

# Introduction to the Peripheral Nervous System

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## ●●● INTRODUCTION

The nervous system comprises the central nervous system (CNS) and the peripheral nervous system (PNS). The CNS is surrounded and protected by the skull (neurocranium) and vertebral column and consists of the brain and the spinal cord. The PNS exists primarily outside these bony structures.

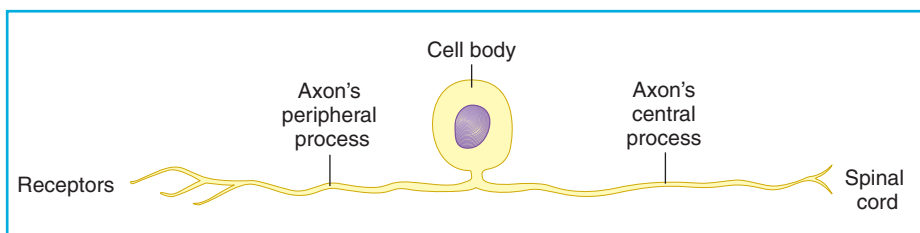
The entire nervous system is composed of neurons, which are characterized by their ability to conduct information in the form of impulses (action potentials), and their supporting cells plus some connective tissue. A neuron has a cell body (perikaryon) with its nucleus and organelles that support the functions of the cell and its processes. Dendrites are the numerous short processes that carry an action potential

toward the neuron's cell body, and an axon is the long process that carries the action potential away from the cell body. Some neurons appear to have only a single process extending from only one pole (a differentiated region of the cell body) that divides into two parts (Fig. 2-1). This type of neuron is called a pseudounipolar neuron because embryonically it develops from a bipolar neuroblast in which the two axons fuse. Multipolar neurons (Fig. 2-2) have multiple dendrites and typically a single axon arising from an enlarged portion of the cell body called the axon hillock. These processes extend from different poles of the cell body.

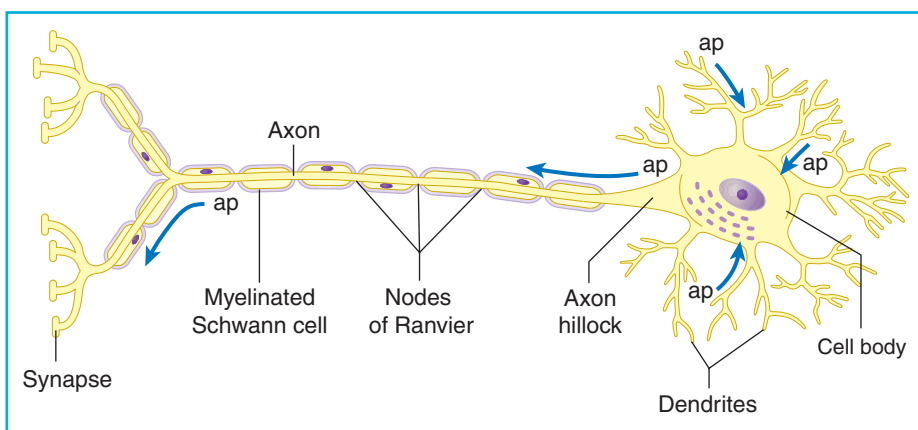
One neuron communicates with other neurons or glands or muscle cells across a junction between cells called a synapse. Typically, communication is transmitted across a synapse by means of specific neurotransmitters, such as acetylcholine, epinephrine, and norepinephrine, but in some cases in the CNS by means of electric current passing from cell to cell.

Many axons are ensheathed with a substance called myelin, which acts as an insulator. Myelinated axons transmit impulses much faster than nonmyelinated axons. Myelin consists of concentric layers of lipid-rich material formed by the plasma membrane of a myelinating cell. In the CNS, the myelinating cell is the oligodendrocyte, and in the PNS it is the Schwann cell. The myelinated sheath is periodically interrupted by segments lacking myelin, called the *nodes of Ranvier*.

The CNS regions that contain myelinated axons are termed *white matter* because myelinated processes appear white in color, whereas the portions of the CNS composed mostly of nerve cell bodies are called *gray matter*.



**Figure 2-1. An afferent (sensory) neuron.** Note the cell body and the peripheral and central processes, which form an axon. For a spinal nerve, the cell body is located in the dorsal root ganglion of the dorsal root.



**Figure 2-2. A myelinated efferent (motor) neuron.** Note the direction of the action potential (ap) toward the synapse with another neuron or with skeletal muscle.

## PHYSIOLOGY

### Action Potential in the Nodes of Ranvier

The exposed portions of the axon at the nodes of Ranvier have a high density of voltage-dependent  $\text{Na}^+$  channels while the voltage-dependent  $\text{K}^+$  channels are located in the myelinated portions of the axon. This arrangement allows the action potential to “jump” from one node to another in a rapid saltatory, or leaping, conduction. Thus, the conduction velocity of myelinated axons is higher than the conduction velocity of nonmyelinated axons of the same size.

## CLINICAL MEDICINE

### Multiple Sclerosis

Multiple sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. Extensive loss of myelin, which occurs predominantly in the white matter, produces axonal degeneration and even loss of the cell bodies. In some cases, remyelination occurs, resulting in partial or complete recovery periods. This relapsing-remitting form of MS is the most common form of MS at the time of initial diagnosis.

(involuntary movements). These divisions can be traced back to the embryonic origins of the structures that they innervate, starting at the level of the trilaminar embryo. The somatic nervous system innervates structures derived from ectoderm, paraxial mesoderm, and lateral plate somatic mesoderm. The autonomic nervous system supplies structures derived from endoderm, intermediate mesoderm, and lateral plate visceral mesoderm.

In both the somatic system and autonomic system, neurons and their nerves are classified according to function. Individual neurons that carry impulses away from the CNS are called *efferent*, or *motor* neurons. The axons of these multipolar neurons are also referred to as efferent fibers and they synapse on muscles or glands. Neurons that carry impulses to the CNS are called *afferent*, or *sensory*, neurons. In the somatic system, these neurons carry impulses that originate from receptors for external stimuli (pain, touch, and temperature), referred to as *exteroceptors*. In addition, receptors located in tendons, joint capsules, and muscles convey position sense that is known as *proprioception*. Afferent neurons that run with the autonomic system carry impulses from interoceptors located within visceral organs that convey stretch as well as pressure, chemoreception, and pain.

