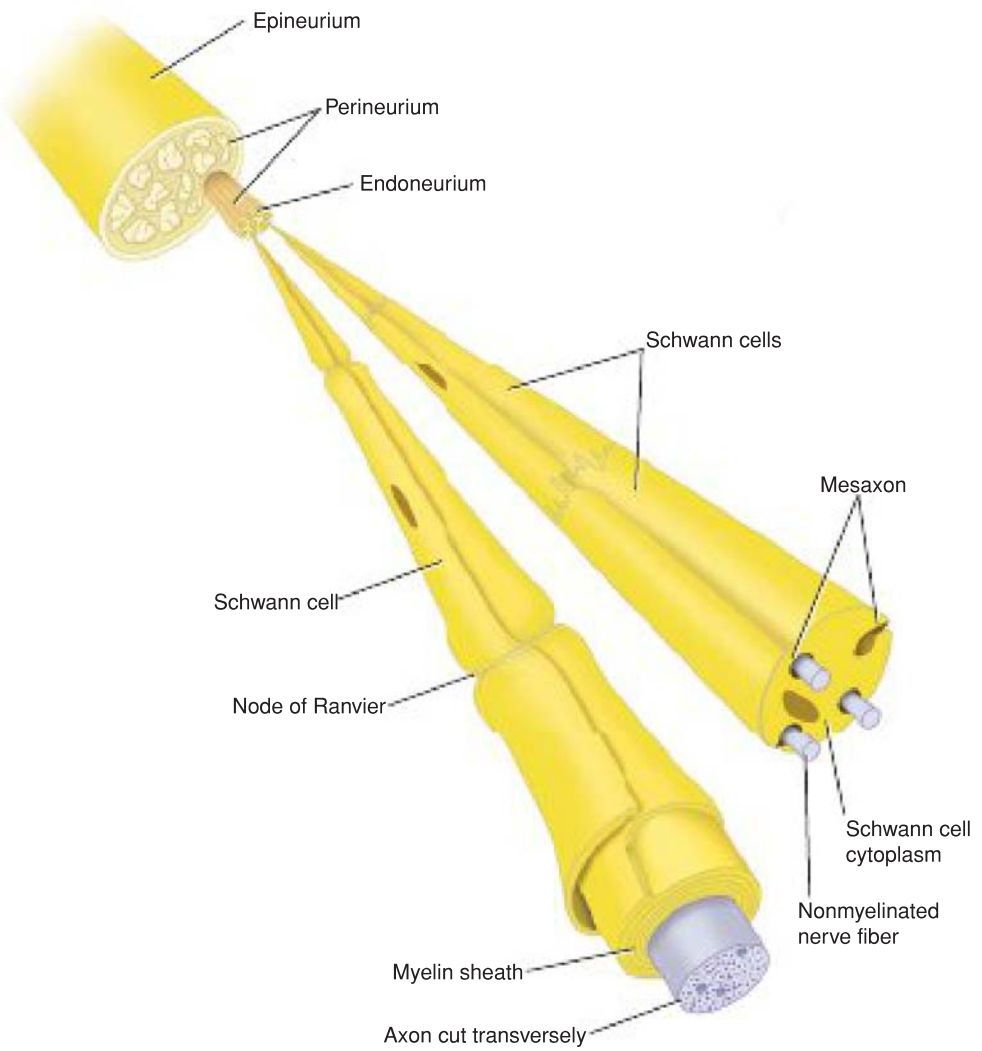

Figure 3-2 Exploded view of a peripheral nerve showing the connective tissue sheaths and the structure of myelinated and nonmyelinated nerve fibers.

of the plasma membrane that are fused together. The lighter **minor dense line**, about 10 nm thick, is formed by the approximation of the outer surfaces of adjacent plasma membranes and is made up of lipid. The fused outer protein layers of the plasma membranes are very thin and form a thin intraperiod line situated in the center of the lighter lipid layer. At the node of Ranvier, two adjacent Schwann cells terminate, and the myelin sheaths become thinner by the turning off of the lamellae (Fig. 3-5). At these regions, the plasma membrane of the axon, the axolemma, is exposed.

The **incisures of Schmidt–Lanterman** are seen on longitudinal sections of myelinated nerve fibers. They represent areas where the dark major dense line is not formed as a result of the localized persistence of Schwann cell cytoplasm (Fig. 3-7). This persistence of cytoplasm involves all the layers of the myelin, and thus, there is a continuous spiral of cytoplasm from the outermost region of the Schwann cell to the region of the axon. This spiral of cytoplasm may provide a pathway for the conduction of metabolites from the surface region of the Schwann cell to the axon.

In the **central nervous system** (**CNS**), oligodendrocytes are responsible for the formation of the myelin sheaths. The plasma membrane of the oligodendrocyte becomes wrapped around the axon, and the number of layers will determine the thickness of the myelin sheath (Fig. 3-3). The **nodes of Ranvier** are situated in the intervals between adjacent oligodendrocytes. A single oligodendrocyte may be connected to the myelin sheaths of as many as 60 nerve fibers. For this reason, the process of myelination in the CNS cannot take place by rotation of the oligodendrocyte on the axon, as did the Schwann cell in the PNS. Myelination in the CNS possibly occurs by the growth in length of the process of the oligodendrocyte, the process wrapping itself around the axon. Incisures of Schmidt–Lanterman exist in CNS nerve fibers. Table 3-1 provides a summary of facts concerning CNS and PNS myelination.

(*text continue on page 79*)

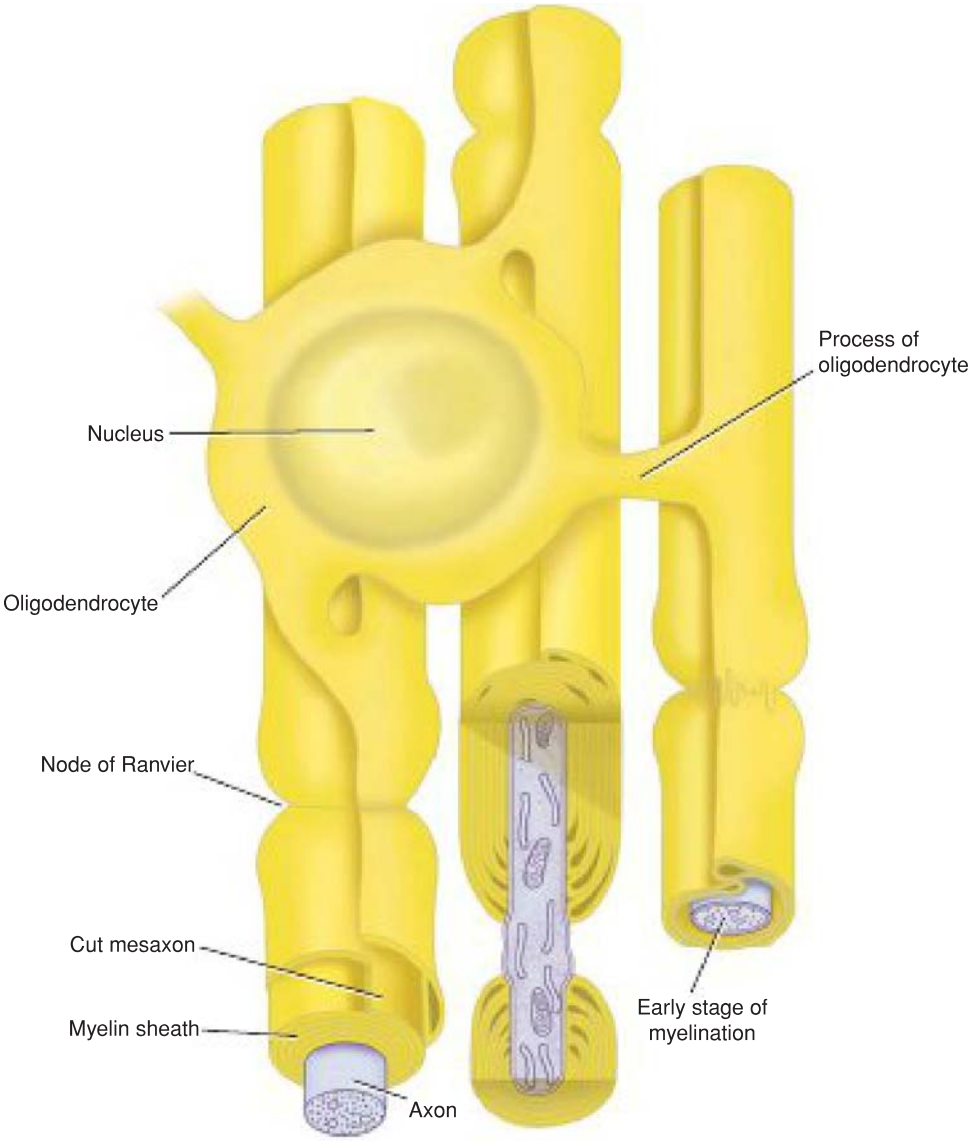

Figure 3-3 The relationship between an oligodendrocyte and myelinated nerve fibers in the central nervous system. Note the absence of a basement membrane.

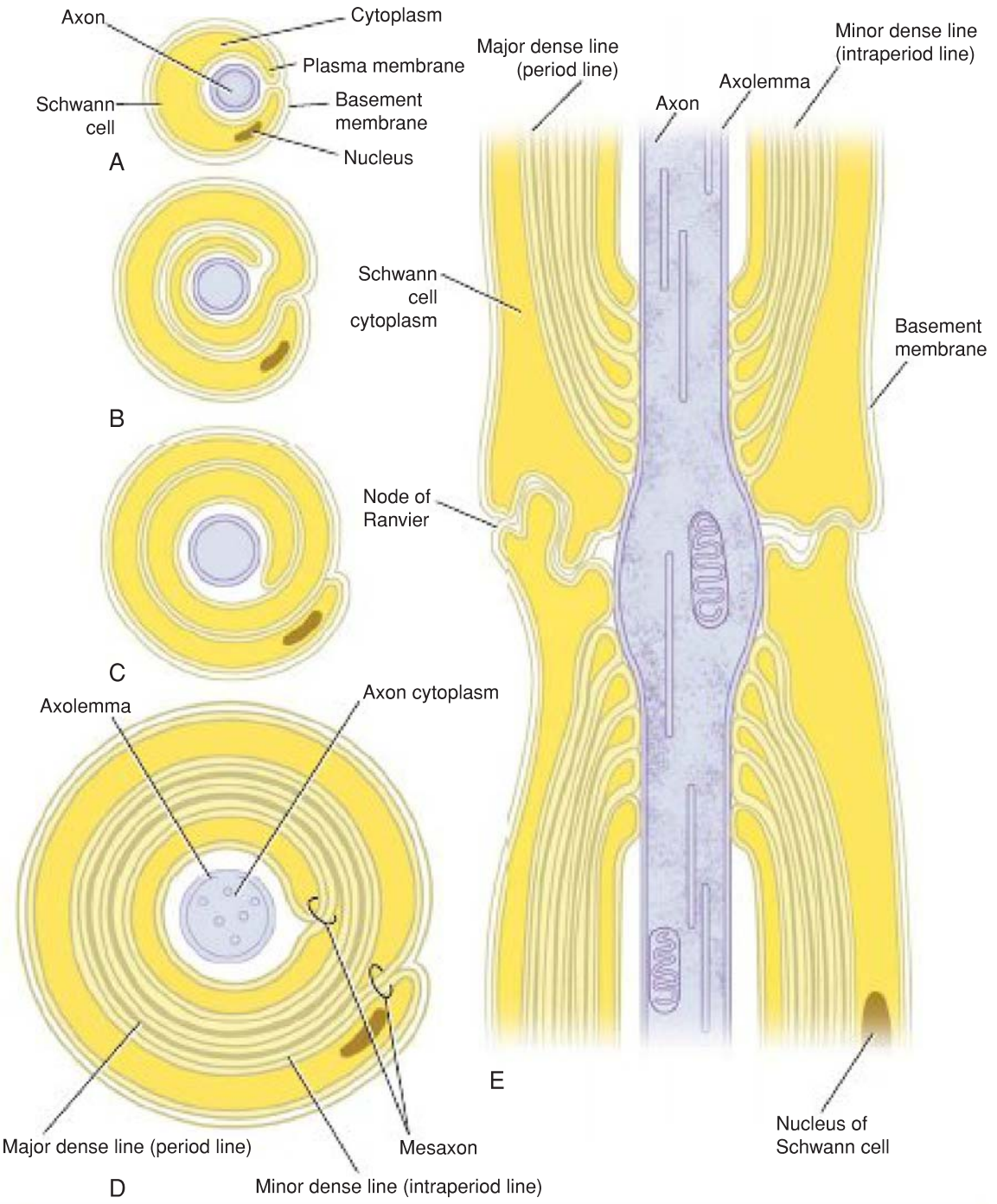

Figure 3-4 A myelinated nerve fiber in the peripheral nervous system. **A–D:** Cross sections showing the stages in the formation of the myelin sheath. **E:** A longitudinal section of a mature myelinated nerve fiber showing a node of Ranvier. Note the presence of a basement membrane.

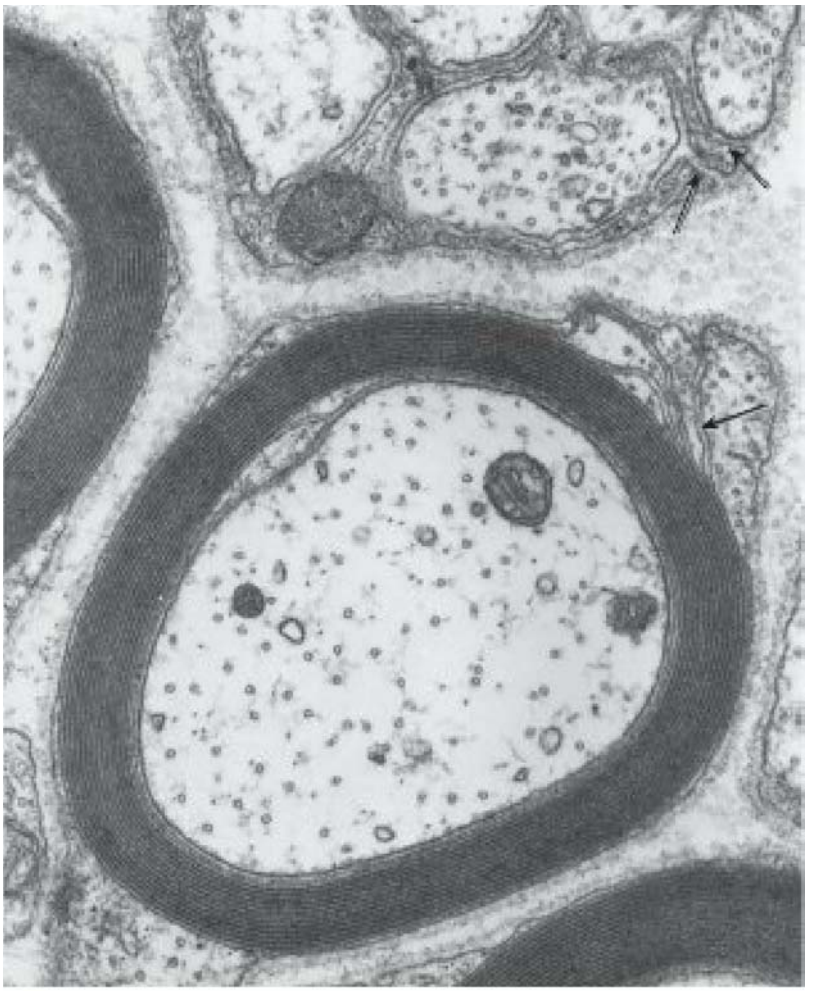

Figure 3-5 Electron micrograph of a longitudinal section of several myelinated axons showing the structure of a node of Ranvier (*arrow*). At the node, two adjacent Schwann cells terminate, and the myelin sheaths become thinner by the turning off of the lamellae. Note the many microtubules and microfilaments within the axons (×12,220). (Courtesy Dr. H. de F. Webster.)

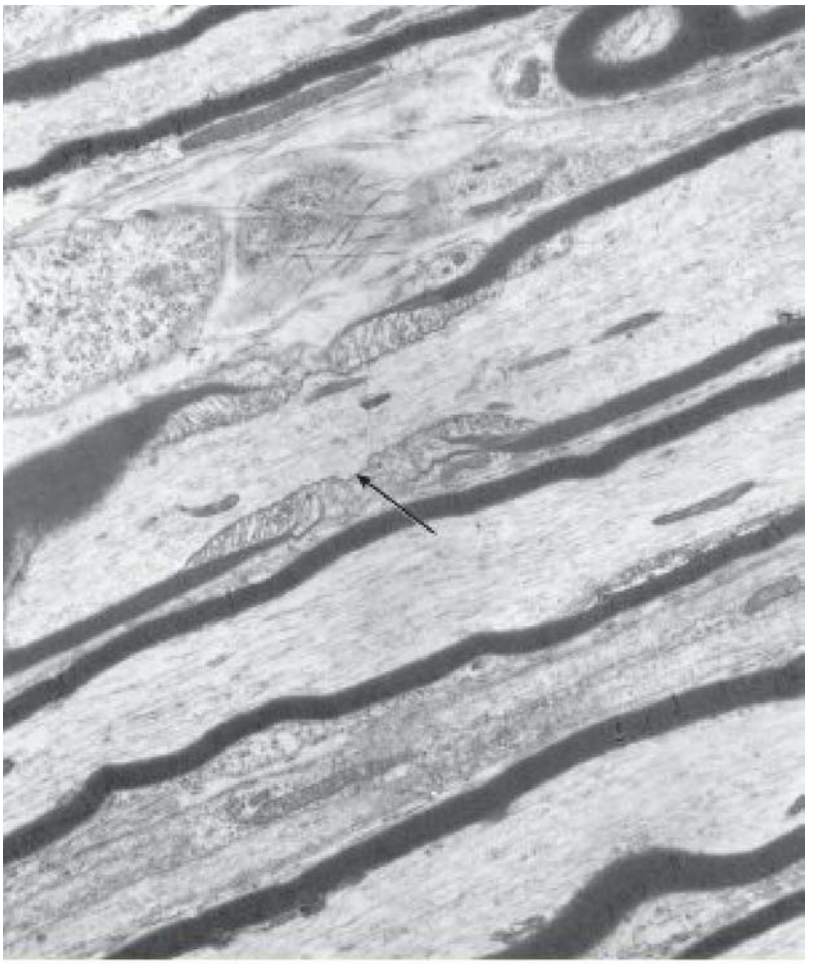

Figure 3-6 Electron micrograph of a transverse section of a peripheral nerve showing a myelinated axon with spiral myelin lamellae (**center**). Note the mesaxon (*arrow*). Parts of two other myelinated fibers are also shown. A number of nonmyelinated axons are enclosed in the peripheral cytoplasm of a Schwann cell (**top**). The mesaxons are indicated by *arrows* (×28,000). (Courtesy Dr. H. de F. Webster.)

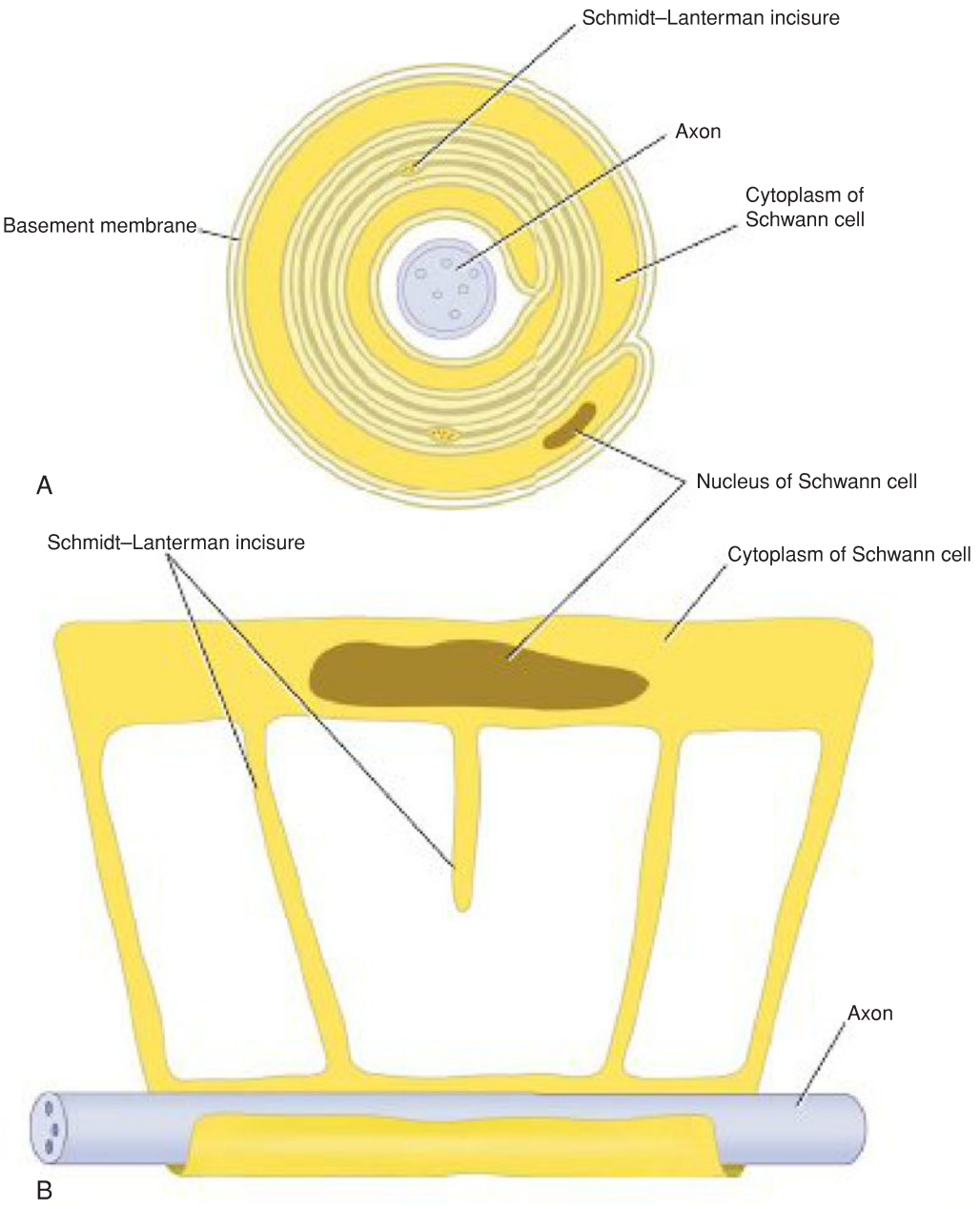

Figure 3-7 Schmidt–Lanterman incisures in the myelin sheath of a peripheral nerve. **A:** Transverse section of a myelinated nerve fiber. **B:** Schematic diagram of a myelinated nerve fiber in which the myelin sheath has been unrolled.

Table 3-1 Classification of Neurons

Location	Cell Responsible	Number of Nerve Fibers Served by Cell	Nodes of Ranvier	Schmidt–Lanterman Incisures	Mesaxon
Peripheral nerve	Schwann cell	1	Present	Present	Present
CNS tract	Oligodendrocyte	Up to 60	Present	Present	Absent

CNS, central nervous system.

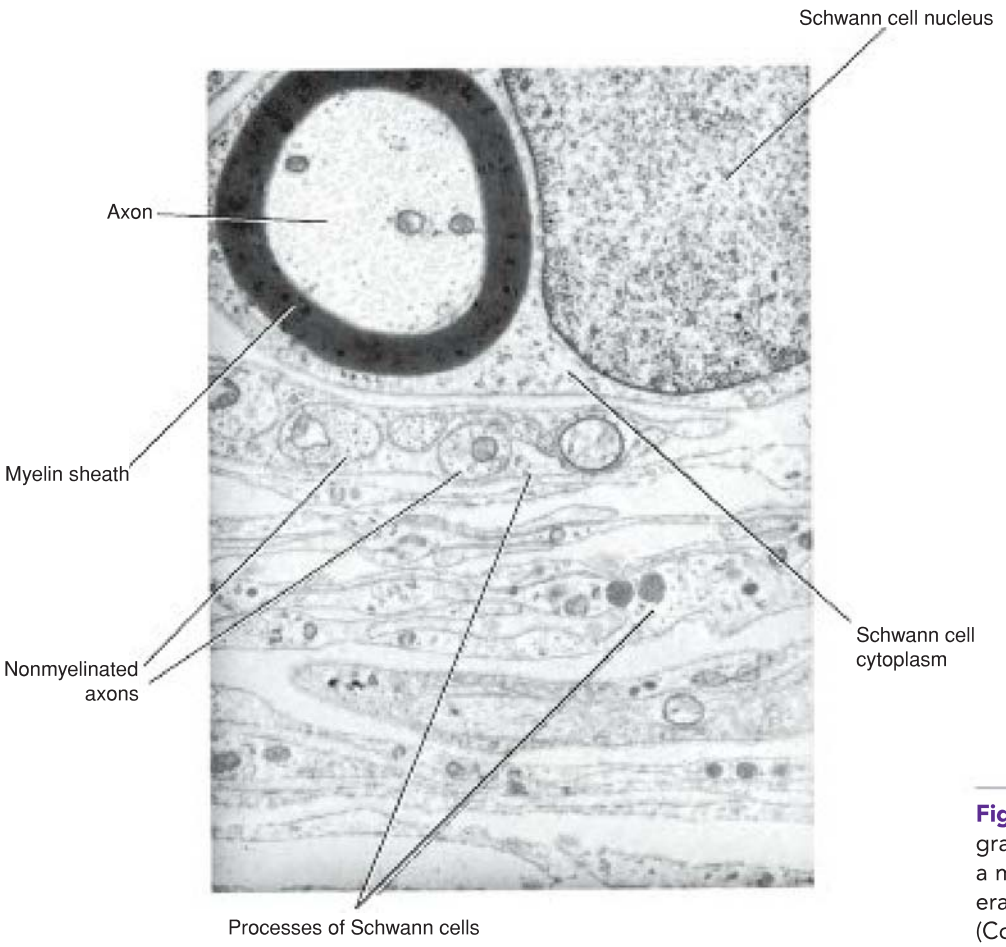

Figure 3-8 Electron micrograph of a transverse section of a myelinated nerve fiber and several nonmyelinated nerve fibers. (Courtesy Dr. J. M. Kerns.)

Nonmyelinated Nerve Fibers

The smaller axons of the CNS, the postganglionic axons of the autonomic part of the nervous system, and some fine sensory axons associated with the reception of pain are nonmyelinated.

In the **PNS**, each axon, which is usually less than 1 μm in diameter, indents the surface of the Schwann cell so that it lies within a trough (Fig. 3-2). As many as 15 or more axons may share a single Schwann cell, each lying within its own trough or sometimes sharing a trough. In some situations, the troughs are deep and the axons are embedded deep in the Schwann cells, forming a **mesaxon** from the Schwann cell plasma membrane (Fig. 3-8; also see Fig. 3-6). The Schwann cells lie close to one another along the length of the axons, and nodes of Ranvier do not exist.

In areas with synapses or where motor transmission occurs, the axon emerges from the trough of the Schwann cell for a short distance, thus exposing the active region of the axon (Fig. 3-9).

In the **CNS**, nonmyelinated nerve fibers run in small groups and are not particularly related to the oligodendrocytes.

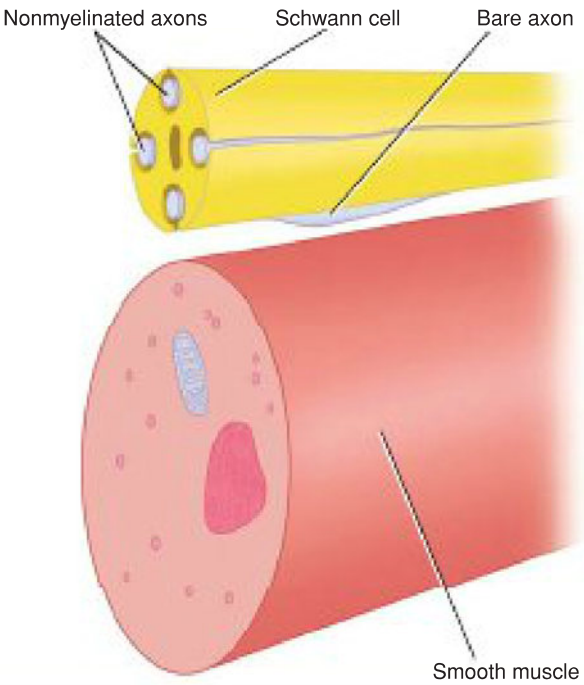

Figure 3-9 Autonomic neuromuscular junction between a nonmyelinated axon and a smooth muscle fiber.

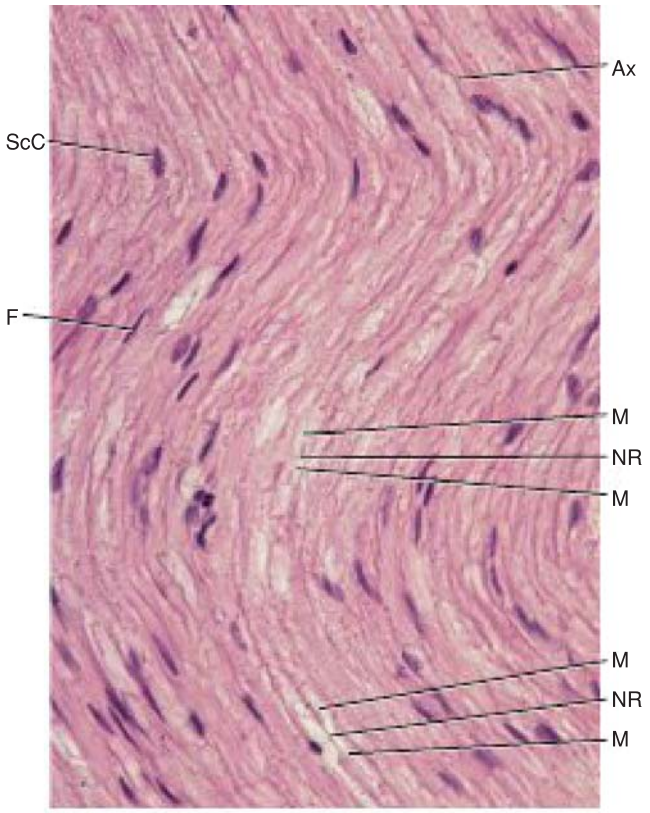

Figure 3-10 Peripheral nerve. l.s. Paraffin section. ×270. This is a higher magnification of a region similar to the boxed area of Figure 1a. A distinguishing characteristic of longitudinal sections of peripheral nerves is that they appear to follow a zigzag course, particularly evident in this photomicrograph. The sinuous course of these fibers is accentuated by the presence of nuclei of Schwann cells (ScC), fibroblasts (F), and endothelial cells of capillaries belonging to the endoneurium. Many of these nerve fibers are myelinated (M) as corroborated by the presence of the nodes of Ranvier (NR) and myelin proteins around the axons (Ax). (From Gartner, L. P. *Color Atlas and Text of Histology*, 7e. Baltimore: Wolters Kluwer, 2018.)

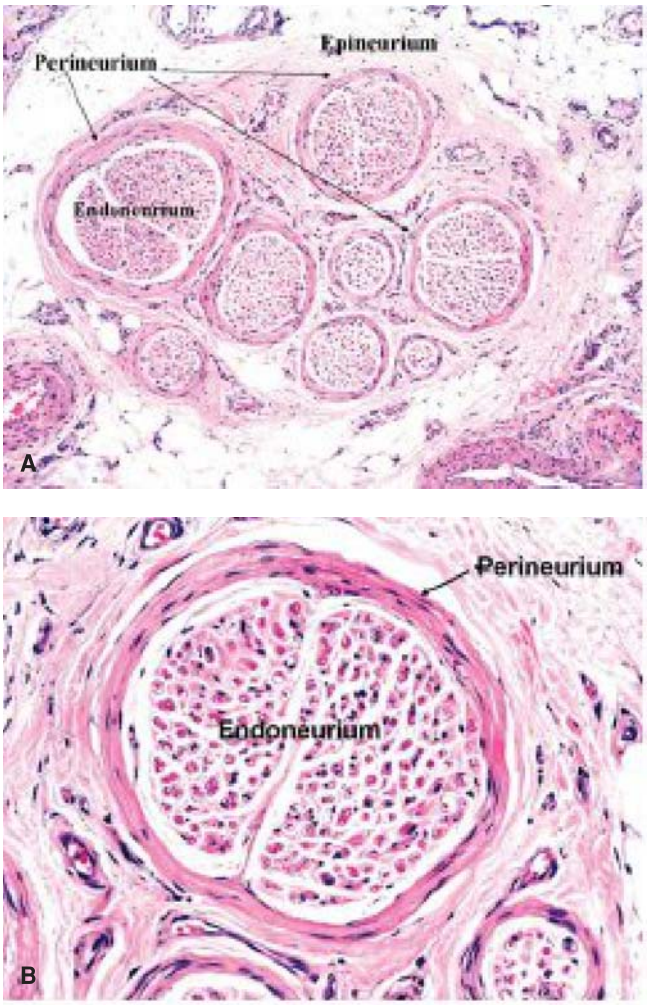

Figure 3-11 Peripheral nerve sheaths and compartments. **A:** A low-power view of a transverse section of a normal sural nerve. The nerve fascicles with roughly circular outlines are surrounded by perineurium and embedded in the connective tissue of the epineurium. Epineurial blood vessels (A) are also cut in cross section and there is adherent adipose tissue. The 1 µm sections are stained with hematoxylin and eosin (×16). **B:** The endoneurial compartment containing myelinated and non-myelinated nerve fibers and their accompanying Schwann cells is surrounded by perineurium. Paraffin section stained with hematoxylin and eosin (×45). (From Mills, S. E. *Histology for Pathologists*, 4e. Philadelphia, PA: Wolters Kluwer, 2013.)

PERIPHERAL NERVES

Peripheral nerves is a collective term for the cranial and spinal nerves. Each peripheral nerve consists of parallel bundles of nerve fibers, which may be efferent or afferent axons, may be myelinated or nonmyelinated, and are surrounded by connective tissue sheaths (Figs. 3-10 and 3-11).

The nerve trunk is surrounded by a dense connective tissue sheath called the **epineurium** (Fig. 3-12). Within the sheath are bundles of nerve fibers, each of which is surrounded by a connective tissue sheath called the **perineurium**. Between the individual nerve fibers is a loose, delicate connective tissue referred to as the **endoneurium**. The connective tissue sheaths serve to support the nerve fibers and their associated blood vessels and lymph vessels. Peripheral nerve fibers can be classified according to their speed of conduction and size (see Table 2-3).

Spinal Nerves and Spinal Nerve Roots

The 31 pairs of spinal nerves leave the spinal cord and pass through intervertebral foramina in the vertebral column. (For details, see Fig. 1-5.) Each spinal nerve is connected to the spinal cord by **two roots**: the **anterior root** and the **posterior root** (Fig. 3-13). The anterior root consists of bundles of nerve fibers carrying nerve impulses *away from* the CNS, the **efferent fibers**. The **posterior root** consists of bundles of nerve fibers

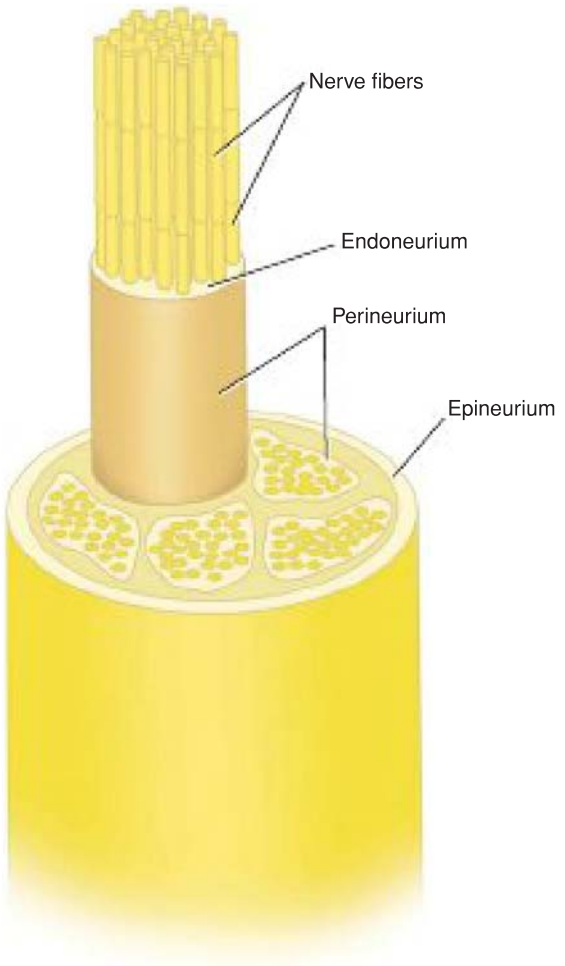

Figure 3-12 Structure of a peripheral nerve.

carrying nerve impulses *to* the CNS, the **afferent fibers**. Because these fibers are concerned with conveying information to the CNS, they are called **sensory fibers**. The cell bodies of these nerve fibers are situated in a swelling on the posterior root called the **posterior root ganglion**.

Cranial Nerves

The 12 pairs of cranial nerves (see Fig. 3-13) leave the brain and pass through foramina in the skull. Some of these nerves are composed entirely of afferent nerve fibers bringing sensations to the brain (olfactory, optic, and vestibulocochlear), others are composed entirely of efferent fibers (oculomotor, trochlear, abducent, accessory, and hypoglossal), while the remainder possess both afferent and efferent fibers (trigeminal, facial, glossopharyngeal, and vagus). The cranial nerves are described in detail in Chapter 11.

Sensory Ganglia

The sensory ganglia of the posterior spinal nerve roots and of the trunks of the trigeminal, facial, glossopharyngeal, and vagal cranial nerves have the same structure. Each ganglion is surrounded by a layer of connective tissue that is continuous with the epineurium and perineurium of the peripheral nerve. The neurons are unipolar, possessing cell bodies that are rounded or oval in shape (Fig. 3-14). The cell bodies tend to be aggregated and separated by bundles of nerve fibers. A single nonmyelinated process leaves each cell body and, after a convoluted course, bifurcates at a T junction into peripheral and central branches. The former axon terminates in a series of dendrites in a peripheral sensory ending, and the latter axon enters the CNS. The nerve impulse, on reaching the T junction, passes directly from the peripheral axon to the central axon, thus bypassing the nerve cell body.

Each nerve cell body is closely surrounded by a layer of flattened cells called **capsular cells** or **satellite cells**. The capsular cells are similar in structure to Schwann cells and are continuous with these cells as they envelop the peripheral and central processes of each neuron.

Autonomic Ganglia

The autonomic ganglia (sympathetic and parasympathetic ganglia) are situated at a distance from the brain and spinal cord. They are found in the sympathetic trunks, in prevertebral autonomic plexuses (e.g., in the cardiac, celiac, and mesenteric plexuses), and as ganglia in or close to viscera. Each ganglion is surrounded by a layer of connective tissue that is continuous with the epineurium and perineurium of the peripheral nerve. The neurons are multipolar and possess cell bodies that are irregular in shape (Fig. 3-15). The dendrites of the neurons make synaptic connections with the myelinated axons of preganglionic neurons. The axons of the neurons are of small diameter (C fibers) and unmyelinated, and they pass to viscera, blood vessels, and sweat glands.

Just as with sensory ganglia, each nerve cell body is closely surrounded by **capsular cells** (or **satellite cells**). Unlike those of sensory ganglia, however, these capsular cells are similar in structure to Schwann cells and are continuous with them as they envelop the peripheral and central processes of each neuron.

Peripheral Nerve Plexuses

Peripheral nerves are composed of bundles of nerve fibers. In their course, peripheral nerves sometimes divide into branches that join neighboring peripheral nerves. If this occurs frequently, a network of nerves, called a **nerve plexus**, forms. Note that the formation of a nerve plexus allows individual nerve fibers to pass from one peripheral nerve to another, and **in most instances**, **branching of nerve fibers does not take place**. A plexus thus permits a redistribution of the nerve fibers within the different peripheral nerves.

At the root of the limbs, the anterior rami of the spinal nerves form complicated plexuses. The cervical and brachial plexuses are at the root of the upper limbs (Fig. 3-16), and the lumbar and sacral plexuses are at the root of the lower limbs. This allows the nerve fibers

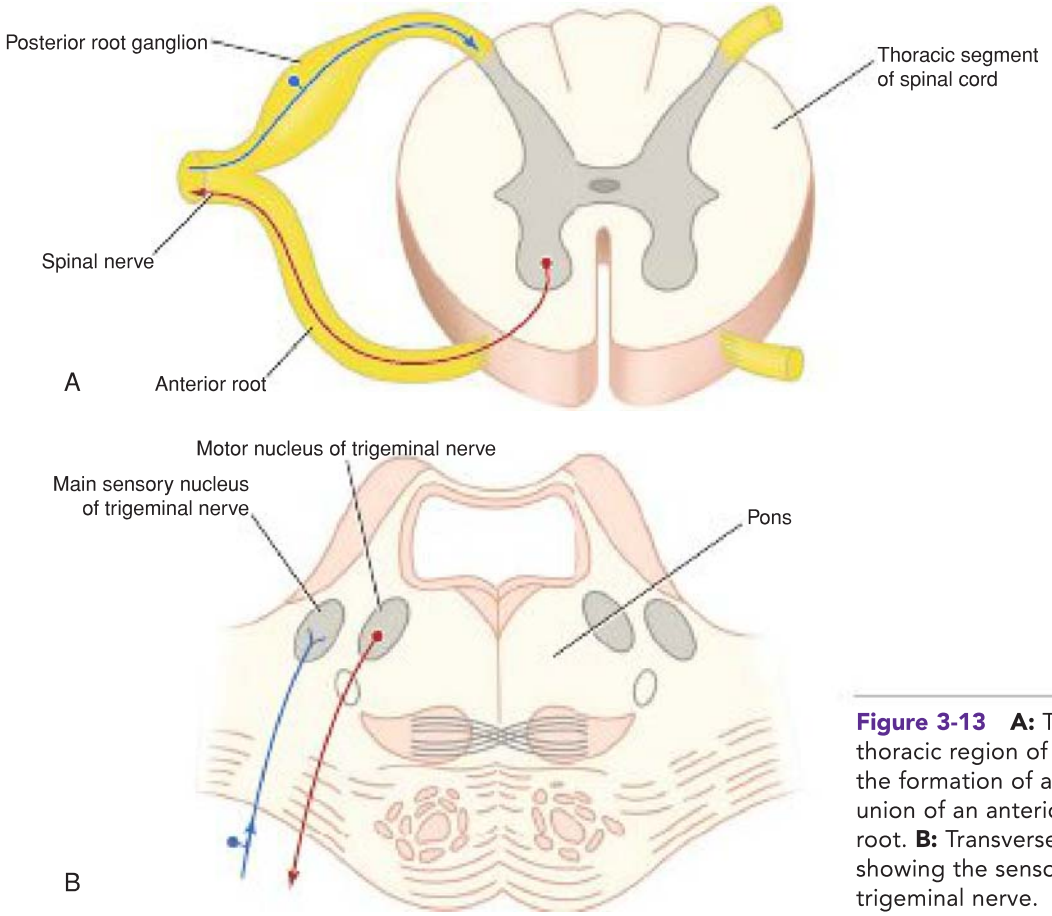

Figure 3-13 **A:** Transverse section of the thoracic region of the spinal cord showing the formation of a spinal nerve from the union of an anterior and a posterior nerve root. **B:** Transverse section of the pons showing the sensory and motor roots of the trigeminal nerve.

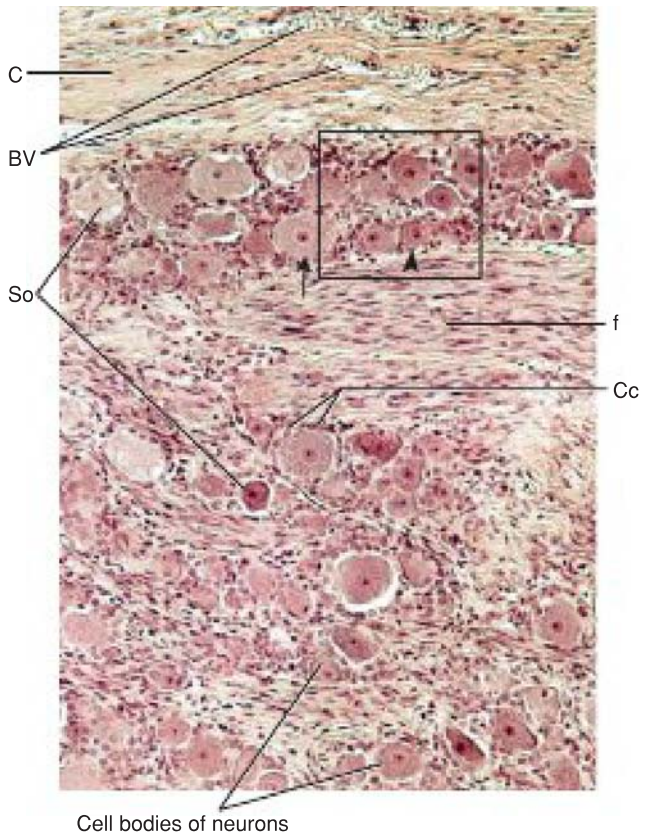

Figure 3-14 Sensory ganglion. l.s. Human. Paraffin section. ×132. The dorsal root ganglion provides a good representative example of a sensory ganglion. It possesses a **vascular** (BV) connective tissue **capsule** (C), which also envelops its sensory root. The neurons of the dorsal root ganglion are pseudounipolar in morphology; therefore, their **somata** (So) appear spherical in shape. The **fibers** (f), many of which are myelinated, alternate with rows of cell bodies. Note that some somata are large (*arrow*), whereas others are small (*arrowhead*). Each soma is surrounded by neuroectodermally derived **capsule cells** (Cc). A region similar to the *boxed area* is presented at a high magnification in Figure 4. (From Gartner, L. P. *Color Atlas and Text of Histology,* 7e. Baltimore: Wolters Kluwer, 2018.)

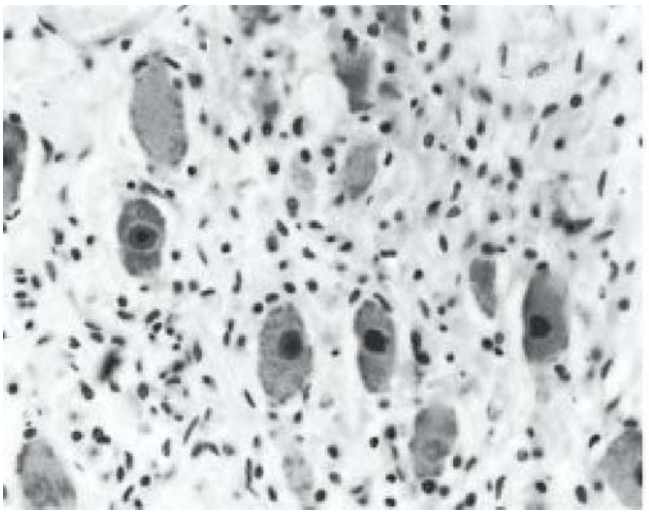

Figure 3-15 Photomicrograph of a longitudinal section of a ganglion of the sympathetic trunk stained with hematoxylin and eosin (×300).

derived from different segments of the spinal cord to be arranged and distributed efficiently in different nerve trunks to the various parts of the upper and lower limbs.

Cutaneous nerves, as they approach their final destination, commonly form fine plexuses that again permit a rearrangement of nerve fibers before they reach their terminal sensory endings.

The autonomic nervous system also possesses numerous nerve plexuses that consist of preganglionic and postganglionic nerve fibers and ganglia.

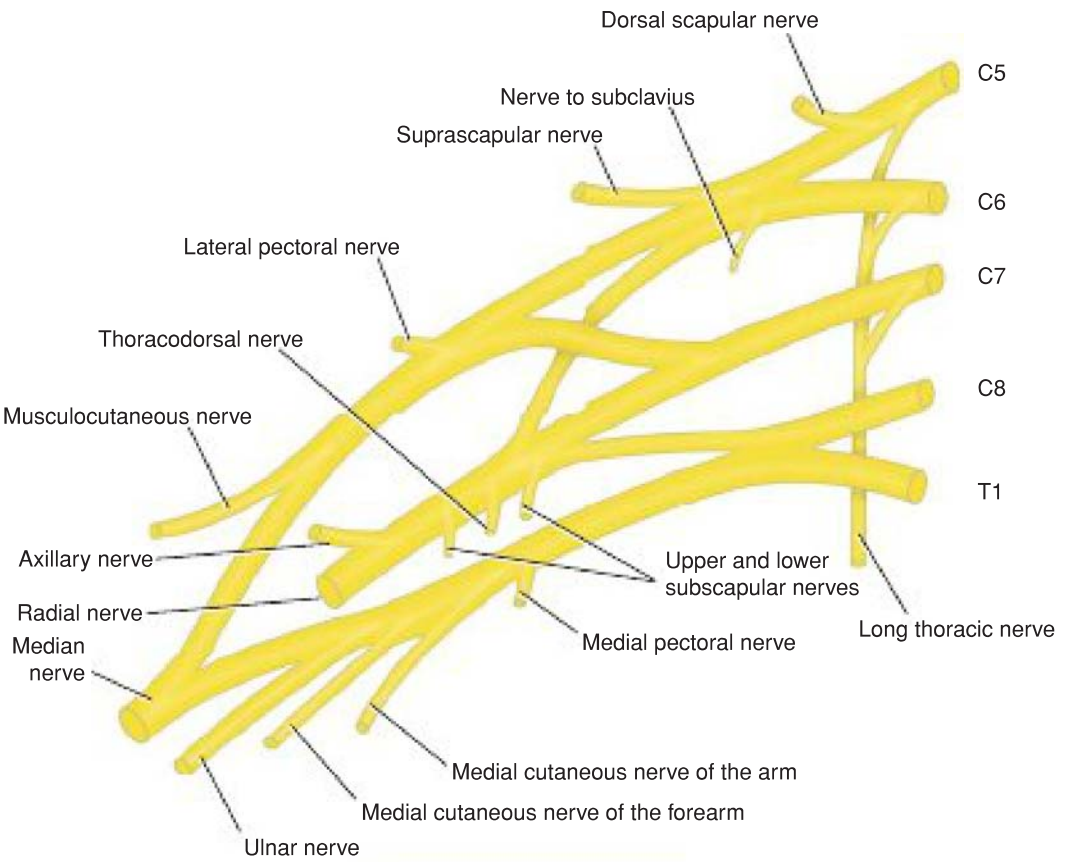

Figure 3-16 Brachial plexus.

RECEPTOR ENDINGS

An individual receives impressions from the outside world and from within the body by special sensory nerve endings or receptors.

Sensory receptors can be classified into five basic functional types:

Mechanoreceptors respond to mechanical deformation.
Thermoreceptors respond to changes in temperature; some receptors respond to cold and others to heat.
Nociceptors respond to any stimuli that bring about damage to the tissue.
Electromagnetic receptors, the rods and cones of the eyes, are sensitive to changes in light intensity and wavelength.
Chemoreceptors respond to chemical changes associated with taste and smell and oxygen and carbon dioxide concentrations in the blood.

Anatomical Types of Receptors

For convenience, the sensory endings can be classified, on a structural basis, into nonencapsulated and encapsulated receptors. Table 3-2 classifies and compares the receptor types.

Nonencapsulated Receptors

Free Nerve Endings

Free nerve endings are widely distributed throughout the body (Fig. 3-17). They are found between the epithelial cells of the skin, the cornea, and the alimentary tract, and in connective tissues, including the dermis, fascia, ligaments, joint capsules, tendons, periosteum, perichondrium, haversian systems of bone, tympanic membrane, and dental pulp; they are also present in muscle.

The afferent nerve fibers from the free nerve endings are either myelinated or nonmyelinated. The terminal endings are devoid of a myelin sheath as well as Schwann cells covering their tips.

Most of these endings detect pain, while others detect crude touch, pressure, and tickle sensations, and possibly cold and heat.

Merkel Discs

Merkel discs are found in hairless skin, for example, the fingertips (Figs. 3-18 and 3-19), and in hair follicles. The nerve fiber passes into the epidermis and terminates as a disc-shaped expansion that is applied closely to a dark-staining epithelial cell in the deeper part of the epidermis, called the **Merkel cell**. In hairy skin, clusters of Merkel discs, known as **tactile domes**, are found in the epidermis between the hair follicles.

Merkel discs are slowly adapting touch receptors that transmit information about the degree of pressure exerted on the skin, such as from holding a pen.

Hair Follicle Receptors

Nerve fibers wind around the follicle in its outer connective tissue sheath below the sebaceous gland. Some branches surround the follicle, while others run parallel to its long axis (Figs. 3-20 and 3-21). Many naked axon filaments terminate among the cells of the outer root sheath.

Table 3-2 Classification and Comparison of Receptor Types

Type of Receptor	Location	Stimulus	Sensory Modality	Adaptability	Fibers
Nonencapsulated Receptors					
Free nerve endings	Epidermis, cornea, gut, dermis, ligaments, joint capsules, bone, dental pulp, etc.	Mechanoreceptor	Pain (fast), pain (slow), touch (crude), pressure, heat and cold	Rapid	A δ, C
Merkel discs	Hairless skin	Mechanoreceptor	Touch	Slow	A β
Hair follicle receptors	Hairy skin	Mechanoreceptor	Touch	Rapid	A β
Encapsulated Receptors					
Meissner corpuscles	Dermal papillae of skin of palm and sole of foot	Mechanoreceptor	Touch	Rapid	A β
Pacinian corpuscles	Dermis, ligaments, joint capsules, peritoneum, external genitalia, etc.	Mechanoreceptor	Vibration	Rapid	A β
Ruffini corpuscles	Dermis of hairy skin	Mechanoreceptor	Stretch	Slow	A β
Neuromuscular spindles	Skeletal muscle	Mechanoreceptor	Stretch—muscle length	Fast	A α, A β
Neurotendinous spindles	Tendons	Mechanoreceptor	Compression—muscle tension	Fast	A α

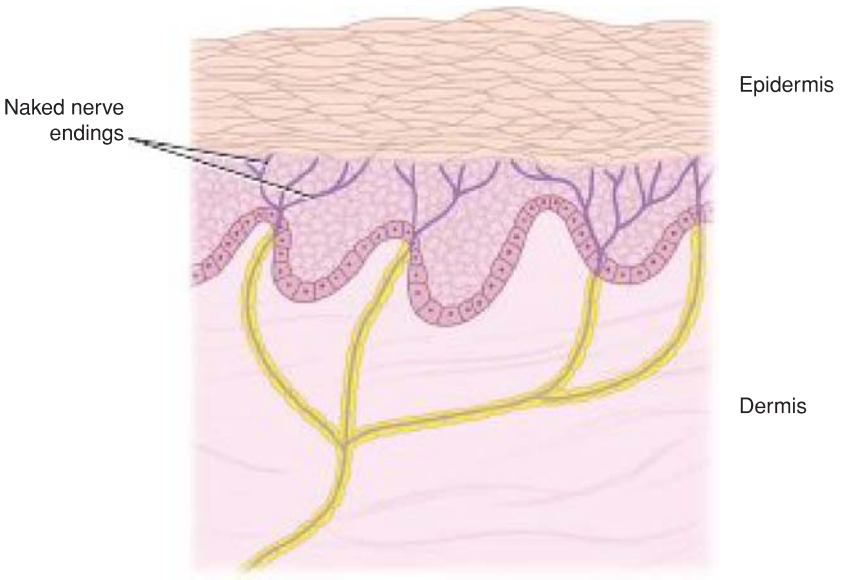

Figure 3-17 Free nerve endings in the skin. The nerve fibers in the epidermis are naked.

Bending of the hair stimulates the follicle receptor, which belongs to the rapidly adapting group of mechanoreceptors. While the hair remains bent, the receptor is silent, but when the hair is released, a further burst of nerve impulses is initiated.

Encapsulated Receptors

Encapsulated receptors show wide variations in size and shape, and the termination of the nerve is covered by a capsule.

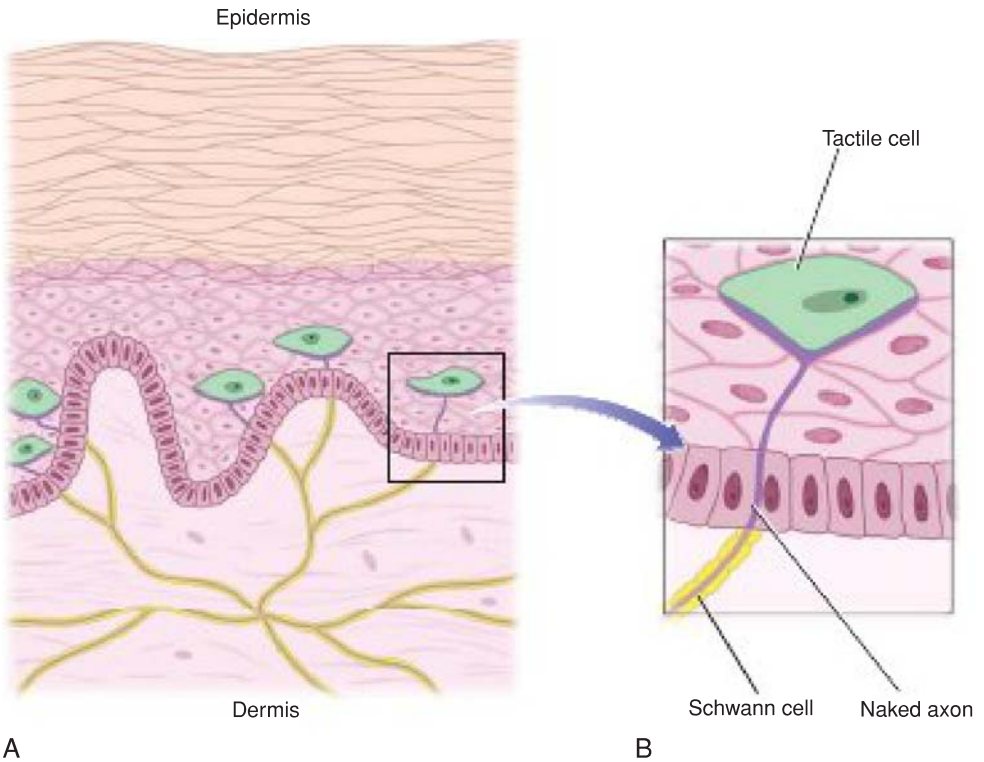

Figure 3-18 Merkel discs in the skin. **A:** Low magnification. **B:** Merkel disc showing the expanded ending of an axon with a stippled tactile cell.

