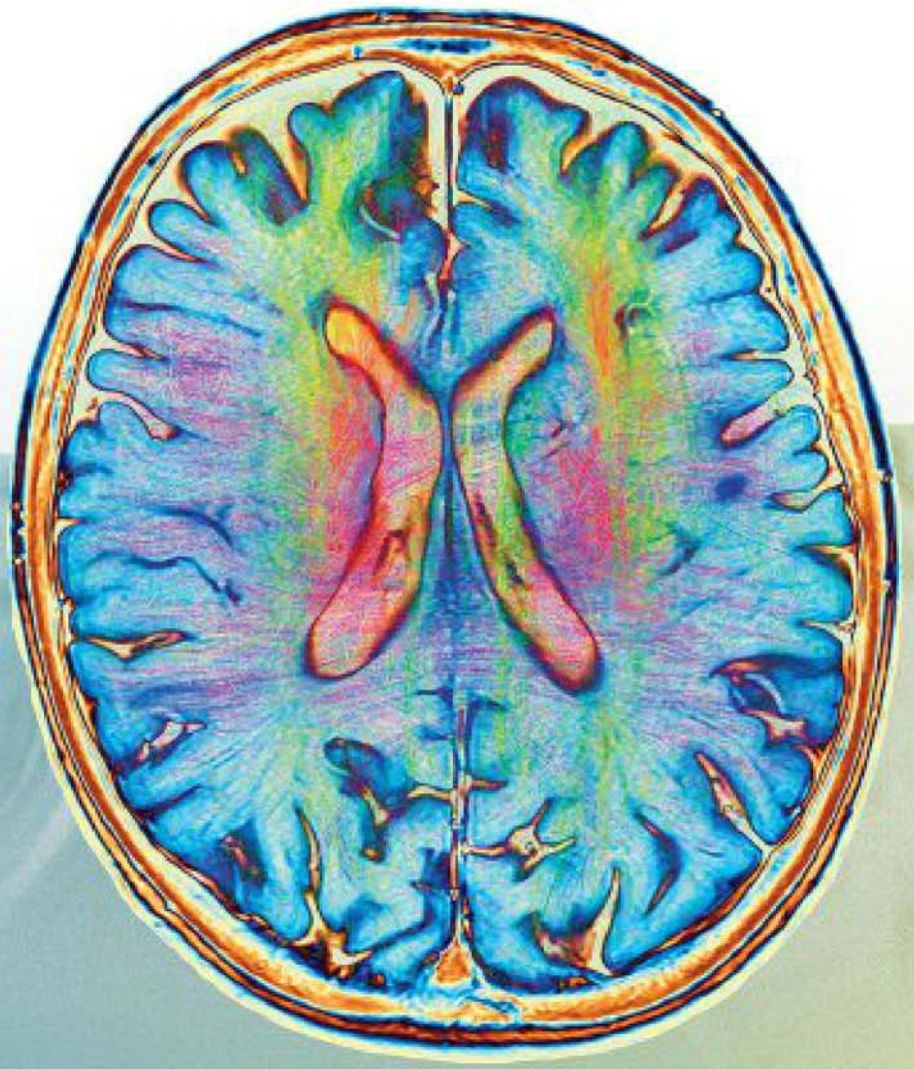
SNELL'S CLINICAL NEUROANATOMY

EIGHTH EDITION



RYAN SPLITTGERBER

Wolters Kluwer

SNELL'S CLINICAL NEUROANATOMY

EIGHTH EDITION

IN MEMORIAM

Richard S. Snell, MRCS, LRCP, MB, MD, PhD

1925–2015

Clinical Anatomy by Regions
Clinical Anatomy by Systems
Clinical Neuroanatomy

SNELL'S CLINICAL NEUROANATOMY

EIGHTH EDITION

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The trip has been long and the cost has been high . . . but no great thing was attained easily. A long tale, like a tall Tower, must be built a stone at a time.

—Stephen King

To my wife, Brienne
For providing more love and support than I deserve.
To my boys, Carter and Caden
For providing inspiration and humor . . . a lot of humor.