## PERIPHERAL NERVOUS SYSTEM

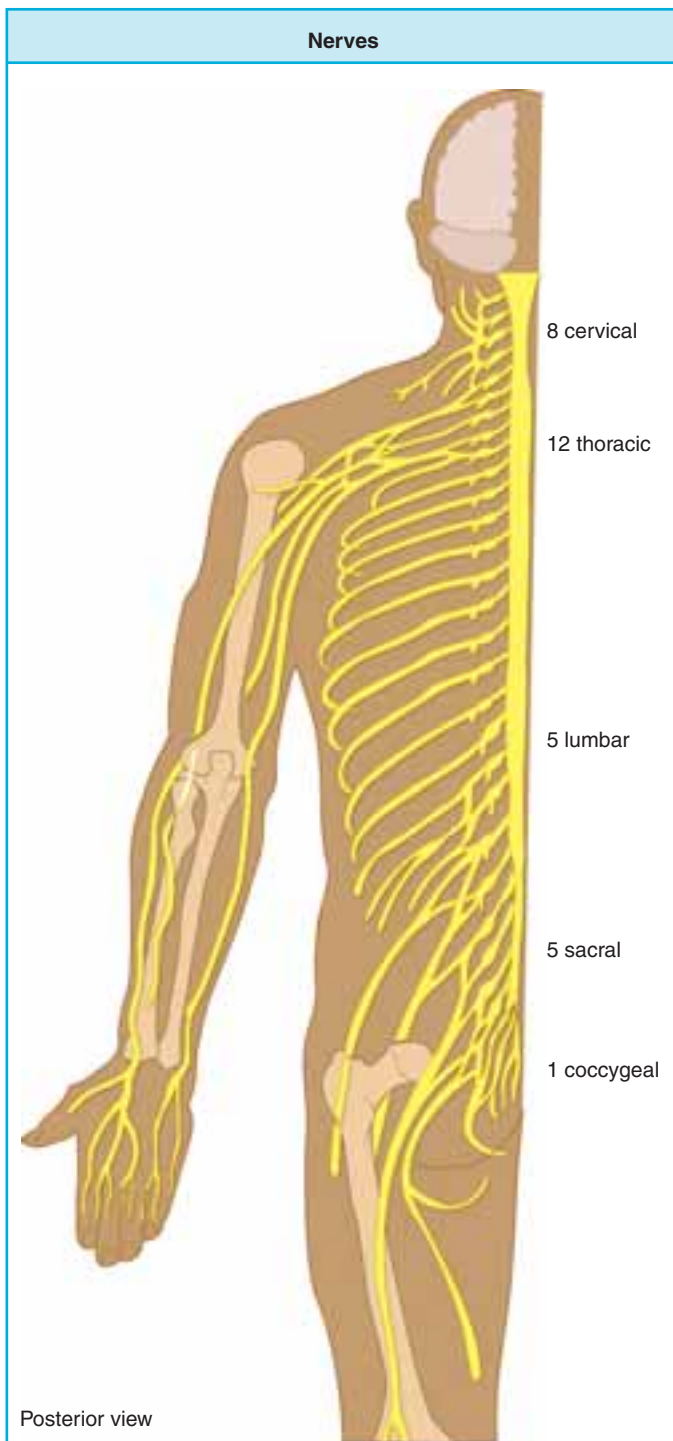
The PNS encompasses the nervous system external to the brain and spinal cord. In the PNS, axons (fibers) are collected into bundles supported by connective tissue to form a nerve.

The PNS consists of 31 pairs of spinal nerves (Fig. 2-3), which arise from the spinal cord, and 12 pairs of cranial nerves, which originate from the brainstem. In addition, the nervous system contains both the somatic system and the autonomic system, each with portions within the CNS and PNS. The somatic system mediates information between the CNS and the skin, skeletal muscles (voluntary movements), bones, and joints. The autonomic system, in contrast, mediates information between the CNS and visceral organs

## HISTOLOGY

### Nerve Tissue

The epineurium, perineurium, and endoneurium organize the nerve into smaller and smaller bundles. The epineurium is continuous with the dura mater at or just distal to the intervertebral foramen; the arachnoid mater follows the ventral and dorsal roots to join the pia mater. Laterally the layers of arachnoid that follow the nerve roots fuse with each other, sealing the subarachnoid space and joining the perineurium. The pia mater is closely associated with the CNS, but the pia mater is reflected off the CNS to cover the arteries, which are now described as lying in a subpial space that is continuous with the perivascular spaces.



**Figure 2-3.** Thirty-one pairs of spinal nerves.

### ●●● SPINAL CORD (CENTRAL NERVOUS SYSTEM)

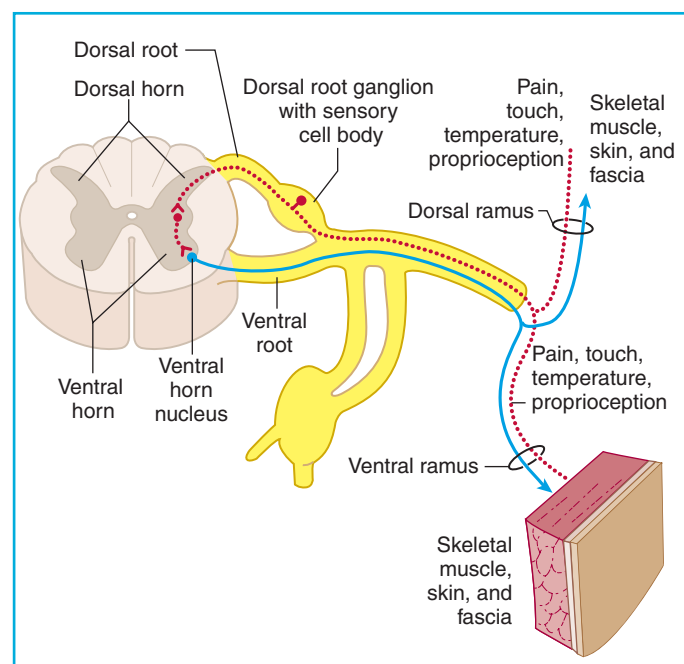
The spinal cord is a long tubular structure that is divided into a peripheral white matter (composed of myelinated axons) and a central gray matter (cell bodies and their connecting fibers). When viewed in cross section, the gray matter has pairs of horn-like projections into the surrounding white

matter. These horns are called ventral horns, dorsal horns, and lateral horns, but in three dimensions they represent columns that run the length of the spinal cord.

The ventral horns contain the cell bodies of motor neurons and their axons (Fig. 2-4). A collection of neuronal cell bodies in the CNS is a nucleus. Axons of the ventral horn nuclei leave the spinal cord in bundles called ventral roots. These motor fibers innervate skeletal muscles.