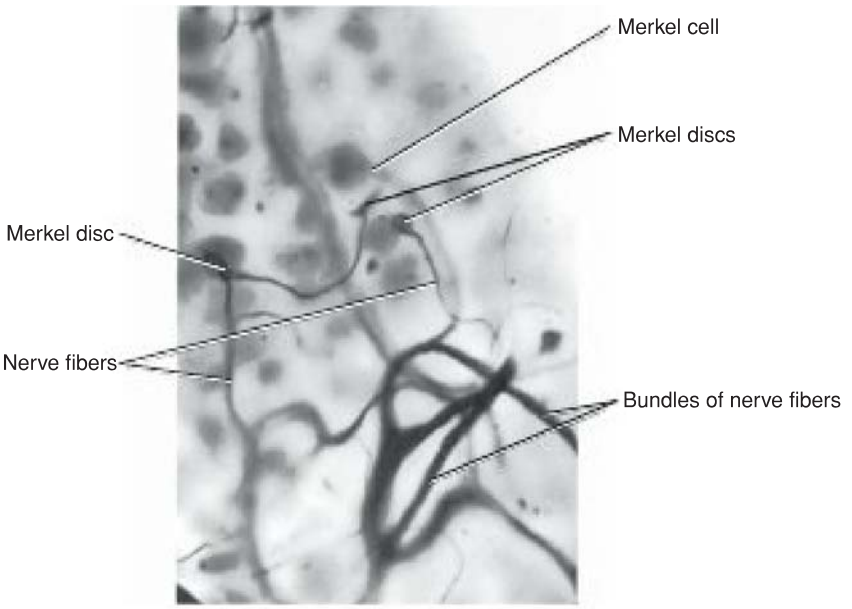

Figure 3-19 Photomicrograph of digital skin showing fine nerve terminals ending in Merkel discs, stained by the silver method. (Courtesy Dr. N. Cauna.)

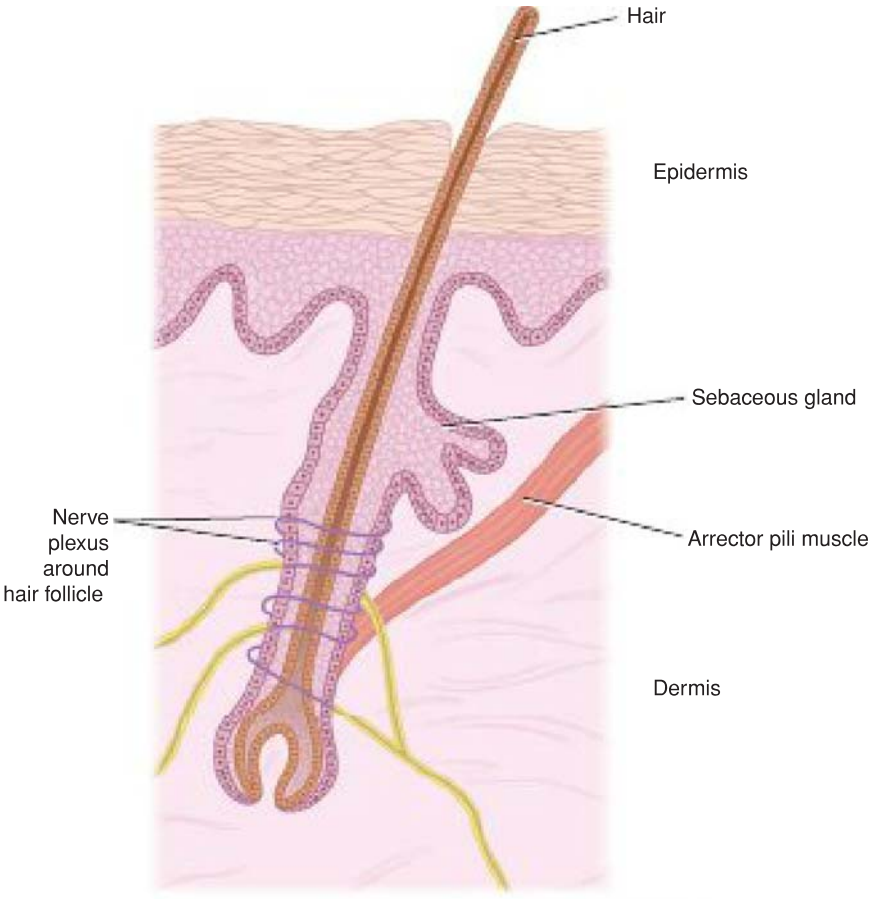

Figure 3-20 Nerve endings around a hair follicle.

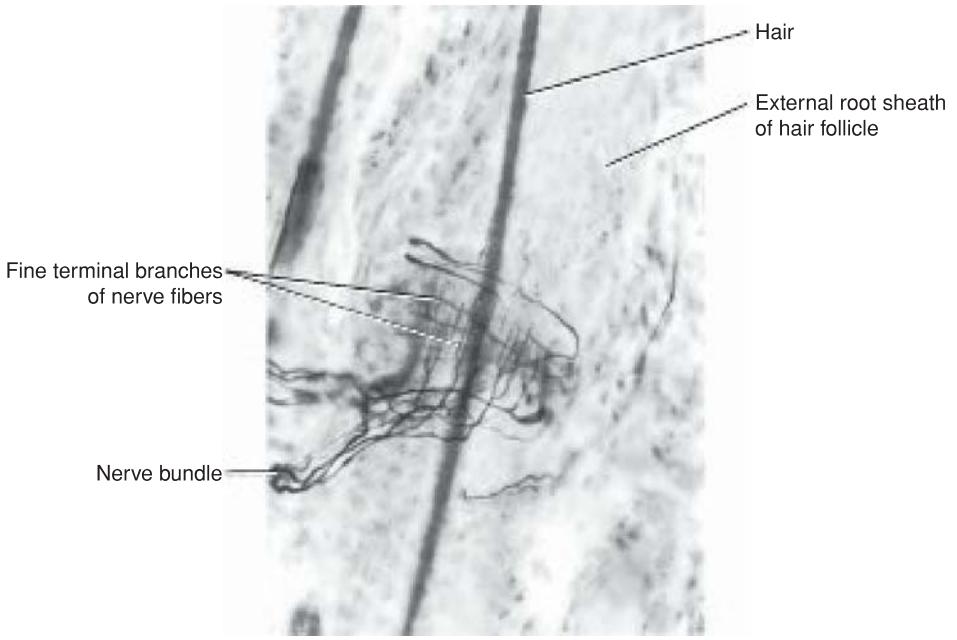

Figure 3-21 Photomicrograph of nerve endings around a hair follicle stained by the silver method. (Courtesy Dr. M. J. T. Fitzgerald.)

Meissner Corpuscles

Meissner corpuscles are located in the dermal papillae of the skin (Figs. 3-22 and 3-23), especially that of the palm of the hand and the sole of the foot. Many also are present in the skin of the nipple and the external genitalia. Each corpuscle is ovoid in shape and consists of a stack of modified flattened Schwann cells arranged transversely across the long axis of the corpuscle. The corpuscle is enclosed by a capsule of connective tissue that is continuous with the endoneurium of the nerves that enter it. A few myelinated nerve fibers enter the deep end of the corpuscle; myelinated and unmyelinated branches

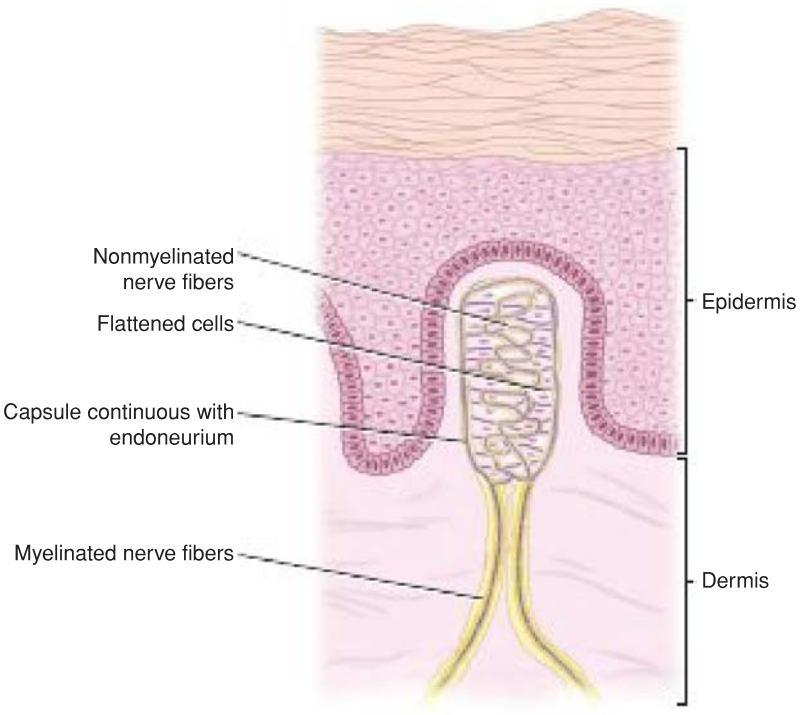

Figure 3-22 Detailed structure of a Meissner corpuscle in the skin.

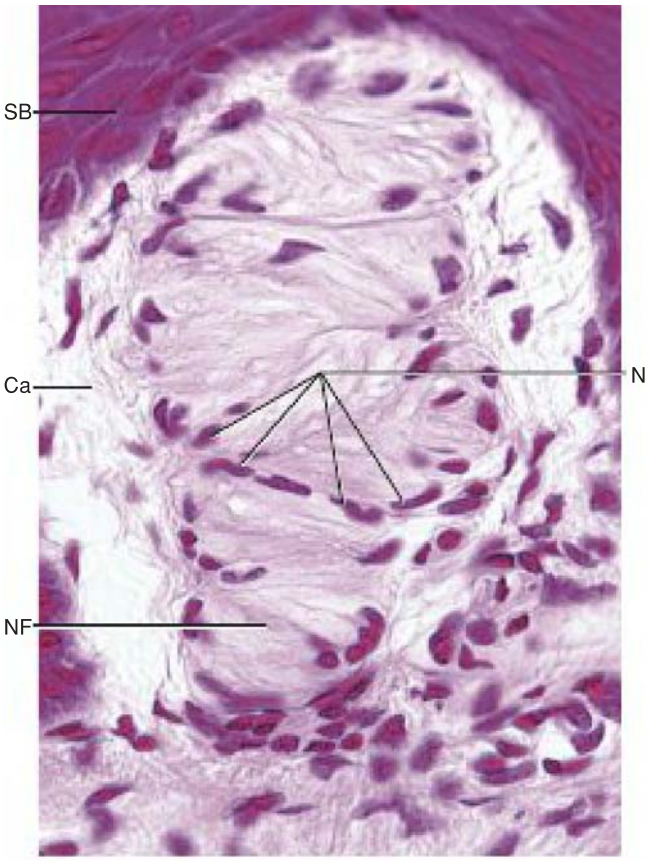

Figure 3-23 Photomicrograph of a Meissner corpuscle of the skin. (Courtesy Dr. N. Cauna.)

decrease in size and ramify among the Schwann cells. The number of Meissner corpuscles considerably diminishes between birth and old age.

Meissner corpuscles are very sensitive to touch and are rapidly adapting mechanoreceptors. They enable an individual to distinguish between two pointed structures when they are placed close together on the skin (two-point tactile discrimination).

Pacinian Corpuscles

Pacinian corpuscles (Figs. 3-24 and 3-25) are widely distributed throughout the body and are abundant in the dermis, subcutaneous tissue, ligaments, joint capsules, pleura, peritoneum, nipples, and external genitalia. Each corpuscle is ovoid in shape, measuring about 2 mm long and about 100 to 500 μm across. It consists of a capsule and a central core containing the nerve ending. The capsule consists of numerous concentric lamellae of flattened cells. A large myelinated nerve fiber enters the corpuscle and loses its myelin sheath and then its Schwann cell covering. The naked axon, surrounded by lamellae formed of flattened cells, passes through the center of the core and terminates in an expanded end.

The Pacinian corpuscle is a rapidly adapting mechanoreceptor that is particularly sensitive to vibration. It can respond to up to 600 stimuli per second.

Ruffini Corpuscles

Ruffini corpuscles are located in the dermis of hairy skin. Each corpuscle consists of several large unmyelinated nerve fibers ending within a bundle of collagen fibers and surrounded by a cellular capsule. These

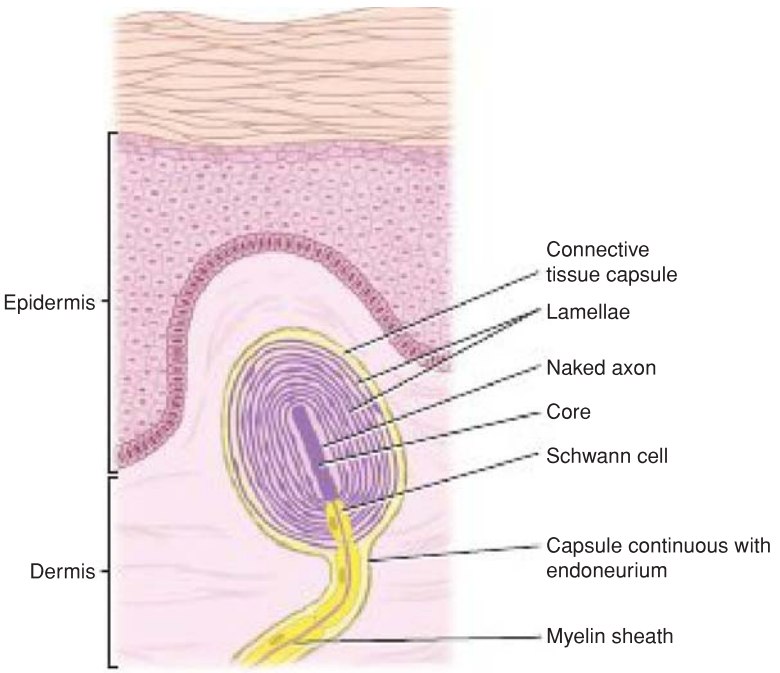

Figure 3-24 Detailed structure of a Pacinian corpuscle in the skin.

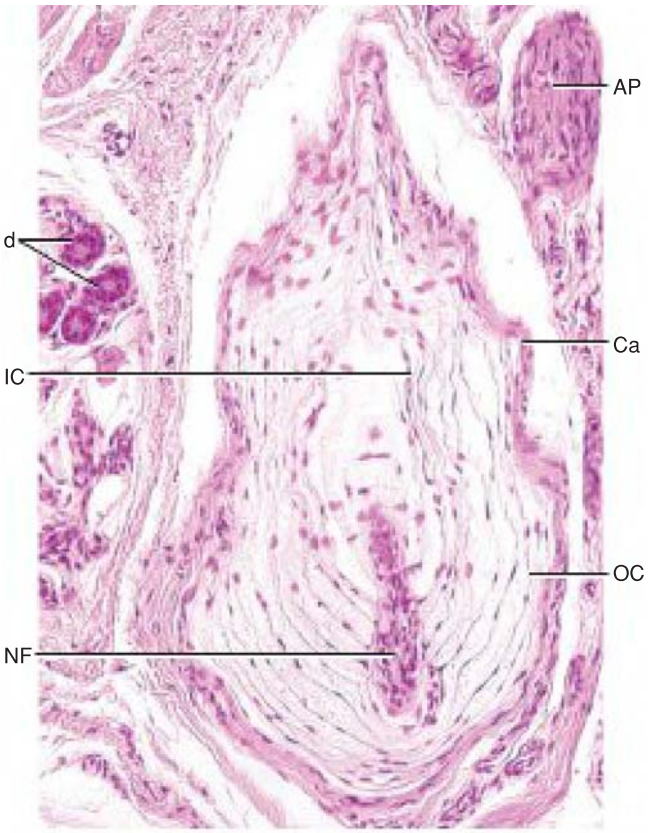

Figure 3-25 Pacinian corpuscle. Paraffin section. 132. Pacinian corpuscles, located in the dermis and hypodermis, are mechanoreceptors. They are composed of a core with an inner (IC) and an outer (OC) region, as well as a capsule (Ca) that surrounds the core. The inner core invests the afferent nerve fiber (NF), which loses its myelin sheath soon after entering the corpuscle. The core cells are modified Schwann cells, whereas the components of the capsule are continuous with the endoneurium of the afferent nerve fiber. Pacinian corpuscles are readily recognizable in section since they resemble the cut surface of an onion. Observe the presence of an arrector pili muscle (AP) and profiles of ducts (d) of a sweat gland in the vicinity of, but not associated with, the pacinian corpuscle. (From Gartner, L. P. *Color Atlas and Text of Histology,* 7e. Baltimore: Wolters Kluwer, 2018.)

slowly adapting mechanoreceptors are stretch receptors, which respond when the skin is stretched.

Cutaneous Receptor Function

The different histologic types of receptors were previously thought to correspond to specific types of sensation, until scientists pointed out that some areas of the body have only one or two histologic types of receptors and yet are sensitive to a variety of different stimuli. Moreover, although the body has these different receptors, all nerves only transmit nerve impulses. Now scientists generally agree that the type of sensation felt is determined by the specific area of the CNS to which the afferent nerve fiber passes. For example, if a pain nerve fiber is stimulated by heat, cold, touch, or pressure, the individual will experience only pain.

Sensory Stimulus Transduction into Nerve Impulse

Transduction is the process by which one form of energy (the stimulus) is changed into another form of energy (electrochemical energy of the nerve impulse). The stimulus, when applied to the receptor, brings about a change in potential of the plasma membrane of the nerve ending. Because this process takes place in the receptor, it is referred to as the **receptor potential**. The amplitude of the receptor potential is proportional to the intensity of the stimulus. By opening more ion channels for a longer time, a stronger mechanical pressure, for example, can produce a greater depolarization than does weak pressure. With chemoreceptors and photoreceptors, the receptor potential is produced by second messengers activated when the stimulus agent binds to the membrane receptors coupled to G proteins. If large enough, the receptor potential will generate an AP that will travel along the afferent nerve fiber to the CNS.

Joint Receptors

Four types of sensory endings can be located in the capsule and ligaments of synovial joints. Three of these endings are encapsulated and resemble Pacinian, Ruffini, and tendon stretch receptors. They provide the CNS with information regarding the position and movements of the joint. A fourth type of ending is nonencapsulated and is thought to be sensitive to excessive movements and to transmit pain sensations.

Neuromuscular Spindles

Neuromuscular spindles, or muscular spindles (Figs. 3-26 and 3-27), are found in skeletal muscle and are most numerous toward the tendinous attachment of the muscle. They provide the CNS with sensory information regarding the muscle length and the rate of change in the muscle length. The CNS uses this information to control muscle activity.

Each spindle measures about 1 to 4 mm in length and is surrounded by a fusiform capsule of connective tissue (Fig. 3-28). Within the capsule are 6 to 14 slender **intrafusal muscle fibers**; the ordinary muscle fibers situated outside the spindles are referred to as **extrafusal fibers**. The intrafusal fibers of the spindles are of two types: the **nuclear bag** and **nuclear chain** fibers. The nuclear bag fibers are recognized by the presence of numerous nuclei in the equatorial region, which consequently is expanded; also, cross striations are absent in this region. In the nuclear chain fibers, the nuclei form a single longitudinal row or chain in the center of each fiber at the equatorial region. The nuclear bag fibers are larger in diameter than the nuclear chain fibers, and they extend beyond the capsule at each end to be attached to the endomysium of the extrafusal fibers.

The two types of sensory innervation of muscle spindles are annulospiral and flower spray. The **annulospiral**

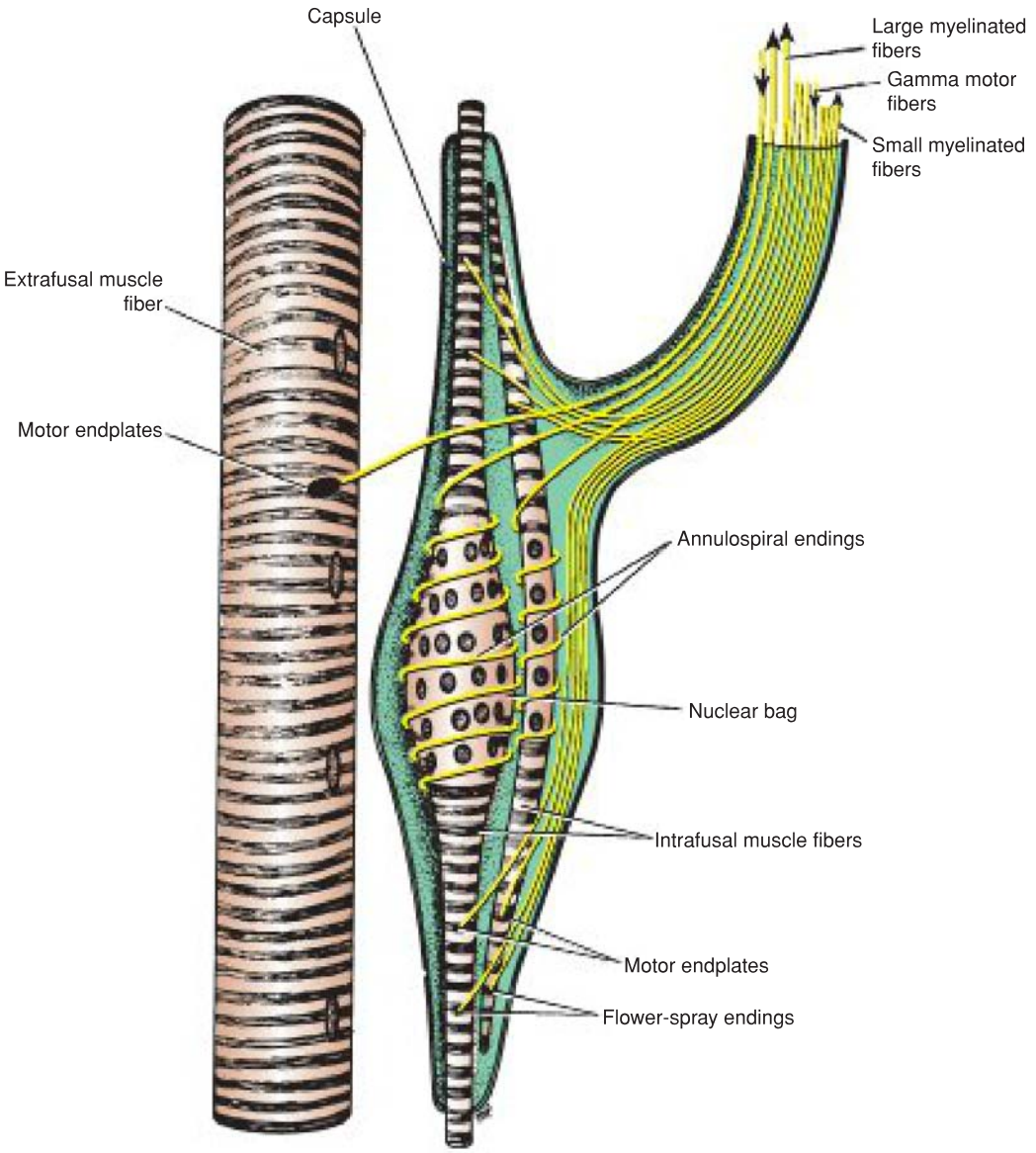

Figure 3-26 Neuromuscular spindle showing two types of intrafusal fibers: the nuclear bag and nuclear chain fibers.

endings are situated at the equator of the intrafusal fibers. As the large myelinated nerve fiber pierces the capsule, it loses its myelin sheath, and the naked axon winds spirally around the nuclear bag or chain portions of the intrafusal fibers.

The **flower-spray endings** are situated mainly on the nuclear chain fibers some distance away from the equatorial region. A myelinated nerve fiber slightly smaller than that for the annulospiral ending pierces the capsule and loses its myelin sheath, and the naked axon branches terminally and ends as varicosities; it resembles a spray of flowers.

Stretching (elongation) of the intrafusal fibers results in stimulation of the annulospiral and flower-spray endings, and nerve impulses pass to the spinal cord in the afferent neurons.

Motor innervation of the intrafusal fibers is provided by fine γ motor fibers. The nerves terminate in small motor endplates situated at both ends of the intrafusal fibers. Stimulation of the motor nerves causes both ends of the intrafusal fibers to contract and activate the sensory endings. The equatorial region, which lacks cross striations, is noncontractile. The extrafusal fibers of the remainder of the muscle receive their innervation in the usual way from large α-size axons.

Neuromuscular Spindle Function

Under resting conditions, the muscle spindles give rise to afferent nerve impulses all the time, and most of this information is not consciously perceived. When muscle activity occurs, either actively or passively, the

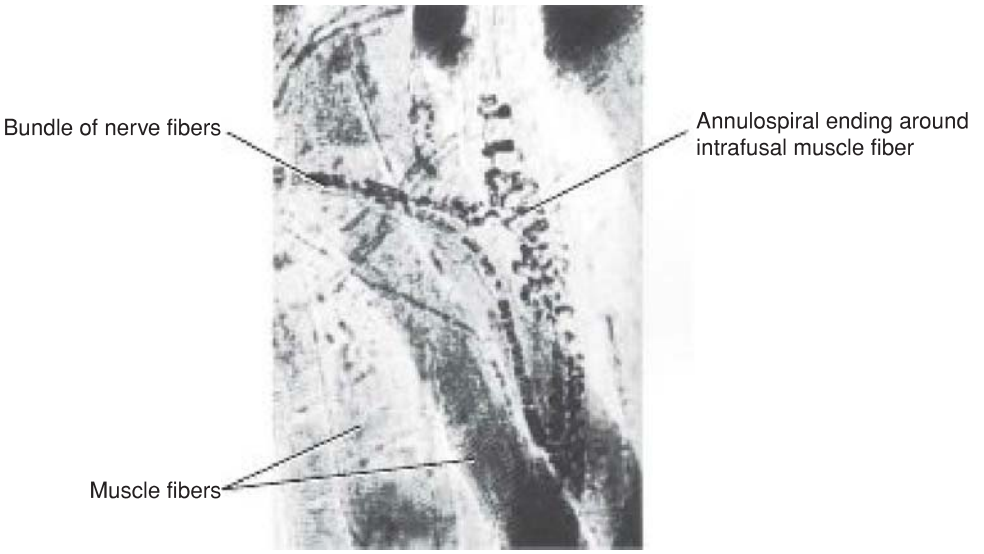

Figure 3-27 Photomicrograph of a neuromuscular spindle.

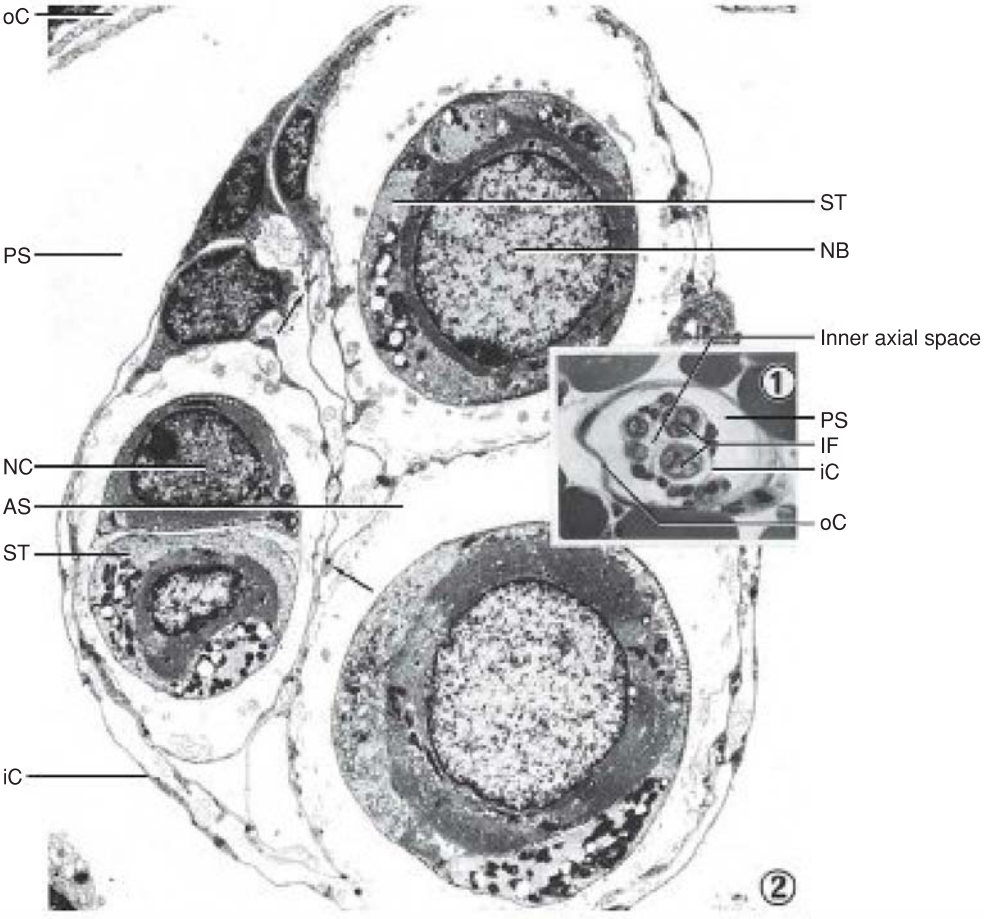

Figure 3-28 Muscle spindle. Mouse. Electron microscopy. ×6,300. Parts of the outer capsule (oC) may be observed at the corners of this electron micrograph. The periaxial space (PS) surrounds the slender inner capsule (iC), whose component cells form attenuated branches, subdividing the axial space (AS) into several compartments for the nuclear chain (NC) and nuclear bag (NB) intrafusal fibers and their corresponding sensory terminals (ST). Note that the attenuated processes of the inner capsule cells establish contact with each other (*arrows*). (From Ovalle, W., Dow, P. (1983). Comparative ultrastructure of the inner capsule of the muscle spindle and the tendon organ. *American Journal of Anatomy, 166*, 343–357.)

intrafusal fibers are stretched, and the rate of passage of nerve impulses to the spinal cord or brain increases in the afferent neurons. Similarly, if the intrafusal fibers are now relaxed due to the cessation of muscle activity, the result is a decrease in the rate of passage of nerve impulses. The neuromuscular spindle thus plays a very important role in keeping the CNS informed about the length of a muscle and the rate of change of its length, thereby indirectly influencing the control of voluntary muscle.

Stretch Reflex

The neurons of the spinal cord involved in the simple stretch reflex are as follows. Stretching a muscle results in elongation of the intrafusal fibers of the muscle spindle and stimulation of the annulospiral and flower-spray endings. The nerve impulses reach the spinal cord in the afferent neurons and synapse with the large α motor neurons situated in the anterior gray horns of the spinal cord. Nerve impulses now pass via the efferent motor nerves and stimulate the extrafusal muscle fibers, and the muscle contracts. This simple stretch reflex depends on a two-neuron arc consisting of an afferent neuron and an efferent neuron. Interestingly, the muscle spindle afferent impulses inhibit the α motor neurons supplying the antagonist muscles. This effect is called **reciprocal inhibition**.

Intrafusal Fiber Control

In the brain and spinal cord, certain centers give rise to tracts that synapse with γ motor neurons in the spinal cord. The reticular formation, the basal ganglia, and the cerebellum are examples of such centers. By these means, these centers can greatly influence voluntary muscle activity. The γ efferent motor fibers cause shortening of the intrafusal fibers, stretching the equatorial regions and stimulating the annulospiral and flower-spray endings. This, in turn, initiates the reflex contraction of the extrafusal fibers described previously.

Approximately one-third of all the motor fibers passing to a muscle are γ efferents; the remaining two-thirds are the large α motor fibers. The nuclear bag fibers are believed to be concerned with dynamic responses and are associated more with position and velocity of contraction, whereas the nuclear chain fibers are associated with slow static contractions of voluntary muscle.

Neurotendinous Spindles

Neurotendinous spindles (Golgi tendon organs) are present in tendons and are located near the junctions of tendons with muscles (Fig. 3-29). They provide the CNS with sensory information regarding the tension of muscles.

Each spindle consists of a fibrous capsule that surrounds a small bundle of loosely arranged tendon (collagen) fibers (intrafusal fibers). The tendon cells are

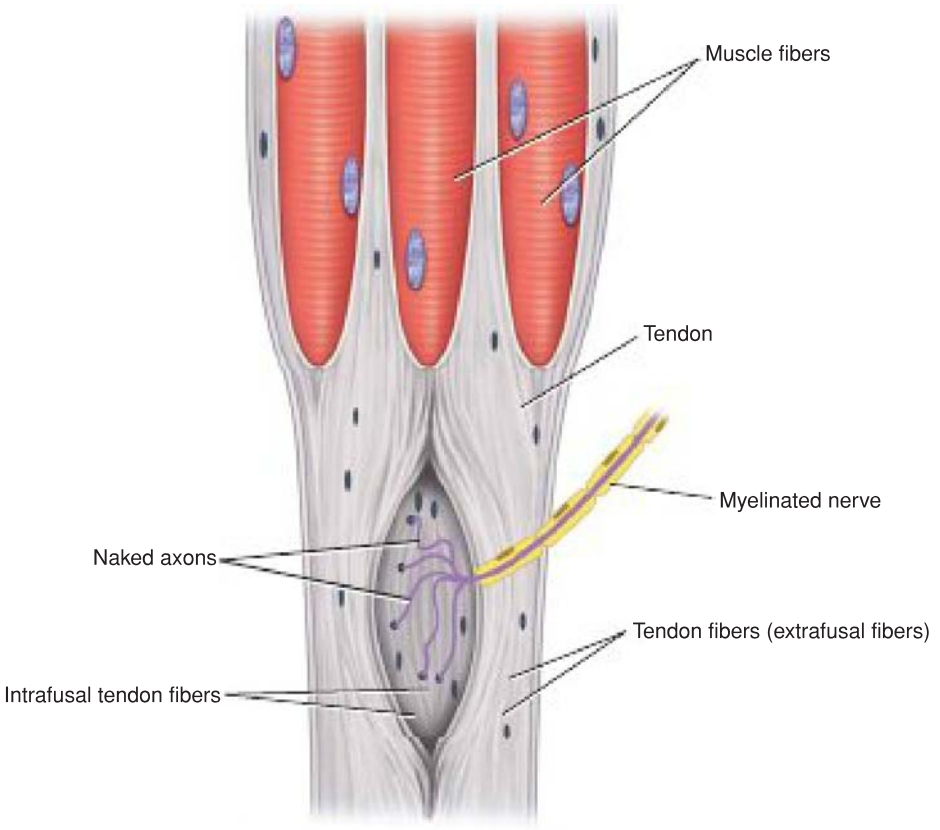

Figure 3-29 A neurotendinous spindle.

larger and more numerous than those found elsewhere in the tendon. One or more myelinated sensory nerve fibers pierce the capsule, lose their myelin sheath, branch, and terminate in club-shaped endings.

The nerve endings are activated by being squeezed by the adjacent tendon fibers within the spindle when tension develops in the tendon. Unlike the neuromuscular spindle, which is sensitive to changes in muscle length, the neurotendinous organ detects changes in muscle tension.

Neurotendinous Spindle Function

Increased muscle tension stimulates the neurotendinous spindles, and an increased number of nerve impulses reach the spinal cord through the afferent nerve fibers. These fibers synapse with the large α motor neurons situated in the anterior gray horns of the spinal cord. Unlike the muscle spindle reflex, this reflex is inhibitory and inhibits muscle contraction. In this manner, the tendon reflex prevents the development of too much tension in the muscle. Although this function is probably important as a protective mechanism, its main function is to provide the CNS with information that can influence voluntary muscle activity.

EFFECTOR ENDINGS

The PNS controls muscle and secretory cell functions. These axonal endings establish chemical synapses on nonneuronal cells such as skeletal, smooth, and cardiac muscle cells and to the cells of glandular tissue.

Skeletal Muscle Innervation

Skeletal muscle is innervated by one or more nerves. In the limbs and head and neck, the innervation is usually single, but, in the large muscles of the abdominal wall, the innervation is multiple, the latter muscles having retained their embryonic segmental nerve supply.

The nerve supply and blood supply to a muscle enter it at a more or less constant position called the **neurovascular** hilus. The nerve to a muscle contains motor and sensory fibers. The motor fibers are of three types: (1) large α myelinated fibers, (2) small γ myelinated fibers, and (3) fine unmyelinated C fibers. The large myelinated axons of the α anterior horn cells supply the extrafusal fibers that form the main mass of the muscle. The small γ myelinated fibers supply the intrafusal fibers of the neuromuscular spindles. The fine unmyelinated fibers are postganglionic autonomic efferents that supply the smooth muscle in the walls of blood vessels.

The sensory fibers are of three main types: (1) myelinated fibers that originate in annulospiral and flower-spray endings of the neuromuscular spindles, (2) myelinated fibers that originate in neurotendinous spindles; and (3) myelinated and nonmyelinated fibers that originate from a variety of sensory endings in muscle connective tissue.

Motor Unit

The motor unit may be defined as the single α motor neuron and the muscle fibers that it innervates (Fig. 3-30). The muscle fibers of a single motor unit are widely scattered throughout the muscle. Where

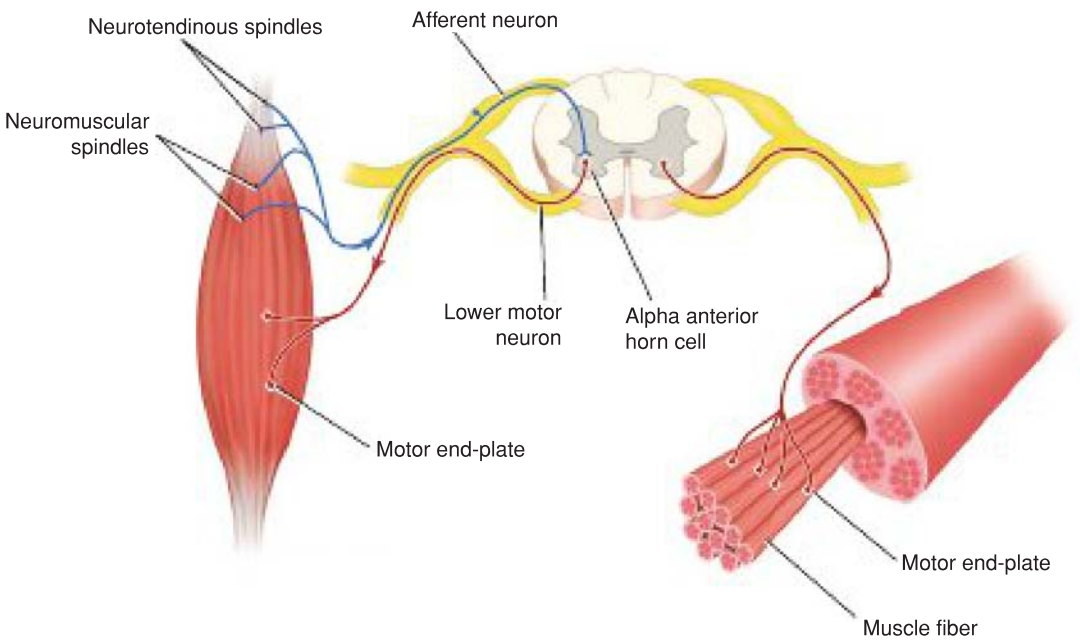

Figure 3-30 Simple reflex arc consisting of an afferent neuron arising from neuromuscular spindles and neurotendinous spindles and an efferent lower motor neuron whose cell body is an α anterior horn cell within the spinal cord. Note that the efferent neuron terminates on muscle fibers at motor endplates.

fine, precise muscle control is required, such as in the extraocular muscles or the small muscles of the hand, the motor units possess only a few muscle fibers. Where precise control is not necessary, however, as in a large limb muscle such as the gluteus maximus, a single motor nerve may innervate many hundreds of muscle fibers.

Skeletal Muscle Neuromuscular Junctions

Skeletal muscle fibers are innervated by large, α myelinated nerve fibers derived from large motor neurons in the anterior gray columns (horns) of the spinal cord or from cranial nerve motor nuclei. As each myelinated fiber enters a skeletal muscle, it branches many times. The number of branches depends on the size of the motor unit. A single branch then terminates on a muscle fiber at the **neuromuscular junction** or **motor endplate** (Figs. 3-31 and 3-32).

The great majority of muscle fibers are innervated by just one motor endplate. On reaching the muscle fiber, the nerve loses its myelin sheath and breaks up into a number of fine branches. Each branch ends as a naked axon and forms the **neural element** of the motor endplate (Fig. 3-33). The axon is expanded slightly and contains many mitochondria and vesicles (approximately 45 nm in diameter). At the site of the motor endplate, the surface of the muscle fiber is elevated slightly to form the **muscular element** of the plate, often referred to as the **sole plate** (see Fig. 3-31A). The elevation is due to the local accumulation of granular sarcoplasm beneath the sarcolemma and the presence of numerous nuclei and mitochondria, the latter providing the ATP, which is the energy source for acetylcholine (ACh) synthesis.

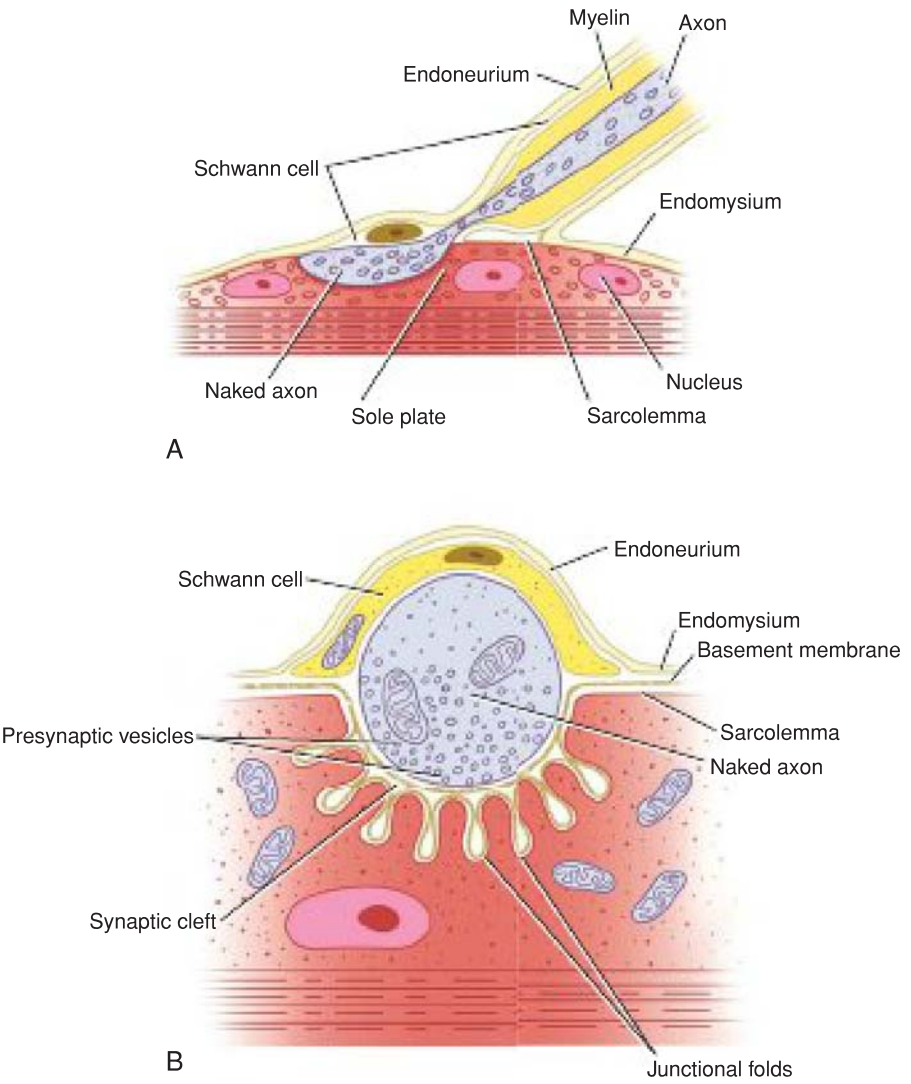

Figure 3-31 **A:** A skeletal neuromuscular junction. **B:** Enlarged view of a muscle fiber showing the terminal naked axon lying in the surface groove of the muscle fiber.

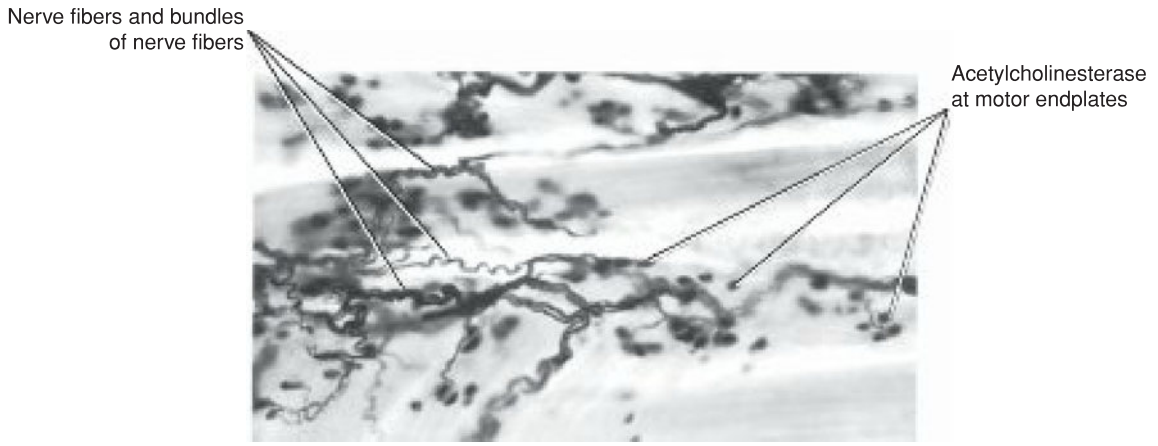

Figure 3-32 Photomicrograph showing nerve fibers terminating on skeletal muscle fibers at motor endplates, stained histochemically for acetylcholinesterase and counterstained with silver. (Courtesy Dr. M. J. T. Fitzgerald.)

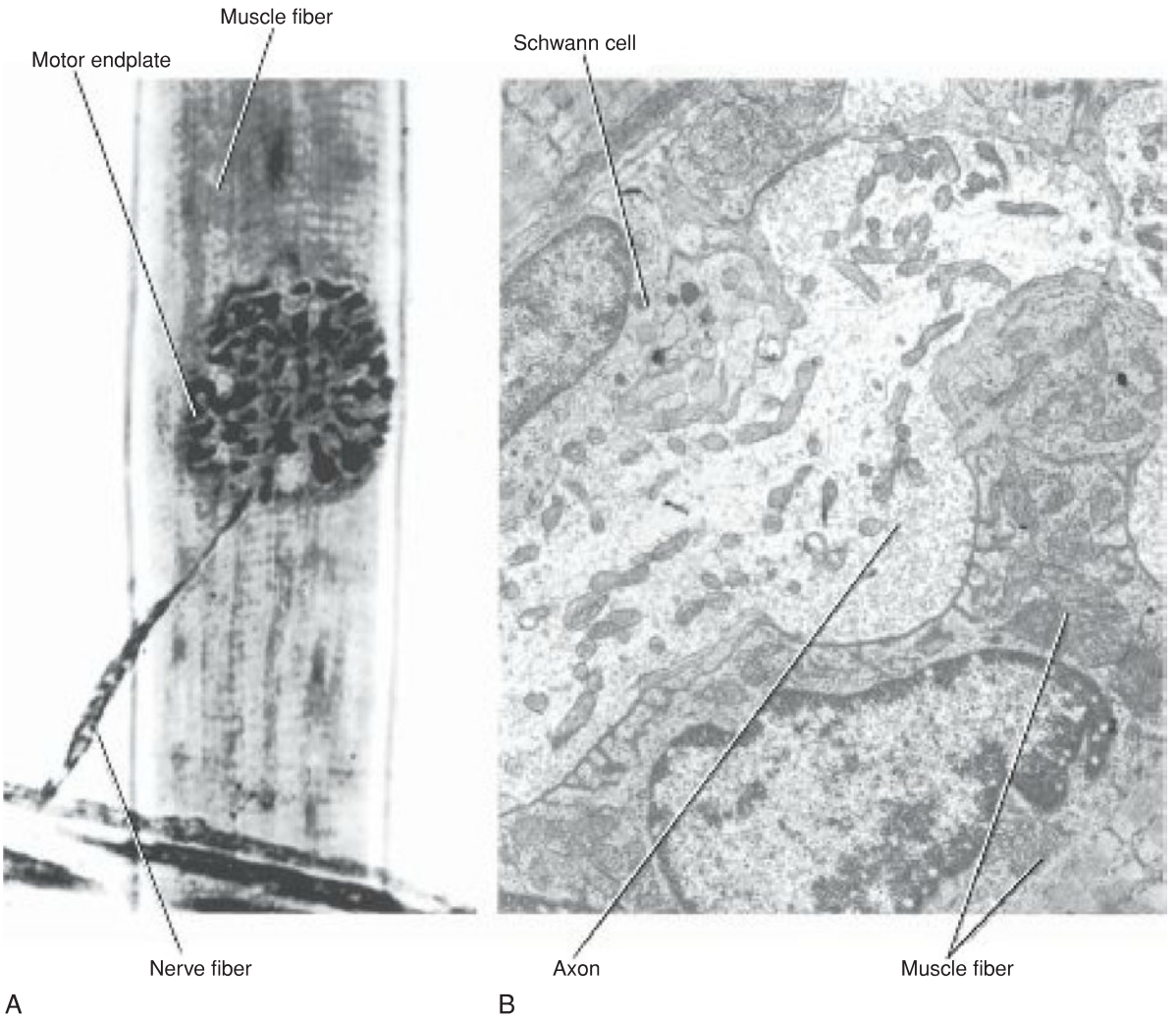

Figure 3-33 **A:** Photomicrograph of a motor endplate showing terminal branching of a nerve fiber. **B:** Electron micrograph of a terminal axon at a motor endplate showing the axon lying in a groove on the surface of the muscle fiber. (Courtesy Dr. J. M. Kerns.)

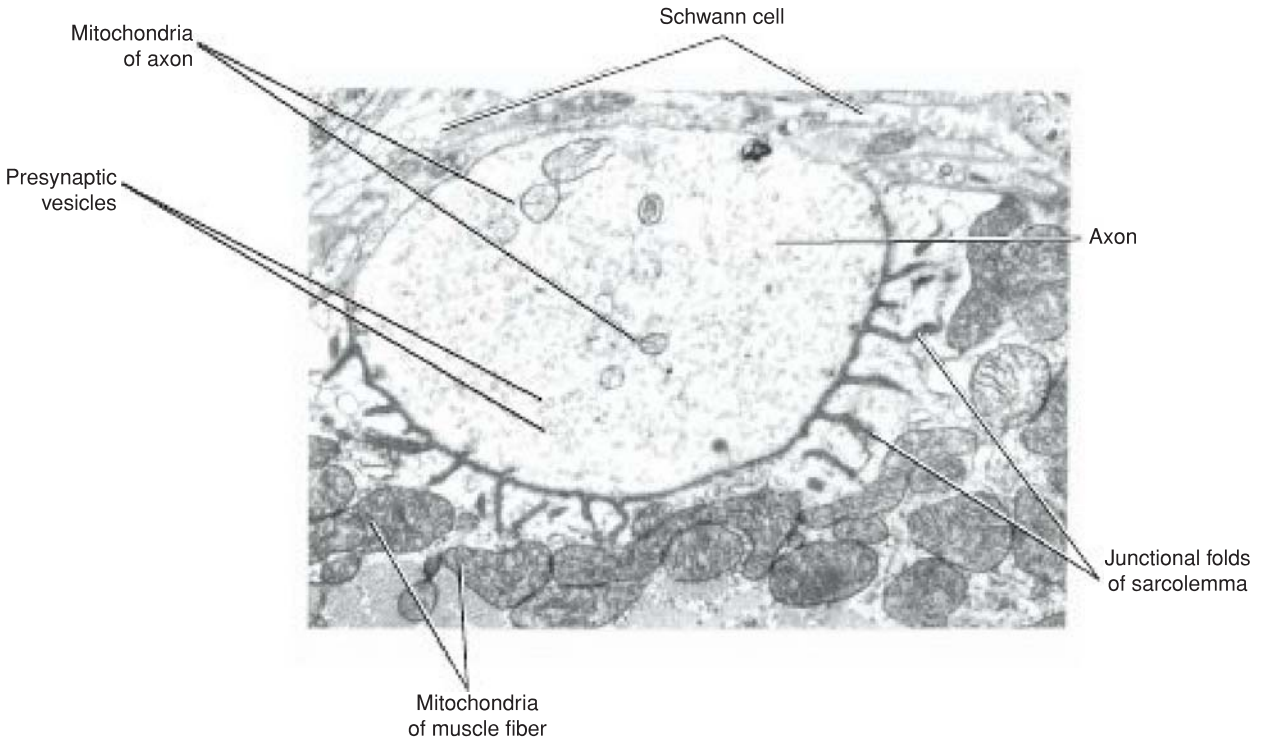

Figure 3-34 Electron micrograph of a cross section of an axon at a motor endplate showing the axon lying in a groove of folded sarcolemma. (Courtesy Dr. J. M. Kerns.)

The expanded naked axon lies in a groove on the surface of the muscle fiber outside the plasma membrane (sarcolemma). Each groove is formed by the infolding of the plasma membrane. The groove may branch many times, with each branch containing a division of the axon. Importantly, the axons are truly naked; the Schwann cells merely serve as a cap or roof to the groove and never project into it. The floor of the groove is formed of the plasma membrane, which is thrown into numerous small folds, called **junctional folds**, which increase the surface area of the plasma membrane that lies close to the naked axon (Fig. 3-34).

The plasma membrane of the axon (the axolemma or presynaptic membrane) is separated, by a space about 30 to 50 nm wide, from the plasma membrane of the muscle fiber (the sarcolemma or postsynaptic membrane). This space constitutes the **synaptic cleft**. The synaptic cleft is filled with the basement membranes of the axon and the muscle fiber (see Fig. 3-31B). The motor endplate is strengthened by the connective tissue sheath of the nerve fiber (endoneurium), which becomes continuous with the connective tissue sheath of the muscle fiber (endomysium).

A nerve impulse (AP), on reaching the presynaptic membrane of the motor endplate, causes the opening of voltage-gated Ca^{2+} channels that allow Ca^{2+} ions to enter the axon. This stimulates the fusion of some of the synaptic vesicles with the presynaptic membrane and causes the release of ACh into the synaptic cleft. The ACh is thus discharged into the cleft by a process of **exocytosis** and diffuses rapidly across the cleft to reach the nicotinic type of ACh receptors on the postsynaptic membrane of the junctional folds. The postsynaptic membrane possesses large numbers of ACh-gated channels.

Once the ACh-gated channels are opened, the postsynaptic membrane becomes more permeable to Na^+ ions, which flow into the muscle cell, and a local potential called the **endplate potential** is created. (The ACh-gated channels are also permeable to K^+ ions, which flow out of the cell but to a lesser extent.) If the endplate potential is large enough, the voltage-gated channels for Na^+ ions are opened, and an AP will be initiated and spread along the surface of the plasma membrane (sarcolemma). The wave of depolarization is carried into the muscle fiber to the contractile myofibrils through the system of T tubules. This leads to the release of Ca^{2+} ions from the sarcoplasmic reticulum, which, in turn, causes the muscle to contract.

The amount of ACh released at the motor endplate will depend on the number of nerve impulses arriving at the nerve terminal. Once the ACh crosses the synaptic cleft and triggers the ionic channels on the postsynaptic membrane, it immediately undergoes hydrolysis due to the presence of the enzyme **acetylcholinesterase** (**AChE**) (see Fig. 3-32). The enzyme adheres to the fine collagen fibrils of the basement membranes in the cleft; some of the ACh diffuses away from the cleft. The ACh remains in contact with the postsynaptic membrane for about 1 msec, and it is rapidly destroyed to prevent re-excitation of the muscle fiber. After the fall in concentration of ACh in the cleft, the ionic channels close and remain closed until more ACh arrives.

Skeletal muscle fiber contraction is thus controlled by the frequency of the nerve impulses that arrive at the motor nerve terminal. A resting muscle fiber shows small occasional depolarizations (endplate potentials) at the motor endplate, which are insufficient to cause an AP and make the fiber contract. These are believed to be due to the sporadic release of ACh into the synaptic cleft from a single presynaptic vesicle.