To my students
May you find your Tower.

Preface

This book contains the basic neuroanatomical facts necessary for the practice of medicine. It is suitable for medical students, dental students, nurses, and allied health students. Residents find this book useful during their rotations.

The functional organization of the nervous system has been emphasized and indicates how injury and disease can result in neurologic deficits. **The amount of factual information has been strictly limited to that which is clinically important.**

In this edition, authorship has transitioned from the late Dr. Richard Snell, who, with brilliance and dedication, fathered the previous seven editions and provided the framework for the eighth. The content of each chapter has been reviewed and edited to be more straightforward and concise. The traditional artwork has been recolored and updated to enhance the clarity and to provide additional information to each image. High-quality magnetic resonance images and histologic photomicrographs have been updated to provide greater visual details.

Each chapter introduces the relevance of neuroanatomy through a short case report.

- **Clinical Example.** A short case report that serves to dramatize the relevance of neuroanatomy introduces each chapter.
- **Chapter Objectives.** This section details the material that is most important to learn and understand in each chapter.
- **Basic Neuroanatomy.** This section provides basic information on neuroanatomical structures that are of clinical importance. Numerous examples of normal radiographs, CT scans, MRIs, and PET scans are also provided. Many cross-sectional diagrams have been included to stimulate students to think in terms of three-dimensional anatomy, which is so important in the interpretation of CT scans and MR images.
- **Clinical Notes.** This section provides the practical application of neuroanatomical facts that are essential in clinical practice. It emphasizes the structures that the clinician will encounter when making a diagnosis and treating a patient. It also provides the information necessary to understand many procedures and techniques and notes the anatomical "pitfalls" commonly encountered.
- **NEW! Key Concepts.** These quick, bulleted reviews of key topics and information are provided at the end of each chapter.
- **Clinical Problem Solving.** This section provides the student with many examples of clinical situations in which a knowledge of neuroanatomy is necessary to solve clinical problems and to institute treatment; solutions to the problems are provided at the end of the chapter.
- **Review Questions.** The purpose of the questions is threefold: to focus attention on areas of importance, to enable students to assess their areas of weakness, and to provide a form of self-evaluation when questions are answered under examination conditions. Some of the questions are centered around a clinical problem that requires a neuroanatomical answer. Solutions to the problem are provided at the end of each chapter.

An interactive **Review Test**, including over 450 questions, is provided online.

The book is extensively illustrated. The majority of the figures have been kept simple and are in color. As in the previous edition, a concise **Color Atlas** of the dissected brain is included prior to the text. This small but important group of colored plates enables the reader to quickly relate a particular part of the brain to the whole organ.

R.S.
R.S.S.

Acknowledgments

Starting with the first edition of Clinical Neuroanatomy published in 1980, many people have provided their expertise and should be recognized for their contributions. First and foremost, thanks to Richard S. Snell whose shoulders we stand upon to advance our own intellectual progress.

Throughout this text and in previous editions, the following individuals provided valuable contributions and are gratefully acknowledged: N. Cauna, L. Clerk, D. O. Davis, H. Dey, M. Feldman, T. M. J. Fitzgerald, I. Grunther, J. M. Kerns, T. McCarthy, A. Peters, G. Sze, and L. Wener.

EIGHTH EDITION

I am greatly indebted to the staff of Wolters Kluwer, including Crystal Taylor, who brought me in and provided me with this wonderful opportunity, as well as Andrea Vosburgh, development editor, and John Larkin, editorial coordinator. Thanks also to freelance development editor Kelly Horvath, who provided invaluable direction and patience with me throughout the entire process.

SPi Global is gratefully acknowledged for their brilliant art recoloring and enhancing the personality of this textbook.

My special thanks to Stephanie Vas, Program Director of the Magnetic Resonance Imaging Program at the University of Nebraska Medical Center, who produced exceptional MR images for this edition.

I would like to extend my gratitude to my students, colleagues, and mentors for their encouragement and wisdom---especially, Sabra Peetz, Art Dalley, Cathy Pettepher, Lillian Nanney, and Kyle Meyer.