The lateral (intermediolateral) horns contain the cell bodies for the sympathetic nervous system at spinal cord levels T1–L2 and for the parasympathetic nervous system at spinal cord levels S2–S4. The axons from these neurons also leave the spinal cord through the ventral root and will synapse in various peripheral ganglia. A collection of neuronal cell bodies in the PNS is a ganglion. It is important to note that synapses occur within ganglia of the autonomic nervous system but not within the sensory ganglia of the somatic nervous system.

The dorsal horns receive the sensory fibers originating in the peripheral nervous system. Sensory fibers reach the dorsal horn by means of a bundle called the dorsal root (see Fig. 2-4). The dorsal root ganglion is part of the dorsal root. The sensory fibers have their cell bodies located in swellings called the *dorsal root ganglia*. The dorsal root contains sensory fibers (axons), while the dorsal root ganglia contain sensory cell bodies (and their axons). The central axons of the sensory neuron enter the dorsal horn of the gray matter. Some of these fibers will run in tracts (a bundle of fibers in the CNS) of the white matter to reach other parts of the CNS. Other axons will synapse with intercalated neurons (interneurons), which in turn synapse with motor neurons in the ventral horn to form a reflex arc.



**Figure 2-4.** A typical cross-section of the spinal cord demonstrates the central location of the gray matter and the peripheral location of the white matter.

Although the dorsal root is essentially sensory and the ventral root is motor, the two roots come together within the bony intervertebral foramen to form a mixed spinal nerve (i.e., it contains both sensory and motor fibers). The spinal cord is defined as part of the CNS, but the ventral and dorsal roots are considered parts of the PNS. Outside the intervertebral foramen, the mixed nerve divides into a ventral ramus (from the Latin for “branch”) and a dorsal ramus (see Fig. 2-4). The larger ventral ramus supplies the ventrolateral body wall and the limbs; the smaller dorsal ramus supplies the back. Since the ventral and dorsal rami are branches of the mixed nerve, they both carry sensory and motor fibers.

A spinal cord segment is the portion of the spinal cord that gives rise to a pair of spinal nerves. Thus, the spinal cord gives rise to 8 pairs of cervical nerves (C1–C8), 12 pairs of thoracic nerves (T1–T12), 5 pairs of lumbar nerves (L1–L5), 5 pairs of sacral nerves (S1–S5), and 1 pair of coccygeal nerves (Co1) (see Fig. 2-3). The spinal cord segments are numbered in the same manner as these nerves.

## OVERVIEW OF THE AUTONOMIC NERVOUS SYSTEM

The autonomic nervous system differs structurally and physiologically from the somatic nervous system. The autonomic nervous system is often defined as a motor neuronal system, generally concerned with involuntary body functions, in contrast to the somatic nervous system, which has both motor and sensory neurons responsible for voluntary muscle function and general sensation. The autonomic nervous system innervates smooth muscle, cardiac muscle, and glands. Again, there are sensory fibers from the viscera that run with the autonomic nerves but are historically not considered part of it.

Anatomically, the motor component of the somatic nervous system consists of a single neuron: an efferent neuron with its cell body located in the ventral horn of the spinal cord and whose axon runs to innervate skeletal muscle. However, the autonomic nervous system consists of a chain of two efferent neurons to innervate smooth muscle or glands. The first-order neuronal cell body is located in a CNS nucleus, and its fiber (axon) travels peripherally to synapse with a second-order neuron, which is located in a PNS ganglion. Physiologically, smooth and cardiac muscles are not completely dependent on autonomic motor neurons for contraction. In contrast, skeletal muscle is completely dependent on somatic motor innervation to contract and to remain viable. Indeed, first paralysis, followed by atrophy, results when skeletal muscle loses its innervation.

The first-order autonomic neurons have their cell bodies located in the CNS, either in the lateral (intermediolateral) horn of the spinal cord or in the brain stem. The cell bodies of first-order neurons give rise to myelinated axons that run from the CNS to synapse on second-order neurons in a ganglion, located completely outside the CNS. These cell bodies give rise to unmyelinated axons that innervate smooth muscle, cardiac muscle, and glands.

The first-order neurons and their fibers are referred to as *preganglionic* (presynaptic), and the second-order neurons and their fibers are *postganglionic* (postsynaptic). Each autonomic preganglionic fiber synapses with several postganglionic neurons. This arrangement allows preganglionic neurons to stimulate multiple postganglionic neurons whose postganglionic fibers reach smooth muscle and glands by means of several different pathways.

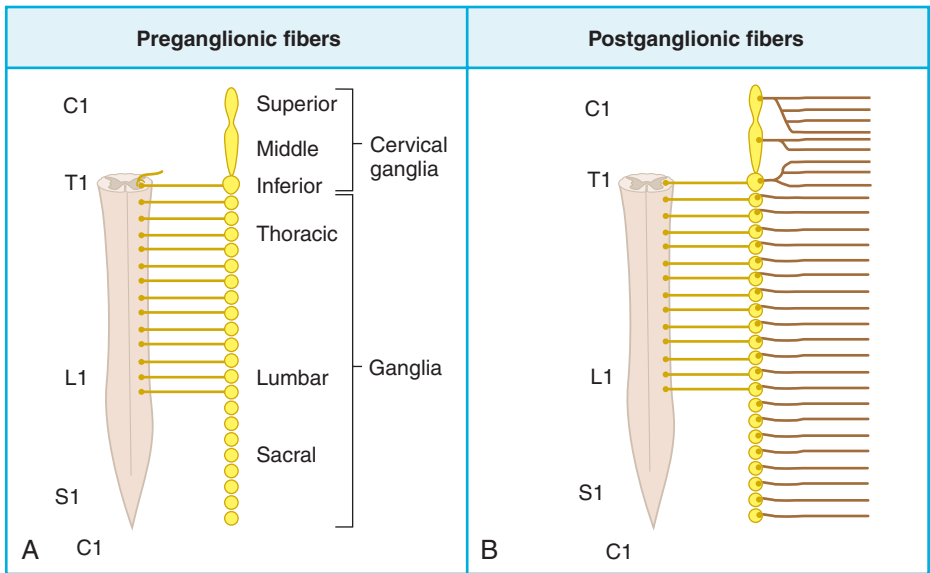
The autonomic nervous system is subdivided into the sympathetic and parasympathetic nervous systems. These terms refer to the specific locations of preganglionic and postganglionic cell bodies, as well as neurohumoral transmitters and function.