The sequence of events that takes place at a motor endplate on stimulation of a motor nerve can be briefly summarized as follows:

ACh → Nicotinic type of ACh receptor, ACh-gated channels opened → Na^+ influx → Endplate potential created
Endplate potential (if large enough) → Na^+-gated channels opened → Na^+ influx → AP created
AP → Increased release of Ca^{2+} → Muscle fiber contraction
Immediate hydrolysis of ACh by AChE → ACh-gated channels closed → Muscle fiber repolarization

If drugs having a similar chemical structure to ACh were to arrive at the receptor site of a motor endplate, they might bring about the same changes as ACh and mimic its action. Two examples of such drugs are **nicotine** and **carbamylcholine**. If, on the other hand, drugs having a similar chemical structure to ACh were to arrive at the receptor site of a motor endplate and were unable to bring about the sequence of changes normally induced by ACh, they would occupy the receptor site and block access of ACh. Such drugs would be competing with ACh and are called **competitive blocking agents**. An example of such a drug is ***d*-tubocurarine**, which causes skeletal muscle to relax and not contract by preventing the action of locally produced ACh (see p. 114).

Smooth Muscle Neuromuscular Junctions

In smooth muscle, where the action is slow and widespread, such as within the wall of the intestine, the autonomic nerve fibers branch extensively; thus, a single neuron exerts control over a large number of muscle fibers. In some areas (e.g., the longitudinal layer of smooth muscle in the intestine), only a few muscle fibers are associated with autonomic endings, the wave of contraction passing from one muscle cell to another by means of gap junctions (Fig. 3-35).

In smooth muscle, in which the action is fast and precision is required, such as in the iris, the branching of the nerve fibers is less extensive; thus, a single neuron exerts control over only a few muscle fibers.

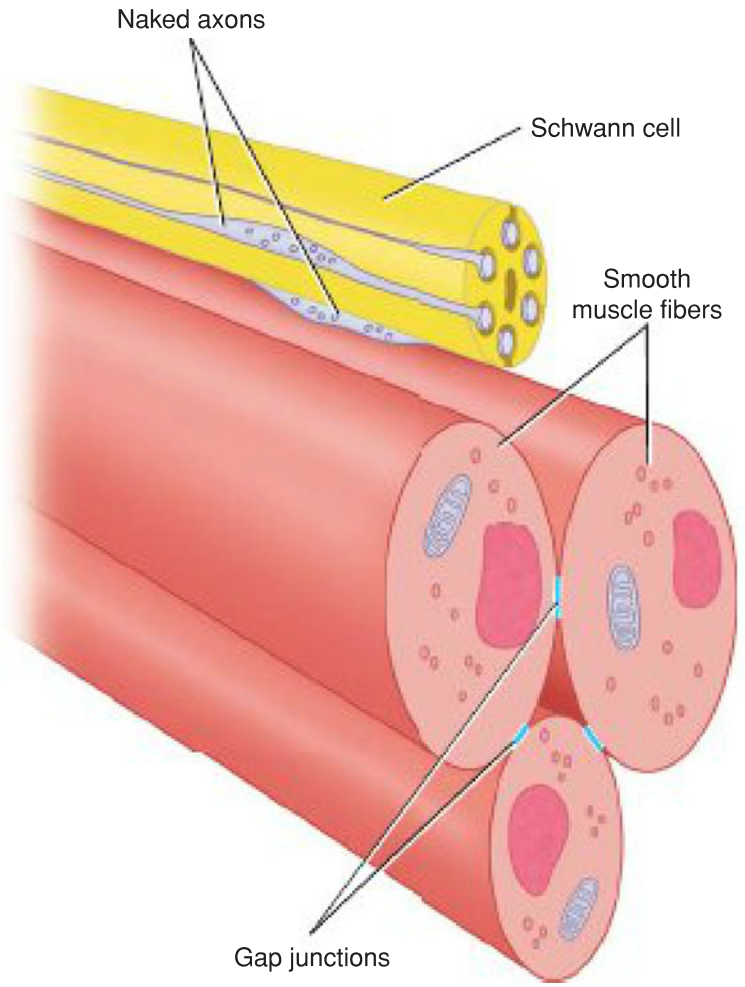

Figure 3-35 Autonomic neuromuscular junction. The exposed axons are close to the smooth muscle fibers.

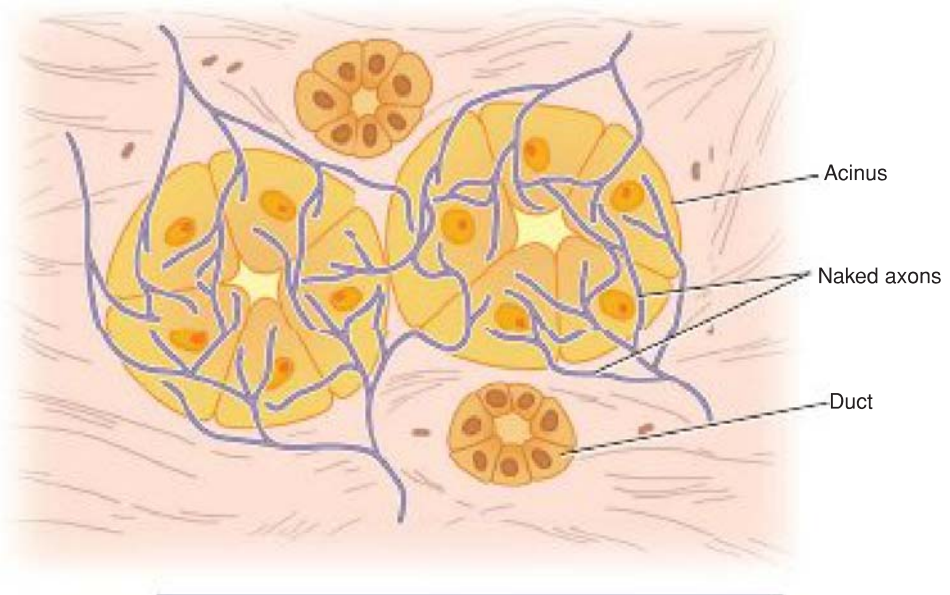

Figure 3-36 Nerve fibers ending around glandular acini.

The autonomic nerve fibers, which are postganglionic, are nonmyelinated and terminate as a series of varicosed branches. An interval of 10 to 100 nm may exist between the axon and the muscle fiber. At the site where transmission is to occur, the Schwann cell is retracted so that the axon lies within a shallow groove on its surface. Therefore, part of the axon is naked, permitting free diffusion of the transmitter substance from the axon to the muscle cell. Here, the axoplasm contains numerous vesicles similar to those seen at the motor endplate of skeletal muscle.

Smooth muscle is innervated by sympathetic and parasympathetic parts of the autonomic system. Those nerves that are cholinergic liberate ACh at their endings by a process of exocytosis, with the ACh being present in the vesicles at the nerve ending. Those nerves that are noradrenergic liberate **norepinephrine** (**NE**) at their endings by a process of exocytosis, with the NE being present in dark-cored vesicles at the nerve endings. Both ACh and NE bring about depolarization of the muscle fibers innervated, which thereupon contract. The fate of these neurotransmitter substances differs. ACh is hydrolyzed in the presence of AChE in the synaptic cleft of the muscle fiber, and NE is taken up by the nerve endings. Notably, in some areas of the body (e.g., bronchial muscle), the NE liberated from postganglionic sympathetic fibers causes smooth muscle to relax and not contract.

Cardiac Muscle Neuromuscular Junctions

Nonmyelinated postganglionic sympathetic and parasympathetic autonomic nerves extend into the connective tissue between the muscle fibers and terminate in close proximity to the individual cardiac muscle fibers. At the site where transmission takes place, the axon becomes naked because of the retraction of the Schwann cell. This permits free diffusion of the neurotransmitter substance from the axon to the muscle fiber. Because of the presence of intermittent desmosomes and gap junctions between abutting muscle fibers, excitation and contraction of one muscle fiber rapidly spread from fiber to fiber.

Nerve Endings on Secretory Cells of Glands

Nonmyelinated postganglionic autonomic nerves extend into the connective tissue of glands and branch close to the secretory cells (Fig. 3-36). In many glands, the nerve fibers have been found to innervate only the blood vessels.

SEGMENTAL INNERVATION OF SKIN

The area of skin supplied by a single spinal nerve and, therefore, a single segment of the spinal cord is called a **dermatome**. On the trunk, dermatomes extend round the body from the posterior to the anterior median plane. Adjacent dermatomes overlap considerably, so to produce a region of complete anesthesia, at least three contiguous spinal nerves have to be sectioned. Note that the area of tactile loss is always greater than the area of loss of painful and thermal sensations. The reason for this difference is that the degree of overlap of fibers carrying pain and thermal sensations is much more extensive than the overlap of fibers carrying tactile sensations. Dermatomal charts for the anterior and posterior surfaces of the body are shown in Figures 3-37 and 3-38.

In the limbs, the arrangement of the dermatomes is more complicated because of the embryologic rotation of the limbs as they grow out from the trunk.

In the face, the divisions of the trigeminal nerve supply a precise area of skin, with little or no overlap to the cutaneous area of another division.

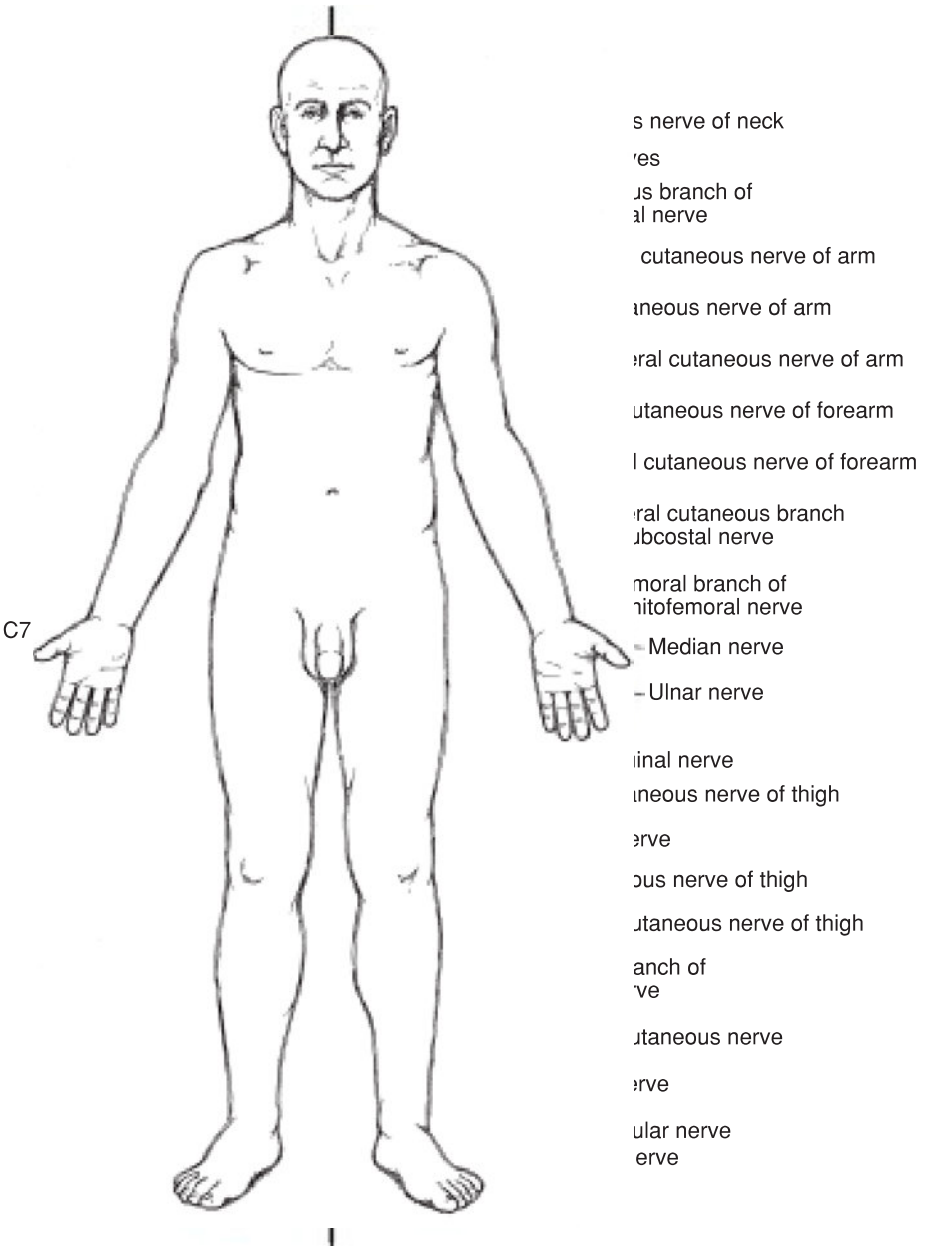

Figure 3-37 Anterior aspect of the body showing the distribution of cutaneous nerves on the left side and dermatomes on the right side.

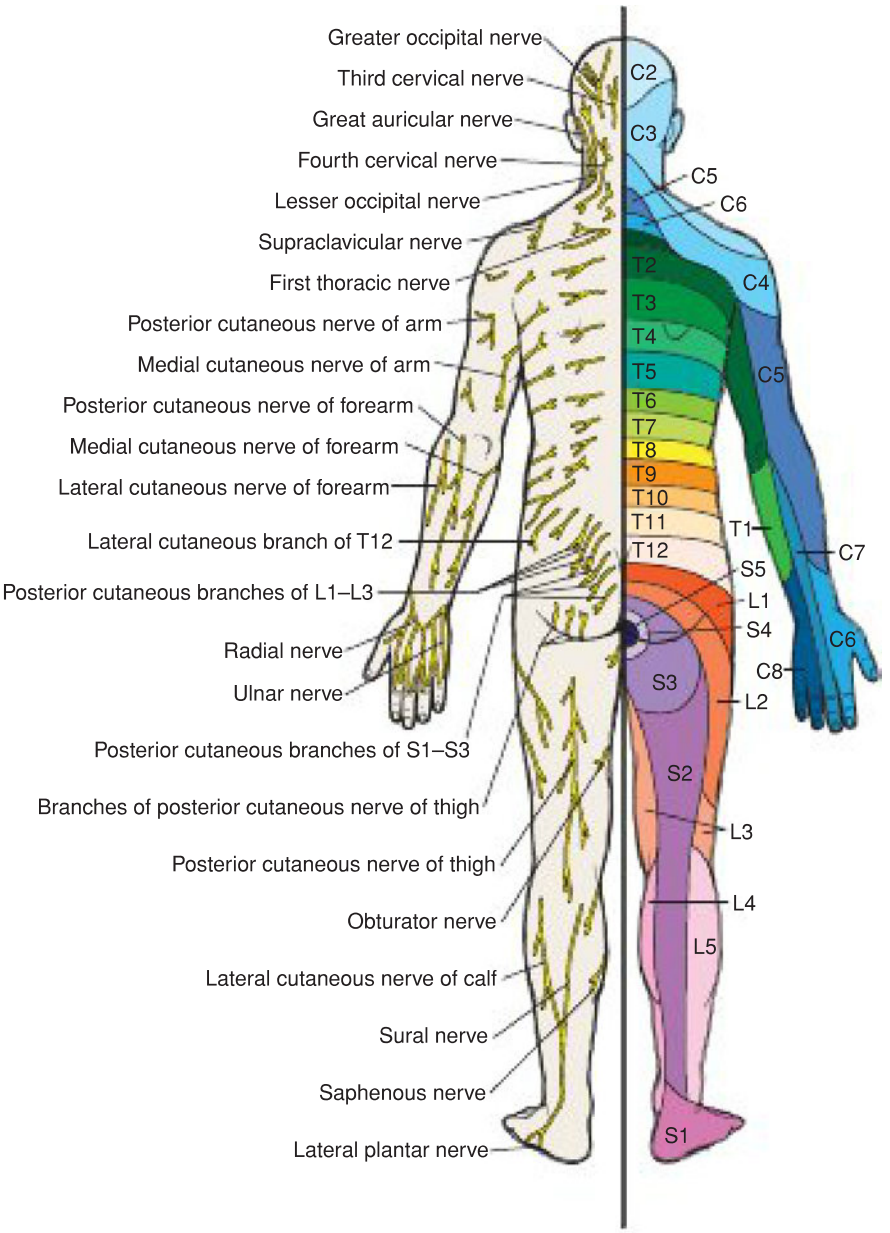

Figure 3-38 Posterior aspect of the body showing the distribution of cutaneous nerves on the left side and dermatomes on the right side.

SEGMENTAL INNERVATION OF MUSCLES

Skeletal muscle also receives a segmental innervation. Most of these muscles are innervated by more than one spinal nerve and, therefore, by the same number of segments of the spinal cord. Thus, to paralyze a muscle completely, sectioning several spinal nerves or destroying several segments of the spinal cord would be necessary.

Learning the segmental innervation of all the muscles of the body is an impossible task. Nevertheless, the segmental innervation of the following muscles should be known because testing them by eliciting simple muscle reflexes in the patient is possible (Fig. 3-39):

Biceps brachii tendon reflex C5–C6: Flexion of the elbow joint by tapping the biceps tendon

Triceps tendon reflex C6–C7 and C8: Extension of the elbow joint by tapping the triceps tendon

Brachioradialis tendon reflex C5–C6 and C7: Supination of the radioulnar joints by tapping the insertion of the brachioradialis tendon

Abdominal superficial reflexes: Contraction of underlying abdominal muscles by stroking the skin: upper abdominal skin T6–T7, middle abdominal skin T8–T9, lower abdominal skin T10–T12

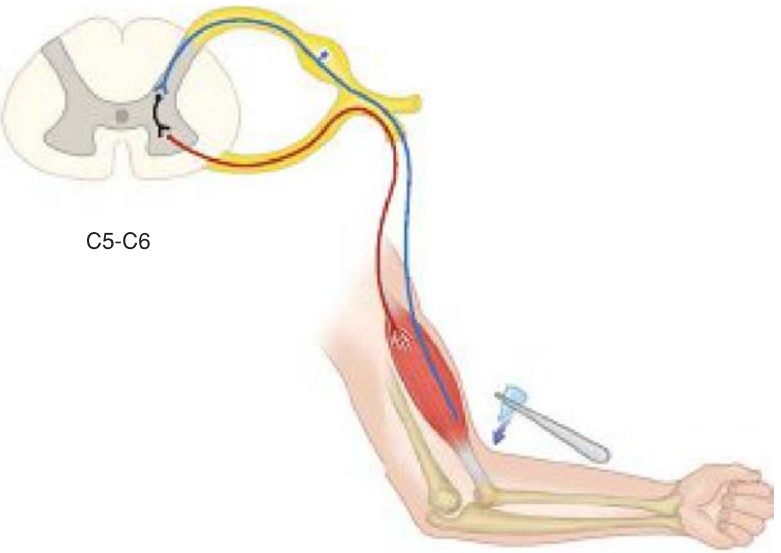

Figure 3-39 Biceps brachii tendon reflex. Note that the reflex arc passes through the fifth and sixth cervical segments of the spinal cord. This is usually monosynaptic, and the internuncial neuron (*black*) is absent.

Patellar tendon reflex (knee jerk) L2, L3, and L4: Extension of knee joint on tapping the patellar tendon

Achilles tendon reflex (ankle jerk) S1 and S2: Plantar flexion of ankle joint on tapping the Achilles tendon (calcaneus tendon)

MUSCLE TONE AND MUSCLE ACTION

A **motor unit** consists of a motor neuron in the anterior gray column (horn) of the spinal cord and all the muscle fibers it supplies (Fig. 3-40). In a large buttock muscle, such as the gluteus maximus, where fine control is unnecessary, a given motor neuron may supply as many as 200 muscle fibers. In contrast, in the small muscles of the hand or the extrinsic muscles of the eyeball, where fine control is required, one nerve fiber supplies only a few muscle fibers.

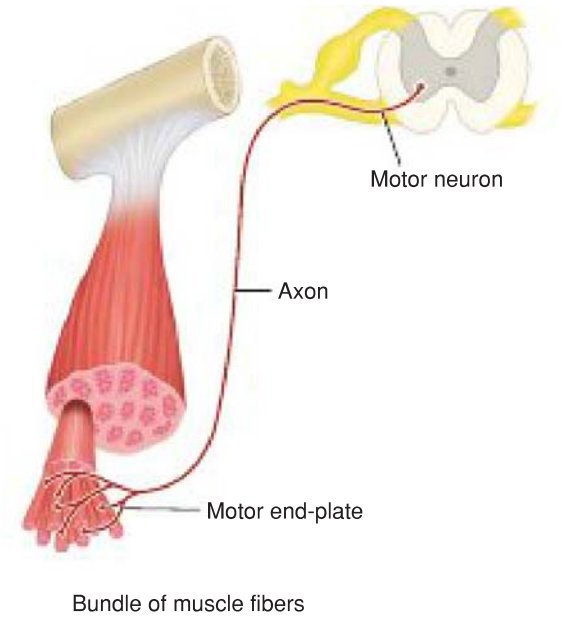

Figure 3-40 Components of a motor unit.

Every skeletal muscle, while resting, is in a partial state of contraction, a condition referred to as **muscle tone**. With no intermediate stage, muscle fibers are either fully contracted or relaxed; therefore, a few muscle fibers within a muscle are fully contracted all the time. To bring about this state and to avoid fatigue, different groups of motor units and, thus, different groups of muscle fibers are activated at different times. This is accomplished by the asynchronous discharge of nervous impulses in the motor neurons in the anterior gray horn of the spinal cord.

Basically, muscle tone is dependent on the integrity of a simple monosynaptic reflex arc composed of two neurons in the nervous system (Fig. 3-41). The lengthening and shortening in a muscle are detected by sensitive sensory endings called **muscle spindles** (see p. 90), and the tension is detected by **tendon spindles** (see p. 92). The nervous impulses travel in the large afferent fibers to the spinal cord. There, they synapse with the motor neurons situated in the anterior gray column, which, in turn, send impulses down their axons to the muscle fibers. The muscle spindles themselves are innervated by small γ efferent fibers that regulate the response of the muscle spindles, acting synergically with external stretch. In this manner, muscle tone is maintained reflexly and adjusted to the needs of posture and movement.

Should the afferent or efferent pathways of the reflex arc be cut, the muscle would lose its tone immediately and become flaccid. A flaccid muscle, on palpation, feels like a mass of dough that has completely lost its resilience. It

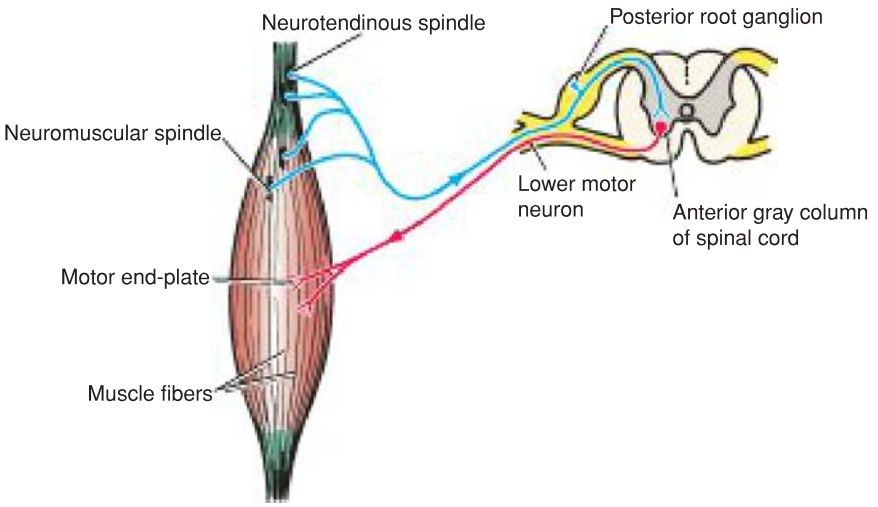

Figure 3-41 Simple reflex arc consisting of an afferent neuron arising from neuromuscular spindles and neurotendinous spindles and an efferent neuron whose cell body lies in the anterior gray column (horn) of the spinal cord. Note that for simplicity, the afferent fibers from the neurotendinous spindle and the neuromuscular spindle are shown as one pathway; in fact, the neurotendinous receptor is inhibitory and reduces tone, whereas the neuromuscular spindle is excitatory and increases tone.

quickly atrophies and becomes reduced in volume. The degree of activity of the motor anterior column cells and, therefore, the degree of muscle tone depends on the summation of the nerve impulses received by these cells from other neurons of the nervous system.

Muscle movement is accomplished by activating increasing numbers of motor units and, at the same time, reducing the activity of the motor units of muscles that will oppose or antagonize the movement. When the maximum effort is required, all the motor units of a muscle are active.

MOTOR UNIT SUMMATION

When a muscle begins to contract, the smaller motor units are stimulated first. This is because the smaller motor units are innervated by smaller neurons in the spinal cord and brainstem, and they have a lower threshold of excitability. As the contraction increases, progressively larger motor units are recruited. This phenomenon causes a gradual increase in muscle strength as the muscle contracts.

MUSCLE FATIGUE

The progressive loss of strength of a muscle with prolonged strong contraction is due to the reduction in the amounts of ATP within the muscle fibers. Nerve impulses continue to arrive at the neuromuscular junction, and normal depolarization of the plasma membrane of the muscle fiber occurs.

POSTURE

Posture is the position adopted by the individual within his or her environment. In the standing position, the line of gravity passes through the odontoid process of the axis, behind the centers of the hip joints, and in front of the knee and ankle joints. In order to stabilize the body and prevent it from collapsing, humans have well-developed antigravity muscles that exhibit the greatest degree of tone. Therefore, posture depends on the degree and distribution of muscle tone, which, in turn, depends on the normal integrity of simple reflex arcs centered in the spinal cord.

An individual may assume a particular posture (sitting or standing) over long periods of time with little evidence of fatigue. The reason for this is that muscle tone is maintained through different groups of muscle fibers contracting in relays, with only a small number of muscle fibers within a muscle being in a state of contraction at any one time. The active muscle fiber groups are scattered throughout the muscle.

In order to maintain posture, the simple muscle reflex, on which muscle tone is dependent, must receive adequate nervous input from higher levels of the nervous system (Fig. 3-42). For example, impulses arising from the labyrinths and neck muscles, information arising from the cerebellum, midbrain, and cerebral centers, and general information arising from other muscle groups, joints, and even skin receptors will result in nervous impulses impinging on the large anterior gray column cells (i.e., the final common pathway) controlling the muscle fibers.

When an individual assumes a given posture, the tone of the muscles controlling that posture is constantly undergoing fine adjustments so that the posture is maintained. Normal posture thus depends not only on the integrity of the reflex arc but also on the summation of the nervous impulses received by the motor anterior gray column cells from other neurons of the nervous system (Fig. 3-43). The detail of the different nervous pathways involved in bringing the information to the anterior gray column cells is dealt with in Chapter 4.

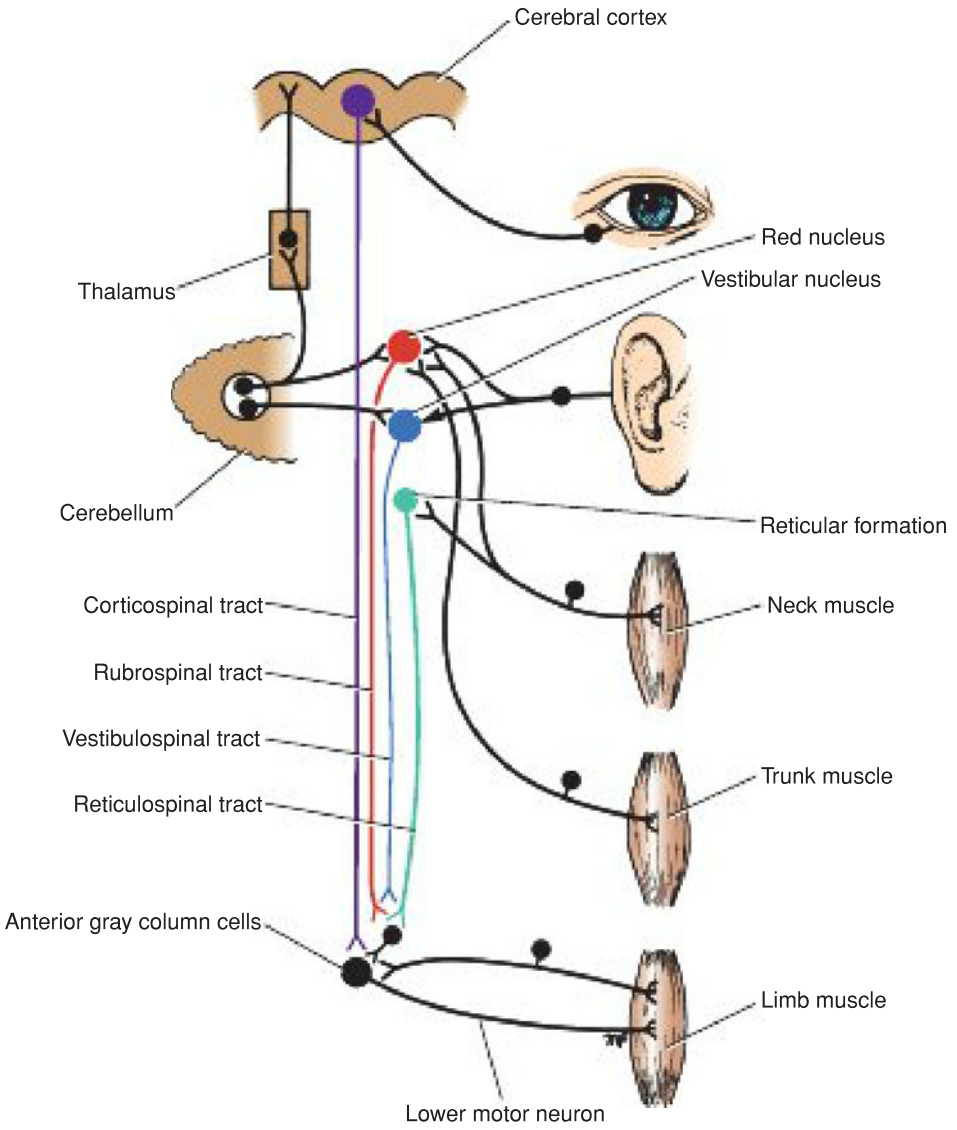

Figure 3-42 Nervous input from higher levels of the central nervous system, which can influence the activity of the anterior gray column (horn) cells of the spinal cord.

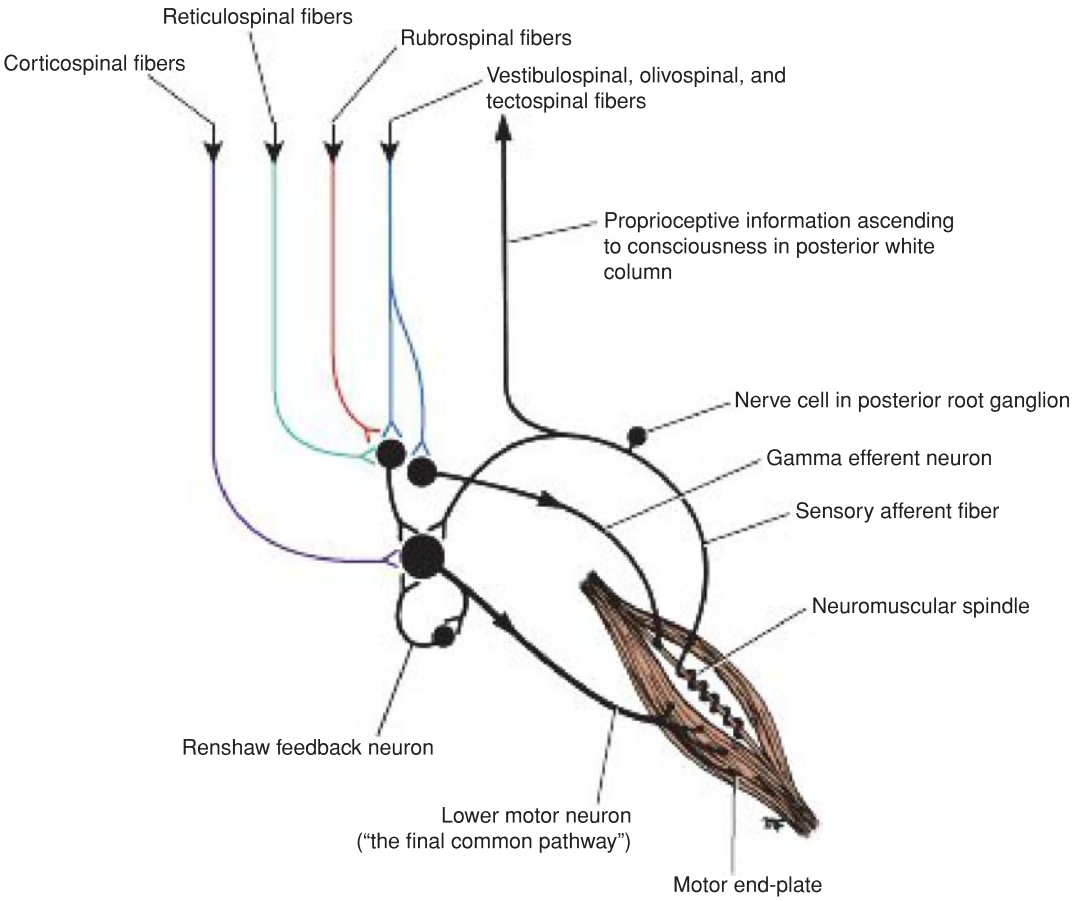

Figure 3-43 Normal postural tone of skeletal muscle is dependent not only on the integrity of the reflex arc but also on the summation of the nervous impulses received by the motor anterior gray column (horn) cells from other neurons of the nervous system.

Clinical Notes

Neuronal Response to Injury

The survival of a neuron's cytoplasm depends on its being connected, however indirectly, with the nucleus. The nucleus plays a key role in the synthesis of proteins, which pass into the cell processes and replace proteins that have been metabolized by cell activity. Thus, the cytoplasm of axons and dendrites will undergo degeneration quickly if these processes are separated from the nerve cell body.

Nerve Cell Body Injury

Severe damage of the nerve cell body due to trauma, interference with the blood supply, or disease may result in degeneration of the entire neuron, including its dendrites and synaptic endings. In the brain and spinal cord, the neuronal debris and the fragments of myelin (if the processes are myelinated) are engulfed and phagocytosed by the microglial cells. Later, the neighboring astrocytes proliferate and replace the neuron with scar tissue.

In the peripheral nervous system (PNS), the tissue macrophages remove the debris, and the local fibroblasts replace the neuron with scar tissue.

Nerve Cell Process Injury

If the axon of the nerve cell is divided, degenerative changes will take place in (1) the distal segment that is separated from the cell body, (2) a portion of the axon proximal to the injury, and (3) possibly the cell body from which the axon arises.

CHANGES IN THE DISTAL SEGMENT OF THE AXON

The changes spread distally from the site of the lesion (Fig. 3-44) and include its terminations; the process is referred to as **wallerian degeneration**. In the PNS, on the first

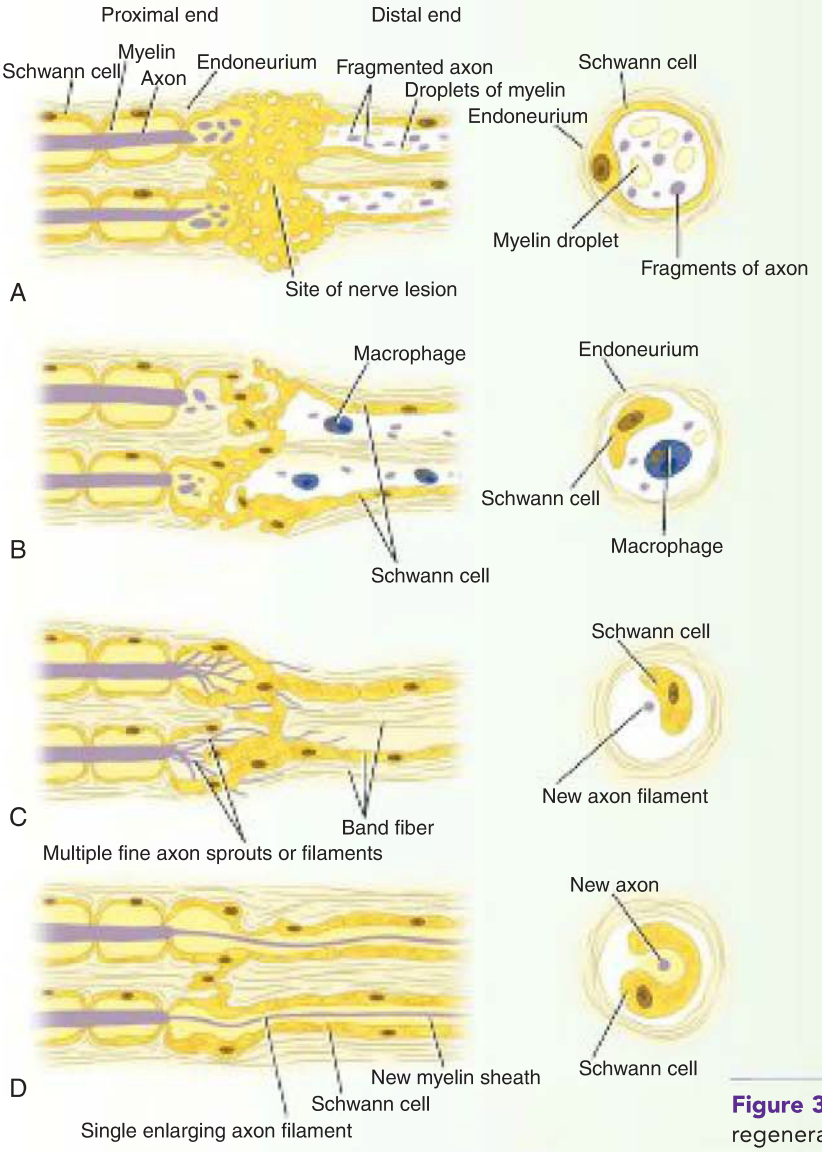

Figure 3-44 **A–D:** Degeneration and regeneration in a divided nerve.

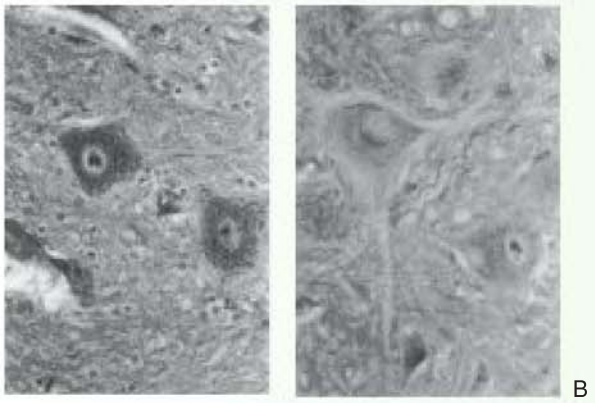

Figure 3-45 Photomicrographs of motor neurons of the anterior gray column of the spinal cord. **A:** Nissl substance in normal neurons. **B:** Following section of anterior roots of spinal nerve, showing chromatolysis.

day, the axon becomes swollen and irregular; by the third or fourth day, the axon is broken into fragments, and the debris is digested by the surrounding Schwann cells and tissue macrophages. The entire axon is destroyed within a week.

Meanwhile, the myelin sheath slowly breaks down, and lipid droplets appear within the Schwann cell cytoplasm. Later, the droplets are extruded from the Schwann cell and subsequently phagocytosed by tissue macrophages. The Schwann cells now begin to proliferate rapidly and become arranged in parallel cords within the persistent basement membrane. The endoneurial sheath and the contained cords of Schwann cells are referred to as a **band fiber**. If regeneration does not occur, the axon and the Schwann cells are replaced by fibrous tissue produced by local fibroblasts.

In the central nervous system (CNS), degeneration of the axons and the myelin sheaths follows a similar course, and the debris is removed by the phagocytic activity of the microglial cells. Little is known about the role of oligodendrocytes in this process. The astrocytes now proliferate and replace the axons.

CHANGES IN THE PROXIMAL SEGMENT OF THE AXON

The changes in the proximal segment of the axon are similar to those that take place in the distal segment (see Fig. 3-44) but extend only proximally above the lesion as far as the first node of Ranvier. The proliferating cords of Schwann cells in the peripheral nerves bulge from the cut surfaces of the endoneurial tubes.

CHANGES IN THE NERVE CELL BODY

The changes that occur in the cell body following injury to its axon are referred to as **retrograde degeneration**; the changes that take place in the proximal segment of the axon commonly are included under this heading. The possible reason for these changes is that section of the axon cuts off the cell body from its supply of trophic factors derived from the target organs at the distal end of the axon.

The most characteristic change occurs in the cell body within the first 2 days following injury and reaches its maximum within 2 weeks. The Nissl material becomes fine, granular (Figs. 3-45 and 3-46), and dispersed throughout the cytoplasm, a process known as **chromatolysis**. Chromatolysis begins near the axon hillock and spreads to all

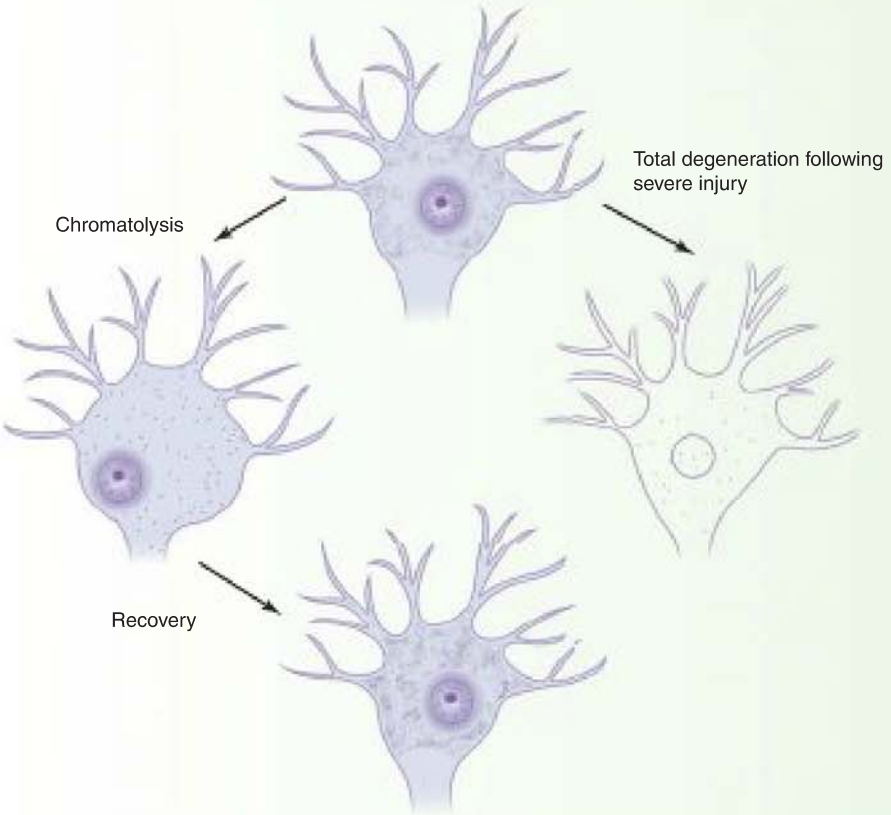

Figure 3-46 The changes that may take place in a nerve cell body following division of one of its processes.

parts of the cell body. In addition, the nucleus moves from its central location toward the periphery of the cell, and the cell body swells and becomes rounded. The degree of chromatolysis and the degree of swelling of the cell are greatest when the injury to the axon is close to the cell body. In some neurons, very severe damage to the axon close to the cell body may lead to death of the neuron. On the other hand, damage to the most distal process may lead to little or no detectable change in the cell body. The dispersal of the Nissl material—that is, the cytoplasmic RNA—and the swelling of the cell are caused by cellular edema. The apparent loss of staining affinity of the Nissl material is due to the wide dispersal of the cytoplasmic RNA. The movement of the nucleus away from the center of the cell may be due to the cellular edema.

Synaptic terminals are seen to withdraw from the surface of the injured nerve cell body and its dendrites and are replaced by Schwann cells in the PNS and microglial cells or astrocytes in the CNS, a process called **synaptic stripping**. Its possible causes are (1) loss of plasma membrane adhesiveness following injury and (2) stimulation of the supporting cells by chemicals released from the injured neuron. If the injury is sufficiently great, the cells of the immune system—namely, monocytes and macrophages—may migrate into the area.

Neuronal Recovery

In contrast to the rapid onset of retrograde degeneration, the recovery of the nerve cell body and regeneration of its processes may take several months.

Nerve Cell Body Recovery

The nucleolus moves to the periphery of the nucleus, and polysome clusters reappear in the cytoplasm. This indicates that RNA and protein synthesis is being accelerated in preparation for the reformation of the axon. Thus, the original Nissl structure reconstitutes, cell body swelling decreases, and the nucleus returns to its characteristic central position (Fig. 3-46).

Regeneration of Peripheral Nerve Axons

Regrowth of the axons (motor, sensory, and autonomic) is possible in peripheral nerves and appears to depend on the presence of endoneurial tubes and the special qualities possessed by Schwann cells. Sprouts from the axons grow from the proximal stump and into the distal stump toward the nerve's end organs. The following mechanisms are thought to be involved: (1) the axons are attracted by chemotropic factors secreted by the Schwann cells in the distal stump, (2) growth-stimulating factors exist within the distal stump, and (3) inhibitory factors are present in the perineurium to inhibit the axons from leaving the nerve.

The satisfactory regeneration of axons and the return of normal function depend on the following factors:

1. In crush nerve injuries, in which the axon is divided or its blood supply has been interfered with but the endoneurial sheaths remain intact, regeneration is likely.
2. In nerves that have been completely severed, the chance of recovery is much less because the regenerating fibers from the proximal stump may be directed to an incorrect destination in the distal stump—that is, cutaneous fibers entering incorrect nerve endings or motor nerves supplying incorrect muscles.
3. If the distance between the proximal and distal stumps of the completely severed nerve is greater than a few millimeters or the gap becomes filled with proliferating fibrous tissue or is simply filled by adjacent muscles that bulge into the gap, then the chances of recovery are very poor. The outgrowing axonal sprouts escape into the surrounding connective tissue and form a tangled mass or **neuroma**. In these cases, early close surgical approximation of the severed ends, if possible, greatly facilitates the chances of recovery.
4. When mixed nerves (those containing sensory, motor, and autonomic fibers) are completely severed, the chances of a good recovery are very much less than when the nerve is purely sensory or purely motor. The reason for this is that the regenerating fibers from the proximal stump may be guided to an incorrect destination in the distal stump; for example, cutaneous fibers may enter motor endoneurial tubes and vice versa.
5. Inadequate physiotherapy to the paralyzed muscles will result in their degeneration before the regenerating motor axons have reached them.
6. The presence of infection at the site of the wound will seriously interfere with the process of regeneration.

If the proximal and distal stumps of the severed nerve are in close apposition, the following regenerative processes take place (see Fig. 3-44). The Schwann cells, having undergone mitotic division, now fill the space within the basal lamina of the endoneurial tubes of the proximal stump as far proximally as the next node of Ranvier and in the distal stump as far distally as the end organs. Where a small gap exists between the proximal and distal stumps, the multiplying Schwann cells form a number of cords to bridge the gap.

Each proximal axon end now gives rise to multiple fine sprouts or filaments with bulbous tips. These filaments, as they grow, advance along the clefts between the Schwann cells and thus cross the interval between the proximal and distal nerve stumps. Many such filaments now enter the proximal end of each endoneurial tube and grow distally in contact with the Schwann cells (Fig. 3-47). Although the filaments from many different axons may enter a single endoneurial tube, only one filament persists, the remainder degenerate, and that one filament grows distally to reinnervate a motor or sensory end organ. While crossing the gap between the severed nerve ends, many filaments fail to enter an endoneurial tube and grow out into the surrounding connective tissue. Note that the formation of multiple sprouts or filaments from a single proximal axon greatly increases the chances that a neuron will become connected to a sensory or motor ending. Why one filament within a single endoneurial tube should be selected to persist while the remainder degenerate remains unknown.

Once the axon has reached the end organ, the adjacent Schwann cells start to lay down a myelin sheath. This process begins at the site of the original lesion and extends in a distal direction. By this means, the nodes of Ranvier and the Schmidt–Lanterman incisures are formed.

Many months may elapse before the axon reaches its appropriate end organ, depending on the site of the nerve injury. The rate of growth has been estimated to be approximately 2 to 4 mm per day. However, in light of the almost certain delay incurred by the axons as they cross the site of the injury, an overall regeneration rate of 1.5 mm per

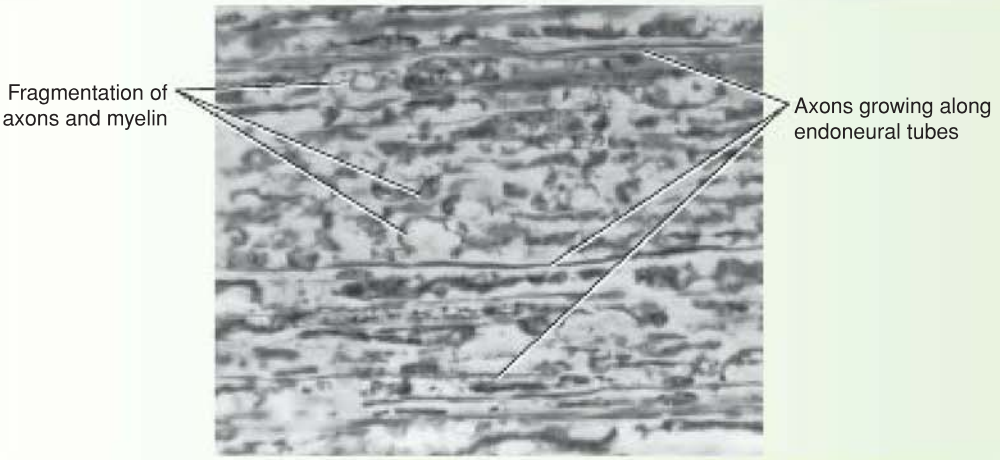

Figure 3-47 Photomicrograph of a longitudinal section of the distal stump of the sciatic nerve showing evidence of degeneration and axon regeneration following injury. (Courtesy Dr. M. J. T. Fitzgerald.)

day is a useful figure to remember clinically. Even if all the difficulties outlined above are overcome and a given neuron reaches the original end organ, the enlarging axonal filament within the endoneurial tube reaches only about 80% of its original diameter. For this reason, the conduction velocity will not be as great as that of the original axon. Moreover, a given motor axon tends to innervate more muscle fibers than formerly; thus, the control of muscle is less precise.

Regeneration of Central Nervous System Axons

In the CNS, axons attempt to regenerate, as evidenced by sprouting of the axons, but the process ceases after about 2 weeks. Long-distance regeneration is rare, and the injured axons make few new synapses. Evidence that restoration of function takes place does not exist. The regeneration process is aborted by the absence of endoneurial tubes (which are necessary to guide the regenerating axons), the failure of oligodendrocytes to serve in the same manner as Schwann cells, and the laying down of scar tissue by the active astrocytes. Absence of nerve growth factors in the CNS or that the neuroglial cells may produce nerve growth-inhibiting factors is also possible.

Research has shown that the Schwann cell basal laminae contain laminin and cell-adhesion molecules of the immunoglobulin family, both of which stimulate axon growth. The CNS contains only low concentrations of these molecules. In the embryo, when axon growth actively takes place in both the CNS and PNS, growth-promoting factors are present in both systems. Later in development, these factors disappear in the CNS. Myelin in the CNS inhibits axonal growth, and myelination in the CNS occurs late in the development process when growth of the main nervous pathways is complete.

Central axons may not be as good at regeneration as peripheral axons. In tissue culture, peripheral axons are more successful at growth than central axons. Moreover, the ability of central axons to grow decreases with age.

NEUROBIOLOGIC RESEARCH INTO CENTRAL NERVOUS SYSTEM REGENERATION

Because traumatic injury to the CNS produces such devastating disabilities that are largely irreversible, neurobiologists are now enthusiastically pressing forward with research in this area. Differences are known to exist between the environment in the CNS and PNS. Moreover, the ability of central axons in lower vertebrates, such as frogs, to regenerate provides an enormous stimulus for future work.

Research has taken the following directions:

1. Molecules present in the PNS, such as laminins and neurotrophins, have been introduced into the CNS at the site of injury to promote axon growth.
2. Schwann cells have been grafted into the CNS, and central axons will grow into the graft.
3. Attempts have been made to reduce the inhibitory factors present in the CNS. Infusion of antibodies at the site of injury has been carried out with some success.
4. The introduction of anti-inflammatory agents to suppress the neuroglial and monocyte response has been used with success. **Methylprednisolone** is now commonly used as soon as possible after the incident in all patients with spinal cord injuries.

Although a vast amount of research still needs to be done, a combination of treatments may provide the return of some function to these patients with CNS injuries.

Transneuronal Degeneration

The responses of a single neuron to injury were considered in the previous section. In the CNS, if one group of neurons is injured, then a second group farther along the pathway, serving the same function, may also show degenerative changes. This phenomenon is referred to as **anterograde transneuronal degeneration**. For example, if the axons of the ganglion cells of the retina are severed, not only do the distal ends of the axons that go to the lateral geniculate bodies undergo degeneration but also the neurons in the lateral geniculate bodies with which these axons form synapses undergo degeneration. In fact, a further set of neurons may be involved in the degenerative process in the visual cortex.

In situations in the CNS in which multiple neurons synapse with a single distal neuron, injury to one of the proximal neurons is not followed by degeneration of the distal neuron.

Experimentation on animals with artificial lesions of the CNS has shown that **retrograde transneuronal degeneration** may occur in certain situations.

Neuronal Degeneration Associated with Senescence

Many neurons degenerate and disappear during fetal development. This process is believed to be due to their failure to establish adequate functional connections. During postnatal life, further gradual neuronal degeneration continues to occur. In old age, an individual may have lost up to 20% of the original number of neurons. This may account to some extent for the loss of efficiency of the nervous system that is associated with senescence.

Atrophy of Voluntary Muscle and Other End Organs Following Peripheral Nerve Degeneration

Voluntary muscle undergoes degenerative changes following motor nerve section. First, the response to acetylcholine (ACh) is altered, followed by gradual wasting of the sarcoplasm, and finally loss of the fibrils and striations. Eventually, the muscle completely atrophies and is replaced by fibrous tissue. Reinnervation of the muscle halts its degeneration, and, if the muscle atrophy is not too advanced, normal structure and function return.

Furthermore, if the motor nerve that supplies fast white voluntary muscle fibers is exchanged for a motor nerve that supplies slow red voluntary muscle fibers, the muscle fibers change their structural and functional properties to comply with the new type of innervation. This experimental result strongly suggests not only that voluntary muscle cells are dependent on the presence of intact motor nerves but also that the nerve has some trophic influence on the muscle and even determines the type of muscle that it innervates.

Another end organ, the taste bud, also depends on the integrity of the sensory nerve. If the nerve is sectioned, the taste bud quickly atrophies. Once the sensory nerve regenerates into the mucous membrane, new taste buds develop.

Traumatic Lesions of Peripheral Nerves

Seddon (1944) described three clinical types of nerve injury:

- **Neuropraxia** is a transient block. The paralysis is incomplete, recovery is rapid and complete, and microscopic evidence of nerve degeneration does not exist. Pressure is the most common cause. It is essentially a temporary interference in function.
- **Axonotmesis** is a nerve lesion in which the axons are damaged but the surrounding connective tissue sheaths remain more or less intact. Wallerian degeneration occurs peripherally. Functional recovery is more rapid and more complete than after complete section of the nerve trunk because the nerve fibers, although severely damaged, for the most part retain their normal anatomical relationships to one another, owing to the preservation of the connective tissue sheaths. Crush injuries, traction, and compression are the most common causes.
- **Neurotmesis** is complete section of the nerve trunk.

Symptoms and Signs of Neurotmesis

Completely dividing a peripheral nerve can be seen in the clinic as paralysis or anesthesia, or both. The magnitude of injury is assessed by reflexive response, muscle strength, and distribution of cutaneous sensation loss.

MOTOR CHANGES

The muscles that are innervated show flaccid paralysis and rapidly waste. The reflexes in which the muscles participate are lost. The paralyzed muscle ceases to respond to faradic stimulation after 4 to 7 days. After 10 days, the muscle responds only sluggishly to galvanic stimulation, and the strength of the current must be greater than that required for a normal innervated muscle. This altered response of muscle to electrical stimulation is known as the **reaction of degeneration**.

SENSORY CHANGES

Cutaneous sensibility is completely lost over the area exclusively supplied by the nerve. This area is surrounded by a zone of partial sensory loss where adjacent sensory nerves overlap. The skin area in which the sensation of light touch is lost is much greater than the area lost to pinprick.

VASOMOTOR, SUDOMOTOR, AND TROPHIC CHANGES

Section of a peripheral nerve results in the interruption of postganglionic sympathetic fibers traveling in the nerve. As a result of the loss of vascular control, the skin area at first becomes red and hot. Later, the affected area becomes blue and colder than normal, especially in cold weather. Because of the loss of sudomotor control, the sweat glands cease to produce sweat, and the skin becomes dry and scaly. Nail growth becomes retarded as the direct result of poor peripheral circulation. If a large area of the body is denervated, as in cases in which the sciatic nerve is sectioned, the bones undergo decalcification as a result of disuse and loss of circulatory control.

