred pain is felt in the dermatomes (T5–T9) on the lower chest and upper abdominal walls. Should the inflammatory process spread to involve the parietal peritoneum of the anterior abdominal wall or peripheral diaphragm, the now severe somatic pain will be felt in the right upper quadrant of the anterior abdominal wall and through to the back below the inferior angle of the scapula. Involvement of the central diaphragmatic parietal peritoneum, which is innervated by the phrenic nerve (C3–C5), may give rise to referred pain to the tip of the shoulder, since the skin in this area is innervated by the supraclavicular nerves (C3–C4).

Causalgia

Causalgia is a painful condition of the arm or leg accompanied by trophic changes in the affected skin and nails. It commonly follows crushing or partial division of the median nerve in the arm or the tibial nerve in the leg. It is thought that the descending impulses in the sympathetic postganglionic fibers in some way evoke ascending impulses in the afferent pain fibers at the site of injury. In many instances, sympathectomy has relieved the pain of causalgia.

Key Concepts

Organization

- The ANS is divided into two parts, sympathetic and parasympathetic.
- The function of the sympathetic system is to prepare the body for emergency by increasing heart rate, constricting peripheral blood vessels, increasing blood supply to muscles, and increasing blood pressure. Thus, it redistributes blood to organs that need high performance in emergency situations.
- Efferent fibers of the sympathetic system originate in the lateral gray columns of the spinal cord. Myelinated axons leave the cord in the anterior root and pass via the white rami communicantes to the paravertebral ganglia of the sympathetic trunk.
- Once these presynaptic fibers reach the sympathetic trunks, they are distributed as follows:
 - Synapse with a postsynaptic sympathetic neuron in the ganglion.