## Sympathetic Nervous System

The sympathetic nervous system supplies visceral structures throughout the entire body. It supplies visceral structures associated with the skin (sweat glands, blood vessels, and arrector pili muscles) and deeper visceral structures of the body (blood vessels, smooth muscle in the walls of organs, and various glands).

The sympathetic preganglionic cell bodies are located in the lateral horns of thoracic spinal cord segments 1 through 12 plus lumbar segments 1 and 2 (Fig. 2-5). The axons of these preganglionic cells leave the spinal cord along with the somatic motor axons by means of the ventral horn and root at each of these levels (T1–L2) to join the mixed spinal nerve (Fig. 2-6). This outflow is referred to as the *thoracolumbar outflow*. The preganglionic sympathetic fibers follow the spinal nerve’s ventral ramus and then leave the ventral ramus to enter the sympathetic ganglia of the sympathetic trunk. The sympathetic trunk is one of the paired elongated nerve strands characterized by ganglia and interganglionic (interconnecting) segments that parallel the vertebral column. The paired sympathetic trunks are lateral to the vertebral column starting at the level of the first cervical vertebra, and they run anterolaterally onto the vertebral column in the lumbar and sacral regions. The myelinated bundle of preganglionic fibers from the ventral ramus to the sympathetic trunk is called a *white ramus communicans* (white communicating branch; plural, *rami communicantes*) (see Figs. 2-6 and 2-7).

Thus, there are 14 pairs of white rami communicantes, arising from the 12 pairs of thoracic spinal nerves and the first two pairs of lumbar spinal nerves. Therefore, only 14 spinal cord segments (T1–L2) contain preganglionic sympathetic cell bodies, and only 14 pairs of white rami communicantes enter the sympathetic trunk carrying preganglionic fibers to synapse with the postganglionic nerve cells in all 22–23 sympathetic chain ganglia. *The preganglionic fibers can synapse in the thoracic and upper lumbar ganglia or run either up or down the chain, but not both, to synapse in cervical, lumbar, or sacral ganglia.* Postganglionic sympathetic fibers leave the sympathetic chain to enter all 31 pairs of spinal ventral rami by means of the 31 pairs of gray rami communicantes.

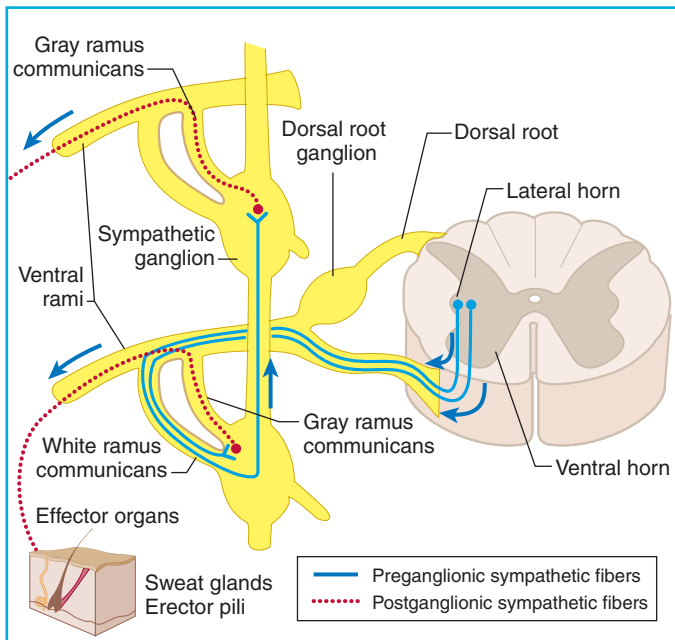


**Figure 2-5.** Preganglionic sympathetic fibers leave the ventral rami of mixed spinal nerves (T1–L2) to enter the sympathetic chain ganglia by means of 14 pairs of white rami communicantes (A), while 31 pairs of gray rami communicantes leave the sympathetic chain ganglia (B). (Only the left half of the thoracolumbar outflow is illustrated.)

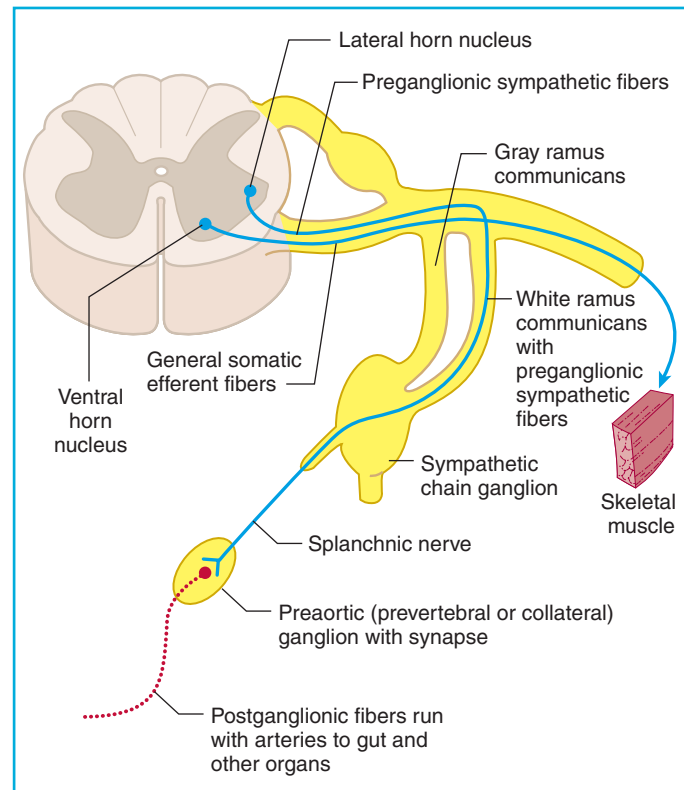
Once the preganglionic sympathetic fibers enter the sympathetic chain ganglion, there are three possibilities to synapse with postganglionic neurons. They can (1) synapse in a chain ganglion as soon as they enter the sympathetic chain, (2) synapse in a chain ganglion after traveling up or down the chain (see Fig. 2-6), or (3) pass through the sympathetic chain ganglion without synapsing and form a specific splanchnic nerve (containing preganglionic fibers) and then synapse in a ganglion closer to the organ that it innervates (see Fig. 2-7).

This last possibility is as if a specific sympathetic chain ganglion for an organ had migrated out of the chain and

moved closer to the organ, lengthening the preganglionic fibers but sometimes shortening the postganglionic ones (see Fig. 2-7). The route that a particular sympathetic neuron takes depends on its ultimate destination. The neurons that supply



**Figure 2-6.** Sympathetic pathway to sweat glands, arrector pili muscles, and the smooth muscle of blood vessels in the body wall.