RECOVERY FROM NEUROTMESIS

Assuming that the divided peripheral nerve has been carefully sutured together, a clinician must be aware of the symptoms and signs of recovery and their sequence.

MOTOR RECOVERY

Regenerating motor axons grow at an average rate of about 1.5 mm per day. The proximal muscles will recover first, and the distal muscles will recover later. The muscles may respond to faradic stimulation before voluntary control returns.

SENSORY RECOVERY

Sensory recovery occurs before voluntary movement returns. The part of the nerve distal to the section becomes very sensitive to mechanical stimulation once the regenerating sensory axons have entered the distal segment. Simple tapping of the distal nerve trunk gives rise to a tingling sensation in the area of cutaneous distribution of the nerve. This sign is referred to as the **Tinel sign**. Recovery of deep cutaneous sensibility—that is, pain caused by deep pressure—is the first sign of recovery. This is followed by the return of poorly localized, superficial cutaneous pain. Vasomotor control also returns at about this time. Later, the sensations of heat and cold are recovered. Light touch and tactile discrimination are the last sensations to return; these sensations return many months later and are often incomplete.

Specific Spinal Nerve Injuries

Table 3-3 summarizes the important features found in cervical and lumbosacral root syndromes (a detailed description of the neurologic deficits following the many spinal nerve injuries seen in clinical practice is beyond the scope of this book). Tables that summarize the branches of the brachial

Table 3-3 Important Features Found in Cervical and Lumbosacral Root Syndromes

Root Injury	Dermatome Pain	Muscles Supplied	Movement Weakness	Reflex Involved
C5	Lateral side of upper part of arm	Deltoid and biceps brachii	Shoulder abduction, elbow flexion	Biceps
C6	Lateral side of forearm	Extensor carpi radialis longus and brevis	Wrist extensors	Brachioradialis
C7	Middle finger	Triceps and flexor carpi radialis	Extension of elbow and flexion of wrist	Triceps
C8	Medial side of forearm	Flexor digitorum superficialis and profundus	Finger flexion	None
L1	Groin	Iliopsoas	Hip flexion	Cremaster
L2	Anterior part of thigh	Iliopsoas, sartorius, hip adductors	Hip flexion, hip adduction	Cremaster
L3	Medial side of knee	Iliopsoas, sartorius, quadriceps, hip adductors	Hip flexion, knee extension, hip adduction	Patellar
L4	Medial side of calf	Tibialis anterior, quadriceps	Foot inversion, knee extension	Patellar
L5	Lateral side of lower leg and dorsum of foot	Extensor hallucis longus, extensor digitorum longus	Toe extension, ankle dorsiflexion	None
S1	Lateral edge of foot	Gastrocnemius, soleus	Ankle plantar flexion	Ankle jerk
S2	Posterior part of thigh	Flexor digitorum longus, flexor hallucis longus	Ankle plantar flexion, toe flexion	None

(Table 3-4) and lumbar and sacral (Table 3-5) plexuses and their distribution are also included. These tables can assist the reader in determining the specific nerve lesion associated with a particular motor or sensory deficit in the upper or lower limbs.

Cranial nerve injuries are considered in Chapter 11.

Basic Clinical Principles Underlying Peripheral Nerve Injuries

- In open, dirty wounds, which carry a high risk of infection, the sectioned nerve should be ignored, and the wound infection should be treated. Later, when the wound has healed satisfactorily, the nerve should be explored, and the cut ends of the nerve should be sutured together.
- For a patient with a healed wound and no evidence of nerve recovery, the treatment should be conservative. Sufficient time should be allowed to elapse to enable the regenerating nerve fibers to reach the proximal muscles. If recovery fails to occur, the nerve should be explored surgically.
- In cases in which connective tissue, bone fragments, or muscles come to lie between the cut ends of a severed nerve, the nerve should be explored; if possible, the cut ends of the nerve should be brought together and sutured.
- The nutrition of the paralyzed muscles must be maintained with adequate physiotherapy. Warm baths, massage, and warm clothing help to maintain adequate circulation.
- The paralyzed muscles must not be allowed to be stretched by antagonist muscles or by gravity. Moreover, excessive shortening of the paralyzed muscles leads to contracture of these muscles.
- Mobility must be preserved by daily passive movements of all joints in the affected area. Failure to do this results in the formation of adhesions and consequent limitation of movement.

Once voluntary movement returns in the most proximal muscles, the physiotherapist can assist the patient in performing active exercises. This not only aids in the return of a normal circulation to the affected part but also helps the patient to learn once again the complicated muscular performance of skilled movements.

Nerve Transplantation

Nerve grafts have been used with some success to restore muscle tone in facial nerve palsy. In mixed nerve injuries, nerve grafts have succeeded only in restoring some sensory function and slight muscle activity. The presence of two suture lines and the increased possibility of mixing the nerve fibers is probably the reason for the lack of success with nerve grafts. In most nerve injuries, even when the gap between the proximal and distal ends is as great as 10 cm, mobilizing the nerve or altering its position in relation to joints so that the proximal and distal ends may be brought together without undue tension is usually possible; the ends are then sutured together.

Peripheral Nerve Tumors

A peripheral nerve consists essentially of nerve fibers (axons), each of which is associated with Schwann cells; the fibers are either myelinated or nonmyelinated. The nerve

Table 3-4 Branches of the Brachial Plexus and Their Distribution

Branches	Distribution
Roots	
Dorsal scapular nerve (C5)	Rhomboid minor, rhomboid major, levator scapulae muscles
Long thoracic nerve (C5–C7)	Serratus anterior muscle
Upper Trunk	
Suprascapular nerve (C5–C6)	Supraspinatus and infraspinatus muscles
Nerve to subclavius (C5–C6)	Subclavius
Lateral Cord	
Lateral pectoral nerve (C5–C7)	Pectoralis major muscle
Musculocutaneous nerve (C5–C7)	Coracobrachialis, biceps brachii, brachialis muscles; supplies skin along lateral border of forearm when it becomes the lateral cutaneous nerve of forearm
Lateral root of median nerve (C5–C7)	See medial root of median nerve
Posterior Cord	
Upper subscapular nerve (C5–C6)	Subscapularis muscle
Thoracodorsal nerve (C6–C8)	Latissimus dorsi muscle
Lower subscapular nerve (C5–C6)	Subscapularis and teres major muscles
Axillary nerve (C5–C6)	Deltoid and teres minor muscles; upper lateral cutaneous nerve of arm supplies skin over lower half of deltoid muscle
Radial nerve (C5–C8, T1)	Triceps, anconeus, part of brachialis, brachioradialis, extensor carpi radialis longus; via deep radial nerve branch supplies extensor muscles of forearm: supinator, extensor carpi radialis brevis, extensor carpi ulnaris, extensor digitorum, extensor digiti minimi, extensor indicis, abductor pollicis longus, extensor pollicis longus, extensor pollicis brevis; skin, lower lateral cutaneous nerve of arm, posterior cutaneous nerve of arm, and posterior cutaneous nerve of forearm; skin on lateral side of dorsum of hand and dorsal surface of lateral 3½ fingers; articular branches to elbow, wrist, and hand
Medial Cord	
Medial pectoral nerve (C8, T1)	Pectoralis major and minor muscles
Medial cutaneous nerve of arm joined by intercostal brachial nerve from second intercostal nerve (C8, T1–T2)	Skin of medial side of arm
Medial cutaneous nerve of forearm (C8, T1)	Skin of medial side of forearm
Ulnar nerve (C8, T1)	Flexor carpi ulnaris and medial half of flexor digitorum profundus, flexor digiti minimi, opponens digiti minimi, abductor digiti minimi, adductor pollicis, third and fourth lumbricals, interossei, palmaris brevis, skin of medial half of dorsum of hand and palm, skin of palmar and dorsal surfaces of medial 1½ fingers
Medial root of median nerve (with lateral root) forms median nerve (C5–C8, T1)	Pronator teres, flexor carpi radialis, palmaris longus, flexor digitorum superficialis, abductor pollicis brevis, flexor pollicis brevis, opponens pollicis, first two lumbricals (by way of anterior interosseous branch), flexor pollicis longus, flexor digitorum profundus (lateral half), pronator quadratus, palmar cutaneous branch to lateral half of palm and digital branches to palmar surface of lateral 3½ fingers; articular branches to elbow, wrist, and carpal joints

Table 3-5 Branches of the Lumbar and Sacral Plexuses and Their Distribution

Branches	Distribution
Femoral nerve (L2–L4)	Iliacus, pectineus, sartorius, quadriceps femoris muscles; skin, medial cutaneous and intermediate cutaneous nerves of thigh, saphenous nerve to medial side of leg, medial side of foot as far as ball of big toe; articular branches to hip and knee joints
Obturator nerve (L2–L4)	Pectineus, adductor longus, adductor brevis, adductor magnus (adductor portion), gracilis muscles; skin, medial side of thigh; articular branches to hip and knee joints
Sciatic nerve (L4–L5, S1–S3)	
Common peroneal nerve	Biceps femoris muscle (short head); skin, lateral cutaneous nerve of calf, sural communicating branch to lateral side of leg, lateral side of foot, and little toe
Superficial peroneal nerve	Peroneus longus and brevis muscles; skin, lower leg, and dorsum of foot
Deep peroneal nerve	Tibialis anterior, extensor hallucis longus, extensor digitorum longus, peroneus tertius, extensor digitorum brevis muscles; skin, cleft between the first and second toes; articular branches to tibiofibular, ankle, and foot joints
Tibial nerve	Semitendinosus, biceps femoris (long head), semimembranosus, adductor magnus (hamstring part), gastrocnemius, soleus, plantaris, popliteus, tibialis posterior, flexor digitorum longus, flexor hallucis longus muscles; skin, medial side of ankle; articular branches to hip, knee, and ankle joints
Medial plantar nerve	Abductor hallucis, flexor digitorum brevis, flexor hallucis brevis, first lumbrical muscles; skin, medial side of sole of foot; articular branches to foot joints
Lateral plantar nerve	Flexor accessorius, abductor digiti minimi, flexor digiti minimi brevis, second, third, and fourth lumbricals, adductor hallucis, all interossei muscles; skin of lateral side of sole of foot

fibers are arranged in parallel bundles and are surrounded by connective tissue sheaths.

A **benign fibroma** or a **malignant sarcoma** may arise in the connective tissue of the nerve and does not differ from similar tumors elsewhere. **Neurilemmomas** are believed to arise from Schwann cells. They arise from any nerve trunk, cranial or spinal, and in any part of its course. Primary tumors of the axons are very rare.

Blood Vessels, Lymphatics, and Endoneurial Spaces within Peripheral Nerves

Peripheral nerves receive branches from arteries in the regions they pass through. The anastomotic network that exists within a nerve is considerable, and local ischemia does not occur if a single artery is obstructed.

A plexus of lymph vessels lies within the epineurial connective tissues, and this drains to regional lymph nodes.

As demonstrated by the results of experiments in which dyes have been injected into peripheral nerves, spaces exist between individual nerve fibers. These endoneurial spaces evidently provide a potential route for the ascent of **tetanus toxin** to the spinal cord.

Local Anesthetic Action on Nerve Conduction

Local anesthetics are drugs that block nerve conduction when applied locally to a nerve fiber in suitable concentrations. Their site of action is the axolemma (plasma membrane), and they interfere with the transient increase in permeability of the axolemma to Na^+, K^+, and other ions. The sensitivity of nerve fibers to local anesthetics is related to the size of the nerve fibers (see Table 2-3). Small nerve fibers are more susceptible than large fibers; small fibers are also slower to recover.

Cocaine has been used clinically to block nerve conduction. Unfortunately, it is a strong stimulant of the cerebral cortex and readily causes addiction. **Procaine** is a synthetic compound that is widely used as a local anesthetic agent.

Apparent Recovery of Central Nervous System Function

Axon regeneration in the brain and spinal cord is minimal following a lesion, yet considerable functional recovery often occurs. Several explanations exist, and more than one mechanism may be involved.

1. Nerve fiber function may be impaired from compression by edema fluid. Once the edema subsides, a substantial recovery may take place.
2. The damaged nerve fiber proximal to the lesion may form new synapses with neighboring normal neurons.
3. Following a lesion to branches of a nerve, all the neurotransmitters may pass down the remaining branches, producing a greater effect.
4. Following a lesion of an afferent neuron, an increased number of receptor sites may develop on a postsynaptic membrane. This may result in the second neuron responding to neurotransmitter substances from neighboring neurons.
5. Nonfunctioning neurons may take over the function of damaged neurons.
6. The damaged nerve fiber proximal to the lesion may form new synapses with neighboring normal neurons.

7. The normal neighboring nerve fibers may give off branches distal to the lesion, which then follow the pathway previously occupied by the damaged fibers.
8. If a particular function, such as the contraction of voluntary muscle, is served by two neural pathways in the CNS and one pathway is damaged, the remaining undamaged pathway may take over the entire function. Thus, conceivably, if the corticospinal tract is injured, the corticoreticulospinal tract may take over the major role of controlling the muscle movement.
9. With intensive physiotherapy, patients may be trained to use other muscles to compensate for the loss of paralyzed muscles.

Herpes Zoster

Herpes zoster, or shingles, is a relatively common condition caused by the reactivation of the latent varicella zoster virus in a patient who has previously had chickenpox. The infection is found in the first sensory neuron in a cranial or spinal nerve. The lesion is seen as an inflammation and degeneration of the sensory neuron with the formation of vesicles with inflammation of the skin. The first symptom is pain in the distribution of the sensory neuron, followed in a few days by a skin eruption. The condition occurs most frequently in patients over age 50 years.

Polyneuropathy

Polyneuropathy is an impairment of function of many peripheral nerves simultaneously. The many causes include infection (endotoxin of diphtheria, Guillain–Barré syndrome [see Clinical Example at beginning of chapter]), metabolic disorders (vitamins B_1 and B_{12} deficiency, poisoning by heavy metals, drugs), and endocrine disorders (diabetes). Axon degeneration and/or segmental demyelination may take place, and the neuron cell body may be involved. In mild cases, the condition is reversible, but in severe cases, it may be permanent. Both sensory and motor symptoms and signs may be evident.

Receptors

Sensory endings are found throughout the body in both somatic and visceral areas. Their wide distribution is fortunate, because they enable us to react to changes in the external and internal environment.

To make a diagnosis or study the effect of treatment on a disease process, a clinician relies almost entirely on the patient's ability to describe changes in subjective sensations or to respond to specific stimuli during a physical examination. Such descriptions, such as "knifelike pain," "dull and aching pain," "colicky pain," "pins and needles," and "cannot feel anything" are very familiar to the practicing clinician. Each main type of sensation that can be experienced, such as pain, temperature, and touch and pressure, is called a **modality** of sensation. The type of modality felt by a patient from a particular part of the body is determined by the specific area of the CNS to which the afferent nerve fiber passes. However, remembering that axons carrying specific modalities are associated with one or more anatomically distinct receptors is clinically useful (Table 3-6).

Table 3-6 Receptors and Associated Functions

Receptor	Associated Function
Free nerve endings	Pain, touch, pressure, tickle sensations, possibly cold and heat
Merkel discs	Touch and pressure
Hair follicle receptor	Touch
Meissner corpuscles	Touch (two-point tactile discrimination)
Pacinian corpuscles	Pressure and vibration
Ruffini corpuscles	Stretch
Neuromuscular spindles	Elongation of muscle (stretch)
Neurotendinous spindles	Tension

Sensory Receptors and Age

With life expectancy increasing, many patients now reach the age when sensory receptor degeneration can cause disequilibrium. This critical age varies in different individuals, but once it starts, the sensory systems progressively deteriorate, involving not only visual and auditory systems but also proprioception and the ability to integrate the afferent information entering the CNS.

Sensory Modality Examination

An accurate physical examination may enable the neurologist to make a precise diagnosis. He or she may be able to determine whether a particular sensation can or cannot be appreciated or whether it is less than normal. The clinician will be able to determine the precise area over the surface of the body where impairment of sensation is found. The following sensations are usually tested:

1. **Light touch.** This is tested by gently touching the skin with a wisp of cotton; the patient has the eyes closed and responds "yes" whenever the stimulus is felt. Recognize that different areas of the skin normally exhibit different thresholds for touch. The back and buttocks are less sensitive than the face or fingertips. On hairy surfaces, the slightest movement of a hair usually can be felt.
2. **Localization of touch.** After detecting the light touch with the eyes closed, the patient is asked to place a finger on the exact site touched. Failure to accomplish this may be due to damage to the cerebral cortex.
3. **Two-point tactile discrimination.** Two blunt points are applied to the skin surface while the patient's eyes are closed. Gradually, the points are brought closer together until the patient is unable to distinguish two definite points. A normal person is able to distinguish two separate points on the tip of the index finger when they are separated by a distance greater than about 3 mm. On the back, however, they have to be separated by as much as 3 to 4 cm.
4. **Pain.** The skin may be touched with the sharp end of a pin. First, the pain threshold is established and then the areas of diminished or lost pain sensation are mapped out. Apply the stimulus in an irregular manner, first using the sharp end of the pin and then the dull head, with the patient responding "sharp" or "dull." Certain diseases, such as tabes dorsalis or polyneuropathy

(polyneuritis), may produce a delay of up to 3 seconds before the patient recognizes the sharp pain.

5. **Pressure pain.** This poorly localized pain is perceived by deep pressure on a muscle or by squeezing a tendon.
6. **Temperature testing.** Test tubes filled with hot or cold water may be used. When the test tubes are applied to the skin, the patient responds with either "warm" or "cold." First, the temperature threshold is established and then the areas of diminished or lost temperature sensation are mapped out.
7. **Vibration.** When the handle of a vibrating tuning fork is applied to the skin over bone (e.g., the medial malleolus of the tibia or the olecranon process of the ulna), a tingling sensation is felt. This is due to the stimulation of superficial and deep pressure receptors. The patient is asked to respond when the first vibration is felt as well as when the vibration can no longer be detected. The perception of vibration in the legs is usually diminished after age 60 years.
8. **Appreciation of form (stereognosis).** With the patient's eyes closed, the examiner places common objects, such as coins or keys, in the patient's hands. The patient normally should be able to identify objects by moving them around in the hand and feeling them with the fingers.
9. **Passive movements of joints.** This test may be carried out on the fingers or toes. With the patient completely relaxed and in the supine position with eyes closed, the digit is flexed or extended irregularly. After each movement, the patient is asked, "Is the digit 'up' or 'down'?" A normal individual not only can determine that passive movement is taking place but also is aware of the direction of the movement.
10. **Postural sensibility.** This is the ability to describe the position of a limb when it is placed in that position while the patient's eyes are closed. Another way to perform the test is to ask the patient, with eyes closed, to place the limb on the opposite side in the same position as the other limb. The application and interpretation of the results of these tests will be understood more fully when the afferent or sensory pathways have been discussed (see Chapter 4).

Phantom Limb

Wherever a particular sensory pathway is stimulated along its course from the receptor to the sensory cortex of the brain, the sensation experienced by the individual is referred to the site of the receptor. For example, if the pain fibers from the receptors in the little finger are stimulated in the ulnar nerve at the elbow, the individual will experience pain in the little finger and not at the elbow.

Following the amputation of a limb, the patient may experience severe pain in the absent limb due to pressure on the nerve fibers at the end of the stump. This phenomenon is referred to clinically as **phantom limb**.

Action of Drugs and Other Agents on Skeletal Neuromuscular Junctions

Table 3-7 gives some examples of drugs and diseases affecting the motor endplates in skeletal muscle.

Neuromuscular Blocking Agents

***d*-Tubocurarine** produces flaccid paralysis of skeletal muscle, first affecting the extrinsic muscles of the eyes and then those of the face, the extremities, and finally the diaphragm.

Table 3-7 Drugs and Diseases Affecting the Motor Endplates in Skeletal Muscle

Drug or Disease	Increasing ACh Release	Decreasing ACh Release	Acting on ACh Receptors		AChE Inhibition
			Depolarizing Blockade	ACh Receptor Blockade	
Drug					
4-Aminopyridines	Yes				
Guanidine hydrochloride	Yes				
Succinylcholine			Yes		
d-Tubocurarine				Yes	
Dimethyltubocurarine				Yes	
Gallamine				Yes	
Benzoquinonium				Yes	
Physostigmine					Yes
Neostigmine					Yes
Disease					
Botulinum toxin		Yes			
Myasthenia gravis			Destruction of receptors		

ACh, acetylcholine; AChE, acetylcholinesterase.

Dimethyltubocurarine, **gallamine**, and **benzoquinonium** have similar effects.

These drugs combine with the receptor sites at the postsynaptic membrane normally used by ACh and thus block the neurotransmitter action of ACh. Therefore, they are referred to as competitive blocking agents, as they are competing for the same receptor site as ACh. As these drugs are slowly metabolized, the paralysis passes off.

Decamethonium and **succinylcholine** also paralyze skeletal muscle, but their action differs from that of competitive blocking agents because they produce their effect by causing depolarization of the motor endplate. Acting like ACh, they depolarize the postsynaptic membrane, and the muscle contracts once. This is followed by flaccid paralysis and blockage of neuromuscular activity. Although the blocking action endures for some time, the drugs are metabolized, and the paralysis passes off. The actual paralysis is produced by the continued depolarization of the postsynaptic membrane. Remember that continuous depolarization does not produce continuous skeletal muscle contraction. Repolarization has to take place before further depolarization can occur.

Neuromuscular blocking agents are commonly used with general anesthetics to produce the desired degree of muscle relaxation without using larger doses of general anesthetics. Because the respiratory muscles are paralyzed, facilities for artificial respiration are essential.

Anticholinesterases

Physostigmine and **neostigmine** have the capacity to combine with acetylcholinesterase (AChE) and prevent the esterase from inactivating ACh. In addition, neostigmine has a direct stimulating action on skeletal muscle. The actions of both drugs are reversible, and they have been used with success in the treatment of myasthenia gravis.

Bacterial Toxins

Clostridium botulinum, the causative organism in certain cases of food poisoning, produces a toxin that inhibits the release of ACh at the neuromuscular junction. Death results from paralysis of the respiratory muscles. The course of the disease can be improved by the administration of calcium gluconate or guanidine, which promotes the release of ACh from the nerve terminals.

Motor Nerve and Skeletal Muscle

Not only does the motor nerve control the activity of the muscle it supplies but also its integrity is essential for the muscle's normal maintenance. Following section of a motor nerve, the muscle fibers rapidly atrophy and are replaced by connective tissue. The total bulk of the muscle may be 75% reduced in as little as 3 months. This degree of atrophy does not occur if the muscle simply is immobilized; that is, it is not just disuse atrophy. Apparently, the maintenance of normal muscle is dependent on the continued reception of ACh at the postsynaptic membrane at the neuromuscular junction.

Denervation Supersensitivity of Skeletal Muscle

After approximately 2 weeks of denervation, skeletal muscle fibers respond to externally applied ACh at sites other than the neuromuscular junctions. This supersensitivity could be explained on the basis that many new ACh receptors have developed along the length of the muscle fibers following denervation.

Myasthenia Gravis

Myasthenia gravis is a common disease characterized by drooping of the upper eyelids (ptosis), double vision (diplopia), difficulty in swallowing (dysphagia), difficulty in talking (dysarthria), and general muscle weakness and fatigue. Initially, the disease most often involves the muscles of the eye and the pharynx, and the symptoms can be relieved with rest. In the progressive form of the disease, the weakness becomes steadily worse, and ultimately death occurs.

The condition is an autoimmune disorder in which antibodies are produced against the nicotinic ACh receptors on the postsynaptic membrane. The cause of the autoimmune disorder is unknown. The antibodies interfere with the synaptic transmission by reducing the number of receptors or by blocking the interaction of ACh with its receptors. The size of the junctional folds is also reduced, and the width of the synaptic cleft is increased. Together, these changes result in reduced amplitude in endplate potentials. The condition can be temporarily relieved by AChE drugs such as **neostigmine,** which potentiates ACh's action.

In adults with myasthenia gravis, about 70% show evidence of hyperplasia of their thymus glands. In the thymus, T cells, which mediate immune protection, undergo maturation. Excessive synthesis of thymic hormones that stimulate the development of T cells may contribute to the autoimmune response.

A rare congenital form of myasthenia gravis may exist from birth, with no abnormal antibody present. The causes of the congenital disease include AChE deficiency at the motor endplates, impaired release of ACh, impaired capacity of the receptors to interact with ACh, and a reduced number of ACh receptors.

Hypokalemic Periodic Paralysis and Hyperkalemic Paralysis

Hypokalemic periodic paralysis and hyperkalemic paralysis are diseases due to decreased or increased blood potassium levels. The ability of ACh to initiate electrical changes in the postsynaptic membrane of the neuromuscular junction can be greatly influenced by the level of blood potassium, and this blood change is responsible for the paralysis in these patients.

Action of Drugs on Neuromuscular Junctions in Smooth and Cardiac Muscle and Nerve Endings on Secretory Cells

In normal body physiology, ACh released from postganglionic parasympathetic fibers can bring about depolarization and resulting contraction of smooth muscle fibers. ACh, however, is a useless drug to be administered by the clinician, because it is rapidly destroyed by the **cholinesterases**. Also, its actions are so widespread that it cannot be used selectively. By slightly changing the structure, as in the case of **methacholine chloride** or **carbachol**, the drugs are less susceptible to destruction by the cholinesterases but still possess the ability to react with the receptors.

Atropine and **scopolamine** are drugs that compete with ACh for the same receptors. These drugs are competitive antagonists of ACh at receptor sites of smooth muscle, cardiac muscle, and various secretory cells.

Norepinephrine is released from postganglionic sympathetic fibers and can bring about depolarization of smooth muscle in the walls of arteries, for example, resulting in their contraction. At other sites, such as the bronchi, it causes

smooth muscle relaxation. Sympathetic receptors have been classified as α and β. The functions associated with α-receptors are vasoconstriction, mydriasis (dilatation of the pupil), and relaxation of the smooth muscle of the intestine. β-Receptors are associated with vasodilatation, cardioacceleration, bronchial relaxation, and intestinal relaxation.

Phenoxybenzamine has been found to block α-receptors, whereas **propranolol** blocks β-receptors. The structure of these receptors is not known.

Sensory Perception Abnormalities

Abnormalities in sensory perception should be looked for on the face, trunk, and limbs. Areas of diminished pain sensation (**hypalgesia**) or touch sensation (**hypesthesia**) or heightened sensation (**hyperesthesia**) should be identified. Abnormal sensations (**paresthesia**), such as pins and needles, may be experienced by a patient who has a lesion located anywhere along the sensory pathway from the peripheral nerve to the cerebral cortex. The areas of sensory abnormality should be precisely defined and recorded, with each modality being recorded separately.

Testing sensory function requires practice and experience. Many patients have difficulty in responding to a clinician's examination of the sensory system. Some individuals try to assist the examiner by wrongfully anticipating the correct response. This problem can largely be overcome by testing for cutaneous sensibility with the patient's eyes closed. In this way, the patient cannot see which areas of skin are being tested. Other patients find it difficult to understand exactly what information is required of them. Some intelligent patients respond more to differences in intensity of stimulation rather than giving a simple "yes" or "no" answer to the question "Can you feel anything?" The clinician must always be aware of the possibility of hysteria, which occurs when a patient complains of sensory loss that has no neuroanatomical explanation. For example, a total loss of skin sensation on one side of the face, including the angle of the jaw, would infer that the patient has a lesion involving the fifth cranial nerve in the pons and the greater auricular nerve (C2–C3), which is anatomically very unlikely. Patience and objectivity are required, and if doubt exists as to the accuracy of the assessment, the patient should be reexamined on another occasion.

Segmental Innervation of the Skin

Because large nerve plexuses are present at the roots of the upper and lower limbs, a single spinal nerve may send both motor and sensory fibers to several peripheral nerves, and conversely, a single peripheral nerve may receive nerve fibers from many spinal nerves. Moreover, a lesion of a segment of the spinal cord, or posterior root, or spinal nerve will result in a sensory loss that is different from that occurring after a lesion of a peripheral nerve.

The area of skin supplied by a single spinal nerve and, therefore, a single segment of the spinal cord is called a **dermatome**. A clinician should remember that dermatomes overlap and that, in the trunk, at least three contiguous spinal nerves have to be sectioned to produce a region of complete anesthesia. Remember also that the degree of overlap for painful and thermal sensations is much greater than that for tactile sensation. A clinician should have a working knowledge of the segmental (dermatomal) innervation of skin, because with a pin or a piece of cotton, he or she can determine whether the sensory function of a particular spinal nerve or segment of the spinal cord is normal. When examining the dermatomal charts, note that because of the development of the upper limbs, the anterior rami of the lower cervical and first thoracic spinal nerves have lost their cutaneous innervation of the trunk anteriorly, and at the level of the second costal cartilage, the fourth cervical dermatome is contiguous with the second thoracic dermatome. In the sensory innervation of the head, the trigeminal (fifth cranial) nerve supplies a large area of the face and scalp, and its cutaneous area is contiguous with that of the second cervical segment.

Because the dermatomes run longitudinally along the long axis of the upper limbs, sensation should be tested by dragging a wisp of cotton or a pin along the long axis of the medial and lateral borders of the limbs. On the trunk, the dermatomes run almost horizontally, so the stimulus should be applied by moving in a vertical direction.

Segmental Innervation of the Muscles

Remember that most skeletal muscles are innervated by more than one spinal nerve and, therefore, by the same number of segments of the spinal cord. Complete destruction of one segment of the spinal cord as the result of trauma or pressure from a tumor will cause weakness of all the muscles that are innervated from that segment. To paralyze a muscle completely, several adjacent segments of the spinal cord have to be destroyed.

Because of the presence of the cervical, brachial, and lumbosacral plexuses, the axons of motor anterior gray column cells are redistributed into a number of peripheral nerves. Knowing this, the clinician, is able to distinguish between a lesion of a segment of the spinal cord, an anterior root, or a spinal nerve on the one hand and a lesion of a peripheral nerve on the other hand. For example, the musculocutaneous nerve of the arm, which receives nerve fibers from the fifth, sixth, and seventh cervical segments of the spinal cord, supplies a finite number of muscles—namely, the biceps brachii, the brachialis, and the coracobrachialis muscles—and section of that nerve would result in total paralysis of these muscles; a lesion of the fifth, sixth, and seventh cervical spinal segments, or their anterior roots or their spinal nerves, would result in paralysis of these muscles and also partial paralysis of many other muscles, including the deltoid, supraspinatus, teres minor, and infraspinatus.

The segmental innervation of the biceps brachii, triceps, brachioradialis, muscles of the anterior abdominal wall, quadriceps femoris, gastrocnemius, and soleus should be memorized, as testing them is possible by eliciting their reflex contraction (see p. 110).

Muscle Tone

Skeletal muscle tone is due to the presence of a few muscle fibers within a muscle being in a state of full contraction all the time. Muscle tone is controlled reflexly from afferent nerve endings situated in the muscle itself. Therefore, any disease process that interferes with any part of the reflex arc will abolish the muscle tone. Some examples are syphilitic infection of the posterior root (tabes dorsalis); destruction of the motor anterior gray column cells, as in poliomyelitis or syringomyelia; destruction of a segment of the spinal cord by trauma or pressure from a tumor; section of an anterior root; pressure on a spinal nerve by a prolapsed intervertebral disc; and section of a peripheral nerve, as in a stab wound. All these clinical conditions will result in loss of muscle tone.

Although the basic mechanism underlying muscle tone is the integrity of the spinal segmental reflex, this reflex activity is influenced by nervous impulses received by the anterior horn cells from all levels of the brain and spinal cord. Spinal shock, which follows injury to the spinal cord and is caused by loss of functional activity of neurons, will result in diminished muscle tone. Cerebellar disease also results in diminished muscle tone because the cerebellum facilitates the stretch reflex. The reticular formation normally tends to increase muscle tone, but its activity is inhibited by higher cerebral centers. Therefore, if the higher cerebral control is interfered with by trauma or disease, the inhibition is lost and the muscle tone is exaggerated (decerebrate rigidity). Primary degeneration of the muscles themselves (myopathies) can also cause loss of muscle tone.

Posture

The posture of an individual depends on the degree and distribution of muscle tone and, therefore, on the activity of the motor neurons that supply the muscles. The motor neurons in the anterior gray columns of the spinal cord are the points where the nervous impulses converge from many posterior nerve roots and the descending fibers from many different levels of the brain and spinal cord. The successful coordination of all these nervous influences results in a normal posture.

When someone is in the standing posture, remarkably little muscular activity is taking place in the muscles of the limbs and trunk. This is because the center of gravity of any part of the body is mainly above the joints on which its weight is directed. Moreover, in many joints, such as the hip and the knee, the ligaments are very strong and support the body in the erect posture. However, a person cannot remain standing if all muscles are paralyzed. Once a person starts to fall, either forward, backward, or laterally, the muscle spindles and other stretch receptors immediately increase their activity, and the reflex arcs come into play; thus, reflex compensatory muscle contractions take place to restore the state of balance. The eyes and the receptors in the membranous labyrinth also play a vital part in the maintenance of balance. The importance of the eyes in maintaining the erect position can easily be tested in a normal person. Once the eyes are closed, the person shows a tendency to sway slightly because he or she now must rely exclusively on muscle and labyrinthine receptors to preserve his or her balance.

Pathologic alteration in muscle tone will therefore affect posture. For example, in hemiplegia or in Parkinson disease, in which hypertonicity exists, posture will be changed. As with cerebellar disease, hypotonicity will cause drooping of the shoulder on the affected side. Lesions involving peripheral nerves that innervate antigravity muscles will produce wristdrop (radial nerve) and footdrop (common peroneal nerve).

Clinical Observation of Muscular Activity

Magnitude of muscle injury is evaluated through observation of size, tone, and the presence of involuntary movements.

Muscular Power

Ask the patient to perform movements for which the muscle under examination is primarily responsible. Next, ask the patient to perform each movement against resistance and compare the strengths of the muscles on the two sides of the body. Section of the peripheral nerve that supplies the muscle or disease affecting the anterior gray column cells (e.g., poliomyelitis) will clearly reduce the power of or paralyze the muscles involved.

Muscle Wasting

Muscle wasting occurs within 2 to 3 weeks after section of the motor nerve. In the limbs, it is easily tested by measuring the diameter of the limbs at a given point over the involved muscle and comparing the measurement obtained with that at the same site on the opposite limb.

Muscular Fasciculation

Twitching of groups of muscle fibers is seen most often in patients with chronic disease that affects the anterior horn cells (e.g., progressive muscular atrophy).

Muscular Contracture

Muscular contracture occurs most commonly in the muscles that normally oppose paralyzed muscles. The muscles contract and undergo permanent shortening.

Muscle Tone

A muscle without tone—that is, one in which the simple spinal reflex arcs are not functioning—is noncontractile and doughlike on palpation. Degrees of loss of tone may be tested by passively moving the joints and comparing the resistance to the movements by the muscles on the two sides of the body. Increase in muscle tone can occur following the removal of the cerebral inhibition on the reticular formation.

Muscular Coordination

To determine muscular coordination, ask the patient to touch, with the eyes open, the tip of the nose with the tip of the forefinger and then ask to repeat the process with the eyes closed. A similar test of the lower limbs may be carried out with the patient lying down. Ask the patient to place one heel on the opposite knee, with the eyes open and then ask to repeat the process with the eyes closed.

Another test is to ask the patient to quickly supinate and pronate both forearms simultaneously. Disease of the cerebellum, for example, which coordinates muscular activity, would result in impaired ability to perform these rapid repetitive movements.

Involuntary Movement of Muscles

Tic is a coordinated, repetitive movement involving one or more muscles.

Choreiform movements are quick, jerky, irregular movements that are nonrepetitive. Swift grimaces and sudden movements of the head or limbs are examples of this condition.

Athetosis consists of slow, sinuous, writhing movements that most commonly involve the distal segments of the limbs.

Tremor is the alternating contraction of the agonists and antagonists of a joint.

Myoclonus consists of shocklike muscular contractions of a portion of a muscle, an entire muscle, or a group of muscles.

Tonic spasm refers to a sustained contraction of a muscle or group of muscles, as in the tonic phase of an epileptic seizure.

Neurologic Sensory and Motor Symptoms—Are They Always of Primary Neurologic Origin?

A neurologic diagnosis depends on determining the site of the lesion and the nature of the pathology causing the disease. The clinician cannot consider the nervous system in isolation, because the neurologic symptoms and signs may depend on disorders mainly involving another system. For example, a cerebral embolism may follow the formation of a blood clot on the ventricular wall of a patient with coronary thrombosis. A cerebral abscess may follow the formation of a lung abscess. Therefore, neurologic examination in many patients should be accompanied by a more general physical examination involving other systems.

Key Concepts

Nerve Fibers

- Myelinated nerve fibers are surrounded by segmented, discontinuous myelin sheaths from supporting neuroglia cells.
- In the PNS, multiple Schwann cells wrap around a single axon in a tight spiral.
- In the CNS, a single oligodendrocyte will extend multiple myelin processes that cover portions of multiple nerve fibers.
- Some smaller axons do not require myelination, such as fine sensory or postganglionic autonomic nerves.

Peripheral Nerves

- The 31 pairs of spinal nerves and 12 pairs of cranial nerves each carry sensory and/or motor nerve fibers.
- Spinal nerves carrying sensory information have a dorsal root ganglion, formed by the collection of unipolar cell bodies. Cranial nerves carrying sensory fibers also have sensory ganglia.
- Sympathetic and parasympathetic nerves have autonomic ganglia, formed by the collection of postsynaptic autonomic cell bodies, located away from the brain and spinal cord.
- Peripheral nerve bundles may divide into branches that join neighboring peripheral nerves, forming a nerve plexus. This allows nerve fibers from different spinal cord segments to be distributed efficiently in different nerve trunks to various parts of the body.

Conduction in Peripheral Nerves

- Reversing the negative resting potential by diffusion of sodium (Na^+) and potassium (K^+) across the plasma membrane, resulting in propagation of electrical depolarization down the fiber, is called an action potential.
- For a short time after the action potential, the nerve is unable to be excited because the sodium channels are inactivated. This is called the absolute refractory period.
- Conduction velocity is positively affected by factors such as fiber diameter and myelination.

Receptor Endings

- Sensory receptors are classified by functional type (mechanoreceptors, thermoreceptors, nociceptors, electromagnetic receptors, and chemoreceptors) and anatomical type (encapsulated or nonencapsulated).
- Free nerve endings are nonencapsulated and typically detect pain, crude touch, pressure, and tickle sensations.
- Merkel discs are nonencapsulated endings found in hairless skin and are considered to be slowly adapting touch receptors.
- Hair follicle receptors are nonencapsulated endings that surround the hair follicle and respond to bending the hair.
- Meissner corpuscles are encapsulated ending found in the dermal papillae of the skin and function as rapidly adapting fine touch detectors.
- Pacinian corpuscles are encapsulated endings in the skin that respond to vibration sensations.
- Ruffini corpuscles are encapsulated stretch receptors in the skin.
- Neuromuscular and neurotendinous spindles are found in muscles and tendons to detect muscle stretch and muscle tension, respectively.

Effector Endings

- Skeletal muscle is innervated by large myelinated nerve fibers derived from motor neurons in the anterior gray horns of the spinal cord.
- A single nerve fiber terminates on multiple muscle fibers at a site referred to as a neuromuscular junction or motor endplate.
- Smooth muscle and cardiac muscle fibers are innervated by sympathetic and parasympathetic parts of the autonomic system.

Clinical Problem Solving

1. A 20-year-old man is seen in the emergency department following an automobile accident. A diagnosis of fracture dislocation of the fourth thoracic vertebra is made, with injury to the spinal cord as a complication. A laminectomy is performed to decompress the spinal cord in order to avoid permanent injury to the tracts of the cord. What is a nerve tract in the spinal cord? How does this differ in structure from a peripheral nerve?
2. Multiple sclerosis is an example of a demyelinating disease of the nervous system. Many other diseases of the nervous system also have the common pathologic feature of destruction of the myelin sheaths of nerve fibers. How does myelination normally take place in peripheral nerves and central nervous system tracts? When does myelination of nerves normally take place?
3. The myelin sheath is said to be formed in the peripheral nervous system (PNS) by the rotation of Schwann cells on the axon so that the plasma membrane becomes wrapped around the axon in a spiral. In the central nervous system (CNS), do the oligodendrocytes rotate on the axons in a similar manner to form myelin?
4. A 26-year-old man is involved in a street brawl and receives a knife wound to the right arm at about the midhumeral level. Physical examination reveals that the median nerve has been sectioned. Motor loss consists of paralysis of the pronator muscles of the forearm and the long flexor muscles of the wrist and fingers, with the exception of the flexor carpi ulnaris and the medial half of the flexor digitorum profundus. As a result, the right forearm is kept in the supine position; wrist flexion is weak and accompanied by adduction. The latter deviation is due to the paralysis of the flexor carpi radialis and the strength of both the flexor carpi ulnaris and the medial half of the flexor digitorum profundus. No flexion is possible at the interphalangeal joints of the index and middle fingers, although weak flexion of the metacarpophalangeal joints of these fingers was attempted by the interossei. When the patient is asked to make a fist of his right hand, the index and, to a lesser extent, the middle fingers tends to remain straight, while the ring and little fingers flex. The latter two fingers are weakened by the loss of the flexor digitorum superficialis. Flexion of the terminal phalanx of the thumb is lost due to paralysis of the flexor pollicis longus. The muscles of the thenar eminence are paralyzed, and the right thumb is laterally rotated and adducted.

   Sensory loss of the skin of the right hand involves the lateral half of the palm and the palmar aspect of the lateral three and a half fingers. There is also sensory loss of the skin of the distal parts of the dorsal surfaces of the lateral three and a half fingers.

   The skin areas involved in sensory loss become warmer and drier than normal, evidencing vasomotor changes. This is due to arteriolar dilatation and absence of sweating resulting from loss of sympathetic nervous control.

   (a) Describe the changes that would take place in the median nerve proximal and distal to the site of section. (b) How would you treat this case? (c) What will be the first signs and symptoms to indicate that the nerve is regenerating adequately? (d) Which function will return first—sensory or muscular? (e) About how long will it take for the nerve to regenerate and reach its end organs?
5. A 45-year-old woman with a right-sided facial palsy is examined. When questioned, she says that 3 years previously she had experienced a weakness of the right side of the face and some degree of loss of taste sensation following a ride in an open car on a cold day. A diagnosis of Bell palsy was made. What is Bell palsy? How would you treat this patient?
6. A family with five small children move into an old house. Six months later, the mother notices that her 1-year-old son is becoming somnolent and quiet. Whereas previously he was very active and crawled around the house, he now tends to lie about the floor, uninterested in his toys. He has also stopped eating well and is very constipated. The mother decides to take him to a pediatrician when, as she puts it, the child suddenly "threw a fit." Examination reveals no positive physical signs except for a dark line between the gums and teeth. When questioned further, the mother admits that the child liked sucking the peeling paint on the railings outside the house. A diagnosis of chronic lead poisoning is made. This is confirmed by finding that the blood lead level was in excess of 50 μg per 100 mL. What effect does lead have on the nervous system?
7. A 54-year-old man suddenly develops severe pain down both legs in the distribution of the sciatic nerve. He also notices numbness in the buttocks and perineum and recently notes that he cannot feel the passage of urine or feces. A diagnosis is made of central protrusion posteriorly of the intervertebral disc between the third and fourth lumbar vertebrae. The symptoms indicate that the cauda equina is being pressed on. Can regeneration occur in the cauda equina?
8. By what anatomical route is tetanus toxin believed to pass from a wound to the central nervous system?
9. Following an automobile accident, a 35-year-old man is seen in the emergency department with fractures of the fifth and sixth ribs on the right side. In order to relieve the pain and discomfort experienced by the patient when breathing, the clinician decides to block the right fifth and sixth intercostal nerves by

injecting a local anesthetic, lidocaine (Xylocaine), around the nerve trunks. What is the effect of the local anesthetic agent on the nerve fibers? Are the large-diameter or the small-diameter nerve fibers more susceptible to the action of the drug?

10. A 65-year-old man, on returning home from a party, finds that he cannot climb the stairs. He has consumed a large amount of whiskey and seems to have lost control of his legs. He sits down on a chair in the hallway and is soon in a deep, stuporous sleep, with his right arm suspended over the back of the chair. The next morning, he wakes with a severe headache and loss of the use of his right arm and hand. During examination in the emergency department, the patient is found to have severe paralysis involving branches of the medial cord of the brachial plexus and the radial nerve. The diagnosis is neuropraxia, which occurred as the result of the pressure of the back of the chair on the involved nerves. What is neuropraxia? How does this differ from axonotmesis and neurotmesis? What is the prognosis in this patient? How would you treat this case?
11. A well-known politician is attending a rally when a youth suddenly steps forward and shoots him in the back. Examination in the emergency department shows that the bullet has entered the back obliquely and is lodged in the vertebral canal at the level of the eighth thoracic vertebra. The patient cannot feel anything below this level and is paralyzed from the waist downward. At the operation, a laminectomy is performed, and the bullet is removed. Considerable damage to the spinal cord is noted. What changes take place in the spinal cord when the nerve fibers are damaged? Does regeneration take place in the central nervous system?
12. An 18-year-old woman visits her physician because she has burns, which she cannot feel, on the tips of the fingers of the right hand. She also mentions that she has weakness of her right hand. On physical examination, severe scarring of the fingers of the right hand is noted. Obvious atrophy of the small muscles of the right hand is also found. Testing the sensory modalities of the skin of the entire patient shows total loss of pain and temperature sensation of the distal part of the right upper limb. The left hand has diminished sensibility to pain and temperature. Definite muscular weakness is demonstrated in the small muscles of the right hand, and a small amount of weakness also is found in the muscles of the left hand. A diagnosis of syringomyelia was made. (a) Using your neuroanatomical knowledge, describe the type of sensory nerve endings that are sensitive to pain and temperature. (b) How would you examine a patient to determine cutaneous pain and temperature sensory loss?
13. A 35-year-old man, while walking past some workmen who are digging a hole in the road, suddenly becomes aware of a foreign body in his left eye. Because the cornea is extremely sensitive, he suffers considerable discomfort. What sensory endings are present in the cornea? Is the cornea sensitive to stimuli other than pain?
14. A 60-year-old man visits his physician because for the past 3 months he has been experiencing an agonizing stabbing pain over the middle part of the right side of his face. The stabs last a few seconds but might be repeated several times. "The pain is the worst I have ever experienced," he tells his clinician. He has noticed particularly that a draft of cold air on his face or the touching of a few scalp hairs in the temporal region can trigger the pain. Physical examination reveals no sensory or motor loss of the trigeminal nerve. A diagnosis of trigeminal neuralgia is made. Using your knowledge of neuroanatomy, explain why hairs are so sensitive to touch.
15. A 50-year-old man is diagnosed as suffering from tabes dorsalis. On physical examination, many signs of the syphilitic disease are present, including a total lack of deep sensation to pain. Intense squeezing of the calcaneus tendon or the testicles produces no response. Using your knowledge of neuroanatomy, explain how deep pain sensation is normally experienced.
16. While carrying out a physical examination of a patient, the clinician asks the patient to cross his knees and relax his leg muscles. The left ligamentum patellae are then struck smartly with a reflex hammer, which immediately produces an involuntary partial extension of the left knee joint (the knee-jerk test is positive). How does the central nervous system receive nervous information from the quadriceps femoris muscle in order that it may respond reflexly by extending the knee?
17. A 55-year-old man suffering from syphilis of the spinal cord presents characteristic symptoms and signs of tabes dorsalis. He has experienced severe stabbing pains in the abdomen and legs for the last 6 months. When asked to walk, the patient is seen to do so with a broad base, slapping the feet on the ground. How would you test the patient's ability to perceive the position of his lower extremities and his vibratory sense? Using your knowledge of neuroanatomy, explain how a normal individual is able to perceive the position of the extremities and detect vibrations.
18. Using your knowledge of pharmacology, name two drugs that act as competitive blocking agents on skeletal neuromuscular junctions. Name the chemical substance against which these agents are competing. Name the sites at which the blocking agents are believed to act.
19. Name a drug that will bring about flaccid paralysis of skeletal muscle by causing depolarization of the postsynaptic membrane.
20. In cases of severe food poisoning, the organism *Clostridium botulinum* may be found to be responsible. How does this organism cause paralysis of the respiratory muscles?
21. During a ward round, an orthopedic surgeon states that the degree of muscular atrophy that occurs in a limb immobilized in a cast is totally different from

the degree of muscular atrophy that follows section of the motor nerve supply to muscles. The surgeon asks a medical student to explain this difference. How would you account for this difference in the degree of muscular atrophy?

22. A 57-year-old man visits his physician because of pain in the right buttock that extends down the right leg, the back of the thigh, the outer side and back of the calf, and the outer border of the foot. The patient gives no history of previous injury but states that the pain started about 3 months ago as a dull, low backache. Since that time, the pain has increased in intensity and has spread down the right leg. When asked if the pain has ever disappeared, he replied that on two separate occasions the pain has diminished in intensity, but his back remains "stiff" all the time. He says the pain is aggravated by stooping or by coughing and sneezing. Sometimes, he experiences a "pins and needles" sensation along the outer border of his right foot. After a complete physical examination, a diagnosis is made of herniation of a lumbar intervertebral disc. Using your knowledge of anatomy, state which intervertebral disc is most likely to have been herniated.
23. A 61-year-old woman is seen by her physician because she is experiencing a shooting, burning pain in the left side of her chest. Three days later, a group of localized papules appears on the skin covering the left fifth intercostal space. One day later, the papules become vesicular; a few days later, the vesicles dry up into crusts. The crusts later separate, leaving small permanent scars. The patient also notices some loss of sensibility over the left side of the chest. A diagnosis of herpes zoster is made. Using your knowledge of anatomy, state the segment of the spinal cord involved with the disease.
24. While examining the sensory innervation of the skin of the head and neck in a patient, a medical student has difficulty remembering the dermatomal pattern at the junction of the head with the neck and at the junction of the neck with the thorax. Are the dermatomes arranged in a special manner in these areas? If so, what is the underlying reason for this?
25. On physical examination, a 30-year-old man is found to have weakness and diminished tone of the rhomboid muscles, deltoids, and biceps brachii on both sides of the body. The degree of weakness is greater on the right side. The biceps tendon jerk is absent on the right side and diminished on the left side. The triceps jerks are normal on both sides of the body. The muscles of the trunk and lower limb show increased tone and exhibit spastic paralysis. Radiology of the vertebral column reveals the presence of vertebral destruction due to a tumor arising within the vertebral canal. Using your knowledge of anatomy, answer the following questions: (a) Which vertebra is likely to have the tumor within the vertebral canal? (b) Name the segments of the spinal cord that are being pressed on by the tumor. (c) Which segments of the spinal cord participate in the reflex arcs responsible for the biceps brachii tendon jerk? (d) Why do the rhomboid and deltoid muscles exhibit diminished muscle tone, whereas the muscles of the lower limb exhibit increased tone?
26. Name three clinical conditions that could result in a loss of tone of skeletal muscle.
27. A 69-year-old man with advanced tabes dorsalis is asked to stand with his toes and heels together and his eyes closed. He immediately starts to sway violently, and if the nurse had not held on to his arm, he would have fallen to the ground (positive Romberg test). Why was it vital for this patient to keep his eyes open in order to remain upright?
28. A 63-year-old man with moderately advanced Parkinson disease is disrobed and asked to walk in a straight line in the examining room. The physician observes that the patient has his head and shoulders stooped forward, the arms slightly abducted, the elbow joints partly flexed, and the wrists slightly extended with the fingers flexed at the metacarpophalangeal joints and extended at the interphalangeal joints. On starting to walk, the patient leaned forward and slowly shuffles his feet. The farther he leans forward, the more quickly he moves his legs, so that by the time he has crossed the room, he is almost running. The patient's face is masklike and exhibits few emotional movements. The hands show a coarse tremor, and the muscles of the upper and lower limbs show increased tone in the opposing muscle groups when the joints are passively moved. Parkinson disease, or the parkinsonian syndrome, can be caused by a number of pathologic conditions, but they usually interfere in the normal function of the corpus striatum or the substantia nigra or both. Using your knowledge of the anatomy and physiology of muscle action, explain the different signs seen in this important syndrome.
29. A 10-year-old girl is taken to a neurologist because of a 6-month history of epileptic attacks. The parents describe the attacks as starting with sudden involuntary movements of the trunk, arms, or legs. Sometimes, the muscle movements are slight, but at other times, they are so violent that she has been known to throw an object in her hand across the room. At yet other times, the patient just falls to the ground as the result of a sudden loss of muscle tone. Having hit the ground, the patient will immediately rise to her feet. On one occasion, she severely bruised her head and shoulder by striking a chair and a table. One month ago, the parents notice that their daughter appears to lose consciousness briefly. On that occasion, she is carrying on a normal conversation when she suddenly stops and her gaze becomes fixed. After a few seconds, she becomes alert and continues her conversation. This patient is suffering from a form of epilepsy known as petit mal. What is the correct term for the sudden involuntary contraction of the muscles of the trunk or extremities? Name the condition of a patient who suddenly loses all muscle tone and falls to the ground.

30. A 45-year-old man suffering from amyotrophic lateral sclerosis is examined by a third-year medical student. The student found that the flexor and extensor muscles of the knee and ankle joints of the right leg are weaker than those of the left leg. However, she is of the opinion that the muscles of the left leg also are somewhat weaker than normal. On palpation of the extensor muscles of the right thigh, twitching of the muscle fibers in the quadriceps muscle is detected. Marked atrophy of the muscles of both legs also is noted. Cutaneous sensory loss in either limb is not evident. Amyotrophic lateral sclerosis is a condition in which the motor anterior horn cells of the spinal cord and brainstem degenerate with secondary degeneration of the nervous tracts in the lateral and anterior portions of the spinal cord. Why do you think this patient had weakness and atrophy of the muscles of the lower limbs? What is the correct clinical term for the twitching of the muscle fibers in the extensor muscles of the right knee?
31. A 12-year-old girl is diagnosed as suffering from a medulloblastoma of the cerebellum. Clinical and radiologic examinations reveal that the tumor is predominantly invading the right cerebellar hemisphere. Knowing that the cerebellum is concerned with the coordination of motor activity so that complex voluntary movements involving antagonistic muscle groups can take place in a precise manner, what should you test for to demonstrate loss of cerebellar function? Describe the test for each parameter.

Answers and Explanations to Clinical Problem Solving

1. Nervous tracts are bundles of nerve fibers found in the brain and spinal cord, most of which are myelinated. Some of the main structural differences between a myelinated nerve tract and a myelinated peripheral nerve fiber are as follows:

   Nerve Tract
   Oligodendrocyte
   Mesaxon absent
   Schmidt–Lanterman incisures present
   Nerve fibers supported by neuroglia
   Peripheral Nerve Fiber
   Schwann cell
   Mesaxon present
   Schmidt–Lanterman incisures present
   Nerve fibers supported by connective tissue sheaths, endoneurium, perineurium, and epineurium

2. Myelination is fully described on page 72. Myelin sheaths begin to form during fetal development and during the first year postnatally.
3. No. In the CNS, a single oligodendrocyte may be responsible for the formation of myelin for as many as 60 nerve fibers. Clearly, it would not be possible for an oligodendrocyte to rotate on each axon as does the Schwann cell in the PNS. In the CNS, the process of the oligodendrocyte is believed to grow in length and wrap itself around the axon.
4. (a) The microscopic changes that occur in the proximal and distal segments of a divided peripheral nerve are fully described on page 105. Remember that in the proximal segment, the changes occur only as far proximally as the next node of Ranvier, whereas the changes spread distally from the site of the lesion and include its terminations. (b) If one bears in mind the considerations outlined on page 109 and that the surgeon has the experience to perform nerve suture, the following treatment should be instituted. If the knife was clean, the nerve should be immediately sutured, and any arterial damage should be repaired. On the other hand, if the knife was contaminated or the wound was more than 6 hours old, the wound should be treated, and the nerve should be ignored. In the latter case, when the wound has healed and there is no sign of residual infection, the nerve ends should be explored and sutured together without tension. In either case, the paralyzed muscles are protected with a suitable splint, and the joints are gently exercised daily. (c) Once the regenerating axons have entered the distal segment, the nerve distal to the section becomes very sensitive to mechanical stimulation (Tinel sign). (d) Sensory recovery occurs first. Deep pressure sensation is the first sign of recovery. This is followed by the return of superficial cutaneous pain and vasomotor control of blood vessels. Later, the sensations of heat and cold return. Later still, light touch and tactile discrimination reappear. Sensory recovery occurs before there is return of voluntary movement. (e) For clinical purposes, a figure of 1.5 mm per day is the average rate of regeneration. Use this figure to determine approximately how long it will take for a regenerating nerve to reach its end organs.
5. Bell palsy is produced by swelling of the seventh cranial nerve (facial nerve) in the facial nerve canal of the skull. Its cause is unknown, although it often follows exposure to cold. Since the facial canal is bony, the nerve cannot expand and consequently becomes compressed and ischemic. In severe cases, the muscles of facial expression are paralyzed on one side of the face, and there is loss of taste sensation in the anterior part of the tongue on the same side. Massage of the paralyzed muscles should be undertaken to preserve their integrity until nerve function returns. The majority of patients recover completely. In this patient, a serious residual palsy existed after 3 years. A treatment that has been successful in many cases is to section the hypoglossal nerve below and behind the angle of the mandible and to anastomose its proximal end to the distal

end of the facial nerve. Although the right half of the tongue would be paralyzed, this causes little disability. A reasonable return of facial movement can be expected. The patient learns to move the face instead of the tongue by practicing in front of a mirror. Note that both the hypoglossal and facial nerves are peripheral nerves; therefore, regeneration is possible. The prognosis is especially good since the hypoglossal nerve is purely a motor nerve.