**Figure 2-7.** Distribution of the splanchnic (visceral) nerves. Preganglionic sympathetic fibers pass through the sympathetic ganglia to form greater, lesser, least, and lumbar splanchnic nerves that supply visceral structures in the abdomen and pelvis.

**TABLE 2-1. Location of Preganglionic and Postganglionic Neuronal Cell Bodies for Splanchnic Nerves Arising from Spinal Cord Levels T5–T12; L1, L2, (L3)**

Name of Nerve	Spinal Cord Level of Origin	Preaortic Ganglia Where Synapse Occurs
Greater splanchnic nerve	T5–T9	Celiac and to a lesser extent superior mesenteric ganglia
Lesser splanchnic nerve	T10–T11	Aorticorenal and superior mesenteric ganglia
Least splanchnic nerve	T12	Renal plexus
Lumbar splanchnic nerve	L1, L2, (L3)	Inferior mesenteric ganglion and minute intermesenteric and hypogastric ganglia

blood vessels, arrector pili muscles, and sweat glands in the skin can use either option one or option two and then leave the sympathetic chain at every level by means of grey rami communicantes (unmyelinated communicating branches) to rejoin all 31 pairs of spinal ventral rami (see Fig. 2-5). These postganglionic sympathetic fibers then run in both ventral and dorsal rami to supply the skin throughout the body.

Fibers that will innervate visceral structures in the head, neck, and thorax can also use either of the first two options, but their postganglionic fibers then leave the sympathetic chain ganglia directly as splanchnic nerves that are named for the organs they supply. For example, cervical and thoracic cardiac nerves and thoracic pulmonary nerves are part of the cardiopulmonary splanchnic nerves that supply the heart and lungs.

The neurons that pass *through* the sympathetic chain ganglia without synapsing will innervate visceral structures in the abdomen and pelvis (see Fig. 2-7). These are the so-called named splanchnics: greater, lesser, least, and lumbar splanchnic nerves (Table 2-1). These nerves travel to autonomic ganglia, which are generically referred to as *preaortic (prevertebral) ganglia*. The postganglionic fibers from these preaortic ganglia run with various arteries to reach the viscera of the abdomen and pelvis. The postganglionic fibers from these preaortic ganglia follow the arteries that have the same names as the ganglia (i.e., the postganglionic fibers of the superior mesenteric ganglion follow the branches of the superior mesenteric artery.)

The term splanchnic is derived from the Greek and means “visceral.” Reminder: not all sympathetic nerves with the designation “splanchnic” are bundles of preganglionic fibers

(Table 2-2). There are many other visceral branches of the sympathetic nervous system that are also called “splanchnic nerves” that contain postganglionic fibers. These splanchnic nerves arise from cervical and upper thoracic sympathetic ganglia and as postganglionic nerves run directly to organs in the head, neck, and thorax that they innervate (see parasympathetic nervous system). Postganglionic sympathetic fibers in branches of the upper thoracic sympathetic ganglia also supply the thoracic aorta. *None of the splanchnic nerves run in gray rami communicantes.*

For the thoracoabdominal outflow to provide preganglionic sympathetic neurons to synapse in the 22–23 chain ganglia, one preganglionic fiber must synapse with approximately 33 postganglionic neurons at different levels of the sympathetic chain. Thus, a preganglionic axon synapses with many postganglionic neuronal cell bodies. In addition, one postganglionic cell body receives many synapses from other preganglionic axons. This may account for the wide dissemination and possibly amplification of sympathetic innervation.

## Parasympathetic Nervous System

The parasympathetic portion of the autonomic nervous system is called the *craniosacral outflow* because it has its preganglionic cell bodies in the brainstem and in the sacral portion of the spinal cord. Parasympathetic fibers run in cranial nerves III, VII, IX, and X. The sacral parasympathetic outflow arises from the intermediolateral horn of sacral spinal cord segments 2, 3, 4, and its fibers are called *pelvic splanchnics* (Fig. 2-8 and Table 2-3).

## Visceral Afferent Neurons

Visceral sensory fibers also run with the autonomic nerves. These neurons carry specific information from the viscera. The sensory impulses arising from the heart, great vessels, respiratory and gastrointestinal system, which run with parasympathetic neurons, are involved in reflexes controlling blood pressure, respiration rate, partial pressures of carbon dioxide, etc. Sensory fibers for pain that arise in receptors from the heart, abdominal gastrointestinal tract, rectum, urogenital system, etc., run with sympathetic and sacral parasympathetic nerves and result from inflammation or excessive distention and contraction of the involved organs.

Not all afferent functions are perceived on a conscious level. We are unaware of sensory information that regulates the respiratory and circulatory systems. However, we are aware of hunger, thirst, and the need to urinate or defecate.

Pain from the viscera is perceived differently from pain from the somatic structures. Visceral pain is typically diffuse. Often visceral pain is *perceived* as arising from a region of the body wall distant from the involved organ, a phenomenon called referred pain. Understanding the mechanism of referred pain helps identify the organ that may be involved and thus aids in the diagnosis of the underlying disease.

**TABLE 2-2. Location of Preganglionic and Postganglionic Neuronal Cell Bodies for Segmental Sympathetic Supply**

Spinal Cord Segment Containing Cell Bodies of Preganglionic Fibers	Location of Postganglionic Cell Bodies in Sympathetic Ganglia/Mode of Exit of Postganglionic Fibers	Region and/or Effector Organ Supplied
T1–T5	Superior and middle cervical chain ganglia fibers exit by means of gray rami communicantes to ventral rami spinal nerves C1–C5	Sweat glands, arrector pili muscles, and blood vessels of neck and face
T3–T6	Inferior cervical and upper thoracic chain ganglia fibers exit by means of gray rami communicantes to ventral rami of spinal nerves C6–C8, T1–T5	Sweat glands, arrector pili muscles, and blood vessels of upper limb and thoracic wall
T1–T6	Superior, middle, and inferior cervical and upper thoracic chain ganglia 1–6 fibers exit directly as visceral branches; <b>they do not use gray rami communicantes</b>	Cardiopulmonary nerves to heart, trachea, lungs, and lower esophagus
T2–L1	Thoracic chain ganglia 1–12 and lumbar ganglia 1, 2 postganglionic fibers exit through gray rami communicantes to ventral rami of spinal nerves T1–L1	Sweat glands, arrector pili muscles, and blood vessels of trunk body wall
T5–L2	Preaortic (celiac, superior mesenteric, inferior mesenteric, aorticorenal) ganglia Postganglionic sympathetic fibers from these ganglia supply	Gastrointestinal and urogenital organs of the abdominopelvic cavity
T9–L2	Lumbosacral chain ganglia fibers exit through gray rami communicantes to ventral rami of spinal nerves T9–L2	Sweat glands, arrector pili muscles, and blood vessels of lower limb

●●● REFERRED PAIN

Referred pain can be defined as pain from deep organs perceived as arising from a dermatome or dermatomes of the body wall distant or remote from the actual diseased organ. The visceral sensory fibers for pain run with sympathetic and parasympathetic splanchnic nerves. The key to understanding referred pain is that both the cutaneous region where the pain is perceived and the involved organ are innervated by fibers associated with the same spinal cord segment or segments.

The general somatic sensory fibers for somatic pain run in spinal nerves. Many visceral sensory pain fibers run in the sympathetic nerves and join the spinal nerves by means of their white rami communicantes (see Table 2-2). Thus, both somatic pain fibers and visceral pain fibers have cell bodies that are in the same dorsal root ganglia and enter the dorsal horn together *to synapse on the same second-order neurons*. The CNS mistakenly recognizes visceral pain as arising from a portion of the body wall, which does not have a direct relationship to the involved organ.

**HISTOLOGY**



**Morphology of Motor and Sensory Cells**

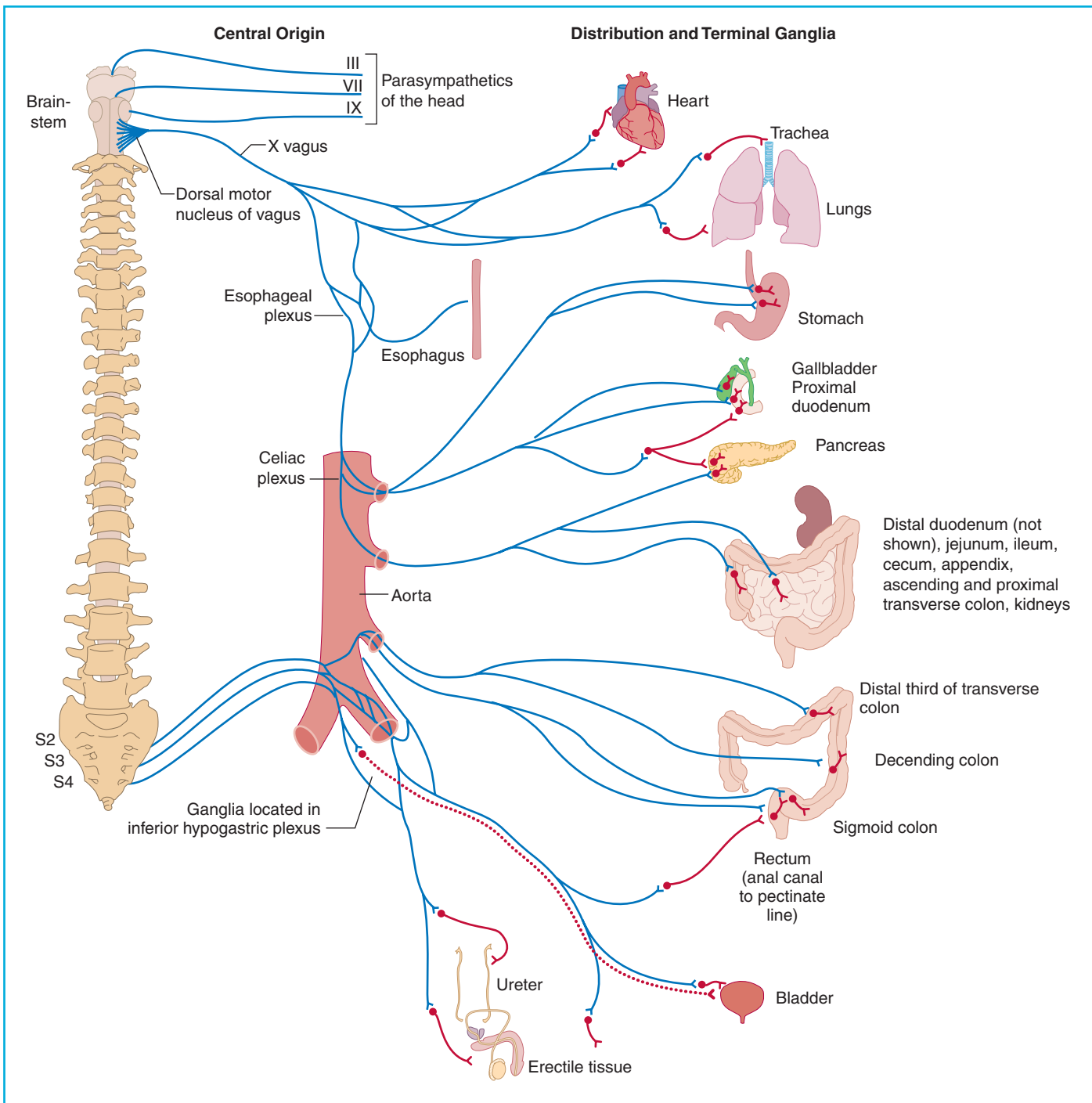
Not only do motor and sensory cells have specific locations, they also have specific morphologies. Motor cells are typically multipolar with numerous dendrites, whereas sensory neurons typically have round cell bodies with one or two axons.

**CLINICAL MEDICINE**



**Sensing Pain**

A myocardial infarction (heart attack) typically produces deep pain on the left side of the chest and radiating pain into the medial side of the left arm, forearm, and even the little finger. Somatic sensory fibers from these regions of the body wall and upper left limb synapse in the same spinal cord segments, T1–T4 or T5, as the visceral sensory fibers from the heart. The CNS does not clearly distinguish the origin of this pain, and it perceives the pain as coming from the body wall and upper left limb.



**Figure 2-8. Diagram of the parasympathetic (craniosacral) outflow.** Cranial nerves III, VII, IX, and X as well as sacral spinal cord segments S2, S3, and S4 have relatively long preganglionic fibers (blue) that synapse in ganglia either in or close to the effector organs. Short postganglionic fibers (red) then innervate specific structures in these organs.