6. Lead causes neuronal degeneration in the central nervous system and demyelination in the tracts of the spinal cord and peripheral nerves. The treatment is to remove the child from the source of the lead and to aid rapid excretion by administering calcium disodium versenate—a chelating agent. Nontoxic lead versenate is excreted in the urine.
7. Yes. The cauda equina consists of the anterior and posterior roots of the spinal nerves below the level of the first lumbar segment of the spinal cord. These are peripheral nerves with endoneurial sheaths and Schwann cells. Therefore, if adequate treatment is promptly instituted, regeneration will take place.
8. As the result of experiments in which dyes have been injected into peripheral nerves, spaces have been demonstrated between individual nerve fibers in the endoneurium. These spaces are believed to provide the route for the ascent of the tetanus toxin to the spinal cord.
9. Lidocaine is a local anesthetic that blocks nerve conduction when applied to a nerve fiber. The anesthetic acts on the axolemma and interferes with the transient increase in permeability of the axolemma to Na^+ ions and, in the resting axon, reduces the permeability of the axolemma to Na^+, K^+, and other ions. The small-diameter pain fibers are more susceptible to the action of this drug.
10. *Neuropraxia* is the term applied to a transient nerve block. Pressure is the most common cause, and this case was due to the pressure of the upper edge of the chair back on the brachial plexus in the axilla. The loss of function is probably caused by ischemia of the nerve fibers. Microscopic evidence of degeneration does not exist. *Axonotmesis* is the term applied to a nerve lesion in which the axons are damaged but the surrounding connective tissue sheaths remain intact. *Neurotmesis* is the term applied to complete section of the nerve trunk.

    The prognosis in this patient is excellent for rapid, complete recovery. The paralyzed muscles must not be stretched by antagonist muscles or by gravity. Therefore, suitable splints should be applied, and gentle passive movement of the joints should be performed once daily.
11. Degeneration in the CNS occurs in a manner similar to that found in the peripheral nervous system. The axon breaks up into small fragments, and the debris is digested by the neighboring microglial cells. The myelin sheath is broken down into lipid droplets, which are also phagocytosed by the microglial cells.

    The axons attempt to regenerate, as evidenced by sprouting of the axons, but no evidence shows that restoration of function ever occurs. The reasons for the failure of regeneration are fully described on page 107.
12. Syringomyelia is a chronic disease of the spinal cord that is due to a developmental abnormality in the formation of the central canal. It is characterized by the appearance of a fluid-filled cavity within the spinal cord that gradually enlarges, causing destruction of surrounding nervous tissue. In this patient, the cavity or syrinx was located in the lower cervical and upper thoracic segments of the cord, causing destruction of the ascending tracts that serve pain and temperature from the upper limbs. The cavity was encroaching on the motor anterior horn cells of both sides as well, causing weakness of the small muscles of the hands.

    (a) As is now generally accepted, the type of sensation felt is determined not by a specific receptor but by the specific area of the central nervous system to which the afferent nerve fiber passes. Free nerve endings are commonly associated with axons serving pain and temperature. (b) The examination of a patient to test different sensory modalities is discussed on page 113.
13. The only sensory receptors present in the cornea are free nerve endings. The cornea is sensitive to touch and temperature changes in addition to pain.
14. All hair follicles are richly innervated. Free nerve endings are found as a branching network that winds around the follicle below the entrance of the sebaceous duct. Merkel discs also are found in the epidermis of the follicle. The hair shaft acts as a lever, so the slightest movement of the hair readily stimulates the nerve endings in the hair follicle. In this patient suffering from trigeminal neuralgia, the temporal region of the scalp was the trigger area, which, on stimulation, initiated the intense stabs of pain in the distribution of the maxillary division of the trigeminal nerve.
15. Numerous free nerve endings are found in the connective tissue of tendons and the testes. Normally, squeezing these structures elicits an aching type of pain. In tabes dorsalis, the disease process affects the sensory neurons in the posterior roots of the spinal nerves.
16. Striking the ligamentum patellae with a reflex hammer causes elongation of the intrafusal fibers of the muscle spindles of the quadriceps muscle and stimulation of the annulospiral and flower-spray endings. The nerve impulses reach the spinal cord in the afferent neurons within the femoral nerve and enter the cord at the level of L2–L4. The afferent neurons synapse with the large α motor neurons in the anterior gray horns of the spinal cord. Nerve impulses now pass via the efferent motor neurons in the femoral nerve and stimulate the extrafusal muscle fibers of the quadriceps muscle, which then contracts. The muscle spindle afferent impulses

inhibit the motor neurons of the antagonist muscles (see reciprocal inhibition, p. 92).

17. To test position sense, the patient is placed in the supine position and is asked to close the eyes. The big toe is grasped at the sides between the thumb and index finger and extended and flexed. The patient is asked, on completion of each movement, "Is the toe pointing up or down?" Another simple test is to ask the patient, again with the eyes closed, to place the right heel on the left shin and run it down the shin to the dorsum of the left foot. The patient is then asked to repeat the performance with the left heel on the right shin.

    Vibratory sense can be tested by placing the handle of a vibrating tuning fork on the tibial tuberosity, the anterior border of the tibia, and the medial or lateral malleoli. The patient is asked to indicate when the vibration is first felt and when it ceases. Symmetrical points on the two limbs may be compared, and the clinician can use his or her own limbs as a control. In the normal individual, the sense of position depends on the central nervous system receiving adequate information from the pressure receptors (Pacinian corpuscles) in the joint capsules and ligaments, touch receptors (free nerve endings) in the tissues in and around joints, and the stretch receptors in the muscles and tendons (especially the neurotendinous spindles).

    Vibration sense is normally believed to be due to the stimulation of superficial and deep pressure receptors (Pacinian corpuscles).

    Appreciation of the passive movements of joints, postural sensibility, and vibration sense is often lost in tabes dorsalis due to syphilitic destruction of the posterior columns of the spinal cord and degeneration of the posterior roots.

18. *d*-Tubocurarine, dimethyltubocurarine, gallamine, and benzoquinonium are examples of competitive blocking agents. These drugs compete with the neurotransmitter acetylcholine (ACh). The competitive blocking agents are believed to combine with the same sites at the postsynaptic membrane (sarcolemma) of the motor endplate normally used by ACh.
19. Decamethonium and succinylcholine paralyze skeletal muscle by depolarizing the motor endplate.
20. *C. botulinum* produces a toxin that inhibits the release of acetylcholine at the motor endplate. Death results from paralysis of the respiratory muscles.
21. Skeletal muscles that are not used, such as in a limb fitted with a splint immobilizing a fracture, undergo disuse atrophy. The longer the muscles are not used, the greater the degree of atrophy. In severe cases, the atrophy may amount to as much as 25% of the muscle mass. The muscle fibers rapidly atrophy following section of a motor nerve, so the total mass of the muscle may be reduced by as much as 75% in as little as 3 months. The precise reason for this severe atrophy is not understood. Apparently, the maintenance of normal muscle depends on the continued reception of acetylcholine and trophic substances from the nerve terminals at the postsynaptic membrane at the neuromuscular junction. The latter mechanism would be impossible if the motor nerve was sectioned and the distal end had degenerated.
22. Your knowledge of the dermatomes of the lower limb will enable you to ascertain that the patient's pain was felt in the area of distribution of the fifth lumbar and first sacral nerve roots. The involvement of these roots is usually due to herniation of the fourth or fifth lumbar intervertebral disc.
23. Herpes zoster is a viral infection of the posterior root ganglia (or sensory ganglia of the cranial nerves), the posterior root, or the posterior gray horn of the spinal cord. This patient experienced pain and had a skin eruption in the area of distribution of the fifth left intercostal nerve. The virus was producing an acute inflammation at some point along the course of the sensory neurons of the fifth segment of the spinal cord on the left side.
24. The trigeminal (5th cranial) nerve innervates the skin of the greater part of the face. The next dermatome that occurs inferior to this is that of the 2nd cervical nerve. The 6th to the 12th cranial nerves do not innervate the skin of the face. At the junction of the neck with the thorax, the 4th cervical dermatome is contiguous with the 2nd thoracic dermatome; the anterior rami of the lower cervical and 1st thoracic spinal nerves lose their cutaneous distribution on the neck and trunk during the development of the upper limb.
25. (a) The physical examination revealed weakness of the rhomboid, deltoid, and biceps brachii muscles, which are innervated by the fifth and sixth cervical segments of the spinal cord. These spinal cord segments lie within the vertebral foramina of the sixth and seventh cervical vertebrae, respectively. (b) The fifth and sixth cervical segments of the spinal cord are being pressed on. (c) The biceps brachii reflex arc involves the fifth and sixth segments of the spinal cord. (d) The rhomboid and deltoid muscles show diminished muscle tone because the reflex arcs on which their tone depends travel through the compressed segments of the spinal cord; that is, the reflex arcs were no longer functioning normally. Because of the pressure of the tumor on the cervical region of the spinal cord, the nervous pathways passing down to lower segments of the spinal cord were interrupted. This resulted in the motor anterior gray column cells of the segments of the cord below the level of compression receiving diminished information from the higher centers, with a consequent increase in muscle tone.
26. Any disease process that can interrupt the normal functioning of the basic spinal reflex arc on which skeletal muscle tone is dependent will cause loss of muscle tone. Some examples are spinal shock following trauma to the spinal cord; section of or pressure on a spinal nerve, a posterior root, or an anterior root; syringomyelia; and poliomyelitis.

27. Tabes dorsalis, which is a syphilitic infection of the brain and spinal cord, produces degeneration of the central processes of the posterior root ganglion cells and also, usually, the ganglion cells themselves. The lower thoracic and lumbar sacral segments of the cord are involved first, and the interruption of the proprioceptive fibers results in impairment of appreciation of posture and the tendency to fall down if one closes the eyes while standing. Eyesight in this patient compensated for lack of proprioception.
28. In a normal individual, standing and walking are largely automatic, but as you have read in this chapter, these activities are highly complex and require the proper integration of neural mechanisms at all levels of the spinal cord and brain. The basic mechanism underlying muscle tone is the spinal segmental reflex. In order to maintain normal posture, these reflex arcs must receive adequate nervous input from higher levels of the nervous system. Diseases involving the corpus striatum (caudate and lentiform nuclei) or the substantia nigra result in an alteration in the pattern of nervous impulses impinging on the anterior horn cells of the spinal cord, hence the abnormal muscle tone. The increased tone is equal in extent in opposing muscle groups. The tremor of the parkinsonian syndrome is produced by the alternating movements of the agonist and antagonist muscles of a joint. The tremor is most prominent when the limb is at rest, ceases temporarily when voluntary movement is performed, and then starts again when the movement is completed. The tremor ceases when the patient is asleep. In Parkinson disease, neuronal degeneration is seen in the substantia nigra, resulting in the loss of inhibitory control of the substantia nigra over the lentiform nucleus, putamen, and caudate nucleus.
29. The syndrome of petit mal commonly has three sets of symptoms: (a) myoclonic jerks, in which the patient experiences sudden involuntary contraction of the muscles of the trunk and extremities; (b) akinetic seizures, in which all muscles of the body suddenly lose tone; and (c) brief losses of consciousness, in which the patient loses contact with the environment for a few seconds.
30. Destruction of the anterior gray column cells in the lumbar and sacral regions of the spinal cord resulted in paralysis and atrophy of the muscles of both legs. The twitching of groups of muscle fibers is referred to as *muscular fasciculation* and is commonly seen in patients with chronic disease affecting the anterior horn cells.
31. (a) Muscular hypotonia, which is present on the same side of the body as the lesion. Passively move the joints on the right side of the body and then on the left side, and compare the resistance to these movements by the muscles on the two sides of the body. (b) Posture. The shoulder girdle on the affected side drops because of loss of muscle tone. With the patient disrobed, ask her to stand up straight with her back toward you. With a unilateral cerebellar lesion, the shoulder on the affected side may be lower than that on the opposite, normal side. (c) Disorders of voluntary movement (ataxia) due to loss of muscle coordination. (d) Nystagmus. This is an involuntary to-and-fro movement of the eyes. It is commonly demonstrated in cerebellar disease and is due to lack of muscle coordination. When the eyes are turned horizontally, quick, rhythmic jerks occur in the direction of gaze. In unilateral cerebellar lesions, the amplitude of nystagmus is greater and its rate is slower when the eyes are rotated toward the side of the lesion than when they are displaced to the opposite side.

Review Questions

Directions: Each of the numbered items in this section is followed by answers. Select the ONE lettered answer that is CORRECT.

1. The following statements concern nerves:
   (a) *Nerve tract* is the name given to a nerve fiber in the peripheral and central nervous systems (PNS and CNS).
   (b) The supporting cell of a myelinated nerve fiber in the CNS is called an oligodendrocyte.
   (c) A node of Ranvier in peripheral nerves is where two Schwann cells come together and cover the exposed part of the plasma membrane of the axon.
   (d) Nodes of Ranvier are absent from myelinated nerve fibers in the CNS.
   (e) The major dense line of myelin consists of two inner lipid layers of the plasma membrane that are fused together.
2. The following statements concern nerves:
   (a) The minor dense line of myelin is made up of protein.
   (b) Incisures of Schmidt–Lanterman are caused by the mesaxons of the Schwann cells.
   (c) Only five or six unmyelinated axons may share a single Schwann cell in the peripheral nervous system (PNS).
   (d) The node of Ranvier is the site of nerve activity.
   (e) *Chromatolysis* is the term used to describe the changes in the arrangement of Nissl material within the axon following injury.

3. The following statements concern an oligodendrocyte:
   (a) A single oligodendrocyte may be associated with one segment of myelin on a single axon.
   (b) Incisures of Schmidt–Lanterman are not present in the myelinated fibers of the central nervous system (CNS).
   (c) Myelination in the CNS occurs by the rotation of the axon within the oligodendrocytic process and the wrapping of it around the axon.
   (d) A nonmyelinated axon in the CNS has a special relationship with the oligodendrocyte.
   (e) A single oligodendrocyte may be associated with the myelin sheaths of as many as 60 axons.
4. The following statements concern spinal nerves:
   (a) There are 26 pairs.
   (b) They are formed by the union of anterior and posterior nerve roots.
   (c) The posterior ramus contains only sensory axons.
   (d) The anterior root contains only sensory axons.
   (e) The posterior root ganglion contains bipolar neurons enveloped in capsular cells.
5. The following statements concern peripheral nerve plexuses:
   (a) They are formed by a network of connective tissue fibers.
   (b) Bundles of nerve fibers do not branch, and, in most instances, the individual nerve fibers do not branch.
   (c) Plexuses at the roots of the limbs are formed from posterior rami of spinal nerves.
   (d) The plexuses of the autonomic nervous system possess a network of efferent nerve fibers and no nerve cells.
   (e) A plexus situated at the root of a limb permits nerve fibers from different segments of the spinal cord to become rearranged so that they more easily travel to different parts of the limb.
6. The following statements concern nerve conduction:
   (a) Adequate stimulus decreases the permeability of the axolemma to Na^+ ions at the point of stimulation.
   (b) During the absolute refractory period, a very strong stimulus will excite the nerve fiber.
   (c) As the action potential moves along the axon, the entry of Na^+ ions into the axon increases and the permeability to K^+ ions decreases.
   (d) A typical action potential is about +40 mV.
   (e) In the resting unstimulated nerve fiber, the interior of the axolemma is positive to the exterior.
7. The following statements concern the propagation of a nerve impulse:
   (a) Conduction velocity is smallest in nerve fibers having a large cross-sectional diameter.
   (b) In nonmyelinated nerve fibers, the action potential occurs along the length of the fiber.
   (c) A myelinated nerve fiber can be stimulated only between the nodes of Ranvier.
   (d) Saltatory conduction occurs only in the central nervous system.
   (e) At the node of Ranvier, the action potential has no effect on the surrounding tissue fluid.
8. The following statements concern Wallerian degeneration:
   (a) Myelin breaks down into droplets that are phagocytosed by the Schwann cells.
   (b) The axon rapidly disappears.
   (c) Schwann cells round off and do not multiply.
   (d) In the central nervous system (CNS), debris is removed by the astrocyte cells.
   (e) In the peripheral nervous system (PNS), tissue macrophages play no part in the digestion of the nerve fragments.
9. The following statements concern the failure of regeneration of nerve fibers in the central nervous system (CNS):
   (a) Endoneurial tubes are present.
   (b) Oligodendrocytes have a basement membrane.
   (c) Oligodendrocytes fail to multiply and form a band fiber, as do Schwann cells in the peripheral nervous system (PNS).
   (d) Blood supply is not usually adequate.
   (e) Nerve growth factors are not present.
10. The following factor may explain the partial return of function following injury to the spinal cord:
   (a) Edema fluid persists at the site of injury.
   (b) Nonfunctional neurons never take over the function of damaged neurons.
   (c) Reduction in the number of receptor sites may occur on the postsynaptic membranes.
   (d) Some of the axons completely regenerate.
   (e) With training, the patient may use other muscles to compensate for the loss of paralyzed muscles.
11. The following statements concern receptor endings:
   (a) Rods and cones of the eyes are chemoreceptors.
   (b) Taste and smell endings are electromagnetic receptors.
   (c) Free nerve endings have no Schwann cells covering their tips.
   (d) Merkel discs are fast-adapting touch receptors.
   (e) Meissner corpuscles are absent from the skin of the palm of the hand and the sole of the foot.
12. The following statements concern receptor endings:
   (a) Pacinian corpuscles are slowly adapting mechanoreceptors.
   (b) Ruffini corpuscles are fast-adapting stretch receptors found in the dermis of hairy skin.
   (c) Each Pacinian corpuscle has no capsule but has a central core containing the nerve ending.
   (d) Annulospiral endings in skeletal muscle do not possess intrafusal muscle fibers.
   (e) The number of Meissner corpuscles considerably diminishes between birth and old age.
13. The following statements concern cutaneous receptors:
   (a) Different histologic types of receptors transmit different types of nerve impulses.

(b) The type of sensation felt is determined by the specific area of the central nervous system (CNS) to which the sensory nerve fiber passes.
(c) Transduction at the receptor is the process by which the stimulus is changed into the mechanical energy of the nerve impulse.
(d) When applied to the receptor, the stimulus brings about a change in the potential of the plasma membranes of the capsule cells and not the nerve ending.
(e) If small enough, the receptor potential will generate an action potential in the afferent sensory nerve fiber.

14. The following statements concern the function of a neuromuscular spindle:
(a) It gives rise to intermittent afferent nerve impulses.
(b) Only active muscle movement causes an increase in the rate of passage of nerve impulses in the afferent nerve fiber.
(c) The neuromuscular spindle keeps the central nervous system (CNS) informed about muscle activity.
(d) The neuromuscular spindle directly influences the control of voluntary movement.
(e) Flower-spray endings are situated mainly on the nuclear bag fibers close to the equatorial region.
15. The following statements concern the neurotendinous spindles:
(a) They are situated in tendons some distance away from the musculotendinous junction.
(b) The nerve terminates in a single club-shaped ending.
(c) Each has a fibrous capsule, loosely arranged collagen fibers, and tendon cells.
(d) Neurotendinous spindles are found only in slow-acting muscles.
(e) The neurotendinous spindle is activated by changes in muscle tension and stimulates muscle contraction.
16. The following statements concern the neuromuscular junctions in skeletal muscle:
(a) Each terminal branch of the motor nerve ends as an axon covered with fine connective tissue.
(b) Each axon lies in a groove on the surface of the muscle fiber formed by the infolding of the muscle plasma membrane (sarcolemma).
(c) Having caused depolarization of the postsynaptic membrane, acetylcholine (ACh) is reabsorbed into the axon terminal.
(d) ACh is released from the axon terminal when the nerve impulse leaves the initial segment of the axon.
(e) Schwann cells form the floor for the groove on the surface of the muscle fiber.
17. The following statements concern the neuromuscular junctions on smooth and cardiac muscle:
(a) In smooth muscle, the autonomic nerve fiber exerts control over a single muscle fiber.
(b) In smooth muscle, the wave of contraction does not pass from one muscle fiber to another.
(c) In cardiac muscle, the wave of contraction spreads slowly from one muscle fiber to another by way of desmosomes and gap junctions.
(d) Autonomic nerve fibers terminate on smooth muscle as unmyelinated fibers.
(e) At the site of the neuromuscular junction, the axon is completely surrounded by Schwann cells.
18. The following statements concern skin sensations and dermatomes:
(a) To produce a region of complete anesthesia on the trunk, at least three segments of the spinal cord have to be damaged.
(b) When contiguous spinal nerves are sectioned, the area of tactile loss is always smaller than the area of loss of painful and thermal sensations.
(c) The dermatome present on the medial side of the wrist is C5.
(d) The dermatome present on the point of the shoulder is C2.
(e) The dermatomes for the limbs run almost horizontally.
19. The following statements concern muscle reflexes:
(a) The biceps brachii tendon reflex involves the C5–C6 segments of the spinal cord.
(b) The triceps tendon reflex involves the T1 segment of the spinal cord.
(c) The patellar tendon reflex (knee jerk) involves L5–S1 segments of the spinal cord.
(d) A tumor pressing on the second, third, and fourth lumbar segments of the spinal cord is likely to interfere with the ankle jerk.
(e) The abdominal superficial reflexes involve T3–T5 segments of the spinal cord.
20. The following statements concern the dermatomes of the trunk and lower limbs:
(a) The T8 dermatome includes the skin of the umbilicus.
(b) The L5 dermatome lies over the lateral side of the knee joint.
(c) The L2 dermatome lies over the medial side of the knee joint.
(d) The S2 dermatome runs along the lateral side of the foot.
(e) The L1 dermatome lies over the inguinal ligament.
21. The following statements concern muscle innervation:
(a) A motor unit consists of the posterior root ganglion and all the neuromuscular spindles to which it is connected.
(b) In the small muscles of the hand, one nerve fiber supplies large numbers of muscle fibers.
(c) Neurotendinous spindles are innervated by nonmyelinated nerve fibers.
(d) Muscle tone is dependent on the integrity of a simple monosynaptic reflex arc.
(e) The γ motor efferent fibers innervate the extrafusal fibers of a muscle spindle.

22. The following statements concern skeletal muscle action:
    (a) When a muscle begins to contract, the larger motor units are stimulated first.
    (b) Muscle fatigue is caused by an exhaustion of the presynaptic vesicles at the neuromuscular junction.
    (c) When a prime mover contracts, the antagonistic muscles are inhibited.
    (d) When a muscle is paralyzed, it does not immediately lose its normal tone.
    (e) To paralyze a muscle completely, destroying several adjacent segments of the spinal cord or their nerve roots is not necessary.
23. The following statements concern posture:
    (a) In the standing position, the line of gravity passes through the odontoid process of the axis, behind the centers of the hip joints, and in front of the knee and ankle joints.
    (b) Posture depends on the strength of the joint ligaments and not on the degree and distribution of muscle tone.
    (c) A particular posture can often be maintained for long periods by groups of muscle fibers in a muscle contracting together continuously.
    (d) The cerebral cortex has no role in the maintenance of normal posture.
    (e) Nerve impulses arising in the eyes and ears cannot influence posture.
24. The following clinical observation on muscle activity can be made:
    (a) Muscle contracture is a condition in which the muscle contracts for a long period of time.
    (b) Muscle fasciculation is seen with chronic disease that affects sensory nerves supplying muscles.
    (c) Muscle atrophy does not take place when a limb is immobilized in a splint.
    (d) Muscle wasting can occur if only the efferent motor nerve fibers to a muscle are sectioned.
    (e) Wasting does not occur in the muscles acting on the shoulder joint in patients with painful pericapsulitis involving that joint.

Answers and Explanations to Review Questions

1. B is correct. The supporting cell of a myelinated nerve fiber in the CNS is called an oligodendrocyte. A. *Nerve tract* is the name given to a nerve fiber in the CNS. C. A node of Ranvier in peripheral nerves is where two Schwann cells terminate and the plasma membrane of the axon is exposed (see p. 72). D. Nodes of Ranvier are present in myelinated nerve fibers in the CNS. E. The major dense line of myelin consists of two inner protein layers of the plasma membrane that are fused together.
2. D is correct. The node of Ranvier is the site of nerve activity. A. The minor dense line of myelin is made up of lipid. B. Incisures of Schmidt–Lanterman represent where the dark major dense line is not formed as a result of the localized persistence of Schwann cell cytoplasm (Fig. 3-7). C. As many as 15 or more unmyelinated axons may share a single Schwann cell in the PNS. E. *Chromatolysis* is the term used to describe the changes in the arrangement of Nissl material within the cytoplasm of the nerve cell body following injury (see p. 106).
3. E is correct. A single oligodendrocyte may be associated with the myelin sheaths of as many as 60 axons (see p. 72). A. A single oligodendrocyte may be associated with several segments of myelin on a single axon. B. Incisures of Schmidt–Lanterman are present in the myelinated fibers of the CNS. C. Myelination in the CNS occurs by the growth in length of the oligodendrocytic process and the wrapping of it around the axon. D. A nonmyelinated axon in the CNS has no special relationship with the oligodendrocyte (see p.79).
4. B is correct. Spinal nerves are formed by the union of anterior and posterior nerve roots (Fig. 3-1). A. There are 31 pairs of spinal nerves. C. The posterior ramus of a spinal nerve contains both motor and sensory axons. D. The anterior root of a spinal nerve contains only motor axons. E. The posterior root ganglion of a spinal nerve contains unipolar neurons enveloped in capsular cells.
5. E is correct. A peripheral nerve plexus situated at the root of a limb permits nerve fibers from different segments of the spinal cord to become rearranged so that they more easily travel to different parts of the limb (see p. 81). A. Peripheral nerve plexuses are formed by a network of nerve fibers. B. In peripheral nerve plexuses, bundles of nerve fibers branch, but in most instances, the individual nerve fibers do not branch. C. The peripheral nerve plexuses at the roots of the limbs are formed from the anterior rami of the spinal nerves. D. The nerve plexuses of the autonomic nervous system possess a network of nerve fibers and nerve cells.
6. D is correct. In nerve conduction, a typical action potential is about +40 mV (see pp. 44–45). A. In nerve conduction, an adequate stimulus increases the permeability of the axolemma to Na^+ ions at the point of stimulation. B. During the absolute refractory period of nerve conduction, no stimulus, no matter how strong, will excite the nerve fiber. C. During nerve conduction, the action potential moves along the axon; the entry of Na^+ ions into the axon ceases, and the permeability of the plasma membrane of the axon to K^+ ions increases (see p. 44). E. In the resting unstimulated nerve fiber, the interior of the plasma membrane (axolemma) is negative to the exterior.
7. B is correct. In nonmyelinated nerve fibers, the action potential occurs along the length of the fiber.

A. Conduction velocity is greatest in nerve fibers having a large cross-sectional diameter. C. A myelinated nerve fiber can be stimulated only at the nodes of Ranvier. D. Saltatory conduction occurs in both the peripheral and central nervous systems. E. At the node of Ranvier, the action potential sets up an electrical current in the surrounding tissue fluid (see p. 72).

8. A is correct. In Wallerian degeneration, the myelin breaks down into droplets that are phagocytosed by the Schwann cells. B. In Wallerian degeneration, the axon first breaks up into fragments before it is phagocytosed by the surrounding Schwann cells (see p. 105). C. In Wallerian degeneration, the Schwann cells proliferate rapidly and become arranged in parallel cords within the persistent basement membrane. D. In Wallerian degeneration in the CNS, the debris is removed by the microglial cells. E. In Wallerian degeneration in the PNS, the tissue macrophages are very active in removing the nerve fragments.
9. C is correct. Following injury to the CNS, the oligodendrocytes fail to multiply and form a band fiber as do Schwann cells in the damaged PNS (see p. 106). A. The absence of endoneurial tubes may be important in the failure in the regeneration of injured CNS tissue (see p. 106). B. Oligodendrocytes have no basement membrane. D. Blood supply to the central nervous tissue is usually adequate. E. In the CNS, no nerve growth factors are present.
10. E is correct. The partial return of function seen in spinal cord injuries may be due in part to the patient using other muscles to compensate for the loss of the paralyzed muscles. A. Following injury to the central nervous system, the edema fluid usually subsides at the site of injury and will result in some clinical improvement (see p. 107). B. Nonfunctional neurons may take over the function of damaged neurons. C. The receptor sites on the postsynaptic membrane may increase in number and be responsible for some posttraumatic improvement. D. Evidence does not show that destroyed axons in the central nervous system completely regenerate after injury.
11. C is correct. Free nerve endings have no Schwann cells covering their tips (see p. 84). A. The rods and cones of the eyes are examples of electromagnetic receptors. B. Taste and smell receptors are chemoreceptors. D. Merkel discs are slow-adapting touch receptors. E. Meissner corpuscles are present in the skin of the palm of the hand and the sole of the foot.
12. E is correct. The number of Meissner corpuscles is considerably reduced between birth and old age. A. Pacinian corpuscles are fast-adapting mechanoreceptors. B. Ruffini corpuscles are slow-adapting stretch receptors found in the dermis of hairy skin. C. Each Pacinian corpuscle has a lamellated capsule and a central core containing the nerve ending (Figs. 3-23 and 3-24). D. Annulospiral endings in skeletal muscle do possess intrafusal muscle fibers.
13. B is correct. The type of sensation felt is determined by the specific area of the CNS to which the sensory nerve fiber passes (see p. 89). A. Although a variety of histologic types of receptors exist, their nerves only transmit the same nerve impulses. C. Transduction at the receptor is the process by which the energy of the stimulus is changed into electrochemical energy of the nerve impulse. D. When applied to the receptor, the stimulus brings about a change in the potential of the plasma membrane of the nerve ending (see p. 89). E. If large enough, the receptor potential will generate an action potential in the afferent sensory nerve fiber.
14. C is correct. The neuromuscular spindle keeps the CNS informed about muscle activity (see p. 89). A. The neuromuscular spindle gives rise to afferent nerve impulses all the time. B. When active or passive muscle movement occurs, the rate of passage of nerve impulses in the afferent nerve fibers of the neuromuscular spindles increases. D. The neuromuscular spindle indirectly influences the control of voluntary movement (see p. 90). E. Flower-spray endings are situated mainly on the nuclear chain fibers some distance from the equatorial region (Fig. 3-25).
15. C is correct. Each neurotendinous spindle has a fibrous capsule, loosely arranged collagen fibers, and tendon cells (see p. 92). A. Neurotendinous spindles are situated in tendons close to the musculotendinous junction. B. The nerve ends within the spindle by branching and terminating in club-shaped endings. D. Neurotendinous spindles are found in fast- and slow-acting muscles. E. The neurotendinous spindle is activated by changes in muscle tension and inhibits muscle contraction.
16. B is correct. At a neuromuscular junction, each axon lies in a groove on the surface of the muscle fiber formed by the infolding of the muscle plasma membrane (sarcolemma) (Fig. 3-30). A. At a neuromuscular junction, each terminal branch of the motor nerve ends as a naked axon. C. Having caused depolarization of the postsynaptic membrane, ACh is immediately hydrolyzed in the synaptic cleft by acetylcholinesterase (see p. 96). D. ACh is released from the axon terminal when the nerve impulse reaches the neuromuscular junction. E. At the neuromuscular junction, the Schwann cells form a cap or roof for the groove on the surface of the muscle fiber.
17. D is correct. Autonomic nerve fibers terminate on smooth muscle fibers as unmyelinated fibers (see p. 98). A. In neuromuscular junctions of smooth muscle, the autonomic nerve fiber exerts control over several muscle fibers (see p. 98). B. In smooth muscle, the wave of contraction passes from one muscle fiber to another by means of gap junctions. C. In cardiac muscle, the wave of contraction spreads rapidly from one muscle fiber to another by way of desmosomes and gap junctions. E. At the site of a neuromuscular junction involving smooth muscle, the axon lies in a shallow groove on the muscle surface, and the Schwann cell is retracted to expose the axolemma (Fig. 3-34).

18. A is correct. To produce a region of complete anesthesia on the trunk, at least three segments of the spinal cord have to be damaged (see p. 98). B. When contiguous spinal nerves are sectioned, the area of tactile loss is always greater than the area of loss of painful and thermal sensations. C. The dermatome present on the medial side of the wrist is C8. D. The dermatomes present on the point of the shoulder are C3–C4. E. Limb dermatomes run almost vertically (see Figs. 3-36 and 3-37).
19. A is correct. The biceps brachii tendon reflex involves C5–C6 segments of the spinal cord (see p. 100). B. The triceps tendon reflex involves the C6–C7 and C8 segments of the spinal cord. C. The patellar tendon reflex (knee jerk) involves the L2–L4 segments of the spinal cord. D. A tumor pressing on the S1–S2 segments of the spinal cord is likely to interfere with the ankle jerk. E. The abdominal superficial reflexes involve T6–T12 segments of the spinal cord.
20. E is correct. The L1 dermatome lies over the inguinal ligament (see Fig. 3-36). A. The T10 dermatome includes the skin of the umbilicus; the T8 dermatome involves the skin between the xiphoid process and the umbilicus. B. The L5 dermatome lies over the anterior and lateral surfaces of the leg below the knee. C. The L2 dermatome lies over the anterior and lateral surfaces of the thigh. D. The S2 dermatome extends down the middle of the posterior surface of the thigh and leg (see Fig. 3-37).
21. D is correct. Muscle tone is dependent on the integrity of a simple reflex arc (see p. 101). A. A motor unit consists of a motor neuron in the anterior gray column (horn) of the spinal cord and all the muscle fibers it supplies (Fig. 3-39). B. In the small muscles of the hand, one nerve fiber supplies only a few muscle fibers. C. Neurotendinous spindles are innervated by myelinated nerve fibers. E. The γ motor efferent fibers innervate the intrafusal fibers of a muscle spindle.
22. C is correct. In voluntary muscle movement, when a prime mover contracts, the antagonistic muscles are inhibited (see p. 92). A. When a muscle begins to contract, the smaller motor units are stimulated first. B. Muscle fatigue is caused by reduced adenosine triphosphate within the muscle fibers. D. When a muscle is paralyzed, it immediately loses its normal tone (see p. 101). E. To paralyze a muscle completely, destroying several adjacent segments of the spinal cord or their nerve roots is usually necessary.
23. A is correct. In the standing position, the line of gravity passes through the odontoid process of the axis, behind the centers of the hip joints, and in front of the knee and ankle joints (see p. 102). B. Posture depends on the degree and distribution of muscle tone. C. A particular posture can often be maintained for long periods by different groups of muscle fibers in a muscle contracting in relays. D. The cerebral cortex makes an important contribution to the maintenance of normal posture (see p. 102). E. Nerve impulses arising in the eyes and the ears can greatly influence posture.
24. D is correct. Muscle wasting can occur if only the efferent motor nerve fibers to a muscle are sectioned (see p. 109). A. Muscle contracture is a condition in which the muscle contracts and undergoes permanent shortening; it occurs frequently in muscles that normally oppose paralyzed muscles. B. Muscle fasciculation is seen with chronic disease that affects anterior horn cells or the motor nuclei of cranial nerves. C. Muscle atrophy takes place when a limb is immobilized in a splint. E. Wasting occurs in the muscles acting on the shoulder joint in patients with painful pericapsulitis involving that joint.

4 Spinal Cord and Ascending, Descending, and Intersegmental Tracts

CHAPTER OBJECTIVES

- To learn how injuries to the spinal cord can occur
- To understand the position of the main nervous pathways and nerve cell groups in the spinal cord as well as be able to correlate radiologic evidence of bone injury with segmental levels of the spinal cord and neurologic deficits
- To review the basic structure of the delicate spinal cord and the positions and functions of the various ascending and descending tracts that lie within it
- To make simple line drawings of each of the ascending and descending tracts, showing their cells of origin, their course through the central nervous system, and their destination

A 35-year-old man is galloping his horse when he attempts to jump over a farm gate. The horse refuses to jump, and he is thrown to the ground. His head strikes a log, and his head and neck are excessively flexed. On initial evaluation in the emergency department after he regains consciousness, he is found to have signs and symptoms of severe neurologic deficits in the upper and lower extremities. A lateral radiograph of the cervical region of the spine shows fragmentation of the body of the fourth cervical vertebra with backward displacement of a large bony fragment on the left side.

After stabilization of the vertebral column by using skeletal traction to prevent further neurologic damage, a complete examination reveals that the patient has signs and symptoms indicating incomplete hemisection of the spinal cord on the left side.

Any medical personnel involved in the evaluation and treatment of a patient with spinal cord injuries must know the structure of the spinal cord and the arrangement and functions of the various nerve tracts passing up and down this vital conduit in the central nervous system.

Because of the devastating nature of spinal cord injuries and the prolonged disability that results, all concerned with the care of such patients must be trained to prevent any additional cord injury and provide the best chance for recovery. All medical personnel must have a clear picture of the extent of the cord lesion and the possible expectations for the return of function.

Spinal cord injuries are common and can occur as a result of automobile and motorcycle accidents, falls, sports injuries, and gunshot wounds. Spinal cord and spinal nerve damage may also be associated with vertebral fractures; vertebral infections; vertebral tumors, both primary and secondary; and herniated intervertebral discs. The student must learn the course and connections of the various tracts within the spinal cord in order to be able to diagnose and understand the treatment of cord injuries. Particular attention should be paid as to whether a specific tract crosses the midline to the opposite side of the central nervous system (CNS) or remains on the same side. If the tract does cross the midline, the level of the crossover is important.

The assessment of neurologic damage requires not only an understanding of the main nervous pathways within the spinal cord but an ability to correlate radiologic evidence of bone injury with segmental levels of the spinal cord. The close relationship of the spinal cord to the bony vertebral column necessitates a brief review of the vertebral column before the spinal cord is considered.

BRIEF REVIEW OF THE VERTEBRAL COLUMN

The vertebral column is the central bony pillar of the body. It supports the skull, pectoral girdle, upper limbs, and thoracic cage and, by way of the pelvic girdle, transmits body weight to the lower limbs. Within its cavity lie the spinal cord, spinal nerve roots, and the covering meninges, to which the vertebral column gives great protection.

Vertebral Column Composition

The vertebral column (Figs. 4-1 and 4-2) is composed of 33 vertebrae—7 cervical, 12 thoracic, 5 lumbar, 5 sacral (fused to form the sacrum), and 4 coccygeal (the lower 3 are commonly fused). Because it is segmented and made up of vertebrae, joints, and pads of fibrocartilage called **intervertebral discs**, it is a flexible structure. The intervertebral discs form about a quarter of the length of the column.

Vertebra General Characteristics

Although vertebrae show regional differences, they all possess a common pattern (Fig. 4-2B). A **typical vertebra** consists of a rounded **body** anteriorly and a **vertebral arch** posteriorly. These enclose a space called the **vertebral foramen**, through which run the spinal cord and its coverings. The vertebral arch consists of a pair of cylindrical **pedicles**, which form the sides of the arch, and a pair of flattened **laminae**, which complete the arch posteriorly.

The vertebral arch gives rise to seven processes: one spinous, two transverse, and four articular.

The **spinous process**, or **spine**, is directed posteriorly from the junction of the two laminae. The transverse processes are directed laterally from the junction of the laminae and the pedicles. Both the spinous and transverse processes serve as levers and receive attachments of muscles and ligaments.

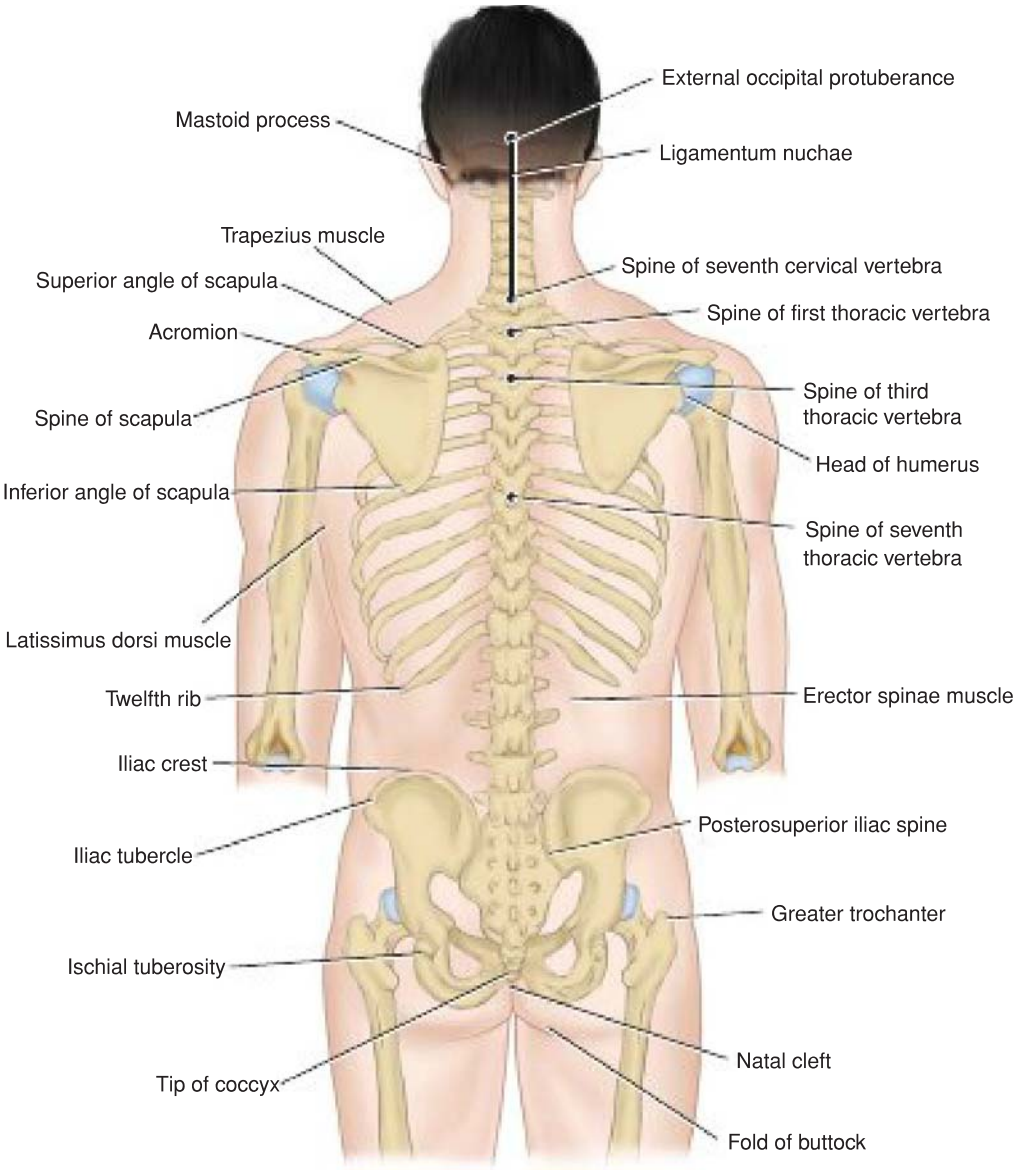

Figure 4-1 Posterior view of the skeleton showing the vertebral column. The surface marking of the external occipital protuberance of the skull, the ligamentum nuchae (*solid black line*) and some important palpable spines (*solid dots*) are also shown.

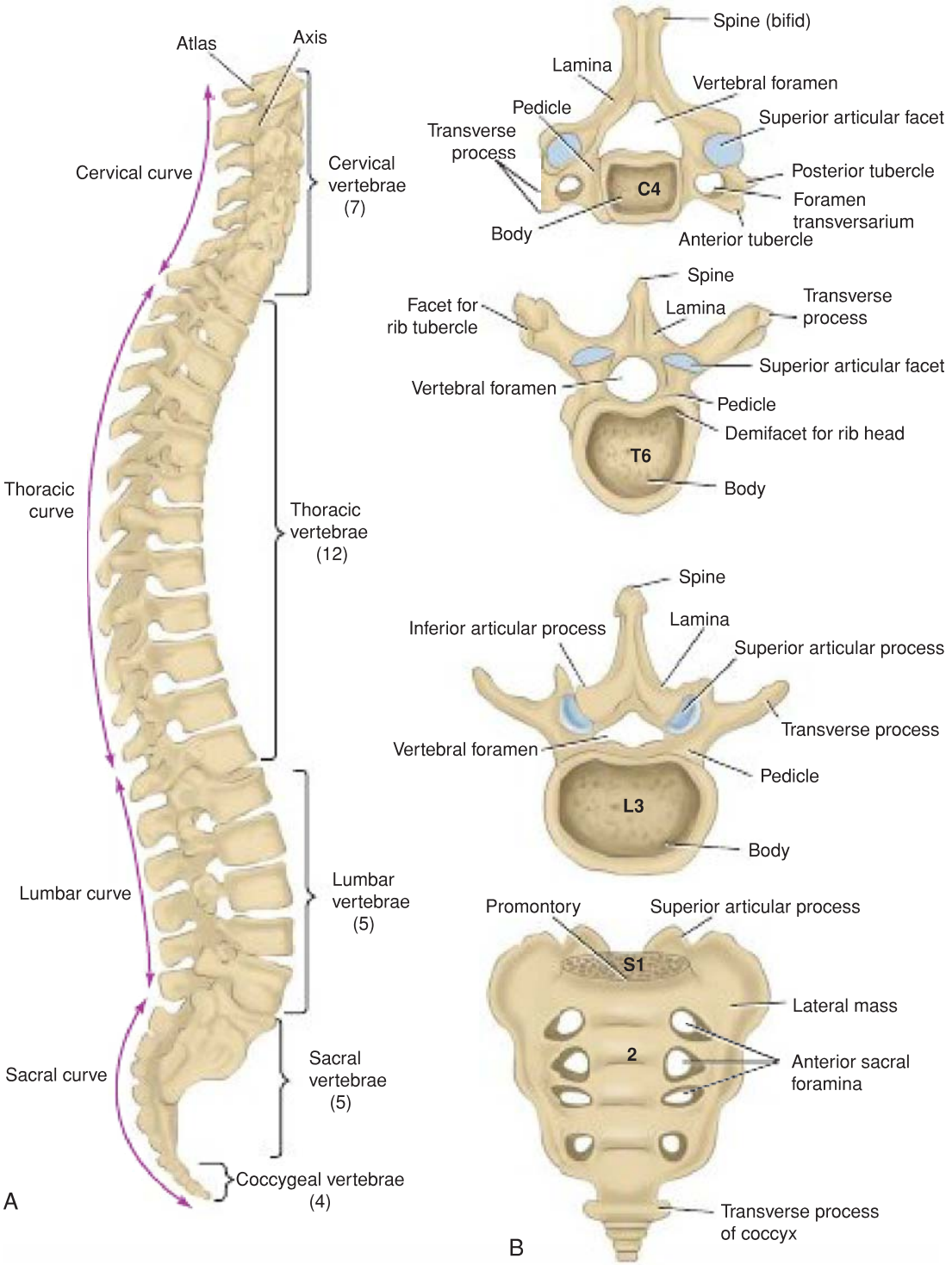

Figure 4-2 **A:** Lateral view of the vertebral column. **B:** General features of different kinds of vertebrae.

The **articular processes** are vertically arranged and consist of two superior and two inferior processes. They arise from the junction of the laminae and the pedicles. The two superior articular processes of one vertebral arch articulate with the two inferior articular processes of the arch above, forming two synovial joints.

The pedicles are notched on their upper and lower borders, forming the **superior** and **inferior vertebral notches**. On each side, the superior notch of one vertebra and the inferior notch of an adjacent vertebra together form an **intervertebral foramen**. These foramina, in an articulated skeleton, serve to transmit

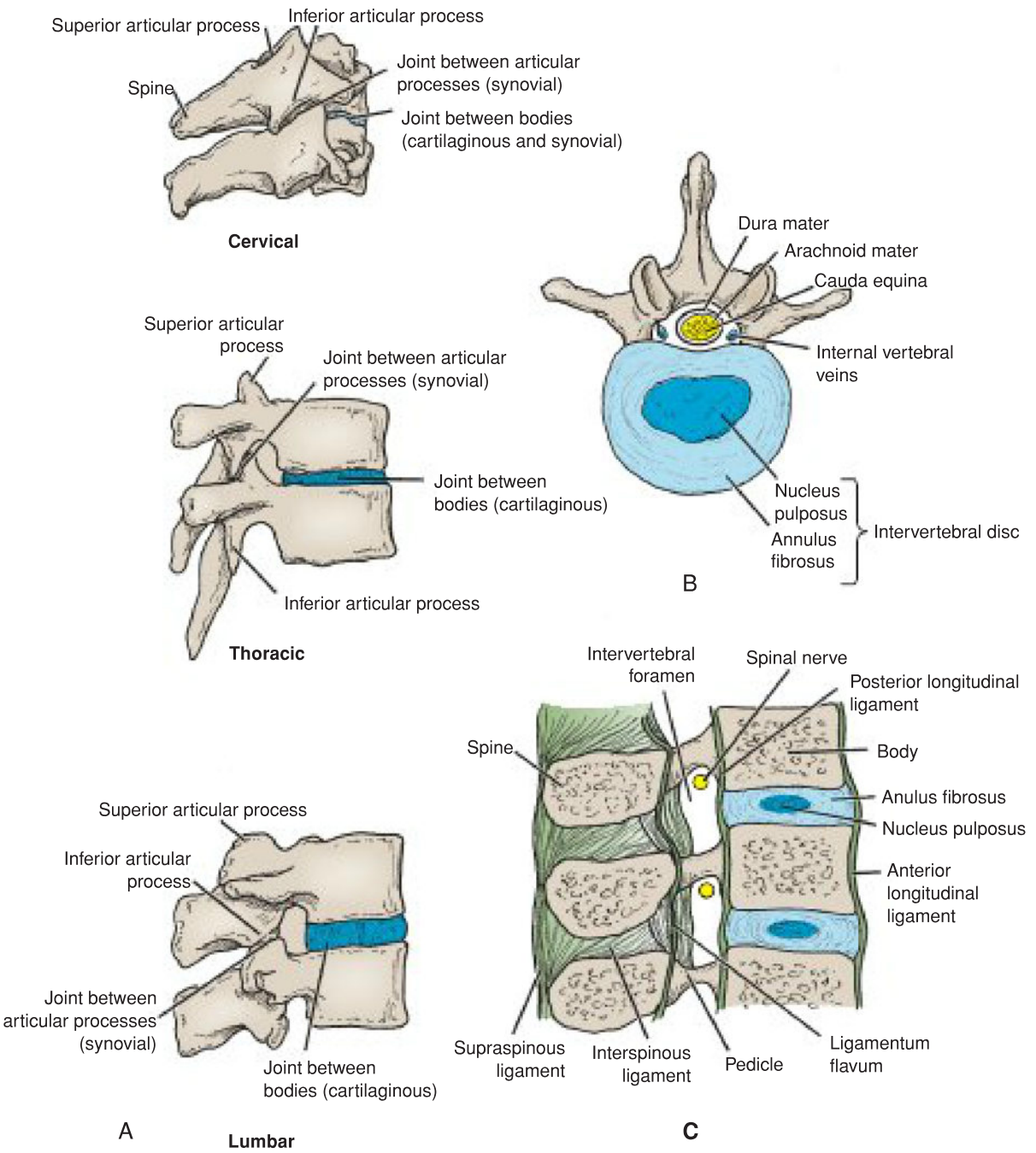

Figure 4-3 **A:** Joints in the cervical, thoracic, and lumbar regions of the vertebral column. **B:** Third lumbar vertebra seen from above showing the relationship between intervertebral disc and cauda equina. **C:** Lumbar vertebrae in sagittal section showing vertebral ligament relationships.

the spinal nerves and blood vessels. The anterior and posterior nerve roots of a spinal nerve unite within these foramina with their coverings of dura to form the segmental spinal nerves.

Vertebral Column Joints

Below the axis, the vertebrae articulate with each other by means of cartilaginous joints between their bodies and by synovial joints between their articular processes.

Joints Between Two Vertebral Bodies

Sandwiched between the vertebral bodies is an intervertebral disc of fibrocartilage (Fig. 4-3).

Intervertebral Discs

The intervertebral discs are thickest in the cervical and lumbar regions, where the movements of the vertebral column are greatest. They serve as shock absorbers when the load on the vertebral column is suddenly

increased. Unfortunately, their resilience is gradually lost with advancing age.

Each disc consists of a peripheral part, the annulus fibrosus, and a central part, the nucleus pulposus (Fig. 4-3B,C). The **annulus fibrosus** is composed of fibrocartilage, which is strongly attached to the vertebral bodies and the anterior and posterior longitudinal ligaments of the vertebral column.

The **nucleus pulposus** in the young is an ovoid mass of gelatinous material. It is normally under pressure and situated slightly nearer to the posterior than to the anterior margin of the disc. The upper and lower surfaces of the bodies of adjacent vertebrae that abut onto the disc are covered with thin plates of hyaline cartilage.

The semifluid nature of the nucleus pulposus allows it to change shape and permits one vertebra to rock forward or backward on another. A sudden increase in the compression load on the vertebral column flattens the nucleus pulposus, which is accommodated by the resilience of the surrounding annulus fibrosus. Sometimes, the outward thrust is too great for the annulus fibrosus and it ruptures, allowing the nucleus pulposus to herniate and protrude into the vertebral canal, where it may press on the spinal nerve roots, the spinal nerve, or even the spinal cord.

With advancing age, the nucleus pulposus becomes smaller and is replaced by fibrocartilage. The collagen fibers of the annulus degenerate, and, as a result, the annulus cannot always contain the nucleus pulposus under stress. In old age, the discs are thin and less elastic, and distinguishing the nucleus from the annulus is no longer possible.

Ligaments

The **anterior** and **posterior longitudinal ligaments** run as continuous bands down the anterior and posterior surfaces of the vertebral column from the skull to the sacrum (Fig. 4-3C). The anterior ligament is wide and is strongly attached to the front and sides of the vertebral bodies and to the intervertebral discs. The posterior ligament is weak and narrow and is attached to the posterior borders of the discs.

Joints Between Two Vertebral Arches

The joints between two vertebral arches consist of synovial joints between the superior and inferior articular processes of adjacent vertebrae (Fig. 4-3A).

Ligaments

Refer to Figure 4-3C.

- The **supraspinous ligament** runs between the tips of adjacent spines.
- The **interspinous ligament** connects adjacent spines.
- The **intertransverse ligaments** run between adjacent transverse processes.
- The **ligamentum flavum** connects the laminae of adjacent vertebrae.

In the cervical region, the supraspinous and interspinous ligaments are greatly thickened to form the strong **ligamentum nuchae**.

Vertebral Joint Nerve Supply

The joints between the vertebral bodies are innervated by the small meningeal branches of each spinal nerve (Fig. 4-4). The joints between the articular processes are innervated by branches from the posterior rami of the spinal nerves; the joints of any particular level receive nerve fibers from two adjacent spinal nerves.

The atlanto-occipital joints and the atlanto-axial joints should be reviewed in a textbook of gross anatomy.

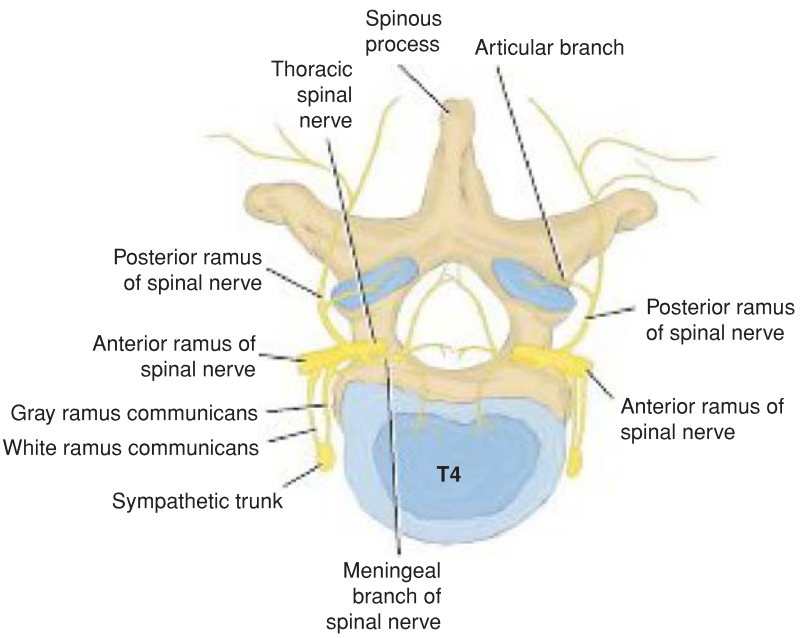

Figure 4-4 The innervation of vertebral joints. At any particular vertebral level, the joints receive nerve fibers from two adjacent spinal nerves.

SPINAL CORD

The spinal cord is roughly cylindrical in shape. It begins superiorly at the foramen magnum in the skull, where it is continuous with the **medulla oblongata** of the brain, and it terminates inferiorly in the adult at the level of the **lower border of the first lumbar vertebra**. In the young child, it is relatively longer and usually ends at the upper border of the third lumbar vertebra. Thus, it occupies the upper two thirds of the **vertebral canal** of the vertebral column and is surrounded by the three meninges, the **dura mater**, the arachnoid mater, and the **pia mater**. Further protection is provided by the **cerebrospinal fluid** (**CSF**), which surrounds the spinal cord in the **subarachnoid space**.

In the cervical region, where it gives origin to the brachial plexus, and in the lower thoracic and lumbar regions, where it gives origin to the lumbosacral plexus, the spinal cord is fusiformly enlarged; the enlargements are referred to as the **cervical** and **lumbar enlargements** (Fig. 4-5). Inferiorly, the spinal cord tapers off into the **conus medullaris**, from the apex of which a prolongation of the pia mater, the **filum terminale**, descends to attach to the posterior

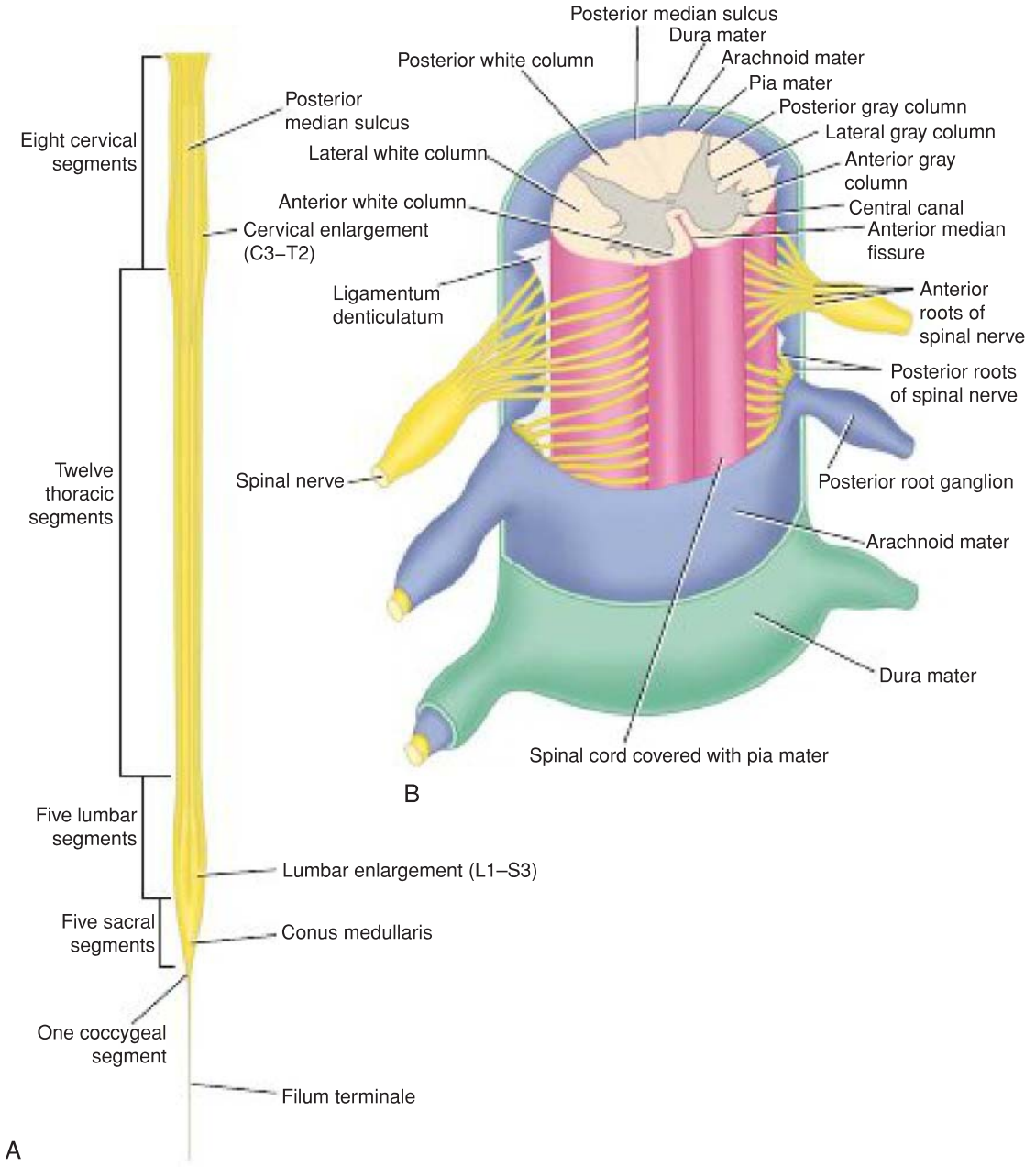

Figure 4-5 Spinal cord. **A:** Posterior view, showing cervical and lumbar enlargements. **B:** Three segments of the spinal cord showing the coverings of dura mater, arachnoid mater, and pia mater.

surface of the coccyx. The cord possesses a deep longitudinal fissure called the **anterior median fissure** in the midline anteriorly and a shallow furrow called the **posterior median sulcus** on the posterior surface (Fig. 4-5B).

Along the entire length of the spinal cord, 31 pairs of spinal nerves are attached by the **anterior** or **motor roots** and the **posterior** or **sensory roots** (Fig. 4-5B). Each root is attached to the cord by a series of rootlets, which extend the whole length of the corresponding segment of the cord. Each posterior nerve root possesses a **posterior root ganglion**, the cells of which give rise to peripheral and central nerve fibers.

Spinal Cord Structure

The spinal cord is composed of an inner core of gray matter, which is surrounded by an outer covering of white matter (Fig. 4-6); there is no indication that the cord is segmented.

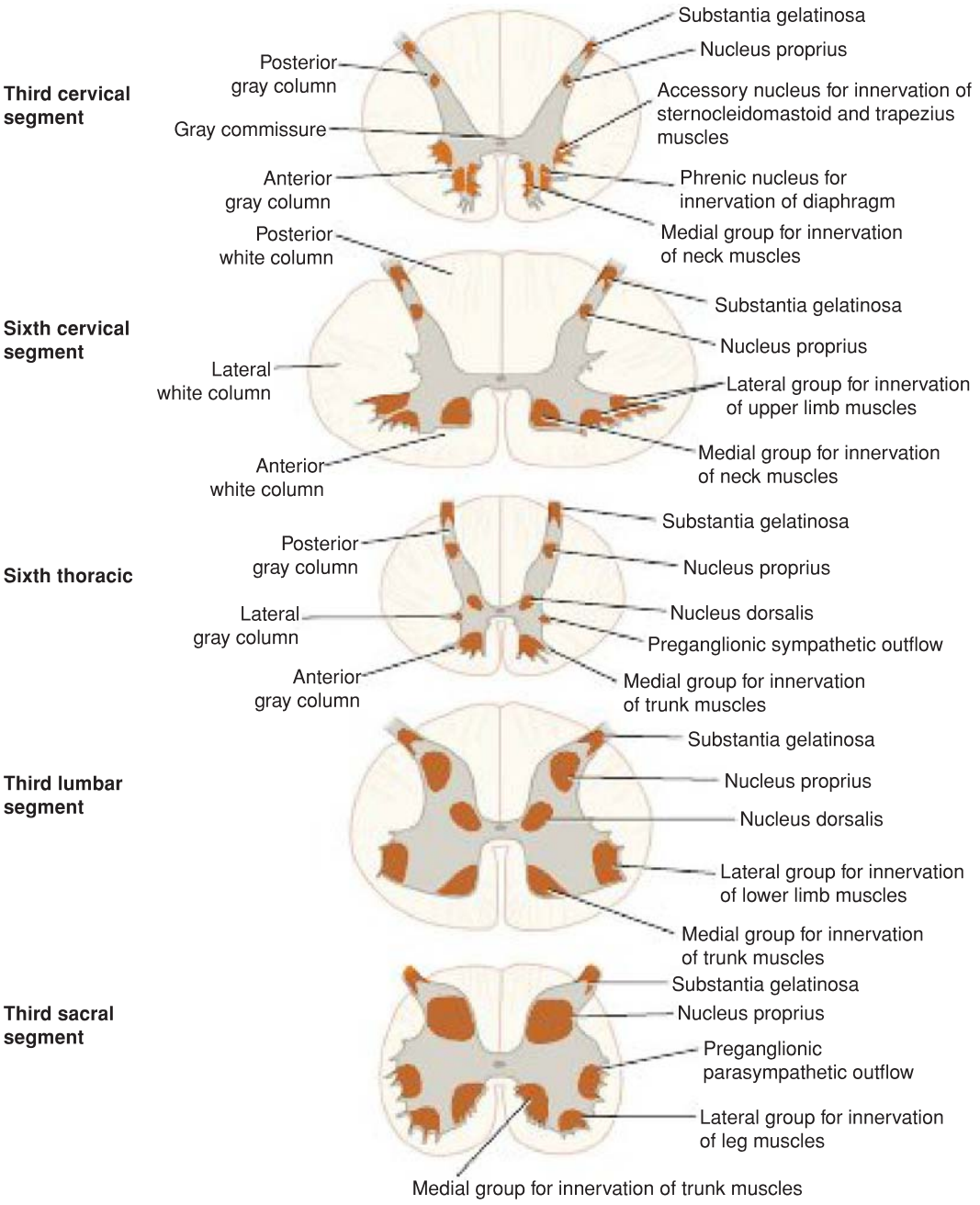

Figure 4-6 Transverse sections of the spinal cord at different levels showing the arrangement of the gray matter and white matter.

Table 4-1 Comparison of Structural Details in Different Regions of the Spinal Cord[a]

Region	Shape	White Matter	Gray Matter		
			Anterior Gray Column	Posterior Gray Column	Lateral Gray Column
Cervical	Oval	Fasciculus cuneatus and fasciculus gracilis present	Medial group of cells for neck muscles; central group of cells for accessory nucleus (C1–C5) and phrenic nucleus (C3–C5); lateral group of cells for upper limb muscles	Substantia gelatinosa present, continuous with Sp.N. of cranial nerve V at level C2; nucleus proprius present; nucleus dorsalis (Clarke column) absent	Absent
Thoracic	Round	Fasciculus cuneatus (T1–T6) and fasciculus gracilis present	Medial group of cells for trunk muscles	Substantia gelatinosa, nucleus proprius, and visceral afferent nucleus present.	Present; gives rise to preganglionic sympathetic fibers
Lumbar	Round to oval	Fasciculus cuneatus absent; fasciculus gracilis present	Medial group of cells for lower limb muscles; central group of cells for lumbosacral nerve	Substantia gelatinosa, nucleus proprius, nucleus dorsalis (Clarke column) at L1–L4, and visceral afferent nucleus present	Present (L1–L2 [3]); gives rise to preganglionic sympathetic fibers
Sacral	Round	Small amount; fasciculus cuneatus absent; fasciculus gracilis present	Medial group of cells for lower limb and perineal muscles	Substantia gelatinosa and nucleus proprius present	Absent; group of cells present at S2–S4, for parasympathetic outflow

[a]The information in this table is useful for identifying the specific level of the spinal cord from which a section has been taken.

For a comparison of the structural details in different regions of the spinal cord, see Table 4-1.

Gray Matter

On cross section, the gray matter is seen as an H-shaped pillar with **anterior** and **posterior gray columns**, or **horns**, united by a thin **gray commissure** containing the small **central canal**. A small **lateral gray column** or **horn** is present in the thoracic and upper lumbar segments of the cord. The amount of gray matter present at any given level of the spinal cord is related to the amount of muscle innervated at that level. Thus, its size is greatest within the cervical and lumbosacral enlargements of the cord, which innervate the muscles of the upper and lower limbs, respectively (Figs. 4-7 to 4-10; also see Fig. 4-6).

Structure

As in other CNS regions, spinal cord gray matter consists of a mixture of nerve cells and their processes, neuroglia, and blood vessels. The nerve cells are multipolar, and the neuroglia forms an intricate network around the nerve cell bodies and their neurites.

ANTERIOR GRAY COLUMN NERVE CELL GROUPS

Most nerve cells are large and multipolar, and their axons pass out in the anterior roots of the spinal nerves as α **efferents,** which innervate skeletal muscles. The smaller nerve cells are also multipolar, and the axons of many of these pass out in the anterior roots of the spinal nerves as γ **efferents**, which innervate the intrafusal muscle fibers of neuromuscular spindles.

For practical purposes, the nerve cells of the anterior gray column can be divided into three basic groups or columns: medial, central, and lateral (Fig. 4-6).

The medial group is present in most segments of the spinal cord and is responsible for innervating the skeletal muscles of the neck and trunk, including the intercostal and abdominal musculature.

The central group is the smallest and is present in some cervical and lumbosacral segments. In the cervical part of the cord, some of these nerve cells (segments C3–C5) specifically innervate the diaphragm and are collectively referred to as the phrenic nucleus (Fig. 4-7). In the upper five or six cervical segments, some of the nerve cells innervate the sternocleidomastoid and trapezius muscles and are referred to as the **accessory nucleus**. The axons of these cells form the spinal part of the accessory nerve. The **lumbosacral nucleus** present in the second lumbar down to the first sacral segment of the cord is made up of nerve cells whose axons have an unknown distribution.

The lateral group is present in the cervical and lumbosacral segments of the cord and is responsible for

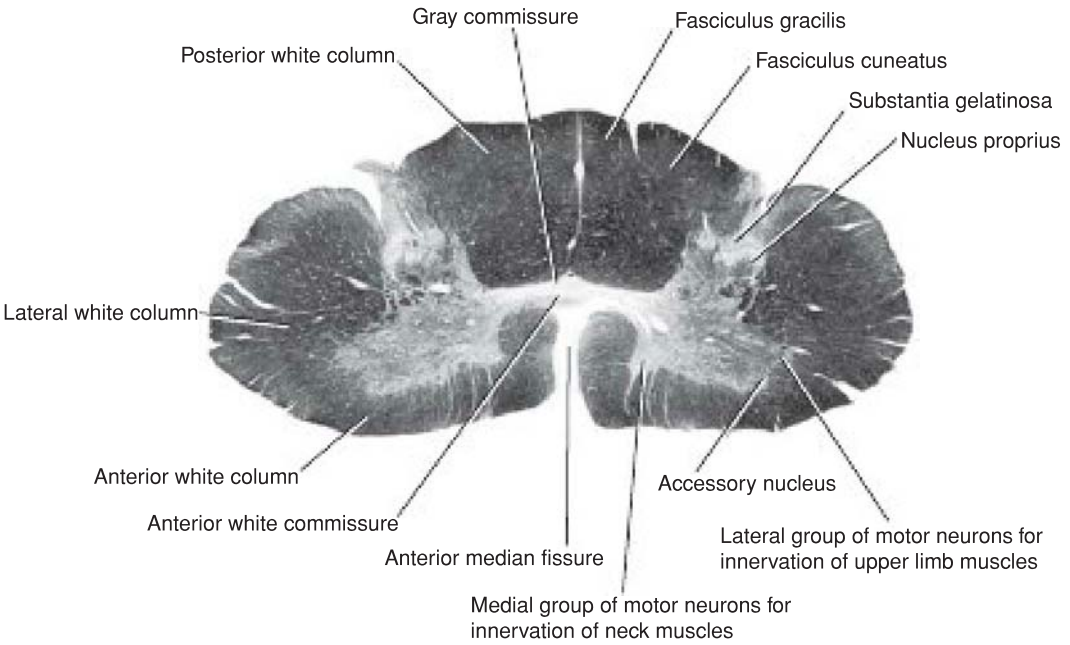

Figure 4-7 Transverse section of the spinal cord at the level of the fifth cervical segment. (Weigert stain.)

innervating the skeletal muscles of the limbs (Figs. 4-6, 4-7, 4-9, and 4-10).

POSTERIOR GRAY COLUMN NERVE CELL GROUPS

Two of the four nerve cell groups of the posterior gray column extend throughout the length of the cord; the other two are restricted to the thoracic and lumbar segments.

The **substantia gelatinosa group** is situated at the apex of the posterior gray column throughout the length of the spinal cord (Figs. 4-6 to 4-10). It is largely composed of Golgi type II neurons and receives afferent fibers concerned with pain, temperature, and touch from the posterior root. Furthermore, it receives input from descending fibers from supraspinal levels. Pain and temperature inputs are thought to be modified by excitatory or inhibitory information from other sensory inputs and by information from the cerebral cortex.

The **nucleus proprius** is a group of large nerve cells situated anterior to the substantia gelatinosa throughout the spinal cord (Figs. 4-6 to 4-10). This nucleus constitutes the main bulk of cells present in the posterior

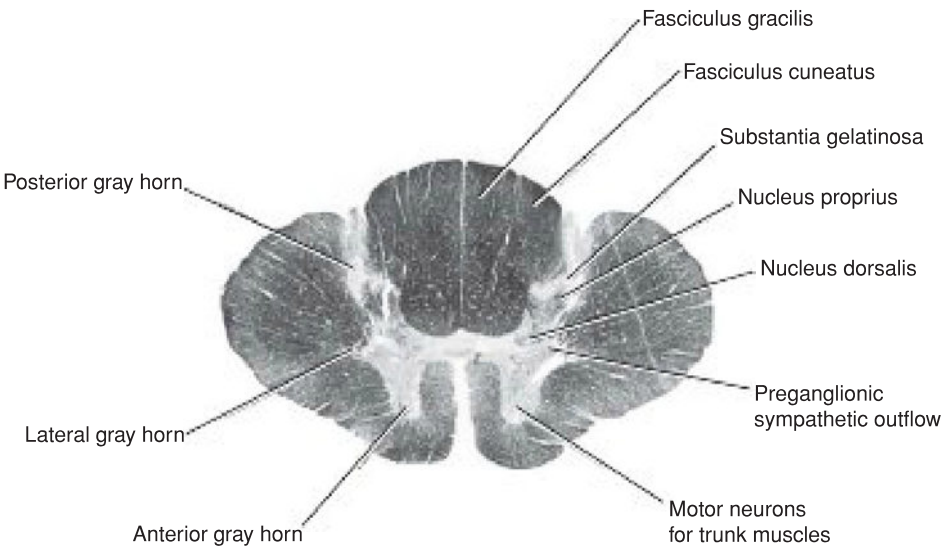

Figure 4-8 Transverse section of the spinal cord at the level of the second thoracic segment. (Weigert stain.)

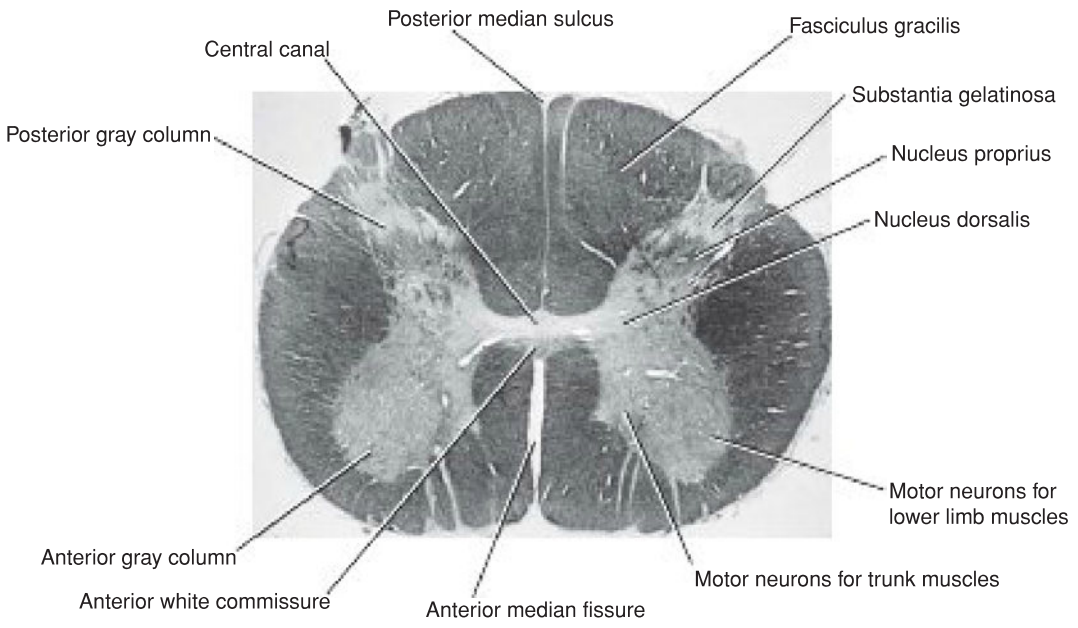

Figure 4-9 Transverse section of the spinal cord at the level of the fourth lumbar segment. (Weigert stain.)

gray column and receives fibers from the posterior white column that are associated with the senses of position and movement (proprioception), two-point discrimination, and vibration.

The **nucleus dorsalis** (**Clarke column**) is a group of nerve cells situated at the base of the posterior gray column and extending from the eighth cervical segment caudally to the third or fourth lumbar segment (Figs. 4-6 to 4-9). Most of the cells are comparatively large and are associated with proprioceptive endings (neuromuscular spindles and tendon spindles).

The **visceral afferent nucleus** is a group of nerve cells of medium size situated lateral to the nucleus dorsalis; it extends from the first thoracic to

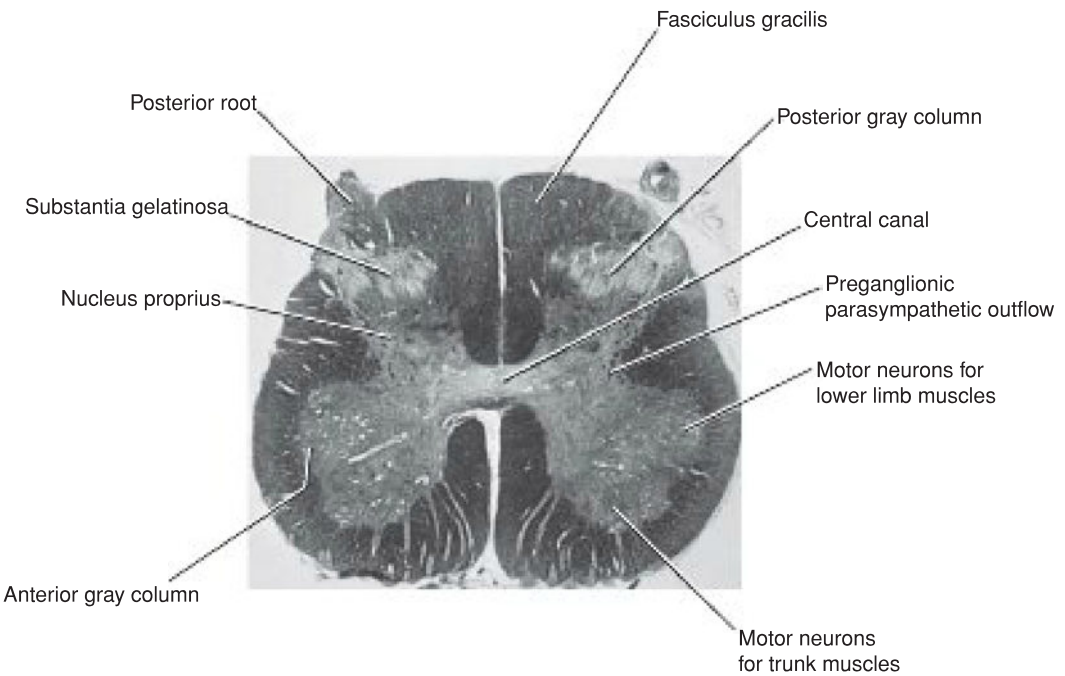

Figure 4-10 Transverse section of the spinal cord at the level of the second sacral segment. (Weigert stain.)

the third lumbar segment of the spinal cord. It is believed to be associated with receiving visceral afferent information.

LATERAL GRAY COLUMN NERVE CELL GROUPS

The intermediolateral group of cells form the small lateral gray column, which extends from the first thoracic to the second or third lumbar segment of the spinal cord (Figs. 4-6 and 4-8). The cells are relatively small and give rise to preganglionic sympathetic fibers.

A similar group of cells found in the second, third, and fourth sacral segments of the spinal cord give rise to preganglionic parasympathetic fibers (Figs. 4-6 and 4-10).

GRAY COMMISSURE AND CENTRAL CANAL

In transverse sections of the spinal cord, the anterior and posterior gray columns on each side are connected by a transverse **gray commissure**; the gray matter resembles the letter H (Figs. 4-6 to 4-10). The **central canal** is situated in the center of the gray commissure. The part of the gray commissure that is situated posterior to the central canal is the **posterior gray commissure**; the anterior part is the **anterior gray commissure**.

The central canal is present throughout the spinal cord. Superiorly, it is continuous with the central canal of the caudal half of the medulla oblongata; above this, it opens into the cavity of the fourth ventricle. Inferiorly in the conus medullaris, it expands into the fusiform **terminal ventricle** and terminates below within the root of the filum terminale. It is filled with CSF and is lined with ciliated columnar epithelium, the **ependyma**. Thus, the central canal is closed inferiorly and opens superiorly into the fourth ventricle.

White Matter

The white matter, for purposes of description, may be divided into **anterior**, **lateral**, and **posterior white columns** or **funiculi** (Figs. 4-5 to 4-10). The anterior column on each side lies between the midline and the point of emergence of the anterior nerve roots; the lateral column lies between the emergence of the anterior nerve roots and the entry of the posterior nerve roots; the posterior column lies between the entry of the posterior nerve roots and the midline.

Structure

As in other CNS regions, the spinal cord white matter consists of a mixture of nerve fibers, neuroglia, and blood vessels. It surrounds the gray matter, and its white color is due to the high proportion of myelinated nerve fibers.

NERVE FIBER TRACT ARRANGEMENT

The arrangement of the nerve fiber tracts within the spinal cord has been deduced as the result of animal experimentation and study of the human spinal cord for degenerative nerve fibers resulting from injury or disease. Although some nerve tracts are concentrated in certain areas of the white matter, considerable overlap is present. For purposes of description, the spinal tracts are divided into ascending, descending, and intersegmental tracts, and their relative positions in the white matter are described below. A simplified diagram, showing the general arrangement of the major tracts, is shown in Figure 4-11.

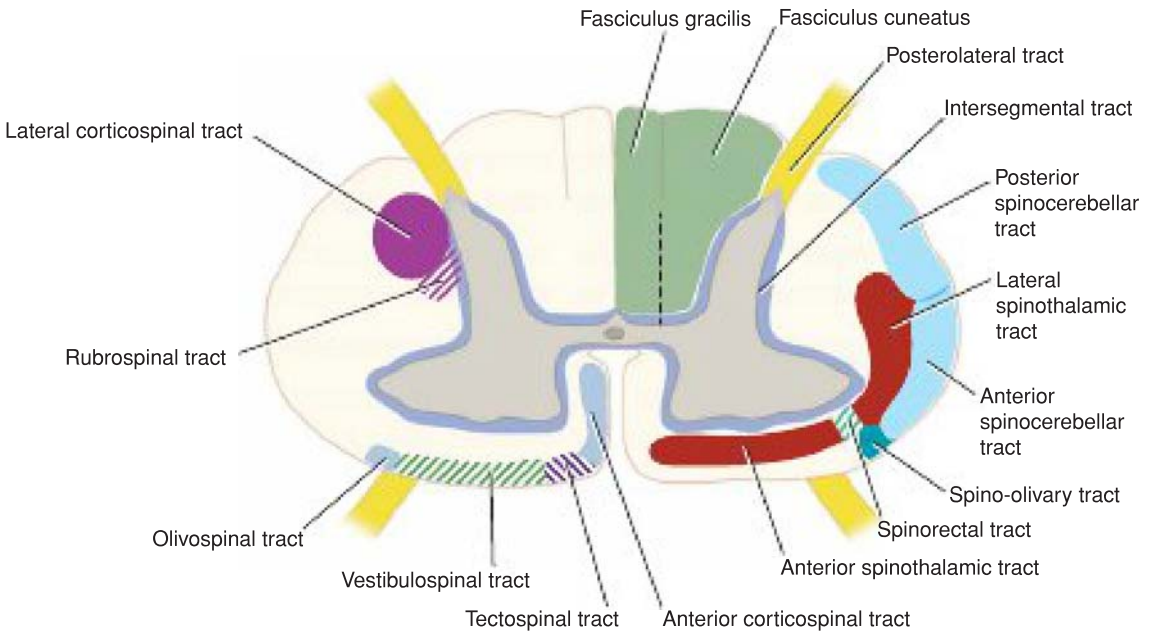

Figure 4-11 Transverse section of the spinal cord at the midcervical level showing the general arrangement of the ascending tracts on the right and the descending tracts on the left.

ASCENDING TRACTS

On entering the spinal cord, the sensory nerve fibers of different sizes and functions are sorted out and segregated into nerve bundles or **tracts** in the white matter (Fig. 4-12; also see Fig. 4-11). Some of the nerve fibers serve to link different segments of the spinal cord, while others ascend from the spinal cord to higher centers and thus connect the spinal cord with the brain. These bundles of the ascending fibers are referred to as the **ascending tracts**.

The ascending tracts conduct two types of afferent information, which may or may not reach consciousness. **Exteroceptive** information originates from outside the body, such as pain, temperature, and touch. **Proprioceptive** information originates from inside the body, for example, from muscles and joints.

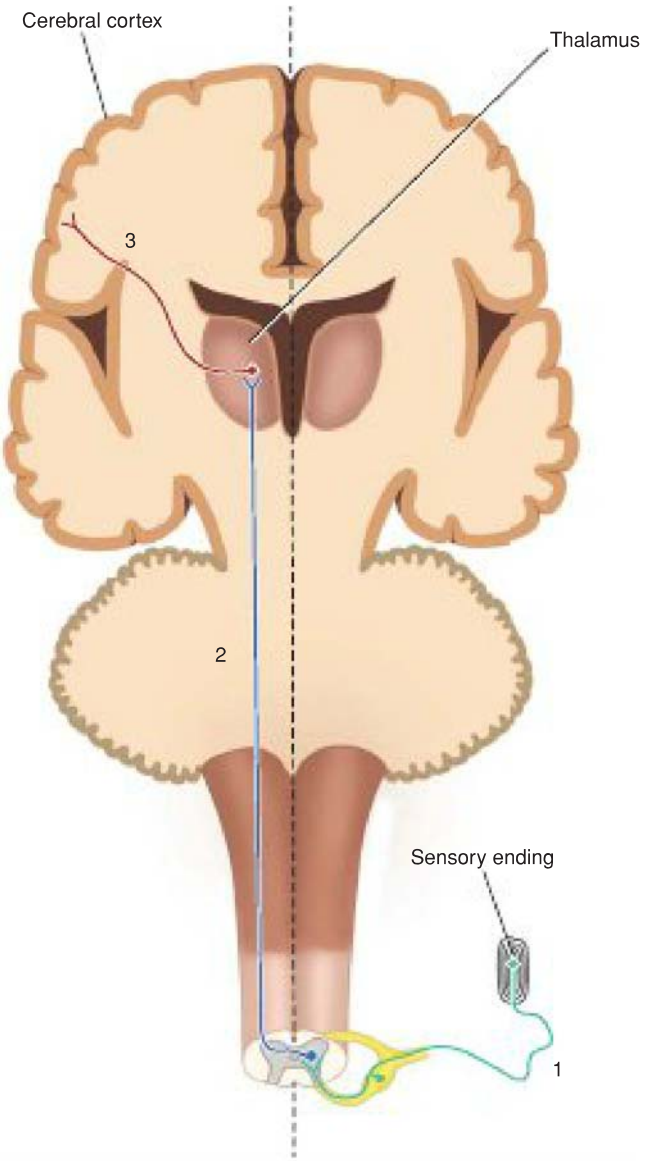

Figure 4-12 Simplest form of the ascending sensory pathway from the sensory nerve ending to the cerebral cortex. Note the three neurons involved.

Anatomical Organization

General information from the peripheral sensory endings is conducted through the nervous system by a series of neurons. In its simplest form, the ascending pathway to consciousness consists of three neurons (Fig. 4-12). The first neuron, the **first-order neuron**, has its cell body in the **posterior root ganglion** of the spinal nerve. A peripheral process connects with a sensory receptor ending, whereas a central process enters the spinal cord through the posterior root to synapse on the second-order neuron. The **second-order neuron** gives rise to an axon that decussates (crosses to the opposite side) and ascends to a higher level of the CNS, where it synapses with the **third-order neuron**. The third-order neuron is usually in the thalamus and gives rise to a projection fiber that passes to a sensory region of the cerebral cortex. This three-neuron chain is the most common arrangement, but some afferent pathways use more or fewer neurons. Many of the neurons in the ascending pathways branch and give a major input into the reticular formation, which, in turn, activates the cerebral cortex, maintaining wakefulness. Other branches pass to motor neurons and participate in reflex muscular activity.

Functions

Painful and thermal sensations ascend in the lateral spinothalamic tract; light (crude) touch and pressure ascend in the anterior spinothalamic tract (Fig. 4-13). Discriminative touch—that is, the ability to localize accurately the area of the body touched and also to be aware that two points are touched simultaneously, even though they are close together (two-point discrimination)—ascends in the posterior white columns. Also ascending in the posterior white columns is information from muscles and joints pertaining to movement and position of different parts of the body. In addition, vibratory sensations ascend in the posterior white column. Unconscious information from muscles, joints, the skin, and subcutaneous tissue reaches the cerebellum by way of the anterior and posterior spinocerebellar tracts and by the cuneocerebellar tract. Pain, thermal, and tactile information are passed to the superior colliculus of the midbrain through the spinotectal tract for the purpose of spinovisual reflexes. The spinoreticular tract provides a pathway from the muscles, joints, and skin to the reticular formation, while the spino-olivary tract provides an indirect pathway for further afferent information to reach the cerebellum.

Pain and Temperature Pathways

The pain and thermal receptors in the skin and other tissues are free nerve endings. The pain impulses are transmitted to the spinal cord in fast-conducting

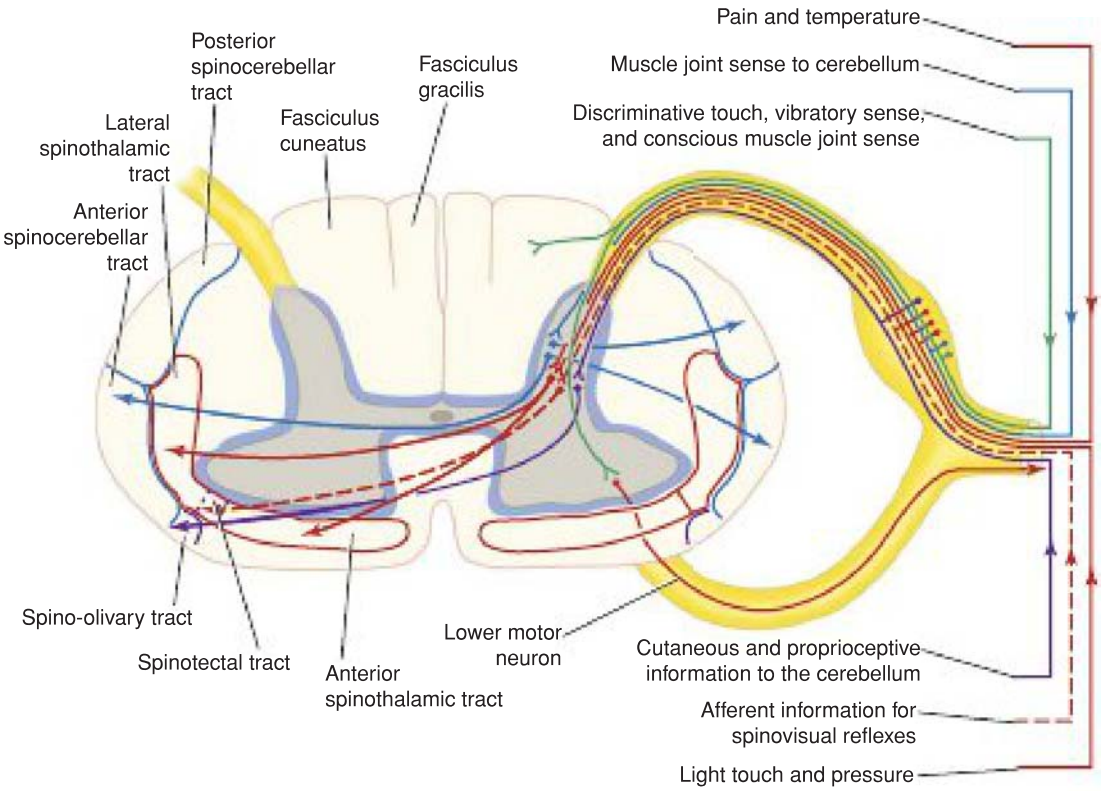

Figure 4-13 Transverse section of the spinal cord showing the origin of the main ascending sensory tracts. Note that the sensations of pain and temperature ascend in the lateral spinothalamic tract, and light touch and pressure ascend in the anterior spinothalamic tract.

δ A-type fibers and slow-conducting C-type fibers. The fast-conducting fibers alert the individual to initial sharp pain, and the slow-conducting fibers are responsible for prolonged burning, aching pain. The sensations of heat and cold also travel by δ A and C fibers.

The main somatosensory pathways are summarized in Table 4-2.

Table 4-2 Main Somatosensory Pathways to Consciousness[a]

Sensation	Receptor	First-Order Neuron	Second-Order Neuron	Third-Order Neuron	Pathways	Destination
Pain and temperature	Free nerve endings	Posterior root ganglion	Substantia gelatinosa	Ventral posterolateral nucleus of thalamus	Lateral spinothalamic, spinal lemniscus	Posterior central gyrus
Light touch and pressure	Free nerve endings	Posterior root ganglion	Substantia gelatinosa	Ventral posterolateral nucleus of thalamus	Anterior spinothalamic, spinal lemniscus	Posterior central gyrus
Discriminative touch, vibratory sense, conscious muscle joint sense	Meissner corpuscles, pacinian corpuscles, muscle spindles, tendon organs	Posterior root ganglion	Nuclei gracilis and cuneatus	Ventral posterolateral nucleus of thalamus	Fasciculi gracilis and cuneatus, medial lemniscus	Posterior central gyrus

[a]Note that all ascending pathways send branches to the reticular activating system.

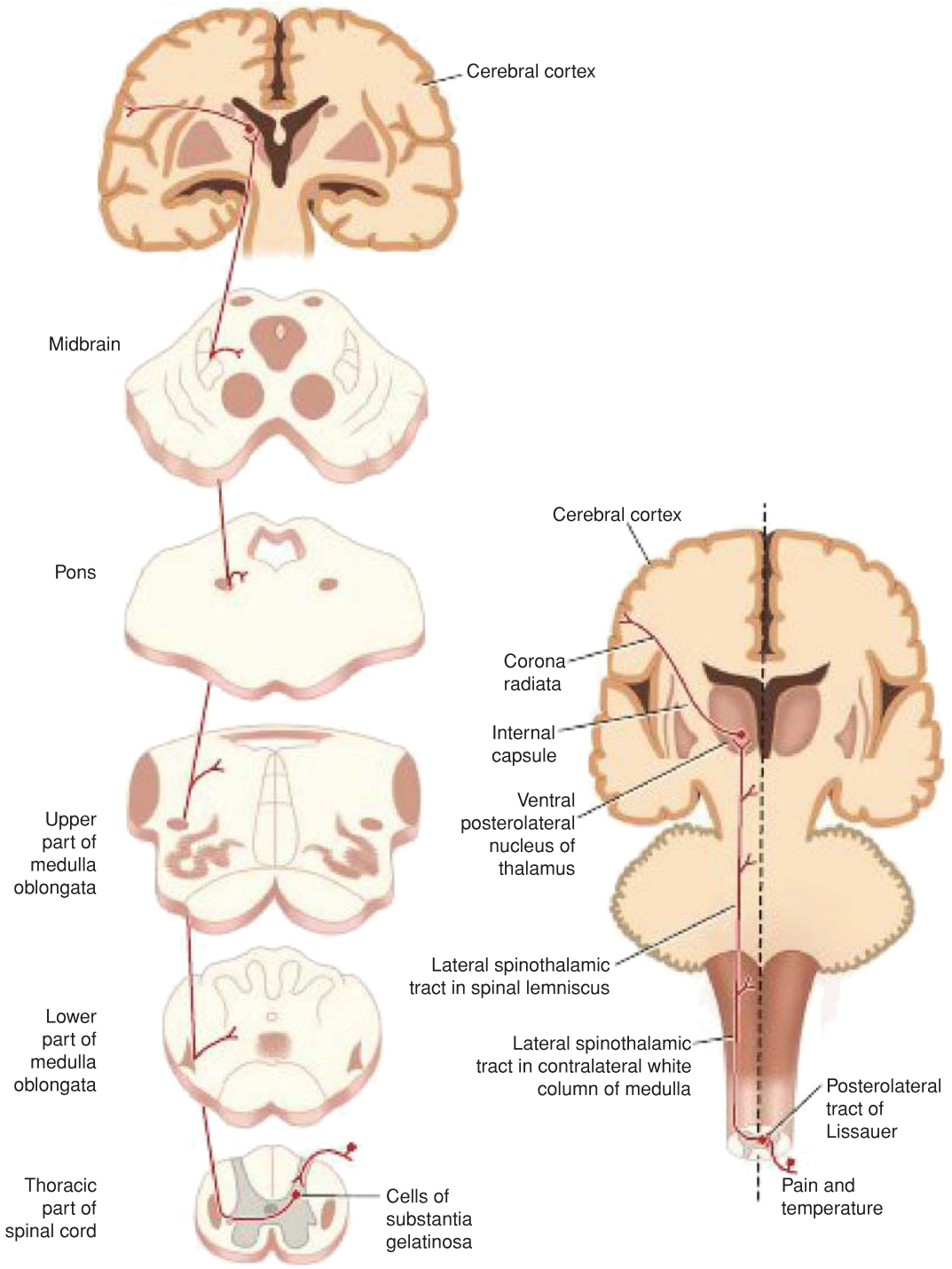

Figure 4-14 Pain and temperature pathways.

Lateral Spinothalamic Tract

Axons entering the spinal cord from the posterior root ganglion proceed to the tip of the posterior gray column and divide into ascending and descending branches (Fig. 4-14). These branches travel for a distance of one or two segments of the spinal cord and form the **posterolateral tract of Lissauer**. These fibers of the first-order neuron terminate by synapsing with cells in the posterior gray column, including cells in the substantia gelatinosa. Substance P, a peptide, is thought to be the neurotransmitter at these synapses.

Axons of the second-order neurons now **cross obliquely to the opposite side in the anterior gray and white commissures within one spinal segment of**

the cord, ascending in the contralateral white column as the lateral spinothalamic tract. The lateral spinothalamic tract lies medial to the anterior spinocerebellar tract. As the lateral spinothalamic tract ascends through the spinal cord, new fibers are added to the anteromedial aspect of the tract. Thus, in the upper cervical segments of the cord, the sacral fibers are lateral and the cervical segments are medial. The fibers carrying pain are situated slightly anterior to those conducting temperature.

As the lateral spinothalamic tract ascends through the medulla oblongata, it lies near the lateral surface and between the inferior olivary nucleus and the nucleus of the spinal tract of the trigeminal nerve. It is now accompanied by the anterior spinothalamic tract and the spinotectal tract; together they form the **spinal lemniscus**.

The spinal lemniscus continues to ascend through the posterior part of the pons. In the midbrain, it lies in the tegmentum lateral to the medial lemniscus. Many of the fibers of the lateral spinothalamic tract end by synapsing with the third-order neuron in the ventral posterolateral nucleus of the thalamus. Crude pain and temperature sensations are probably appreciated and emotional reactions initiated here.

Axons of the third-order neurons in the ventral posterolateral nucleus of the thalamus now pass through the posterior limb of the internal capsule and the corona radiata to reach the somesthetic area in the postcentral gyrus of the cerebral cortex. The contralateral half of the body is represented as inverted, with the hand and mouth situated inferiorly and the leg situated superiorly, and with the foot and anogenital region on the medial surface of the hemisphere. (For details, see Chapter 7.) From here, the information is transmitted to other regions of the cerebral cortex to be used by motor areas and the parietal association area. The role of the cerebral cortex is interpreting the quality of the sensory information at the level of consciousness.

Pain Reception

The perception of pain is a complex phenomenon that is influenced by the emotional state and past experiences of the individual. Pain is a sensation that warns of potential injury and alerts the person to avoid or treat it.

Pain can be divided into two main types: **fast pain** and **slow pain**. Fast pain is experienced within about 0.1 second after the pain stimulus is applied; slow pain is felt 1.0 second or later after the stimulation. Fast pain is described by the patient as sharp pain, acute pain, or pricking pain and is the type of pain felt after pricking the finger with a needle. Fast pain is almost confined to the skin.

Slow pain is described as burning pain, aching pain, and throbbing pain and is produced on tissue destruction, as for example, in the development of an abscess or in severe arthritis. Slow pain can occur in any tissue of the body.

All types of pain reception take place in free nerve endings. Fast pain is experienced by mechanical or thermal types of stimuli, and slow pain may be elicited by mechanical, thermal, and chemical stimuli.

Many chemical substances have been found in extracts from dam**aged tissue that will excite free nerve endings. These include serotonin; histamine; bradykinin; acids**, such as **lactic acid**; and **K^+ ions.** The threshold for pain endings can be lowered by prostaglandins and substance P, but they cannot stimulate the endings directly by themselves.

The individual should be aware of the existence of stimuli that, if allowed to persist, will cause tissue destruction; pain receptors have little or no adaptation.

Pain Conduction to the Central Nervous System

Fast pain travels in peripheral nerves in large diameter A δ axons at velocities between 6 and 30 msec. Slow pain travels in the small-diameter C fibers at velocities between 0.5 and 2.0 msec. The fast pain impulses reach consciousness first to alert the individual to danger so that a suitable protective response may take place. Slow pain is appreciated later and lasts much longer.

Pain Conduction in the Central Nervous System

Afferent pain fibers enter the spinal cord, for example, in the posterior roots of a spinal nerve and terminate predominantly in the superficial layers of the posterior gray horn. The main excitatory neurotransmitter released by A δ fibers and C fibers is the amino acid **glutamate**. Substance P, a neuropeptide, is also released from C fibers. Whereas glutamate is a fast-acting localized neurotransmitter, substance P has a slow release and diffuses widely in the posterior horn and can influence many neurons.

The initial sharp, pricking, fast-acting pain fibers stimulate the second-order neurons of the lateral spinothalamic tract. The axons immediately cross to the opposite side of the spinal cord and ascend to the thalamus where they are relayed to the sensory postcentral gyrus. The burning, aching, slow-acting pain fibers also stimulate the second-order neurons of the lateral spinal thalamic tract in the posterior gray horn and ascend with the axons of the fast-acting pain fibers. However, most of the incoming slow fibers to the spinal cord probably take part in additional relays involving several neurons in the posterior horn before ascending in the spinal cord. The repeated arrival of noxious stimuli through C fibers in the posterior gray horn during severe injury results in an increased response of the second-order neurons. This **winding up** phenomenon is attributed to the release of the neurotransmitter glutamate from C fibers.

The fast type of pain is precisely localized. For example, if someone hits a thumb with a hammer, where the injury has occurred is clear. The slow type of pain is only poorly localized. For example, in a patient with osteoarthritis of the hip joint, the individual can only vaguely localize the pain to the hip area and not to the specific site of the disease. This may

be explained by the fact that fast pain fibers directly ascend the spinal cord in the lateral spinothalamic tract, whereas the slow pain fibers take part in multiple relays in the posterior gray horn before ascending to higher centers.

Other Terminations of the Lateral Spinothalamic Tract

As is now generally agreed, fast pain impulses travel directly up to the ventral posterolateral nucleus of the thalamus and are then relayed to the cerebral cortex.

The majority of the slow pain fibers in the lateral spinothalamic tract terminate in the reticular formation, which then activates the entire nervous system. In the lower areas of the brain, the individual becomes aware of the chronic, nauseous, suffering type of pain.

As the result of research using the positron emission tomography scan, the postcentral gyrus, the cingulate gyrus of the limbic system, and the insular gyrus are sites concerned with the reception and interpretation of nociceptor information. The postcentral gyrus is responsible for the interpretation of pain in relation to past experiences. The cingulate gyrus is involved with the interpretation of the emotional aspect of pain, whereas the insular gyrus is concerned with the interpretation of pain stimuli from the internal organs of the body and brings about an autonomic response.

Reception of pain information by the CNS is modulated first in the posterior gray horns of the spinal cord and at other sites at higher levels.

Pain Control in the Central Nervous System

Massage and the application of liniments to painful areas in the body can relieve pain. The technique of acupuncture, which was discovered several thousand years ago in China, is also beneficial in relieving pain. Low-frequency electrical stimulation of the skin also relieves pain in certain cases.

Gating Theory

Although the precise mechanism for the phenomena described above is not understood, the gating theory suggested that, at the site where the pain fiber enters the CNS, inhibition could occur by means of connector neurons excited by large, myelinated afferent fibers carrying information of nonpainful touch and pressure. The excess tactile stimulation produced by massage, for example, "closed the gate" for pain. Once the nonpainful tactile stimulation ceased, however, "the gate was opened," and information on the painful stimuli ascended the lateral spinothalamic tract. Although the gate theory may partially explain the phenomena, the analgesia system is probably involved with the liberation of enkephalins and endorphins in the posterior gray columns.

Analgesia System

Stimulation of certain areas of the brainstem can reduce or block sensations of pain. These areas include the periventricular area of the diencephalon, the periaqueductal gray matter of the midbrain, and midline nuclei of the brainstem. Fibers of the reticulospinal tract are believed to pass down to the spinal cord and synapse on cells concerned with pain sensation in the posterior gray column. The analgesic system can suppress both sharp pricking pain and burning pain sensations.

Recently, two compounds with morphinelike actions, **enkephalins** and **endorphins**, have been isolated in the CNS. These compounds and **serotonin** serve as neurotransmitter substances in the analgesic system of the brain, and they may inhibit the release of substance P in the posterior gray column.

Light (Crude) Touch and Pressure Pathways

These pathways are summarized in Table 4-2.

Anterior Spinothalamic Tract

Axons enter the spinal cord from the posterior root ganglion and proceed to the tip of the posterior gray column, where they divide into ascending and descending branches (Fig. 4-15). These branches travel for a distance of one or two segments of the spinal cord, contributing to the posterolateral tract of Lissauer. These fibers of the first-order neuron are believed to terminate by synapsing with cells in the substantia gelatinosa group in the posterior gray column.

Axons of the second-order neuron now **cross very obliquely to the opposite side in the anterior gray and white commissures within several spinal segments** and ascend in the opposite anterolateral white column as the anterior spinothalamic tract. As the anterior spinothalamic tract ascends through the spinal cord, new fibers are added to the medial aspect of the tract. Thus, in the upper cervical segments of the cord, the sacral fibers are mostly lateral and the cervical segments are mostly medial.

As the anterior spinothalamic tract ascends through the medulla oblongata, it accompanies the lateral spinothalamic tract and the spinotectal tract, all of which form the **spinal lemniscus**.

The spinal lemniscus continues to ascend through the posterior part of the pons, and the tegmentum of the midbrain and the fibers of the anterior spinothalamic tract terminate by synapsing with the third-order neuron in the ventral posterolateral nucleus of the thalamus. Crude awareness of touch and pressure is believed to be appreciated here.

Axons of the third-order neurons in the ventral posterolateral nucleus of the thalamus pass through the posterior limb of the **internal capsule** and the **corona radiata** to reach the somesthetic area in the postcentral gyrus of the cerebral cortex. The contralateral half of the body is represented inverted, with the hand and mouth situated inferiorly, as described previously. (For details, see Chapter 7.) The conscious appreciation of touch and pressure depends on the activity of the cerebral cortex. The sensations can be only crudely

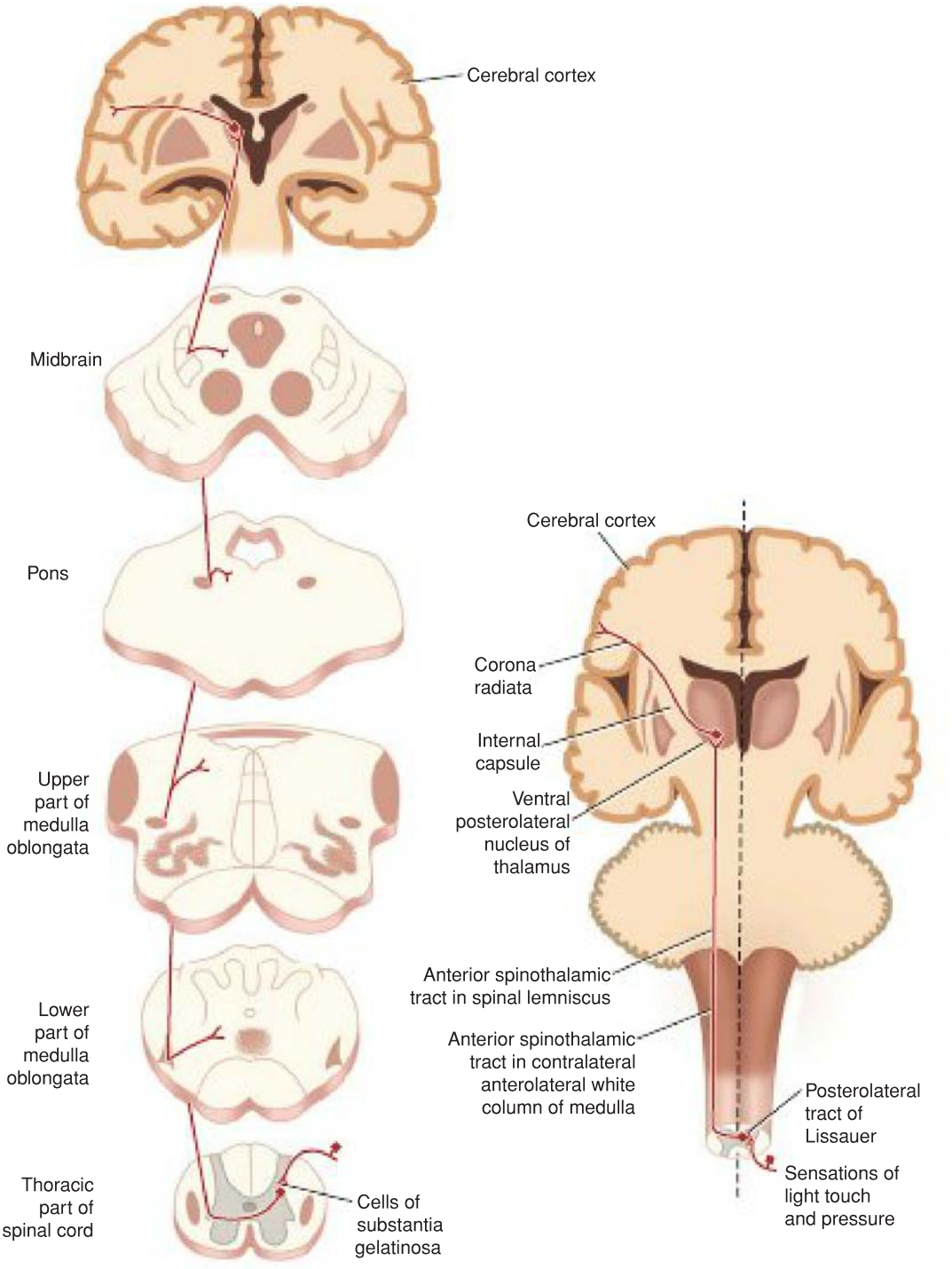

Figure 4-15 Light touch and pressure pathways.

localized, and very little discrimination of intensity is possible.

Discriminative Touch, Vibratory Sense, and Conscious Muscle Joint Sense

These pathways are summarized in Table 4-2.

Posterior White Column: Fasciculus Gracilis and Fasciculus Cuneatus

Axons enter the spinal cord from the posterior root ganglion and pass directly to the posterior white column of the same side (Fig. 4-16). Here, the fibers divide into long ascending and short descending branches. The

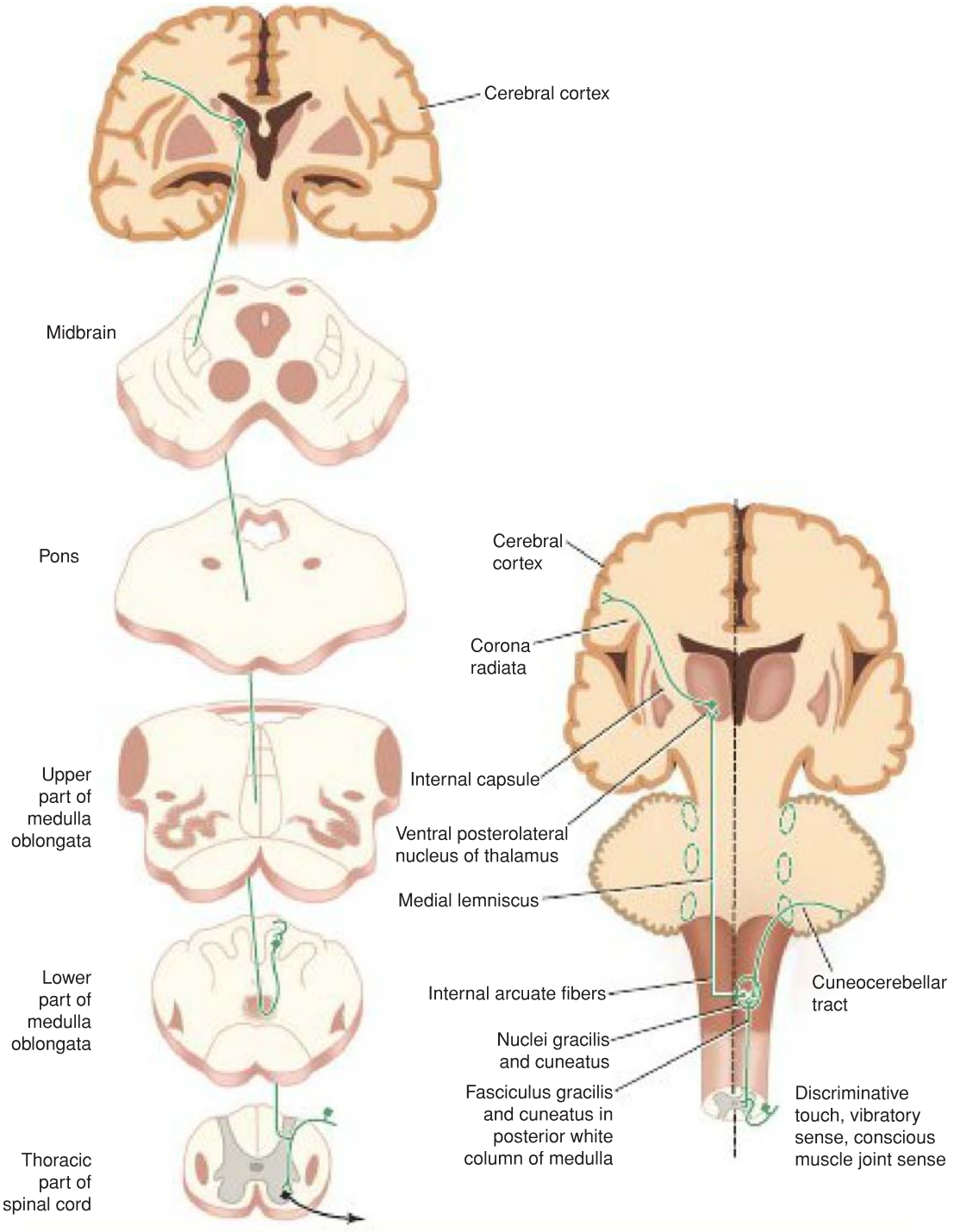

Figure 4-16 Discriminative touch, vibratory sense, and conscious muscle joint sense pathways.

descending branches pass down a variable number of segments, giving off collateral branches that synapse with cells in the posterior gray horn, with internuncial neurons, and with anterior horn cells. These short descending fibers are clearly involved with intersegmental reflexes.