Both the autonomic and visceral sensory innervation to many of the organs of the trunk are well known, whereas this is less clear for other organs. For example, the cardiac sympathetic nerves arise in the lateral horns of thoracic spinal cord segments T1 through T4(T5). Therefore, the visceral sensory fibers that travel in reverse from the heart follow the cardiac sympathetic fibers and synapse in spinal cord segments T1 through T4(T5). This distribution of visceral sensory fibers

that run with the cardiac sympathetic nerves accounts for specific patterns of pain that arise from the heart.

The convergence theory of referred pain indicates that visceral pain fibers in the spinal cord converge on the same second-order neurons that receive input from the somatic sensory neurons. The information is then conveyed to suprasegmental levels, where the CNS interprets the pain as arising from the somatic region (Fig. 2-9).

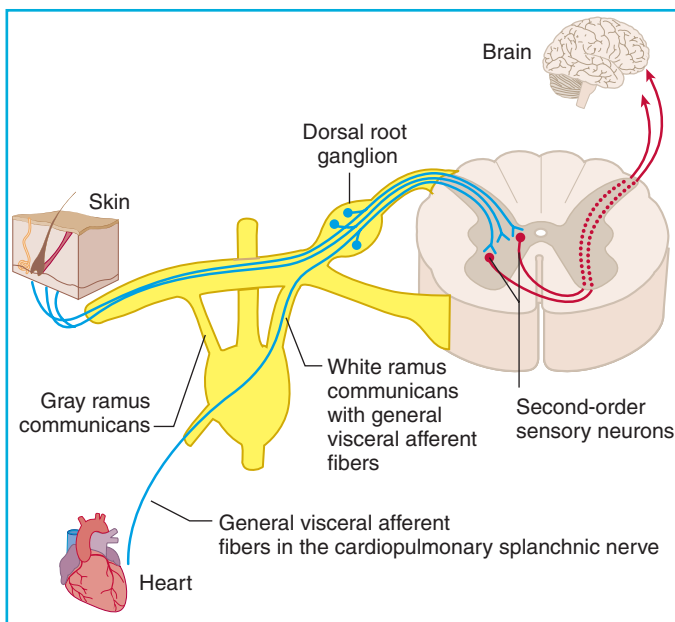


**TABLE 2-3. Comparisons Between the Sympathetic and Parasympathetic Nervous Systems**

Feature	Sympathetic Nervous System	Parasympathetic Nervous System
Location of preganglionic cell bodies	Lateral horns T1–L2 (thoracolumbar outflow)	Brainstem and sacral spinal cord S2–S4 (craniosacral outflow)
Location of ganglia	Sympathetic trunk and collateral ganglia	In organs of the gastrointestinal tract, pelvic organs, or close to other organs
Length of fibers	Short preganglionic fibers, long postganglionic fibers with exception of the named splanchnic nerves	Long preganglionic fibers, short postganglionic fibers
Ratio of preganglionic fibers to postganglionic fibers	Approximately 1 to 33	Approximately 1 to 2–5
Postganglionic transmitter	Norepinephrine (except sweat glands, which use acetylcholine)	Acetylcholine

**TABLE 2-4. Classification of Fiber Types That Supply Trunk and Limbs**

Classification	Function	Structure Innervated	Embryologic Origin
General somatic afferent (GSA)	Pain, touch, temperature, proprioception (deep sensation)	Skin, skeletal muscle, parietal serous membranes	Ectoderm, somites, somatic lateral mesoderm
General somatic efferent (GSE)	Motor innervation to voluntary muscles	Skeletal muscle of the trunk and limbs	Somites
General visceral afferent (GVA)	Visceral afferents for silent information from receptors for blood pressure, serum chemistry, as well as referred pain	Organs such as cardiovascular, respiratory, gastrointestinal and urogenital systems	Visceral lateral mesoderm, intermediate mesoderm, endoderm
General visceral efferent (GVE)	Autonomic innervation	Organs such as cardiovascular, respiratory, gastrointestinal and urogenital systems	Visceral lateral mesoderm, intermediate mesoderm



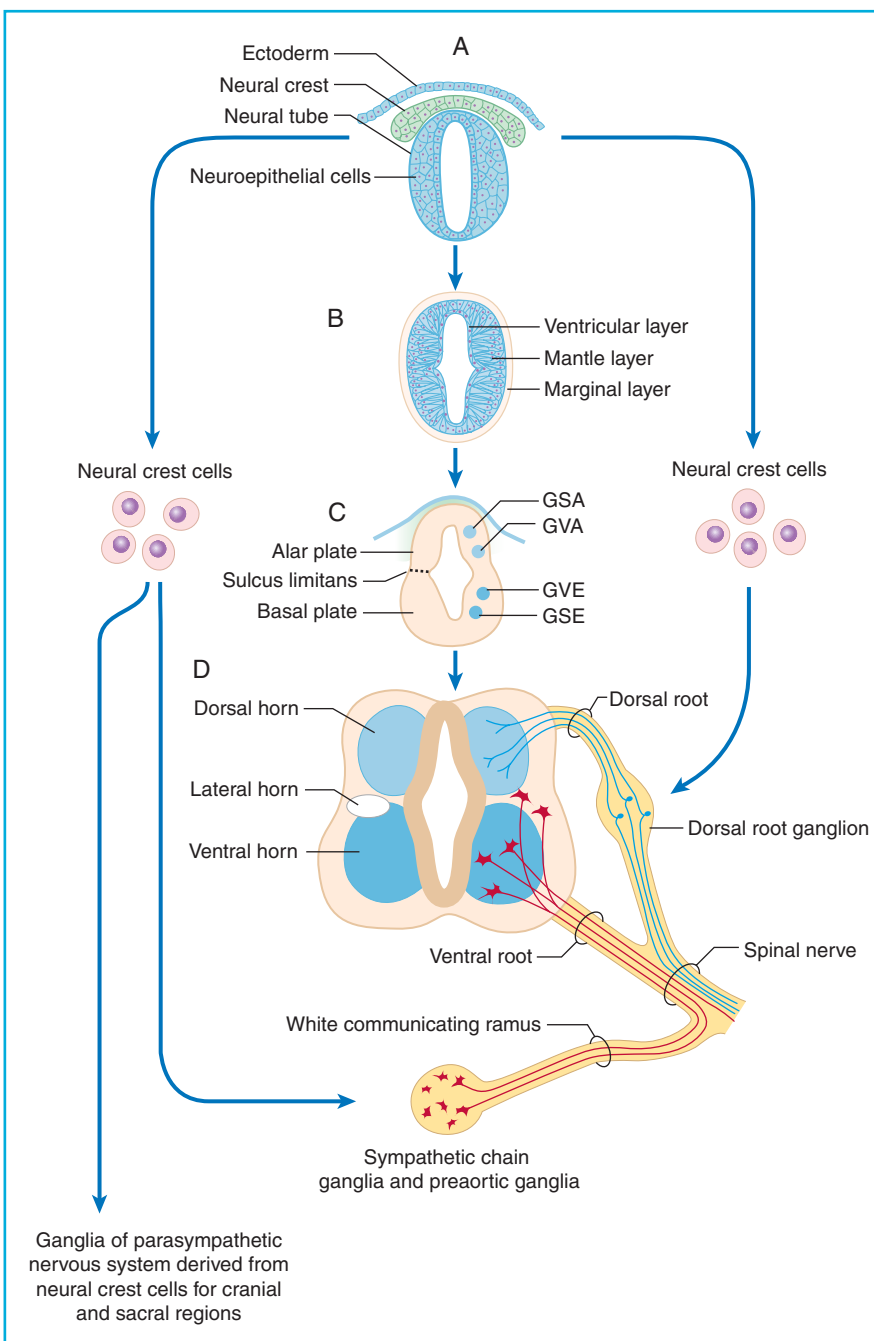
**Figure 2-9.** Convergence theory of referred pain points out that both somatic sensory fibers and visceral sensory fibers have the cell bodies in the same dorsal root ganglion and synapse on the same second-order neurons in the spinal cord.