Long ascending fibers may also end by synapsing with cells in the posterior gray horn, with internuncial neurons, and with anterior horn cells. This distribution may extend over numerous segments of the spinal cord. As in the case of the short descending fibers, they are involved with intersegmental reflexes.

Many of the long ascending fibers travel upward in the posterior white column as the **fasciculus gracilis** and **fasciculus cuneatus**. The fasciculus gracilis is present throughout the length of the spinal cord and contains the long ascending fibers from the sacral, lumbar, and lower six thoracic spinal nerves. The fasciculus cuneatus is situated laterally in the upper thoracic and cervical segments of the spinal cord and is separated from the fasciculus gracilis by a septum. The fasciculus cuneatus contains the long ascending fibers from the upper six thoracic and all the cervical spinal nerves.

Fibers of the fasciculus gracilis and fasciculus cuneatus ascend **ipsilaterally** and terminate by synapsing on the second-order neurons in the **nuclei gracilis** and **cuneatus** of the medulla oblongata. The axons of the second-order neurons, called the **internal arcuate fibers**, sweep anteromedially around the central gray matter and **cross the median plane,** decussating with the corresponding fibers of the opposite side in the **sensory decussation**. The fibers then ascend as a single compact bundle, the **medial lemniscus**, through the medulla oblongata, the pons, and the midbrain. The fibers terminate by synapsing on the third-order neurons in the ventral posterolateral nucleus of the thalamus.

Axons of the third-order neuron leave and pass through the posterior limb of the **internal capsule** and **corona radiata** to reach the somesthetic area in the postcentral gyrus of the cerebral cortex. The contralateral half of the body is represented inverted, with the hand and mouth situated inferiorly, as described previously. (For details, see Chapter 7.) In this manner, the impressions of touch with fine gradations of intensity, exact localization, and two-point discrimination can be appreciated. Vibratory sense and the position of the different parts of the body can be consciously recognized.

Many fibers in the fasciculus cuneatus from the cervical and upper thoracic segments, having terminated on the second-order neuron of the nucleus cuneatus, are relayed and travel as the axons of the second-order neurons to enter the cerebellum through the inferior cerebellar peduncle of the same side. This pathway is the **cuneocerebellar tract**, and the fibers are known as the **posterior external arcuate fibers**. The function of these fibers is to convey information of muscle joint sense to the cerebellum.

Muscle Joint Sense Pathways to the Cerebellum

Muscle joint sense pathways to the cerebellum are summarized in Table 4-3.

Posterior Spinocerebellar Tract

Axons entering the spinal cord from the posterior root ganglion enter the posterior gray column and terminate by synapsing on the second-order neurons at the base of the posterior gray column (Fig. 4-17). These neurons are known collectively as the **nucleus dorsalis** (**Clarke column**). Axons of the second-order neurons enter the posterolateral part of the lateral white column on the **same side** and ascend as the posterior spinocerebellar tract to the medulla oblongata. Here, the tract joins the inferior cerebellar peduncle and terminates in the cerebellar cortex. Note that it does not ascend to the cerebral cortex. Because the nucleus dorsalis (Clarke column) extends only from the eighth cervical segment caudally to the third or fourth lumbar segment, axons entering the spinal cord from the posterior roots of the lower lumbar and sacral segments ascend in the posterior white column until they reach the third or fourth lumbar segment, where they enter the nucleus dorsalis.

The posterior spinocerebellar fibers receive muscle joint information from the muscle spindles, tendon organs, and joint receptors of the trunk and lower limbs. This information concerning tension of muscle tendons and the movements of muscles and joints is used by the cerebellum in the coordination of limb movements and the maintenance of posture.

Anterior Spinocerebellar Tract

Axons entering the spinal cord from the posterior root ganglion terminate by synapsing with the second-order neurons in the **nucleus dorsalis** at the base of the posterior gray column (Fig. 4-17). Most axons of the second-order neurons **cross** to the opposite side and ascend as the anterior spinocerebellar tract in the contralateral white column; a minority ascend as the anterior spinocerebellar tract in the lateral white column of the **same side**. The fibers, having ascended through the medulla oblongata and pons, enter the cerebellum through the superior cerebellar peduncle and terminate in the cerebellar cortex. Those fibers that crossed over to the opposite side in the spinal cord are believed to **cross back** within the cerebellum. The anterior spinocerebellar tract conveys muscle joint information from the muscle spindles, tendon organs, and joint receptors of the trunk and the upper and lower limbs. It is also believed that the cerebellum receives information from the skin and superficial fascia by this tract.

Table 4-3 Muscle Joint Sense Pathways to the Cerebellum

Sensation	Receptor	First-Order Neuron	Second-Order Neuron	Pathways	Destination
Unconscious muscle joint sense	Muscle spindles, tendon organs, joint receptors	Posterior root ganglion	Nucleus dorsalis	Anterior and posterior spinocerebellar	Cerebellar cortex

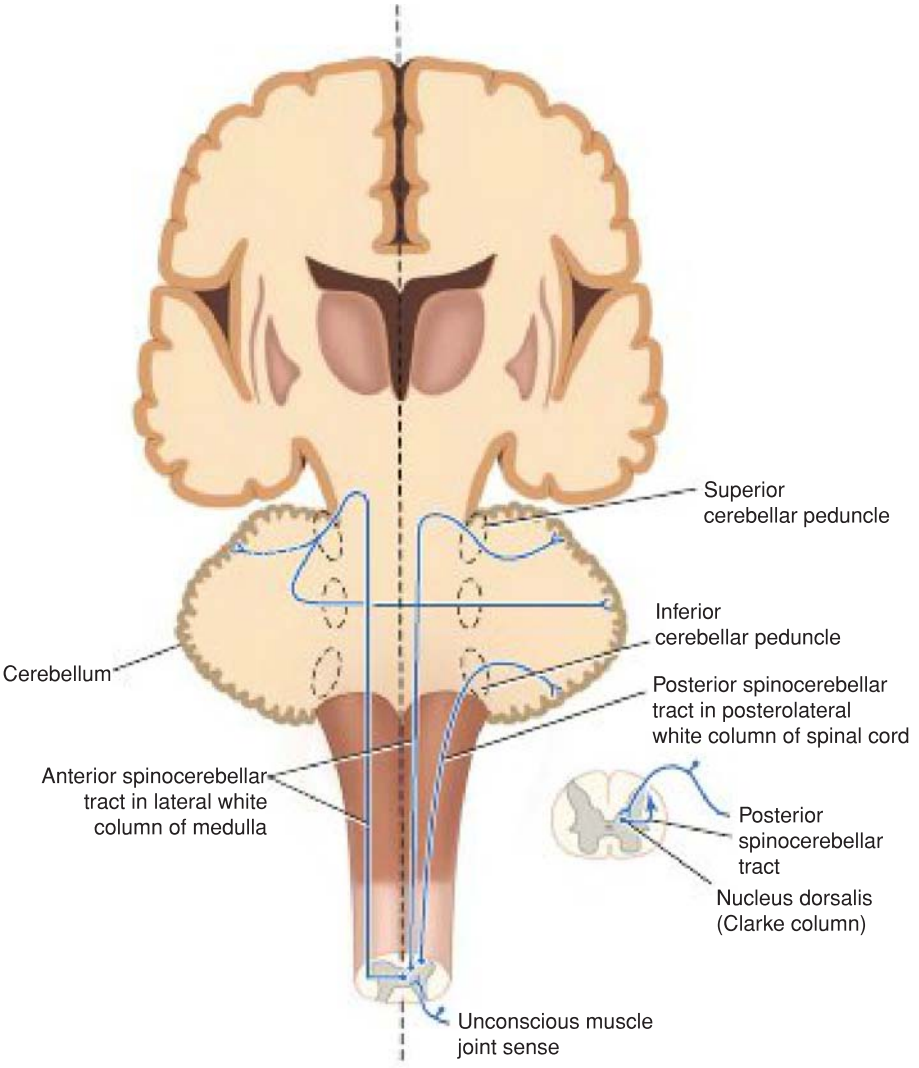

Figure 4-17 Unconscious muscle joint sense pathways to the cerebellum.

Cuneocerebellar Tract

These fibers are described on page 142. They originate in the nucleus cuneatus and enter the cerebellum through the inferior cerebellar peduncle of the **same side** (Fig. 4-16). They are known as the **posterior external arcuate fibers**, and their function is to convey information of muscle joint sense to the cerebellum.

Other Ascending Pathways

The spinotectal, spinoreticular, and spino-olivary tracts are shown in Figure 4-18.

Spinotectal Tract

Axons enter the spinal cord from the posterior root ganglion and travel to the gray matter where they synapse on unknown second-order neurons. Axons of the second-order neurons **cross the median plane** and ascend as the spinotectal tract in the anterolateral white column lying close to the lateral spinothalamic tract. After passing through the medulla oblongata and pons, they terminate by synapsing with neurons in the superior colliculus of the midbrain. This pathway provides afferent information for spinovisual reflexes and brings about movements of the eyes and head toward the source of the stimulation.

Spinoreticular Tract

Axons enter the spinal cord from the posterior root ganglion and terminate on unknown second-order neurons in the gray matter. Axons from these second-order neurons ascend the spinal cord as the spinoreticular tract in the lateral white column mixed with the lateral spinothalamic tract. Most of the fibers are **uncrossed** and terminate by synapsing with neurons of the reticular formation in the medulla oblongata, pons, and midbrain. The spinoreticular tract provides an afferent

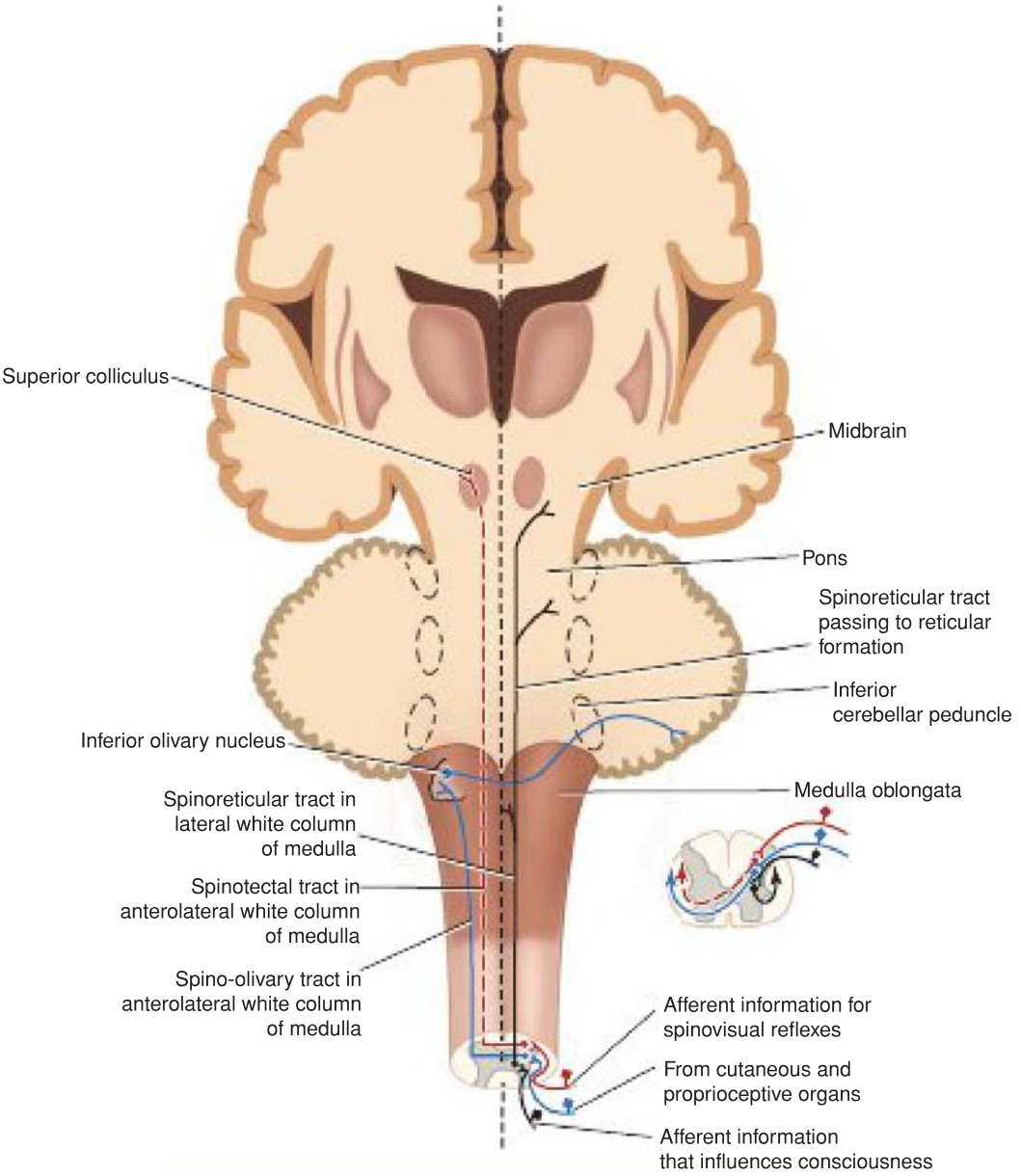

Figure 4-18 Spinotectal, spinoreticular, and spino-olivary tracts.

pathway for the reticular formation, which plays an important role in influencing levels of consciousness. (For details, see p. 204.)

Spino-olivary Tract

Axons enter the spinal cord from the posterior root ganglion and terminate on unknown second-order neurons in the posterior gray column. Axons from the second-order neurons **cross the midline** and ascend as the spino-olivary tract in the white matter at the junction of the anterior and lateral columns. The axons end by synapsing on third-order neurons in the inferior olivary nuclei in the medulla oblongata. Axons of the third-order neurons cross the midline and enter the cerebellum through the inferior cerebellar peduncle. The spino-olivary tract conveys information to the cerebellum from cutaneous and proprioceptive organs.

Visceral Sensory Tracts

Sensations that arise in viscera located in the thorax and abdomen enter the spinal cord through the posterior roots. The cell bodies of the first-order neuron are situated in the posterior root ganglia. The peripheral processes of these cells receive nerve impulses from pain and stretch receptor endings in the viscera. The causes of visceral pain include ischemia, chemical damage, spasm of smooth muscle,

and distention. The central processes, having entered the spinal cord, synapse with second-order neurons in the gray matter, probably in the posterior or lateral gray columns.

Axons of the second-order neurons are believed to join the spinothalamic tracts and ascend and terminate on third-order neurons in the ventral posterolateral nucleus of the thalamus. The final destination of these axons is probably in the postcentral gyrus of the cerebral cortex.

Many of the visceral afferent fibers that enter the spinal cord branch participate in reflex activity.

DESCENDING TRACTS

Motor neurons situated in the anterior gray columns of the spinal cord send axons to innervate skeletal muscle through the anterior roots of the spinal nerves. These motor neurons are referred to as the **lower motor neurons** and constitute the final common pathway to the muscles (Fig. 4-19).

Lower motor neurons are constantly bombarded by nervous impulses that descend from the medulla, pons, midbrain, and cerebral cortex as well as those that enter along sensory fibers from the posterior

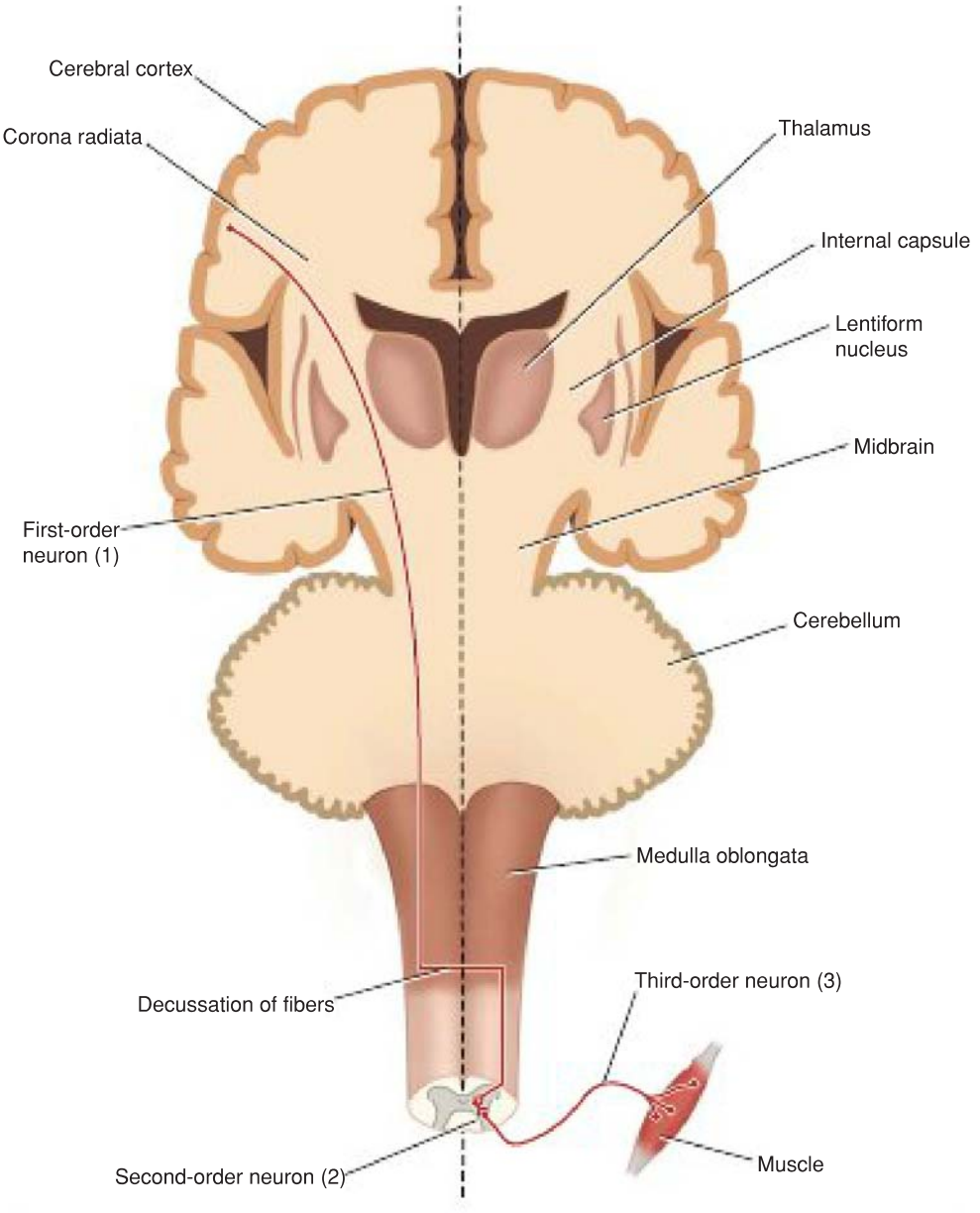

Figure 4-19 Simple form of the descending motor pathway from the cerebral cortex to the skeletal muscle. Note the three neurons involved.

Table 4-4 Main Descending Pathways to the Spinal Cord[a]

Pathway	Function	Origin	Site of Crossover	Destination	Branches to
Corticospinal tracts	Rapid, skilled, voluntary movements, especially distal ends of limbs	Primary motor cortex (area 4), secondary motor cortex (area 6), parietal lobe (areas 3, 1, and 2)	Most cross at decussation of pyramids and descend as lateral corticospinal tracts; some continue as anterior corticospinal tracts and cross over at level of destination	Internuncial neurons or α motor neurons	Cerebral cortex, basal nuclei, red nucleus, olivary nuclei, reticular formation
Reticulospinal tracts	Inhibit or facilitate voluntary movement; hypothalamus controls sympathetic, para-sympathetic outflows	Reticular formation	Some cross at various levels	α and γ motor neurons	Multiple branches as they descend
Tectospinal tract	Reflex postural movements concerning sight	Superior colliculus	Soon after origin	α and γ motor neurons	?
Rubrospinal tract	Facilitates activity of flexor muscles and inhibits activity of extensor muscles	Red nucleus	Immediately	α and γ motor neurons	?
Vestibulospinal tract	Facilitates activity of extensor inhibits flexor muscles	Vestibular nuclei	Uncrossed	α and γ motor neurons	?
Olivospinal tract	??	Inferior olivary nuclei	Cross in brainstem	? α and γ motor neurons	—
Descending autonomic fibers	Control sympathetic and parasympathetic systems	Cerebral cortex, hypothalamus, amygdaloid complex, reticular formation		Sympathetic and parasympathetic outflows	—

[a]Note that the corticospinal tracts are believed to control the prime mover muscles (especially the highly skilled movements), whereas the other descending tracts are important in controlling the simple basic movements. For simplicity, the internuncial neurons are omitted from this table.

roots. Nerve fibers that descend in the white matter from different supraspinal nerve centers are segregated into nerve bundles called the **descending tracts**. These supraspinal neurons and their tracts are referred to as the **upper motor neurons**, and they provide numerous separate pathways that can influence motor activity.

A summary of the main descending pathways in the spinal cord is shown in Table 4-4.

Anatomical Organization

Control of skeletal muscle activity from the cerebral cortex and other higher centers is conducted through the nervous system by a series of neurons (Fig. 4-19). The descending pathway from the cerebral cortex is often made up of three neurons. The first neuron, the **first-order neuron**, has its cell body in the cerebral cortex. Its axon descends to synapse on the **second-order neuron**, an internuncial neuron, situated in the anterior gray column of the spinal cord. The axon of the second-order neuron is short and synapses with the **third-order neuron**, the lower motor neuron, in the anterior gray column. The axon of the third-order neuron innervates the skeletal muscle through the anterior root and spinal nerve. In some instances, the axon of the first-order neuron terminates directly on the third-order neuron (as in reflex arcs).

Functions

Corticospinal tracts (Fig. 4-20) are the pathways concerned with voluntary, discrete, skilled movements, especially those of the distal parts of the limbs. **Reticulospinal tracts** may facilitate or inhibit the activity of the α and γ motor neurons in the anterior gray columns and may, therefore, facilitate or inhibit voluntary

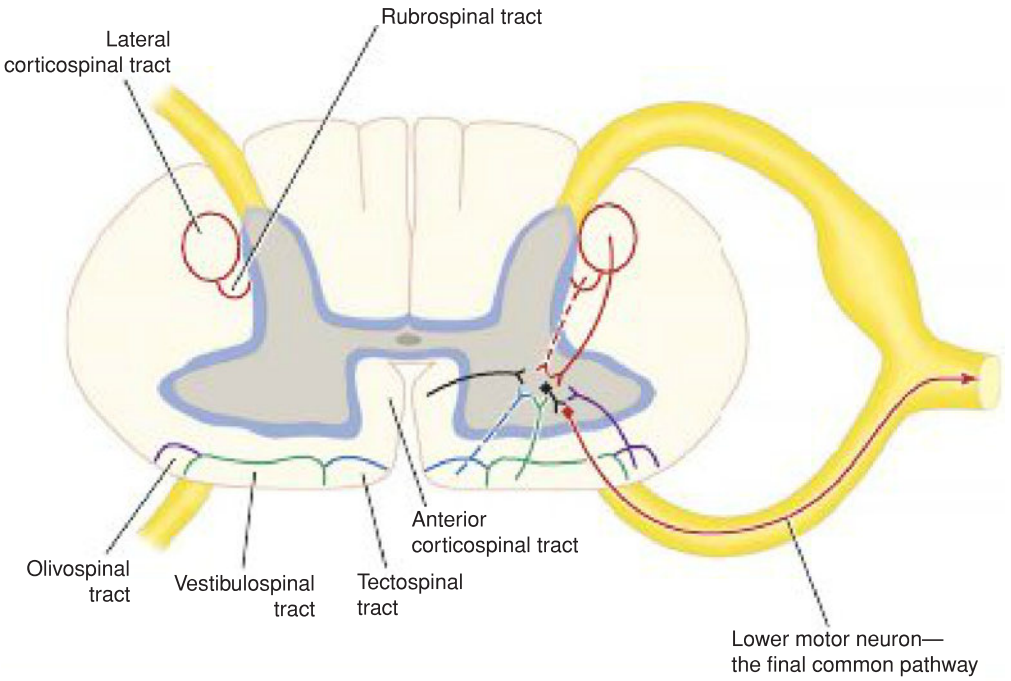

Figure 4-20 Transverse section of the spinal cord showing the termination of the descending motor tracts. Note that the existence of the olivospinal tract as a separate pathway is now in considerably doubt.

movement or reflex activity. The **tectospinal tract** is concerned with reflex postural movements in response to visual stimuli. Those fibers that are associated with the sympathetic neurons in the lateral gray column are concerned with the pupillodilation reflex in response to darkness. The **rubrospinal tract** acts on both the α and γ motor neurons in the anterior gray columns and facilitates the activity of flexor muscles and inhibits the activity of extensor or antigravity muscles. The **vestibulospinal tract**, by acting on the motor neurons in the anterior gray columns, facilitates the activity of the extensor muscles, inhibits the activity of the flexor muscles, and is concerned with the postural activity associated with balance. The **olivospinal tract** may play a role in muscular activity, but some doubt its existence. The **descending autonomic fibers** are concerned with the control of visceral activity.

Corticospinal Tracts

Fibers of the corticospinal tract arise as axons of pyramidal cells situated in the fifth layer of the cerebral cortex (Fig. 4-21). About a third of the fibers originate from the primary motor cortex (area 4), another third from the secondary motor cortex (area 6), and the final third from the parietal lobe (areas 3, 1, and 2); thus, two thirds of the fibers arise from the precentral gyrus, and one third of the fibers arise from the postcentral gyrus. These fibers do not control motor activity but influence sensory input to the nervous system. Because electrical stimulation of different parts of the precentral gyrus produces movements of different parts of the opposite side of the body, we can represent the parts of the body in this area of the cortex. Such a homunculus is shown in Figure 4-21. Note that the region controlling the face is situated inferiorly, and the region controlling the lower limb is situated superiorly and on the medial surface of the hemisphere. The homunculus is a distorted picture of the body, with the various parts having a size proportional to the area of the cerebral cortex devoted to their control. Interestingly, most corticospinal fibers are myelinated and are relatively slow-conducting, small fibers.

The descending fibers converge in the **corona radiata** and then pass through the posterior limb of the **internal capsule**. Here, the fibers are organized so that those closest to the genu are concerned with cervical portions of the body, while those situated more posteriorly are concerned with the lower extremity. The tract then continues through the middle three fifths of the **basis pedunculi of the midbrain**. Here, the fibers concerned with cervical portions of the body are situated medially, while those concerned with the leg are placed laterally.

On entering the pons, the tract is broken into many bundles by the **transverse pontocerebellar fibers** (see Figs. 5-19 to 5-22). In the medulla oblongata, the bundles become grouped together along the anterior border to form a swelling known as the **pyramid** (hence the alternative name, **pyramidal tract**) (see Figs. 5-11 and 5-12). At the junction of the medulla oblongata and the spinal cord, most of the fibers **cross** the midline at the **decussation of the pyramids** (Fig. 4-21) and enter the lateral white column of the

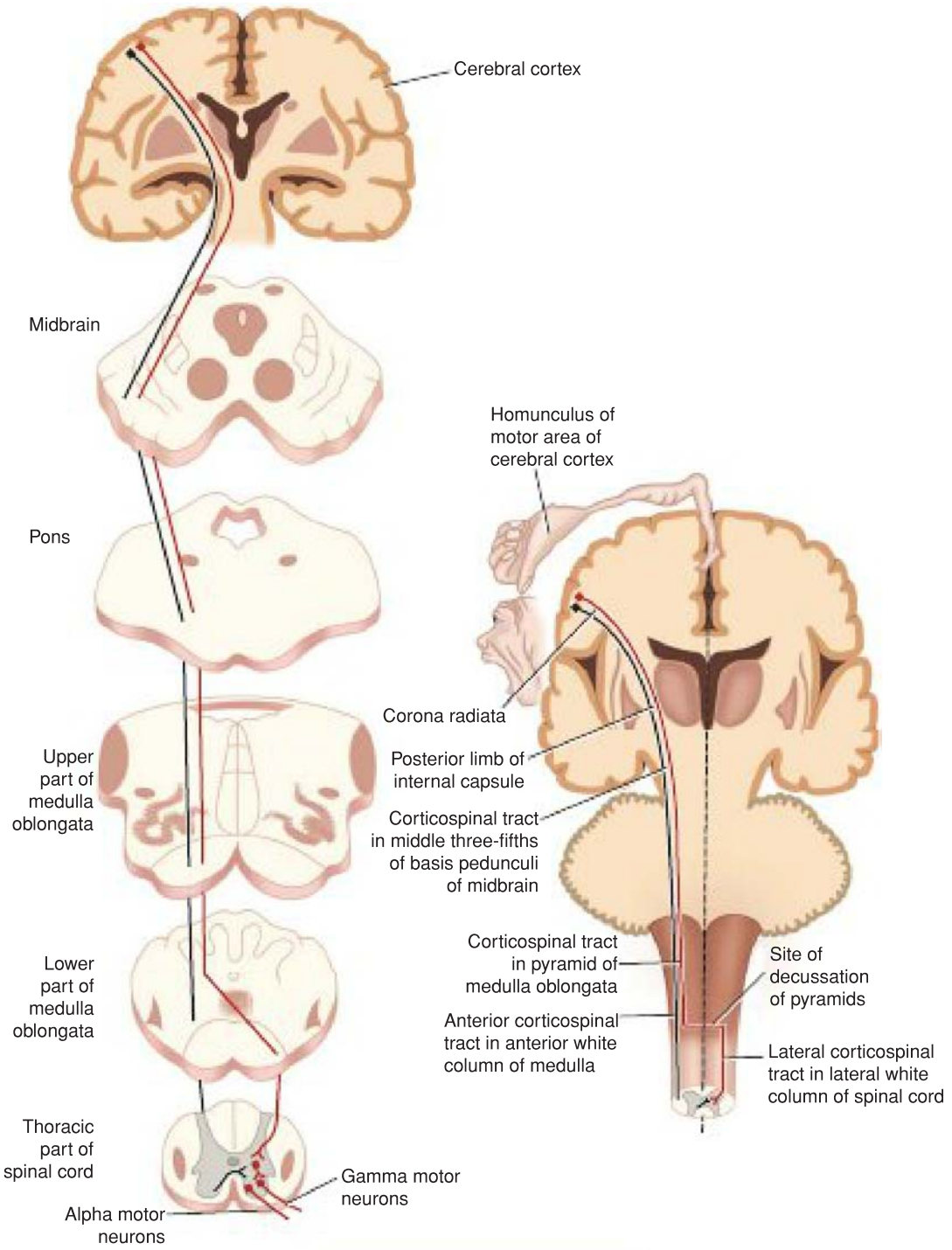

Figure 4-21 Corticospinal tracts.

spinal cord to form the **lateral corticospinal tract** (Fig. 4-20). The remaining fibers do not cross in the decussation but descend in the anterior white column of the spinal cord as the **anterior corticospinal tract** (Figs. 4-20 and 4-21). These fibers eventually **cross** the midline and terminate in the anterior gray column of the spinal cord segments in the cervical and upper thoracic regions.

The lateral corticospinal tract descends the length of the spinal cord; its fibers terminate in the anterior gray column of all the spinal cord segments.

Most corticospinal fibers synapse with internuncial neurons, which, in turn, synapse with α motor neurons and some γ motor neurons. Only the largest corticospinal fibers synapse directly with the motor neurons.

The corticospinal tracts are not the sole pathway for serving voluntary movement. Rather, they form the pathway that confers speed and agility to voluntary movements and is thus used in performing rapid skilled movements. Many of the simple, basic voluntary movements are mediated by other descending tracts.

Branches

1. Branches are given off early in their descent and return to the cerebral cortex to inhibit activity in adjacent regions of the cortex.
2. Branches pass to the caudate and lentiform nuclei, the red nuclei, and the olivary nuclei and the reticular formation. These branches keep the subcortical regions informed about the cortical motor activity. Once alerted, the subcortical regions may react and send their own nervous impulses to the α and γ motor neurons by other descending pathways.

Reticulospinal T racts

Throughout the midbrain, pons, and medulla oblongata, groups of scattered nerve cells and nerve fibers exist that are collectively known as the **reticular formation**. From the pons, these neurons send axons, which are mostly **uncrossed**, down into the spinal cord and form the **pontine reticulospinal tract** (Fig. 4-22). From the medulla, similar neurons send axons, which are crossed and uncrossed, to the spinal cord and form the **medullary reticulospinal tract**.

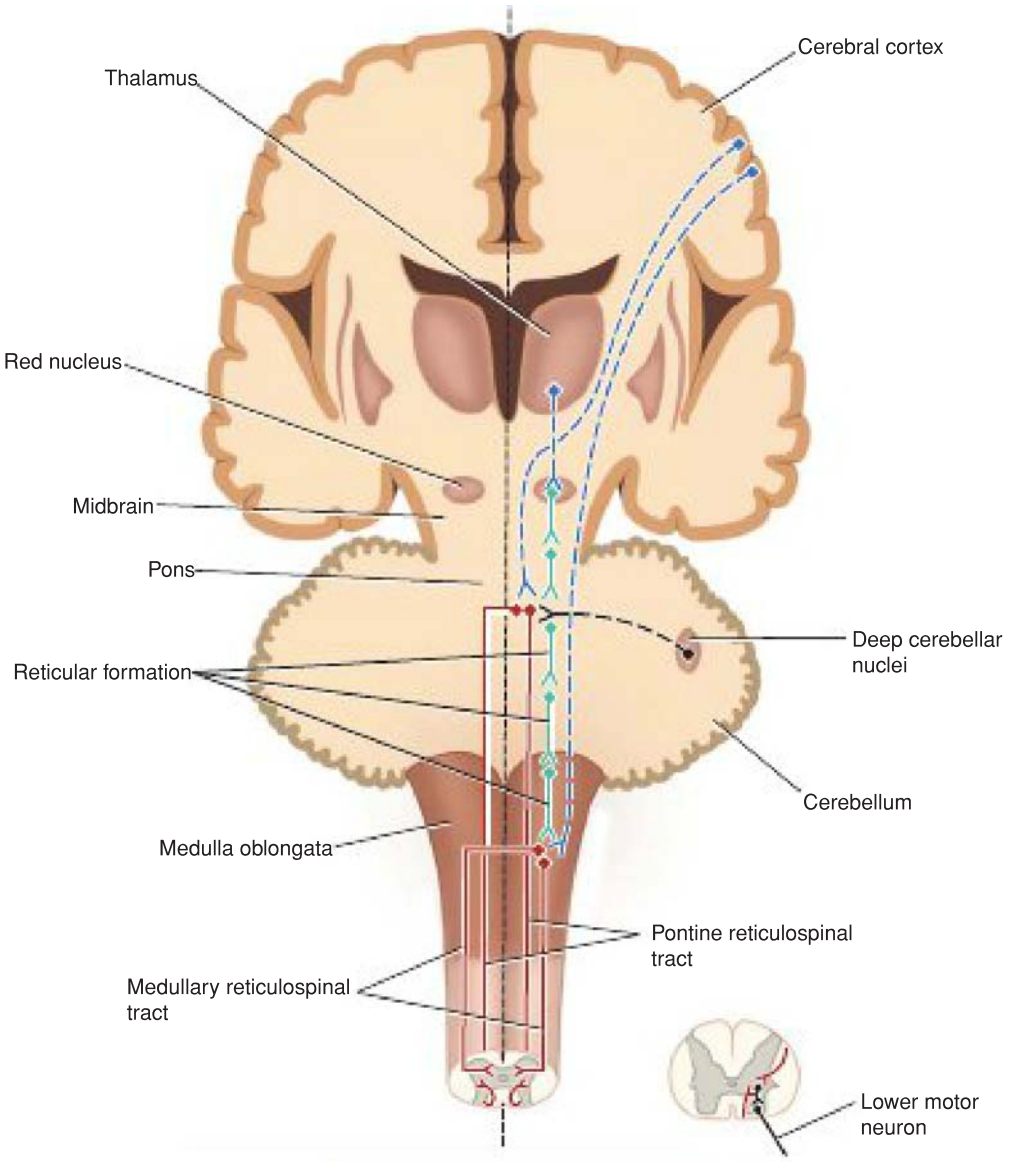

Figure 4-22 Reticulospinal tracts.

Reticulospinal fibers from the pons descend through the anterior white column, while those from the medulla oblongata descend in the lateral white column. Both sets of fibers enter the anterior gray columns of the spinal cord and may facilitate or inhibit α and γ motor neuron activity. By these means, the reticulospinal tracts influence voluntary movements and reflex activity. The reticulospinal fibers are also now thought to include the descending autonomic fibers. The reticulospinal tracts thus provide a pathway by which the hypothalamus can control the sympathetic outflow and the sacral parasympathetic outflow.

Tectospinal Tract

Fibers of this tract arise from nerve cells in the **superior colliculus** of the midbrain (Fig. 4-23). Most of the fibers **cross** the midline soon after their origin and descend through the brainstem close to the **medial longitudinal fasciculus**. The tectospinal tract descends through the anterior white column of the spinal cord close to the anterior median fissure (Fig. 4-20). The majority of the fibers terminate in the anterior gray column in the upper cervical segments of the spinal cord by synapsing with internuncial neurons. These fibers are believed to be concerned with reflex postural movements in response to visual stimuli.

Rubrospinal Tract

The **red nucleus** is situated in the tegmentum of the midbrain at the level of the superior colliculus (Fig. 4-24). The axons of neurons in this nucleus cross

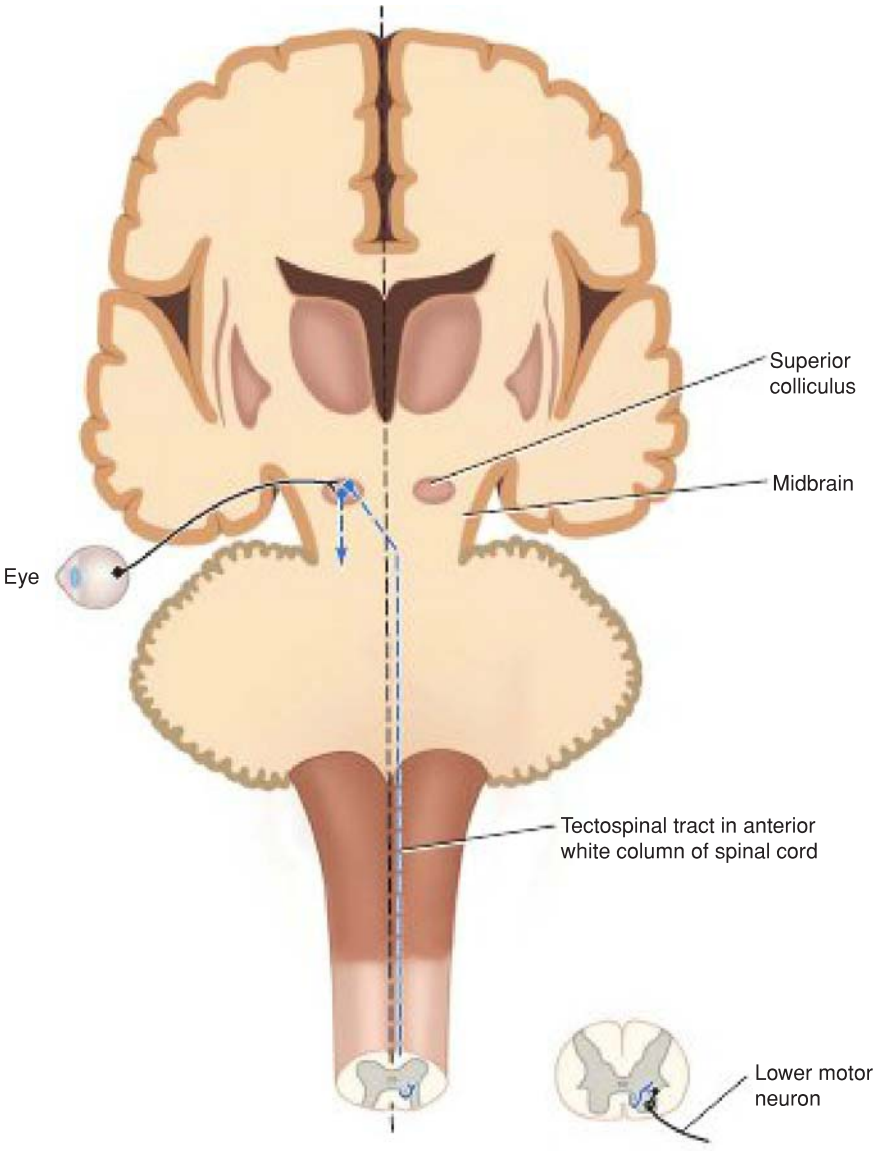

Figure 4-23 Tectospinal tract.

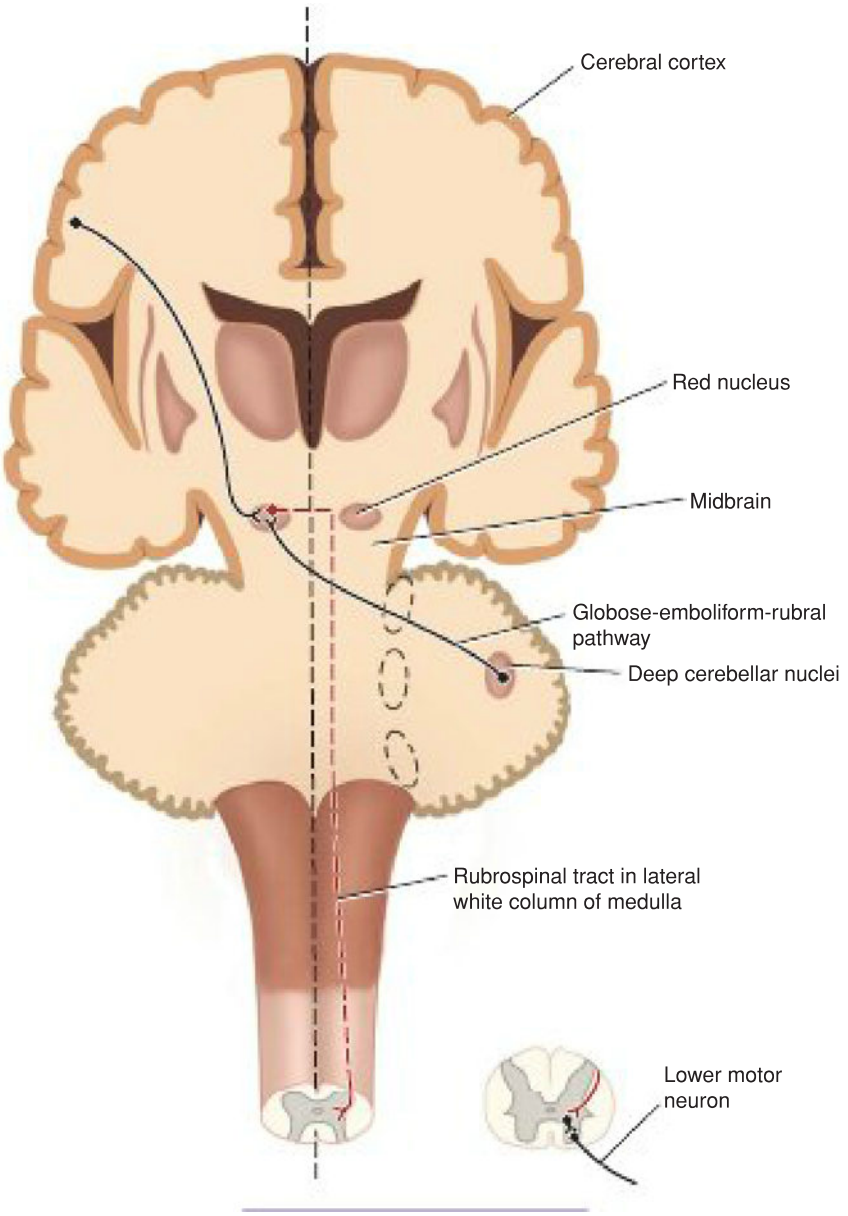

Figure 4-24 Rubrospinal tract.

the midline at the level of the nucleus and descend as the rubrospinal tract through the pons and medulla oblongata to enter the lateral white column of the spinal cord (Fig. 4-20). The fibers terminate by synapsing with internuncial neurons in the anterior gray column of the cord.

Neurons of the red nucleus receive afferent impulses through connections with the cerebral cortex and the cerebellum. This is believed to be an important indirect pathway by which the cerebral cortex and the cerebellum can influence α and γ motor neuron activity. The tract facilitates the activity of the flexor muscles and inhibits the activity of the extensor or antigravity muscles.

Vestibulospinal Tract

Vestibular nuclei are situated in the pons and medulla oblongata beneath the floor of the fourth ventricle (Fig. 4-25). The vestibular nuclei receive afferent fibers from the inner ear through the vestibular nerve and from the cerebellum. Neurons of the lateral vestibular nucleus give rise to the axons that form the vestibulospinal tract. The tract descends **uncrossed** through the medulla and through the length of the spinal cord in the anterior white column (Fig. 4-20). The fibers terminate by synapsing with internuncial neurons of the anterior gray column of the spinal cord.

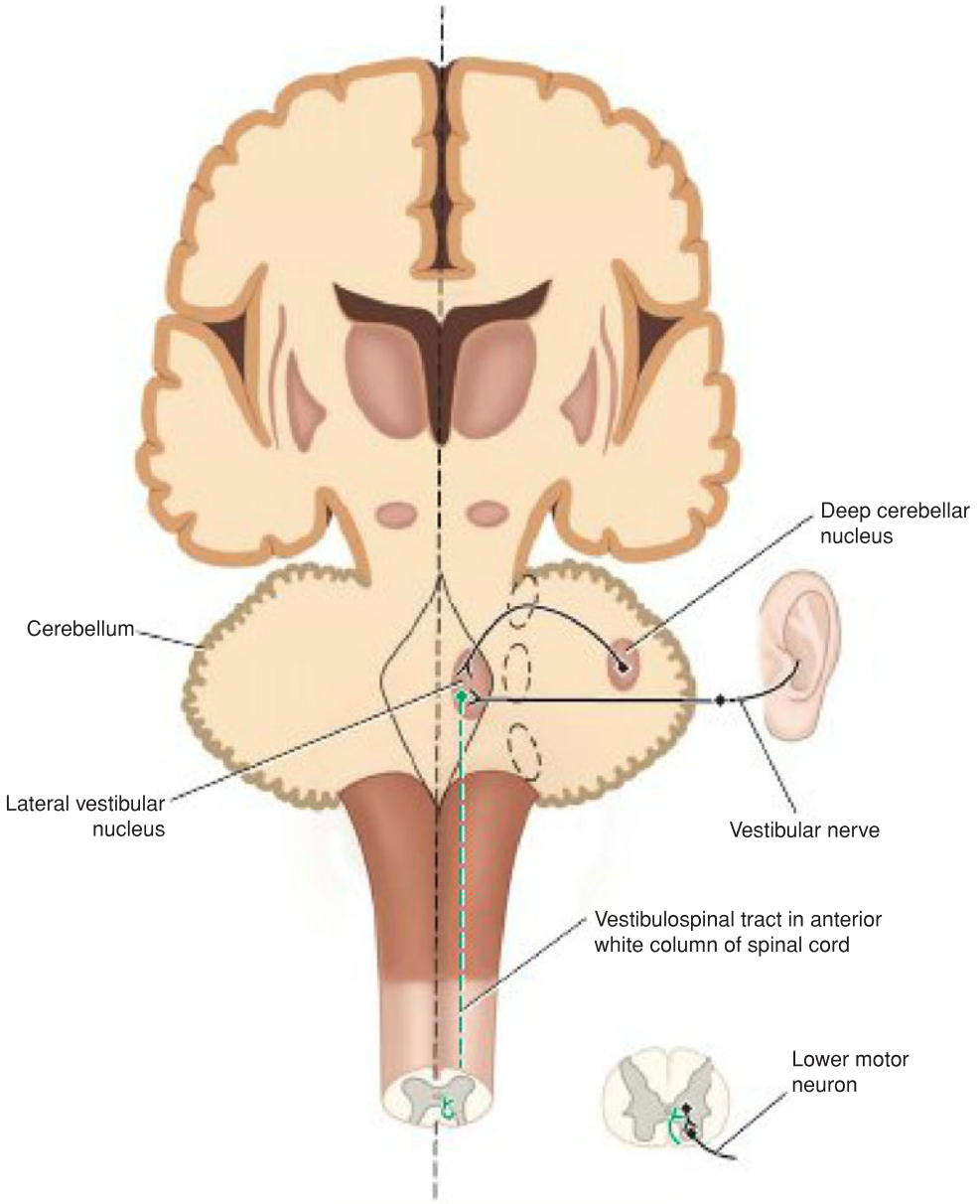

Figure 4-25 Vestibulospinal tract.

The inner ear and the cerebellum, by means of this tract, facilitate the activity of the extensor muscles and inhibit the activity of the flexor muscles in association with the maintenance of balance.

Olivospinal Tract

The olivospinal tract was thought to arise from the inferior olivary nucleus and to descend in the lateral white column of the spinal cord (Fig. 4-26), to influence the activity of the motor neurons in the anterior gray column. Many now doubt that it exists.

Descending Autonomic Fibers

The higher centers of the CNS associated with the control of autonomic activity are situated in the cerebral cortex, hypothalamus, amygdaloid complex, and reticular formation. Although distinct tracts have not been recognized, investigation of spinal cord lesions has demonstrated that descending autonomic tracts do exist and probably form part of the reticulospinal tract.

The fibers arise from neurons in the higher centers and cross the midline in the brainstem. They are

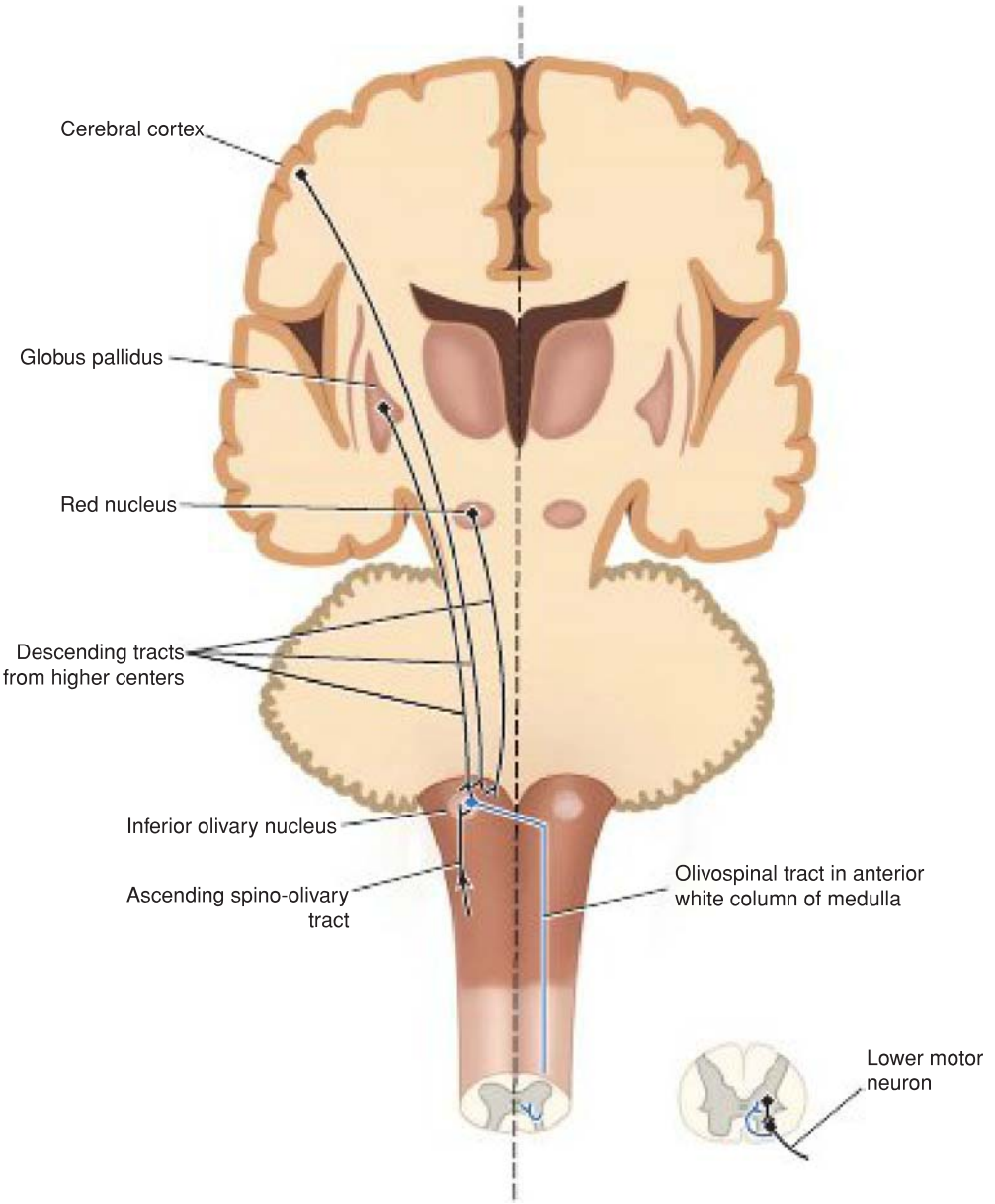

Figure 4-26 Olivospinal tract. The existence of this tract as a separate pathway is doubtful.

believed to descend in the lateral white column of the spinal cord and to terminate by synapsing on the autonomic motor cells in the lateral gray columns in the thoracic and upper lumbar (sympathetic outflow) and midsacral (parasympathetic) levels of the spinal cord.

INTERSEGMENTAL TRACTS

Short ascending and descending tracts that originate and end within the spinal cord exist in the anterior, lateral, and posterior white columns. The function of these pathways is to interconnect the neurons of different segmental levels, and the pathways are particularly important in intersegmental spinal reflexes.

Reflex Arc

A **reflex** may be defined as an involuntary response to a stimulus. It depends on the integrity of the reflex arc (Fig. 4-27). In its simplest form, a reflex arc consists of the following anatomical structures: (1) a receptor organ, (2) an afferent neuron, (3) an effector neuron, and (4) an effector organ. A reflex arc involving only one synapse is referred to as a **monosynaptic reflex arc**. Interruption of the reflex arc at any point along its course would abolish the response.

In the spinal cord, reflex arcs play an important role in maintaining muscle tone, which is the basis for body posture. The receptor organ is situated in the skin, muscle, or tendon. The cell body of the afferent neuron is

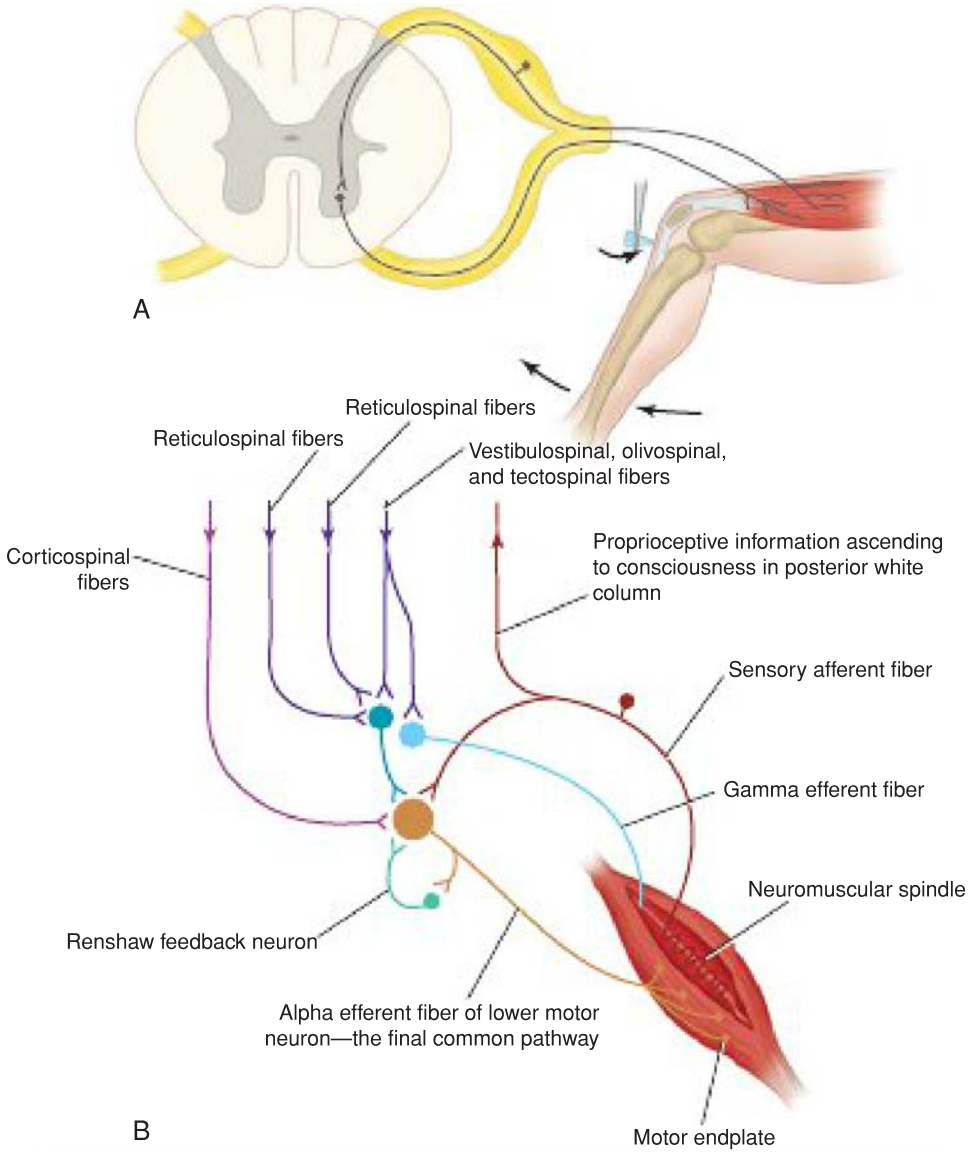

Figure 4-27 **A:** A monosynaptic reflex arc. **B:** Multiple neurons synapsing with the lower motor neuron. Note the presence of the Renshaw feedback neuron.

located in the posterior root ganglion, and the central axon of this first-order neuron terminates by synapsing on the effector neuron. Since the afferent fibers are of large diameter and are rapidly conducting and because of the presence of only one synapse, a very quick response is possible.

Physiologic study of the electrical activity of the effector neuron shows that a prolonged asynchronous discharge follows the very quick monosynaptic discharge. The reason for this later discharge is that the afferent fibers entering the spinal cord frequently branch, and the branches synapse with many internuncial neurons, which ultimately synapse with the effector neuron (Fig. 4-28). These additional neuronal circuits prolong the bombardment of the effector neurons after the initial stimulation by the afferent neuron has ceased. The presence of internuncial neurons also results in the spread of the afferent stimulus to neurons at different segmental levels of the spinal cord.

The **law of reciprocal innervation**is important to understand in considering reflex skeletal muscle activity. Simply stated, it means that the flexor and extensor reflexes of the same limb cannot be made to contract simultaneously. For this law to work, the afferent nerve fibers responsible for flexor reflex muscle action must have branches that synapse with the extensor motor neurons of the same limb, causing them to be inhibited.

Another interesting property of spinal reflexes is that the evocation of a reflex on one side of the body causes opposite effects on the limb of the other side of the body. This **crossed extensor reflex** is demonstrated when afferent stimulation of the reflex arc that causes the ipsilateral limb to flex results in the contralateral limb being extended.

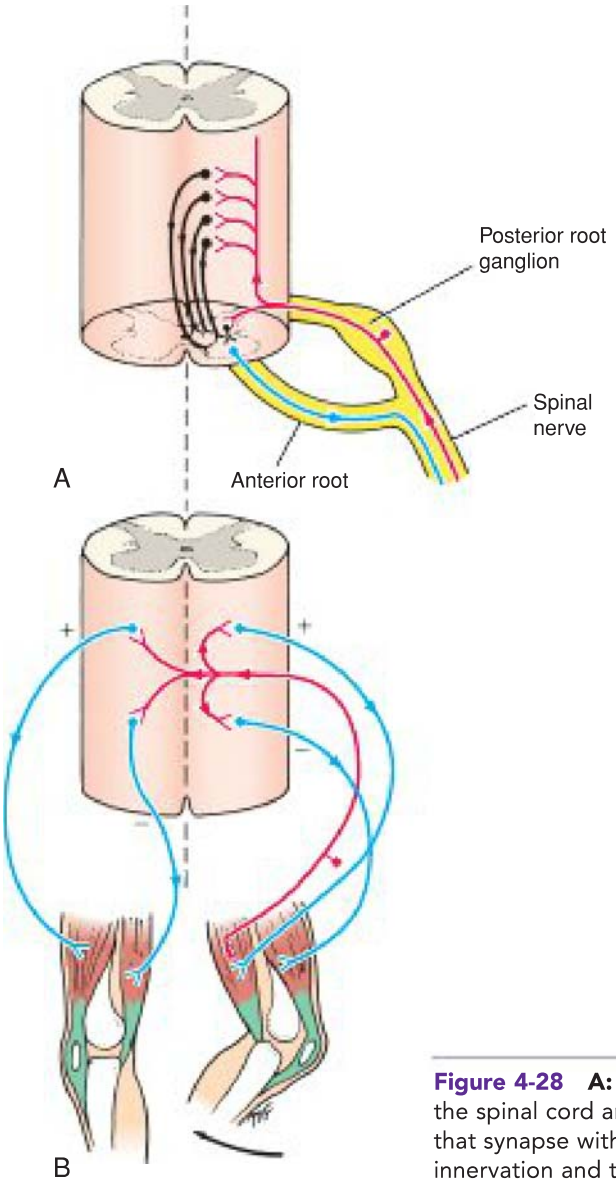

Figure 4-28 **A:** Multiple branching of afferent fibers entering the spinal cord and the presence of many internuncial neurons that synapse with the effector neuron. **B:** Law of reciprocal innervation and the crossed extensor reflex.

Influence of Higher Neuronal Centers on Spinal Reflex Activity

The spinal segmental reflex arc involving motor activity is greatly influenced by higher centers in the brain. These influences are mediated through the corticospinal, reticulospinal, tectospinal, rubrospinal, and vestibulospinal tracts. In the clinical condition known as spinal shock (see p. 167), which follows the sudden removal of these influences by spinal cord severance, the segmental spinal reflexes are depressed. When the spinal shock disappears in a few weeks, the segmental spinal reflexes return, and the muscle tone is increased. This **decerebrate rigidity** is due to the overactivity of the γ efferent nerve fibers to the muscle spindles, which results from the release of these neurons from the higher centers. The next stage may be **paraplegia in extension** with domination of the increased tone of the extensor muscles over the flexor muscles. Some neurologists believe that this condition is due to incomplete severance of all the descending tracts with persistence of the vestibulospinal tract. Should all the descending tracts be severed, the condition of **paraplegia in flexion** occurs. In this condition, the reflex responses are flexor in nature, and the tone of the extensor muscles is diminished.

RENSHAW CELLS AND LOWER MOTOR NEURON INHIBITION

Lower motor neuron axons give off collateral branches as they pass through the white matter to reach the anterior roots of the spinal nerve. These collaterals synapse on neurons described by Renshaw, which, in turn, synapse on the lower motor neurons (Fig. 4-27). These internuncial neurons are believed to provide feedback on the lower motor neurons, inhibiting their activity.

Clinical Notes

General Anatomical Features of Clinical Importance

The spinal cord may be described, for practical purposes, as consisting of columns of motor and sensory nerve cells (gray matter) surrounded by ascending and descending tracts (white matter). It lies within the vertebral canal and is protected by three surrounding fibrous membranes, the meninges. It is cushioned against trauma by cerebrospinal fluid (CSF) and is held in position by the denticulate ligaments on each side and the filum terminale inferiorly. The spinal cord is segmented, and paired posterior (sensory) and anterior (motor) roots corresponding to each segment of the cord leave the vertebral canal through the intervertebral foramina.

The spinal cord is shorter than the vertebral column and terminates inferiorly in the adult at the level of the lower border of the first lumbar vertebra. The subarachnoid space extends inferiorly beyond the end of the cord and ends at the level of the lower border of the second sacral vertebra.

Because of the shortness of the spinal cord relative to the length of the vertebral column, the nerve roots of the lumbar and sacral segments have to take an oblique course downward to reach their respective intervertebral foramina; the resulting leash of nerve roots forms the cauda equina.

A spinal tap needle may be inserted into the subarachnoid space below the level of the second lumbar vertebra without damaging the spinal cord. (For details, see p. 19.)

Anterior and Posterior Nerve Root Lesions

Each nerve root has a covering of pia, arachnoid, and dura mater. The anterior and posterior roots unite in the intervertebral foramina to form the spinal nerves. Here, the meninges fuse with the epineurium of the spinal nerves. Either or both spinal nerve roots may be involved in syphilitic spinal meningitis or pyogenic meningitis. The posterior roots may be involved in tabes dorsalis and herpes zoster. Their anatomical location, both in the vertebral canal and in the intervertebral foramina, exposes them to compression from tumors of the vertebral column and to irritation from abnormal constituents of CSF, such as blood following a subarachnoid hemorrhage. A herniated intervertebral disc, a primary or secondary vertebral tumor, vertebral destruction by tumor or infection, or a fracture dislocation can press on the spinal nerve roots in the intervertebral foramina. Even severe scoliosis can compress the nerve roots.

A lesion of one posterior spinal nerve root will produce pain in the area of skin innervated by that root and in the muscles that receive their sensory nerve supply from that root. Movements of the vertebral column in the region of the lesion will heighten the pain, and coughing and sneezing will also make it worse by raising the pressure within the vertebral canal. Before loss of sensation in the dermatome occurs, the patient might experience hyperalgesia and hyperesthesia.

A lesion of an anterior root will result in paralysis of any muscle that is supplied exclusively by that root and a partial paralysis of any muscle that is supplied partially by that root. In both cases, fasciculation and muscle atrophy occur.

Clinical Significance of Ascending Tract Lamination

Within the anterolateral white column of the spinal cord, the axons of the spinothalamic tracts from the sacral and lumbar segments of the body are deflected laterally by axons crossing the midline at successively higher levels. Within the posterior white column, the axons from the sacral and lumbar segments of the body are pushed medially by the axons from higher segments of the body. This deflection of the tracts produces lamination; thus, in the spinothalamic tracts (anterolateral system), the cervical to sacral segments are located from medial to lateral, whereas in the posterior white column (medial lemniscus system), the sacral to cervical segments are located from medial to lateral. This is shown diagrammatically in Figure 4-29.

Ascending Tract Injury

The detailed information described above is of practical value in patients experiencing external pressure exerted on the spinal cord in the region of the spinothalamic tracts. It explains, for example, why patients will experience a loss of pain and temperature sensations first in the sacral dermatomes of the body and, if the pressure increases, in the other higher segmental dermatomes of the body.

Lateral Spinothalamic Tract

Destruction of this tract produces contralateral loss of pain and thermal sensibilities below the level of the lesion. Therefore, the patient will not respond to pinprick or recognize hot and cold objects placed in contact with the skin.

Anterior Spinothalamic Tract

Destruction of this tract produces contralateral loss of light touch and pressure sensibilities below the level of the lesion. Remember that discriminative touch will still be present, because this information is conducted through the fasciculus gracilis and fasciculus cuneatus. The patient will not feel the light touch of a piece of cotton placed against the skin or feel pressure from a blunt object placed against the skin.

Fasciculus Gracilis and Fasciculus Cuneatus

Destruction of these tracts cuts off the supply of information from the muscles and joints to consciousness; thus, the individual does not know about the position and movements of the ipsilateral limbs below the level of the lesion. With the patient's eyes closed, he or she is unable to tell where the limb or part of the limb is in space. For example, if you passively dorsiflex the patient's big toe, he or she is unable to tell you whether the toe is pointing upward or downward. The patient has impaired muscular control, and the movements are jerky or ataxic.

The patient also has loss of vibration sense below the level of the lesion on the same side. This is easily tested by applying a vibrating tuning fork to a bony prominence, such as the lateral malleolus of the fibula or the styloid process of the radius.

Tactile discrimination will also be lost on the side of the lesion. This is tested most easily by gradually separating the two points of a compass until the patient can appreciate them as two separate points, not as one, when they are applied to the skin surface. Tactile discrimination

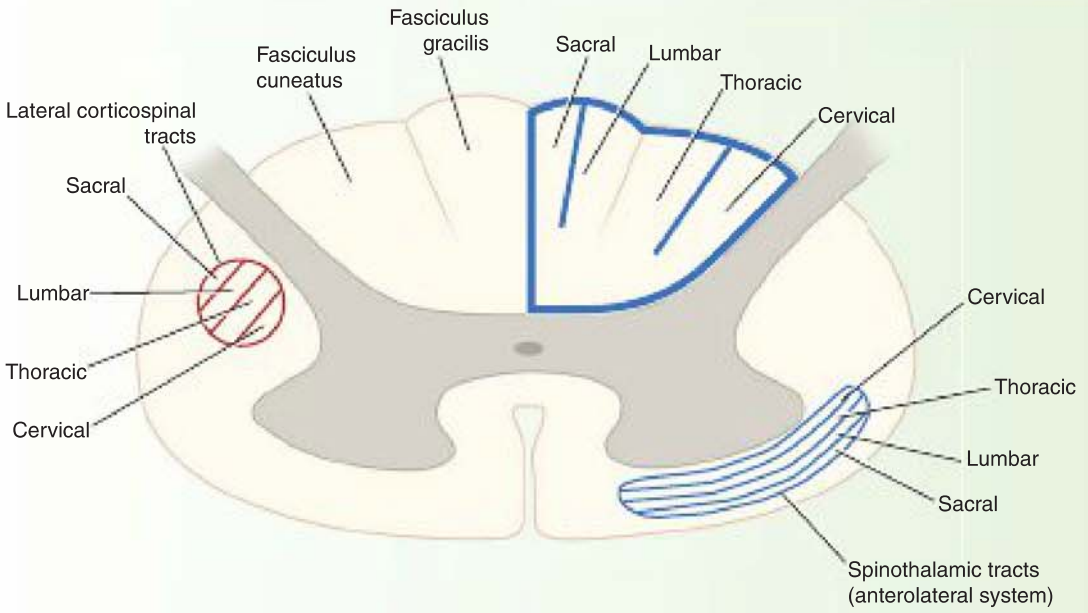

Figure 4-29 Segmental organization of the tracts in the posterior, lateral, and anterior white columns of the spinal cord.

varies from one part of the body to another. In a normal individual, the points have to be separated by about 3 to 4 mm before they are recognized as separate points on the tips of the fingers. On the back, however, the points have to be separated by 65 mm or more before they can be recognized as separate points.

The sense of general light touch would be unaffected, as these impulses ascend in the anterior spinothalamic tracts.

Note that a spinal cord lesion so localized that it affects one sensory tract only is extremely rare; usually, several ascending and descending tracts are involved.

Somatic and Visceral Pain

Somatic pain has been considered extensively in this chapter. The sense organs for somatic pain are the naked nerve endings. The initial sharp pain is transmitted by fast-conducting fibers, and the more prolonged burning pain travels in the slow-conducting nerve fibers (see p. 143).

In the viscera, special receptors, chemoreceptors, baroreceptors, osmoreceptors, and stretch receptors are sensitive to a variety of stimuli, including ischemia, stretching, and chemical damage. Afferent fibers from the visceral receptors reach the central nervous system (CNS) via the sympathetic and parasympathetic parts of the autonomic nervous system. Once within the CNS, the pain impulses travel by the same ascending tracts as the somatic pain and ultimately reach the postcentral gyrus.

Visceral pain is poorly localized and often associated with salivation, nausea, vomiting, tachycardia, and sweating. Visceral pain may be referred from the organ involved to a distant area of the body (**referred pain**).

Treatment of Acute Pain

Drugs such as salicylates can be used to reduce the synthesis of prostaglandin, a substance that sensitizes free nerve endings to painful stimuli. Local anesthetics, such as procaine, can be used to block nerve conduction in peripheral nerves.

Narcotic analgesics, such as morphine and codeine, reduce the affective reaction to pain and act on the opiate receptor sites in the cells in the posterior gray column of the spinal cord as well as other cells in the analgesic system in the brain likely by inhibiting the release of glutamate, substance P, and other transmitters from the sensory nerve endings. To minimize the side effects of morphine given by systemic injection, the narcotic can be given by local injection directly into the posterior gray horn of the spinal cord or by injection indirectly into the CSF in the subarachnoid space. Long-term cancer pain has been treated successfully by the continuous infusion of morphine into the spinal cord.

Treatment of Chronic Pain

New techniques, such as acupuncture and electrical stimulation of the skin, are now being used with success. Relief of pain can be achieved by the use of placebos in a few patients. The anticipation of the relief of pain is thought to stimulate the release of endorphins, which inhibit the normal pain pathway.

Relief of Pain by Rhizotomy or Cordotomy

Surgical relief of pain has been used extensively in patients with terminal cancer. Posterior rhizotomy or division of the posterior root of a spinal nerve effectively severs the conduction of pain into the CNS. It is a relatively simple procedure, but, unfortunately, the operation deprives the patient of other sensations besides pain. Moreover, if the pain sensation is entering the spinal cord through more than one spinal nerve, it may be necessary to divide several posterior roots.

Thoracic cordotomy has been performed with success in patients with severe pain originating from the lower abdomen or pelvis. Essentially, the operation consists of dividing the lateral spinothalamic tracts by inserting a knife into the anterolateral quadrant of the

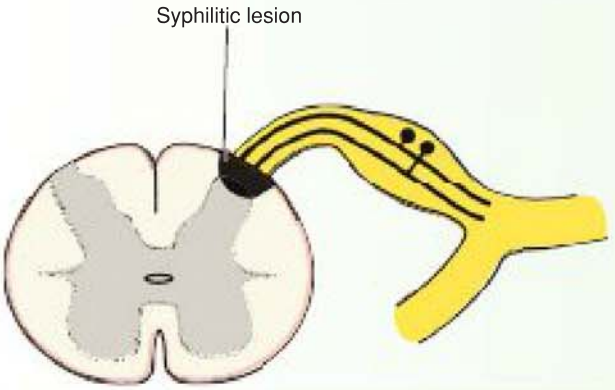

Figure 4-30 Site of a syphilitic lesion on the spinal cord.

spinal cord. Remember that the lateral spinothalamic fibers have originated in cells of the substantia gelatinosa in the opposite posterior gray column and that they cross the spinal cord obliquely and reach their tract in the white column three or four segments higher than their posterior root of entry. Cervical cordotomy has been performed successfully in patients with intractable pain in the neck or thorax.

Tabes Dorsalis

Tabes dorsalis is caused by syphilis. The organism causes a selective destruction of nerve fibers at the point of entrance of the posterior root into the spinal cord, especially in the lower thoracic and lumbosacral regions (Fig. 4-30). The following symptoms and signs may be present: (1) stabbing pains in the lower limbs, which may be very severe; (2) paresthesia, with numbness in the lower limbs; (3) hypersensitivity of skin to touch, heat, and cold; (4) loss of sensation in the skin of parts of the trunk and lower limbs and loss of awareness that the urinary bladder is full; (5) loss of appreciation of posture or passive movements of the limbs, especially the legs; (6) loss of deep pain sensation, such as when the muscles are forcibly compressed or when the Achilles tendon is compressed between the finger and thumb; (7) loss of pain sensation in the skin in certain areas of the body, such as the side of the nose or the medial border of the forearm, the thoracic wall between the nipples, or the lateral border of the leg; (8) ataxia of the lower limbs as the result of loss of proprioceptive sensibility (the unsteadiness in gait is compensated to some extent by vision; however, in the dark or if the eyes are closed, the ataxia becomes worse and the person may fall); (9) hypotonia as the result of loss of proprioceptive information that arises from the muscles and joints; and (10) loss of tendon reflexes, owing to degeneration of the afferent fiber component of the reflex arc (the knee and ankle tendon jerks are lost early in the disease).

Muscle Activity

Muscle tone is a state of continuous partial contraction of a muscle and is dependent on the integrity of a monosynaptic reflex arc (see description on p. 160). The receptor organs are the muscle spindles. The afferent neuron enters the spinal cord through the posterior root and synapses with the effector neuron or lower motor neuron in the anterior gray column. The lower motor neuron supplies the muscle fibers by traveling through the anterior roots, the spinal nerves, and peripheral nerves.

Muscle Tone

Muscle tone is abolished if any part of that simple reflex arc is destroyed. An atonic muscle feels soft and flabby and atrophies rapidly. Normal muscle tone exhibits a certain resilience or elasticity, and, when a muscle is passively stretched by moving a joint, a certain degree of resistance is felt. Normal muscle tone depends on the integrity of the monosynaptic reflex arc described above and the control superimposed on it by impulses received through the descending tracts from supraspinal levels. Note that muscle spindles are excitatory to muscle tone, whereas neurotendinous receptors are inhibitory to muscle tone.

Voluntary Movement

Voluntary movement is initiated by the individual. A series of different muscles are made to contract for the purpose of reaching a goal. This would suggest that the descending tracts that influence the activity of the lower motor neurons are driven by information received by the sensory systems, the eyes, the ears, and the muscles themselves and are affected further by past afferent information that has been stored in the memory. Moreover, the whole process may be colored by past and present emotional input. The limbic structures appear to play a role in emotion, motivation, and memory and may influence the initiation process of voluntary movement by their projections to the cerebral cortex.

The descending pathways from the cerebral cortex and brainstem, that is, the upper motor neurons, influence the activity of the lower motor neurons either directly or through internuncial neurons. Most of the tracts originating in the brainstem that descend to the spinal cord also are receiving input from the cerebral cortex.

The corticospinal tracts are believed to control the prime mover muscles, especially those responsible for the highly skilled movements of the distal parts of the limbs. The other supraspinal descending tracts play a major role in the simple basic voluntary movements and, in addition, adjust muscle tone so that easy and rapid movements of the joints can take place.

Interestingly, the basal ganglia and cerebellum do not give rise directly to descending tracts that influence the activities of the lower motor neuron, yet these parts of the nervous system greatly influence voluntary movements. This influence is accomplished indirectly by fibers that project to the cerebral cortex and brainstem nuclei, which are the sites of origin of the descending tracts.

Pyramidal and Extrapyramidal Tracts

The term **pyramidal tract** is used commonly by clinicians and refers specifically to the corticospinal tracts. The term came into common usage when it was learned that the corticospinal fibers become concentrated on the anterior part of the medulla oblongata in an area referred to as the **pyramids**.

The term **extrapyramidal tracts** refers to all the descending tracts other than the corticospinal tracts.

Upper Motor Neuron Lesions

Damage to descending tracts produces a variety of clinical signs, depending on the specific location.

Corticospinal Tract (Pyramidal Tract) Lesions

Lesions restricted to the corticospinal tracts produce the following clinical signs:

1. The **Babinski sign** is present. The great toe becomes dorsally flexed, and the other toes fan outward in response to scratching the skin along the lateral aspect of the sole of the foot. The normal response is plantar flexion of all the toes. Remember that the Babinski sign is normally present during the first year of life because the corticospinal tract is not myelinated until the end of the first year of life.
2. The explanation for the Babinski sign is thought to be that, normally, the corticospinal tracts produce plantar flexion of the toes in response to sensory stimulation of the skin of the sole. When the corticospinal tracts are nonfunctional, the influence of the other descending tracts on the toes becomes apparent, and a kind of withdrawal reflex takes place in response to stimulation of the sole, with the great toe being dorsally flexed and the other toes fanning out.
3. The **superficial abdominal reflexes** are absent. The abdominal muscles fail to contract when the skin of the abdomen is scratched. This reflex is dependent on the integrity of the corticospinal tracts, which exert a tonic excitatory influence on the internuncial neurons.
4. The **cremasteric reflex** is absent. The cremaster muscle fails to contract when the skin on the medial side of the thigh is stroked. This reflex arc passes through the first lumbar segment of the spinal cord. This reflex is dependent on the integrity of the corticospinal tracts, which exert a tonic excitatory influence on the internuncial neurons.
5. **Fine-skilled voluntary movements are lost.** This occurs especially at the distal end of the limbs.

Lesions of Other Descending Tracts (Extrapyramidal Tracts)

The following clinical signs are present in lesions restricted to the other descending tracts:

1. **Severe paralysis** with little or no muscle atrophy (except secondary to disuse).
2. **Spasticity** or **hypertonicity** of the muscles. The lower limb is maintained in extension, and the upper limb is maintained in flexion.
3. **Exaggerated deep muscle reflexes** and clonus may be present in the flexors of the fingers, the quadriceps femoris, and the calf muscles.
4. **Clasp-knife reaction.** When passive movement of a joint is attempted, muscle spasticity produces resistance. The muscles, on stretching, suddenly give way due to neurotendinous organ-mediated inhibition.

In clinical practice, organic lesions restricted only to the pyramidal tracts or only to the extrapyramidal tracts are rare. Usually, both sets of tracts are affected to a variable extent, producing both groups of clinical signs. As the pyramidal tracts normally tend to increase muscle tone and the extrapyramidal tracts inhibit muscle tone, the balance between these opposing effects will be altered, producing different degrees of muscle tone.

Lower Motor Neuron Lesions

Trauma, infection (poliomyelitis), vascular disorders, degenerative diseases, and neoplasms may all produce a lesion of the lower motor neuron by destroying the cell body in the anterior gray column or its axon in the anterior root or spinal nerve. The following clinical signs are present with lower motor neuron lesions:

1. Muscles exhibit **flaccid paralysis**.
2. Muscles **atrophy**.
3. Muscles **lose reflexes**.
4. **Muscular fasciculation** (muscle twitching) is seen only with slow destruction of the lower motor neuron cell.
5. **Muscular contracture** (shortening of the paralyzed muscles) occurs more often in the antagonist muscles whose action is no longer opposed by the paralyzed muscles.
6. Normally innervated muscles respond to stimulation by the application of faradic (interrupted) current, and the contraction continues as long as the current is passing. Galvanic or direct current causes contraction only when the current is turned on or turned off. When the lower motor neuron is cut, a muscle will no longer respond to interrupted electrical stimulation 7 days after nerve section, although it still will respond to direct current. After 10 days, the response to direct current also ceases. This change in muscle response to electrical stimulation is known as the **reaction of degeneration**.

Types of Paralysis

Hemiplegia is a paralysis of one side of the body and includes the upper limb, one side of the trunk, and the lower limb.
Monoplegia is paralysis of one limb only.
Diplegia is paralysis of two corresponding limbs (i.e., arms or legs).
Paraplegia is paralysis of the two lower limbs.
Quadriplegia is paralysis of all four limbs.

Relationship of Muscular Signs and Symptoms to Nervous System Lesions

The type of abnormal muscle tone resulting from nervous system damage will depend on the location of the lesion.

Hypotonia

Hypotonia exists when the muscle tone is diminished or absent. It occurs when any part of the monosynaptic stretch reflex arc is interrupted. It also occurs in cerebellar disease as the result of diminished influence on the γ motor neurons from the cerebellum.

Hypertonia

Hypertonia (spasticity, rigidity) exists when the muscle tone is increased. It occurs when lesions exist that involve supraspinal centers or their descending tracts but *not* the corticospinal tract. It also may occur at the local spinal segmental level and be produced by local excitation of the stretch reflex by sensory irritation (e.g., spasm of back muscles secondary to prolapsed intervertebral disc, spasm of abdominal muscles secondary to peritonitis).

Tremors

Tremors are rhythmic involuntary movements that result from the contraction of opposing muscle groups. These may be slow, as in **parkinsonism,** or fast, as in toxic tremors from thyrotoxicosis. They may occur at rest, as in parkinsonism, or with action, the so-called intention tremor, as seen in cerebellar disease.

Spasms

Spasms are sudden, involuntary contractions of large groups of muscles. Examples of spasms are seen in paraplegia and are due to lesions involving the descending tracts but not the corticospinal tract.

Athetosis

Athetosis are continuous, slow, involuntary, dysrhythmic movements that are always the same in the same patient and disappear during sleep. They impede voluntary movement. Athetosis occurs with lesions of the corpus striatum.

Chorea

Chorea consists of a series of continuous, rapid, involuntary, jerky, coarse, purposeless movements, which may occur during sleep. Chorea occurs with lesions of the corpus striatum.

Dystonia

Dystonia consists of frequent, maintained contractions of hypertonic muscles, leading to bizarre postures. It occurs with lesions of the lentiform nucleus.

Myoclonus

Myoclonus is a sudden contraction of an isolated muscle or part of a muscle. It occurs irregularly and commonly involves a muscle of a limb. It may be present with diseases that involve the reticular formation and the cerebellum. Normal myoclonic jerks sometimes occur in individuals as they are falling asleep and are believed to be due to a sudden temporary reactivation of the reticular formation.

Hemiballismus

Hemiballismus is a rare form of involuntary movement confined to one side of the body. It usually involves the proximal extremity musculature, and the limb involved is made to fly about in all directions. The lesion responsible occurs in the opposite subthalamic nucleus.

Acute Spinal Cord Injury

The incidence of acute spinal cord injuries in the United States is about 10,000 per year. The injury is catastrophic, because little or no regeneration of the severed nerve tracts takes place (see p. 71) and the individual is permanently disabled. Treatment has been restricted to anatomical realignment and stabilization of the vertebral column or decompression of the spinal cord. During the recovery process, the patient goes through intensive rehabilitation to optimize remaining neurologic function. Apart from improved management of medical complications, very little new therapy has been successful despite an enormous amount of research into the problem of neuronal regeneration in the spinal cord. Recently, the use of certain drugs (GM_1 ganglioside and methylprednisolone) administered to the patient soon after injury has resulted in some improvement in the neurologic deficit. Animal experiments appear to indicate that these drugs enhance the functional recovery of damaged neurons.

Chronic Compression of the Spinal Cord

If acute spinal cord injury is excluded, the causes of compression may be divided into extradural and intradural, which is further divided into those that arise outside the spinal cord (extramedullary) and those that arise within the cord (intramedullary).

Extradural causes include herniation of an intervertebral disc, infection of the vertebrae with tuberculosis, and primary and secondary tumors of the vertebra; leukemic deposits and extradural abscesses may also compress the spinal cord. The two common extramedullary tumors are meningiomas and nerve fibromas. Intramedullary causes include primary tumors of the spinal cord, such as gliomas.

The clinical signs and symptoms are produced by an interference with the normal anatomical and physiologic functions of the spinal cord. Pressure on the spinal arteries causes ischemia of the spinal cord with degeneration of nerve cells and their fibers. Pressure on the spinal veins causes edema of the spinal cord with interference in the function of the neurons. Finally, direct pressure on the white and gray matter of the spinal cord and the spinal nerve roots interferes with nerve conduction. At the same time, CSF circulation is obstructed, and the composition of the fluid changes below the level of obstruction.

Clinical Signs

One of the earliest signs is pain, which may be local pain in the vertebra involved or pain radiating along the distribution of one or more spinal nerve roots. The pain is made worse by coughing or sneezing and is usually worse at night, when the patient is recumbent.

Interference with motor function occurs early. Involvement of the anterior gray column motor cells at the level of the lesion results in partial or complete paralysis of muscles, with loss of tone and muscle wasting. The early involvement of the corticospinal and other descending tracts produces muscular weakness, increased muscle tone (spasticity), increased tendon reflexes below the level of the lesion, and an extensor plantar response. The degree of sensory loss will depend on the nerve tracts involved. A lesion of the posterior white columns of the spinal cord will cause loss of muscle joint sense (proprioception), vibration sense, and tactile discrimination below the level of the lesion on the same side. Involvement of the lateral spinal thalamic tracts will cause loss of pain and heat and cold sensations on the opposite side of the body below the level of the lesion. A more detailed discussion of the symptoms and signs following injury to the ascending and descending tracts in the spinal cord is given on pages 163 and 166.

Because many spinal tumors are benign and can be successfully removed (provided that irreversible damage to the spinal cord has not occurred as a result of compression of the blood supply), an early accurate diagnosis is essential. The following investigations should be performed: (1) radiography of the vertebral column, including computed tomography (CT) and magnetic resonance imaging (MRI); (2) spinal tap; and (3) myelography when determining the diagnosis is difficult.

Clinical Syndromes Affecting the Spinal Cord

Myelopathy stems from a number of causes, including trauma, developmental abnormality, infection, autoimmune destruction, and genetic disease.

Spinal Shock Syndrome

Spinal shock syndrome is a clinical condition that follows acute severe damage to the spinal cord. All cord functions below the level of the lesion become depressed or lost, and

sensory impairment and flaccid paralysis occur. The segmental spinal reflexes are depressed due to the removal of influences from the higher centers that are mediated through the corticospinal, reticulospinal, tectospinal, rubrospinal, and vestibulospinal tracts. Spinal shock, especially when the lesion is at a high level of the cord, may also cause severe hypotension from loss of sympathetic vasomotor tone.

In most patients, the shock persists for less than 24 hours, whereas in others, it may persist for as long as 1 to 4 weeks. As the shock diminishes, the neurons regain their excitability, and the effects of the upper motor neuron loss on the segments of the cord below the lesion, for example, spasticity and exaggerated reflexes, appear.

The presence of spinal shock can be determined by testing for anal sphincter reflex activity. The reflex can be initiated by placing a gloved finger in the anal canal and stimulating the anal sphincter to contract by squeezing the glans penis or clitoris or gently tugging on an inserted Foley catheter. An absent anal reflex indicates spinal shock. A cord lesion involving the sacral segments of the cord would nullify this test, insofar as the neurons giving rise to the inferior hemorrhoidal nerve to the anal sphincter (S2–S4) would be nonfunctioning.

Destructive Spinal Cord Syndromes

When neurologic impairment is identified following the disappearance of spinal shock, it can often be categorized into one of the following syndromes: (1) complete cord transection syndrome, (2) anterior cord syndrome, (3) central cord syndrome, or (4) Brown-Séquard syndrome or hemisection of the cord. Clinical findings often indicate a combination of lower motor neuron injury (at the level of destruction of the cord) and upper motor neuron injury (for those segments below the level of destruction).

COMPLETE CORD TRANSECTION SYNDROME

Complete cord transection syndrome (Fig. 4-31) results in complete loss of all sensibility and voluntary movement below the level of the lesion. It can be caused by fracture dislocation of the vertebral column, by a bullet or stab wound, or by an expanding tumor. The following characteristic clinical features will be seen *after* the period of spinal shock has ended:

1. Bilateral lower motor neuron paralysis and muscular atrophy in the segment of the lesion results from damage to the neurons in the anterior gray columns (i.e., lower motor neuron) and possibly from damage to the nerve roots of the same segment.
2. In bilateral spastic paralysis below the level of the lesion, bilateral Babinski sign is present, and, depending on the level of the segment of the spinal cord damaged, bilateral loss of the superficial abdominal and cremaster reflexes occurs. All these signs are caused by an interruption of the corticospinal tracts on both sides of the cord. The bilateral spastic paralysis is produced by the cutting of the descending tracts other than the corticospinal tracts.
3. In bilateral loss of all sensations below the level of the lesion, loss of tactile discrimination and vibratory and proprioceptive sensations is due to bilateral destruction of the ascending tracts in the posterior white columns. The loss of pain, temperature, and light touch sensations is caused by section of the lateral and anterior spinothalamic tracts on both sides. Because these tracts cross obliquely, the loss of thermal and light touch sensations occurs two or three segments below the lesion distally.
4. Bladder and bowel functions are no longer under voluntary control, because all the descending autonomic fibers have been destroyed.

With a complete fracture dislocation at the L2–L3 vertebral level (i.e., a level below the lower end of the cord in the adult), no cord injury occurs. Neural damage is confined to the cauda equina, and lower motor neuron, autonomic, and sensory fibers are involved.

ANTERIOR CORD SYNDROME

Anterior cord syndrome (Fig. 4-31) can be caused by cord contusion during vertebral fracture or dislocation, from injury to the anterior spinal artery or its feeder arteries with resultant ischemia of the cord, or by a herniated intervertebral disc. The following characteristic clinical features are seen *after* the period of spinal shock has ended:

1. Bilateral lower motor neuron paralysis in the segment of the lesion and muscular atrophy is caused by damage to the neurons in the anterior gray columns (i.e., lower motor neuron) and possibly by damage to the anterior nerve roots of the same segment.
2. In bilateral spastic paralysis below the level of the lesion, the extent depends on the size of the injured area of the cord. The bilateral paralysis is caused by the interruption of the anterior corticospinal tracts on both sides of the cord. The spasticity is produced by the interruption of tracts other than the corticospinal tracts.
3. Bilateral loss of pain, temperature, and light touch sensations below the level of the lesion are caused by interruption of the anterior and lateral spinothalamic tracts on both sides.
4. Tactile discrimination and vibratory and proprioceptive sensations are preserved because the posterior white columns on both sides are undamaged.

CENTRAL CORD SYNDROME

Central cord syndrome is most often caused by hyperextension of the cervical region of the spine (Fig. 4-31). The cord is pressed on anteriorly by the vertebral bodies and posteriorly by the bulging of the ligamentum flavum, causing damage to the central region of the spinal cord. Radiographs of these injuries often appear normal because no fracture or dislocation has occurred. The following characteristic clinical features are seen *after* the period of spinal shock has ended:

1. Bilateral lower motor neuron paralysis in the segment of the lesion and muscular atrophy is caused by damage to the neurons in the anterior gray columns (i.e., lower motor neuron) and possibly by damage to the nerve roots of the same segment.
2. In bilateral spastic paralysis below the level of the lesion with characteristic sacral "sparing," lower limb fibers are affected less than upper limb fibers because the descending fibers in the lateral corticospinal tracts are laminated, with the upper limb fibers located medially and the lower limb fibers located laterally (Fig. 4-29).
3. In bilateral loss of pain, temperature, light touch, and pressure sensations below the level of the lesion with characteristic sacral "sparing," because the ascending fibers in the lateral and anterior spinothalamic tracts are also laminated, with the upper limb fibers located medially and the lower limb fibers located laterally, the upper limb fibers are more susceptible to damage than the lower limb fibers.

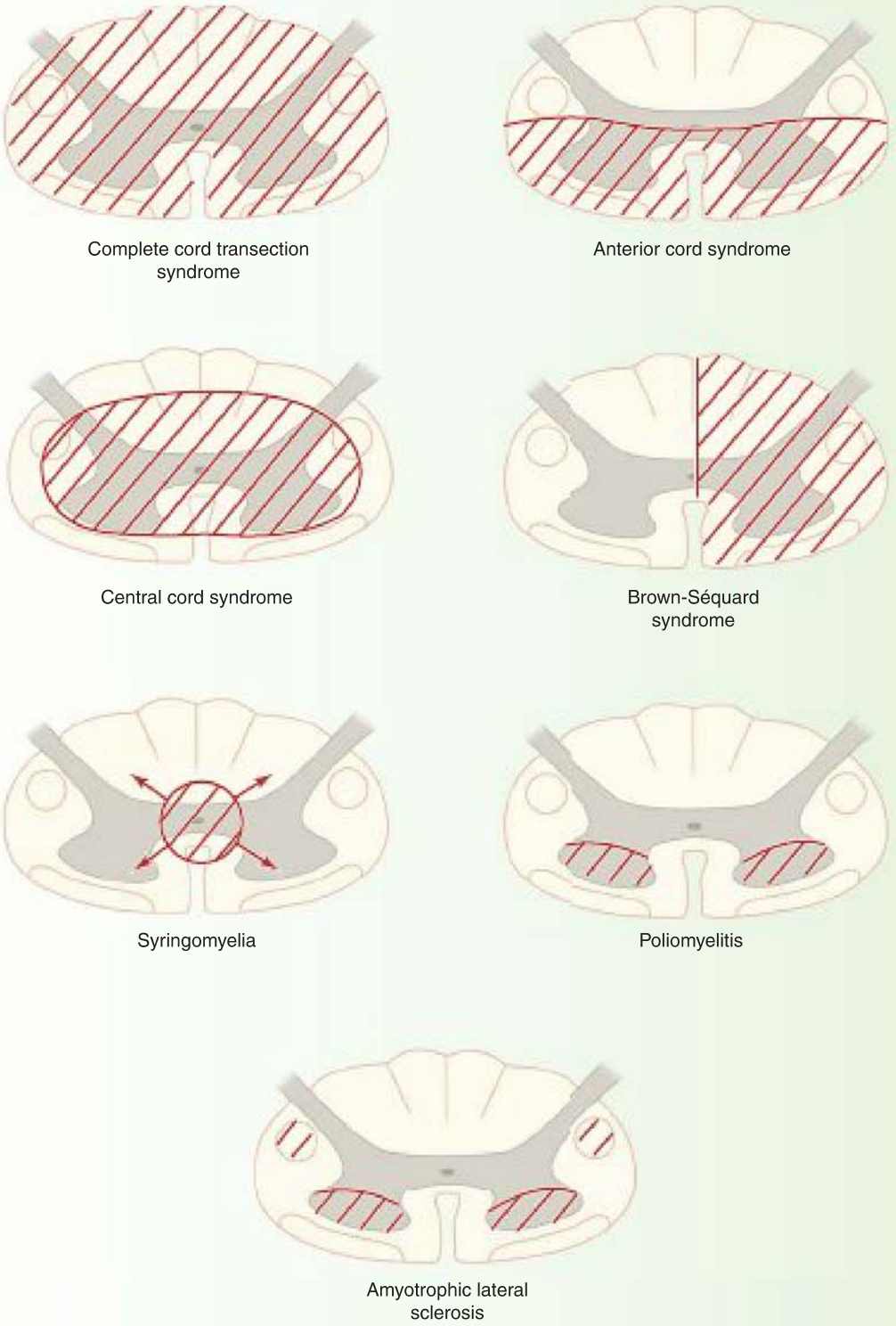

Figure 4-31 Spinal cord syndromes.

Thus, the clinical picture of a patient with a history of a hyperextension injury of the neck, presenting with motor and sensory tract injuries involving principally the upper limb, would strongly suggest central cord syndrome. The sparing of the lower part of the body may be evidenced by (1) the presence of perianal sensation, (2) good anal sphincter tone, and (3) the ability to move the toes slightly. In patients whose damage is caused by edema of the spinal cord alone, the prognosis is often very good. Mild central cord syndrome that consists only of paresthesias of the

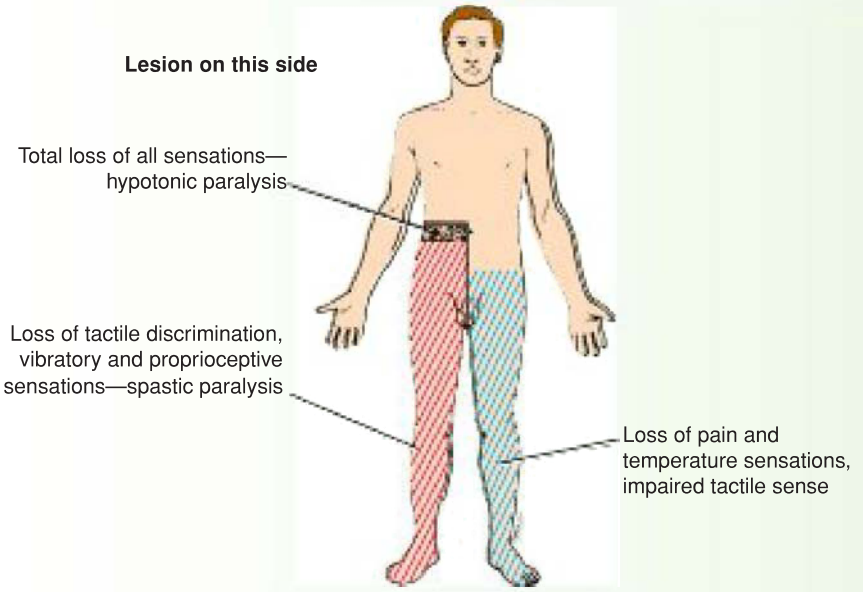

Figure 4-32 Brown-Séquard syndrome with a spinal cord lesion at the right 10th thoracic level.

upper part of the arm and some mild arm and hand weakness can occur.

BROWN-SÉQUARD SYNDROME (CORD HEMISECTION)

Hemisection of the spinal cord can be caused by fracture dislocation of the vertebral column, by a bullet or stab wound, or by an expanding tumor (Fig. 4-31). Incomplete hemisection is common; complete hemisection is rare. The following characteristic clinical features are seen in patients with complete hemisection of the cord (Fig. 4-32) *after* the period of spinal shock has ended:

1. Ipsilateral lower motor neuron paralysis in the segment of the lesion and muscular atrophy are caused by damage to the neurons on the anterior gray column and possibly by damage to the nerve roots of the same segment.
2. In ipsilateral spastic paralysis below the level of the lesion, an ipsilateral Babinski sign is present, and, depending on the segment of the cord damaged, an ipsilateral loss of the superficial abdominal reflexes and cremasteric reflex occurs. All these signs are due to loss of the corticospinal tracts on the side of the lesion. Spastic paralysis is produced by interruption of the descending tracts other than the corticospinal tracts.
3. Ipsilateral band of cutaneous anesthesia in the segment of the lesion results from destruction of the posterior root and its entrance into the spinal cord at the level of the lesion.
4. Ipsilateral loss of tactile discrimination and of vibratory and proprioceptive sensations below the level of the lesion are caused by destruction of the ascending tracts in the posterior white column on the same side of the lesion.
5. Contralateral loss of pain and temperature sensations below the level of the lesion is due to destruction of the crossed lateral spinothalamic tracts on the same side of the lesion. Because the tracts cross obliquely, the sensory loss occurs two or three segments below the lesion distally.
6. Contralateral but not complete loss of tactile sensation below the level of the lesion condition is caused by destruction of the crossed anterior spinothalamic tracts on the side of the lesion. Here, again, because the tracts cross obliquely, the sensory impairment occurs two or three segments below the level of the lesion distally. The contralateral loss of tactile sense is incomplete because discriminative touch traveling in the ascending tracts in the contralateral posterior white column remains intact.

Syringomyelia

Syringomyelia, which is due to a developmental abnormality in the formation of the central canal, most often affects the brainstem and cervical region of the spinal cord. At the site of the lesion, cavitation and gliosis in the central region of the neuroaxis occurs (Fig. 4-33). The following characteristic signs and symptoms are found:

1. Pain and temperature sensations are lost in dermatomes on both sides of the body related to the affected segments of the cord. This loss commonly has a shawllike distribution caused by the interruption of the lateral spinothalamic tracts as they cross the midline in the anterior gray and white commissures. The patient commonly complains of accidental burning injuries to the fingers.
2. Tactile discrimination, vibratory sense, and proprioceptive sense are normal because the ascending tracts in the posterior white column are unaffected.
3. Lower motor neuron weakness is present in the small muscles of the hand. It may be bilateral, or one hand may suffer before the other. As the lesion expands in the lower cervical and upper thoracic region, it destroys the anterior horn cells of these segments. Later, the other muscles of the arm and shoulder girdles undergo atrophy.
4. Bilateral spastic paralysis of both legs may occur, with exaggerated deep tendon reflexes and the presence of a positive Babinski response. These signs are produced by the further expansion of the lesion laterally into the white column to involve the descending tracts.

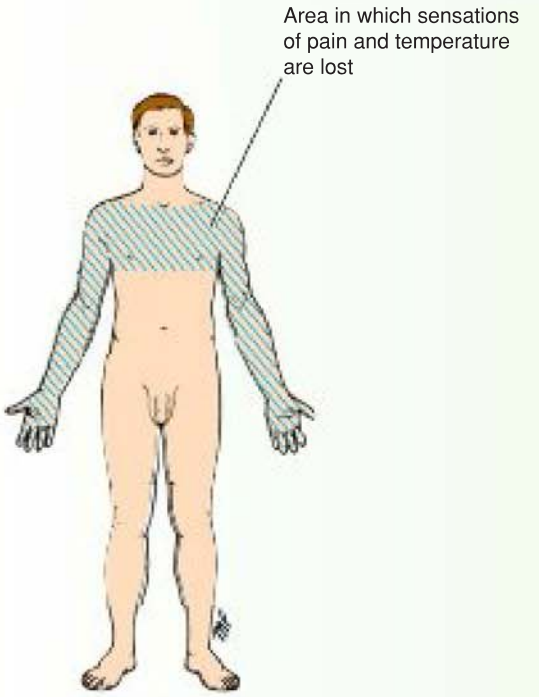

Figure 4-33 Skin area in which the sensations of pain and temperature are lost in syringomyelia.

5. Horner syndrome may be present. This is caused by the interruption of the descending autonomic fibers in the reticulospinal tracts in the lateral white column by the expanding lesion.

Poliomyelitis

Poliomyelitis is an acute viral infection of the neurons of the anterior gray columns of the spinal cord (Fig. 4-31) and cranial nerve motor nuclei. Immunization has greatly reduced the incidence of poliomyelitis, which was once a feared disease. Paralysis and muscle wasting follow motor nerve cell death. Lower limb muscles are more often affected than those of the upper limb. In severe poliomyelitis, respiration may be threatened due to the paralysis spreading to the intercostal muscles and diaphragm. Muscles of the face, pharynx, larynx, and tongue may also be paralyzed. Improvement usually begins at the end of the first week as the edema in the affected area subsides, and function returns to the neurons that have not been destroyed.

Multiple Sclerosis

Multiple sclerosis is a common disease confined to the CNS, causing demyelination of the ascending and descending tracts. It is a disease of young adults, and the cause is unknown. Autoimmunity, infection, and heredity, alone or in combination, may play a role in its etiology. A breach in the integrity of the blood–brain barrier in an individual who is genetically predisposed to the disease may be responsible. This could result in the invasion of the brain and spinal cord by some infection allowing leukocytes to enter the normally immunologically protected CNS. Inflammation and demyelination with loss of the myelin sheath results in the breakdown of the insulation around the axons, and the velocity of the action potentials is reduced and ultimately becomes blocked. Although myelin is relatively rich in lipid (70% to 80%), it also contains proteins that play a role in myelin compaction. Many of these proteins in the myelin of the CNS differ from those in the peripheral nervous system. Experimentally, basic myelin proteins injected into animals have been shown to produce a strong immune response, and CNS demyelination occurs. Mutations in the structure of myelin protein can possibly occur and be responsible for some inherited forms of demyelination. Also possible is that autoantigens develop in multiple sclerosis.

The course of multiple sclerosis is chronic with exacerbations and remissions. Because of the widespread involvement of different tracts at different levels of the neuroaxis, the signs and symptoms are multiple, but remissions do occur. Weakness of the limbs is the most common sign of the disease. Ataxia due to involvement of the tracts of the cerebellum may occur, but spastic paralysis may also be present.

Recent research has suggested that the remissions in multiple sclerosis may in part be explained by the remodeling of the demyelinated axonal plasma membrane so that it acquires a higher than normal number of sodium channels, which permit conduction of action potentials despite the loss of myelin.

Patients who have the progressive form of the disease without remissions have substantial damage to the axons as well as the myelin. This would suggest that multiple sclerosis is not just a demyelinating disease but one with axonal pathology also.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (Lou Gehrig disease) is a disease confined to the corticospinal tracts and the motor neurons of the anterior gray columns of the spinal cord (Fig. 4-31). It is rarely familial and is inherited in about 10% of patients. Amyotrophic lateral sclerosis is a chronic progressive disease of unknown etiology. Typically, it occurs in late middle age and is inevitably fatal in 2 to 6 years. The lower motor neuron signs of progressive muscular atrophy, paresis, and fasciculations are superimposed on the signs and symptoms of upper motor neuron disease with paresis, spasticity, and Babinski response. The motor nuclei of some cranial nerves may also be involved.

Parkinson Disease

Parkinson disease is associated with neuronal degeneration in the substantia nigra and, to a lesser extent, in the globus pallidus, putamen, and caudate nucleus. The degeneration of the inhibitory nigrostriate fibers results in a reduction in the release of the neurotransmitter dopamine within the corpus striatum. This leads to hypersensitivity of the dopamine receptors in the postsynaptic neurons in the corpus striatum, which become overactive. The characteristic signs of the disease include tremor and cogwheel rigidity (hyperkinetic activity) and difficulty initiating voluntary movements, which are slow (hypokinetic activity).

Pernicious Anemia

Pernicious anemia, a form of megaloblastic anemia, is caused by vitamin B_{12} deficiency. The disease may produce

extensive damage to the tracts in the posterior and lateral white columns of the spinal cord as well as peripheral nerve degeneration. Widespread sensory and motor losses may be present due to involvement of the ascending and descending tracts of the spinal cord.

Vertebral Column Radiography

The views commonly used in radiography are anteroposterior, lateral, and oblique. Vertebral destruction due to tuberculosis or primary or secondary tumors of the vertebrae or fractures due to trauma usually can be revealed by radiographic examination. Erosion of the pedicles by a tumor within the intervertebral foramina may be seen. Narrowing of the space between the vertebral bodies with bony spurs because of osteoarthritic changes in adjacent vertebral bodies can also be seen.

Computed Tomography and Magnetic Resonance Imaging

CT scans of the vertebrae and joints can be obtained (Fig. 4-34). A protrusion of an intervertebral disc can be identified, and the presence of narrowing of the vertebral canal (**spinal stenosis**) can be diagnosed.

Sagittal MRI is increasingly being used to replace CT and myelography. The parts of a vertebra, the intervertebral disc, the posterior longitudinal ligament, and meningeal sac (**thecal sac**) can easily be identified (Fig. 4-35).

Myelography

The subarachnoid space can be studied radiographically by the injection of a contrast medium into the subarachnoid space by spinal tap. Iodized oil has been used with success. This technique is referred to as **myelography** (Figs. 4-36 and 4-37).

If the patient is sitting in the upright position, the oil sinks to the lower limit of the subarachnoid space at the level of the lower border of the second sacral vertebra. By placing the patient on a tilting table, the oil can be made to gravitate gradually to higher levels of the vertebral column.

A normal myelogram will show pointed lateral projections at regular intervals at the intervertebral space levels because the opaque medium fills the lateral extensions of the subarachnoid space around each spinal nerve. The presence of a tumor or a prolapsed intervertebral disc may obstruct the movement of the oil from one region to another when the patient is tilted.

With the recent technologic advances in CT scans and MRIs, intrusive procedures such as myelography are usually not required to make a diagnosis.

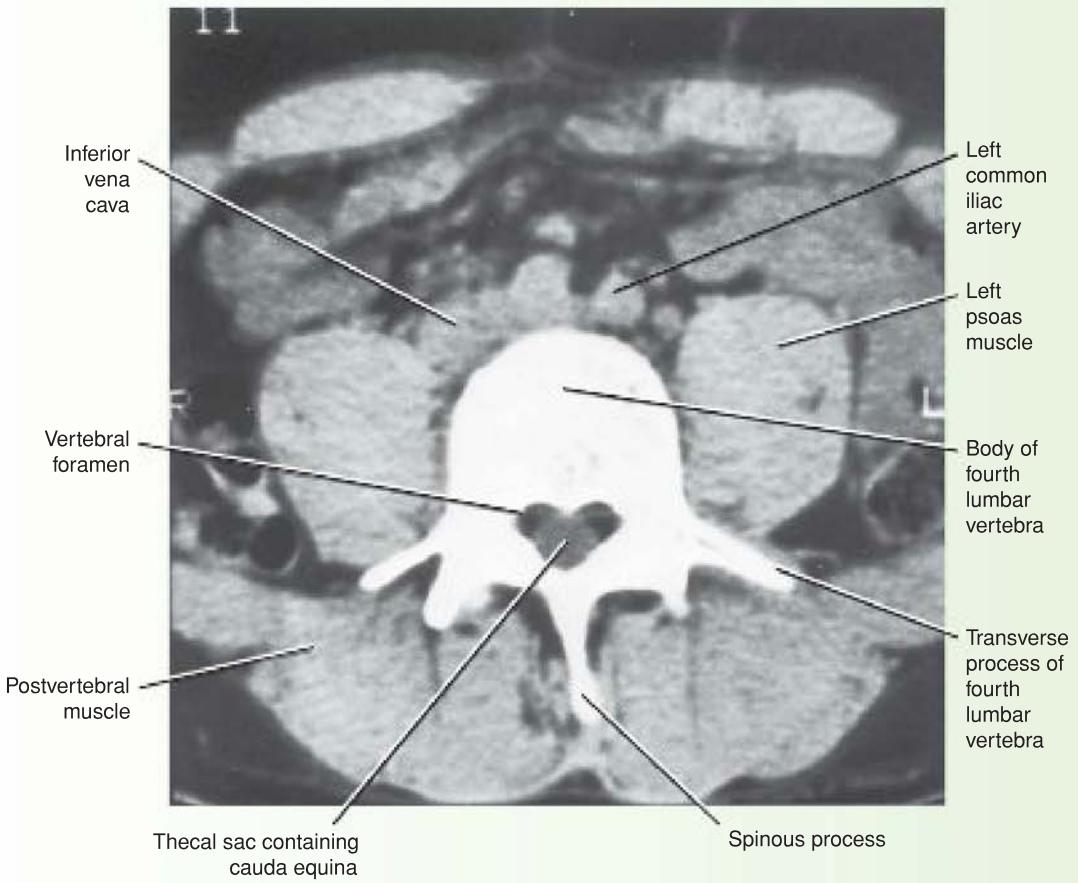

Figure 4-34 Horizontal (axial) CT scan of the fourth lumbar vertebra.