**CLASSIFICATION OF NEURONAL FIBERS**

The fibers of the above neurons are classified according to the structures they supply and the embryologic origin of these structures. The somatic motor and sensory fibers arise from cell bodies in the spinal cord or dorsal root ganglia. Thus, they are widely distributed and their fibers are classified as general somatic sensory (afferent) or motor (efferent) fibers. The autonomic nervous system supplies all of the viscera, so these fibers are also classified as general visceral motor (efferent) fibers, while the sensory fibers from the organs that run with the autonomic nerves are classified as general visceral afferent fibers (Table 2-4).

**DEVELOPMENT OF THE SPINAL CORD AND PERIPHERAL NERVOUS SYSTEM**

The CNS develops from the neural tube, whereas the peripheral nervous system develops from parts of the neural tube and neural crest cells (Fig. 2-10).



**Figure 2-10.** Development of spinal cord and peripheral nervous system.

The neuroepithelial cells surrounding the neural canal go through three waves of proliferation and differentiation (see Fig. 2-10). Initially, they differentiate into neuroblasts that will become the neurons of the CNS. This layer is called the ventricular layer. These newly formed neuroblasts then migrate peripherally to form a new concentric layer called the mantle layer (see Fig. 2-10B). The neuroblasts in the mantle layer further differentiate into primitive neurons. This layer will ultimately become the gray matter of the spinal cord (see Figs. 2-10B to 2-10D). The processes (axons and dendrites) of the primitive neurons in the mantle layer then extend peripherally to form the outermost layer called the marginal

zone. As the oligodendrocytes myelinate the axons, this layer will become the white matter (see Figs. 2-10B and 2-10 D).

In the second wave of differentiation, the neuroepithelial cells in the ventricular layer proliferate and differentiate into glioblasts that will ultimately become oligodendrocytes and astrocytes, the glial or supporting cells of the CNS.

In the third wave, the neuroepithelial cells form the ependymal cells that line the lumen of the neural tube.

Cells from the adjacent mesoderm form the covering layers, called *meninges*, that surround the CNS. These layers, starting from the white matter, are called the pia mater, arachnoid mater, and dura mater, respectively. During

development, the neural tube's central lumen narrows owing to the extensive development of the mantle and marginal zones and is now referred to as the *central canal*. The canal is lined by ependymal cells (which originate from the neural tube's original neuroepithelium) and is located in the center of the transverse portion of gray matter. (The central canal is normally patent throughout life although its terminal ventricle enlargement within the conus medullaris typically regresses in middle age.)

As differentiation continues, the tube enlarges in an asymmetric manner. When viewed in the transverse plane, the mantle (developing gray matter) layer's ventral and dorsal components (plates) have enlarged and the region between them remains relatively narrow (see Figs. 2-10C and 2-10D). The paired, enlarged dorsal portions of the developing gray matter become the alar plates, while the paired ventral portions are called *basal plates*. The narrow groove between the dorsal and ventral plates is the sulcus limitans (see Figs. 2-10C and 2-10D). The ventral and dorsal horns are concerned with the derivatives of the somites.

The alar plates contain developing sensory fibers and second-order neurons in the future dorsal horn (see Fig. 2-10D). The basal plates are the future ventral horns (see Figs. 2-10C and 2-10D). They are found anterior to the sulcus limitans and are the sites of developing neurons whose axons migrate out of the spinal cord to innervate the muscles developing from the adjacent somites.

The portion of the basal plate close to the sulcus limitans produces developing neurons that supply viscera (see Figs. 2-10C and 2-10D). These neurons and their fibers are part of the autonomic nervous system. This portion of the alar plate is designated as the intermediolateral horn.

Concurrent with the development of the spinal cord and somites, the neural crest cells migrate to various points including a dorsolateral position between the alar plate and the somites. Here, the neural crest cells develop into the neuronal cell bodies of the dorsal root ganglia (see Fig. 2-10), which send processes peripherally to supply sensory fibers to skin, dermis, and developing skeletal muscle and centrally to the alar plate (developing dorsal horn). The central processes penetrate the marginal layer (future white matter) to reach suprasegmental levels of the CNS, or they can synapse at this level.

The central processes of the dorsal root ganglion form the dorsal root, and the basal plate's processes form the ventral root. The two roots unite and form the spinal nerve (see Fig. 2-10). The stimulus for much of this is the development of the paraxial mesoderm, which has produced segmented pairs of somites. The somites continuously subdivide to form segmented sclerotomes, myotomes, and dermatomes. The sclerotomes form the vertebrae. The myotomes develop into skeletal muscle, while the dermatomes produce the dermis. This pattern of segmentation results in one pair of developing spinal nerves innervating a specific group of muscles, dermis, and adjacent skin. These specific regions of the body are also referred to as the myotomes and dermatomes of the adult body and are a useful tool in understanding pain or anesthesia as symptoms of injury or disease.

Neural crest cells also migrate into the visceral regions of the body to develop into autonomic ganglia and fibers (see Fig. 2-10). Some of the peripheral fibers of the developing sensory neurons in the dorsal root ganglia also accompany the neural crest cells as they migrate. These sensory fibers carry sensory impulses from viscera to the CNS.