R.S.

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EIGHTH EDITION

Color Atlas of Brain

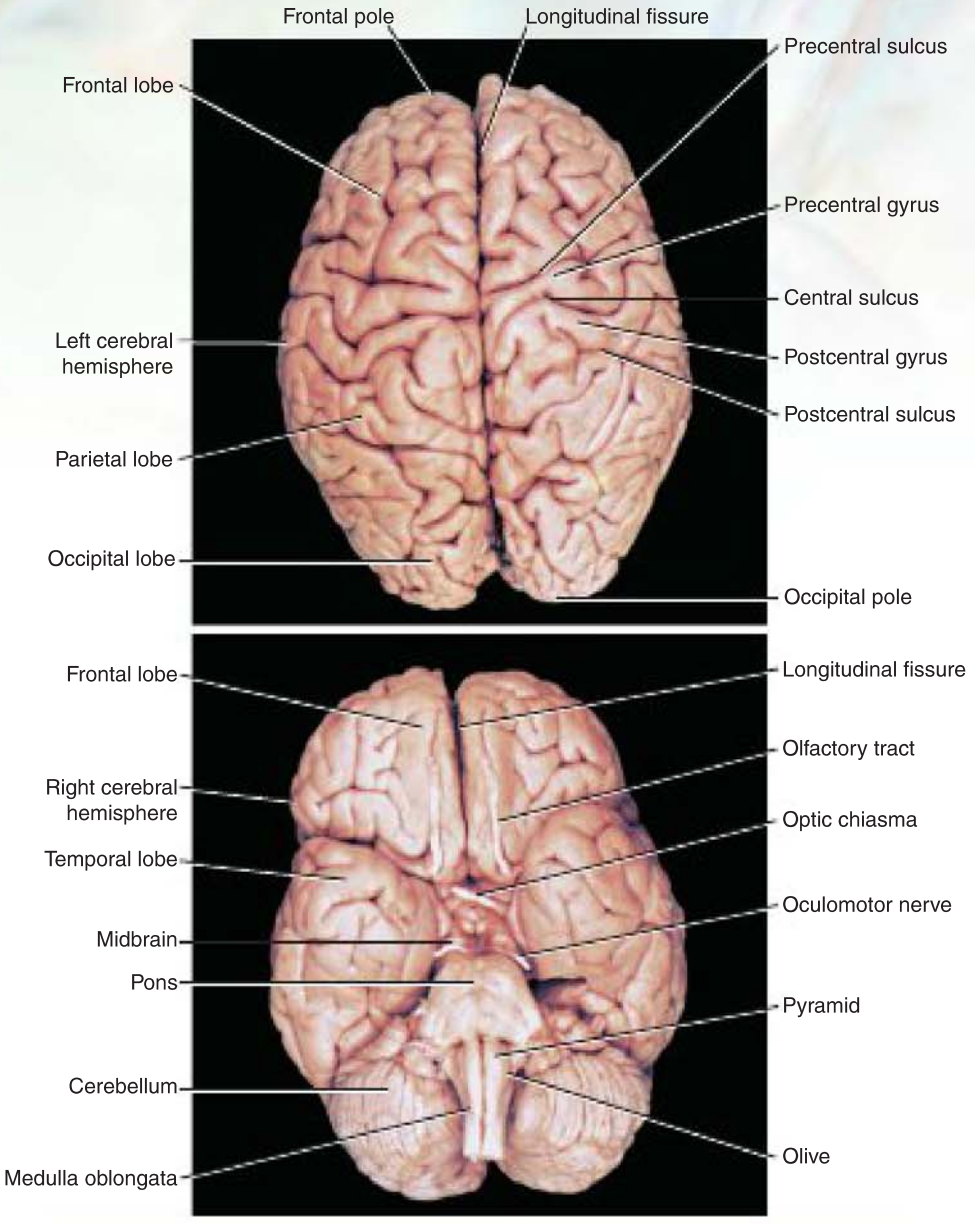

Figure CA-1 **Top:** Superior view of the brain. **Bottom:** Inferior view of the brain.

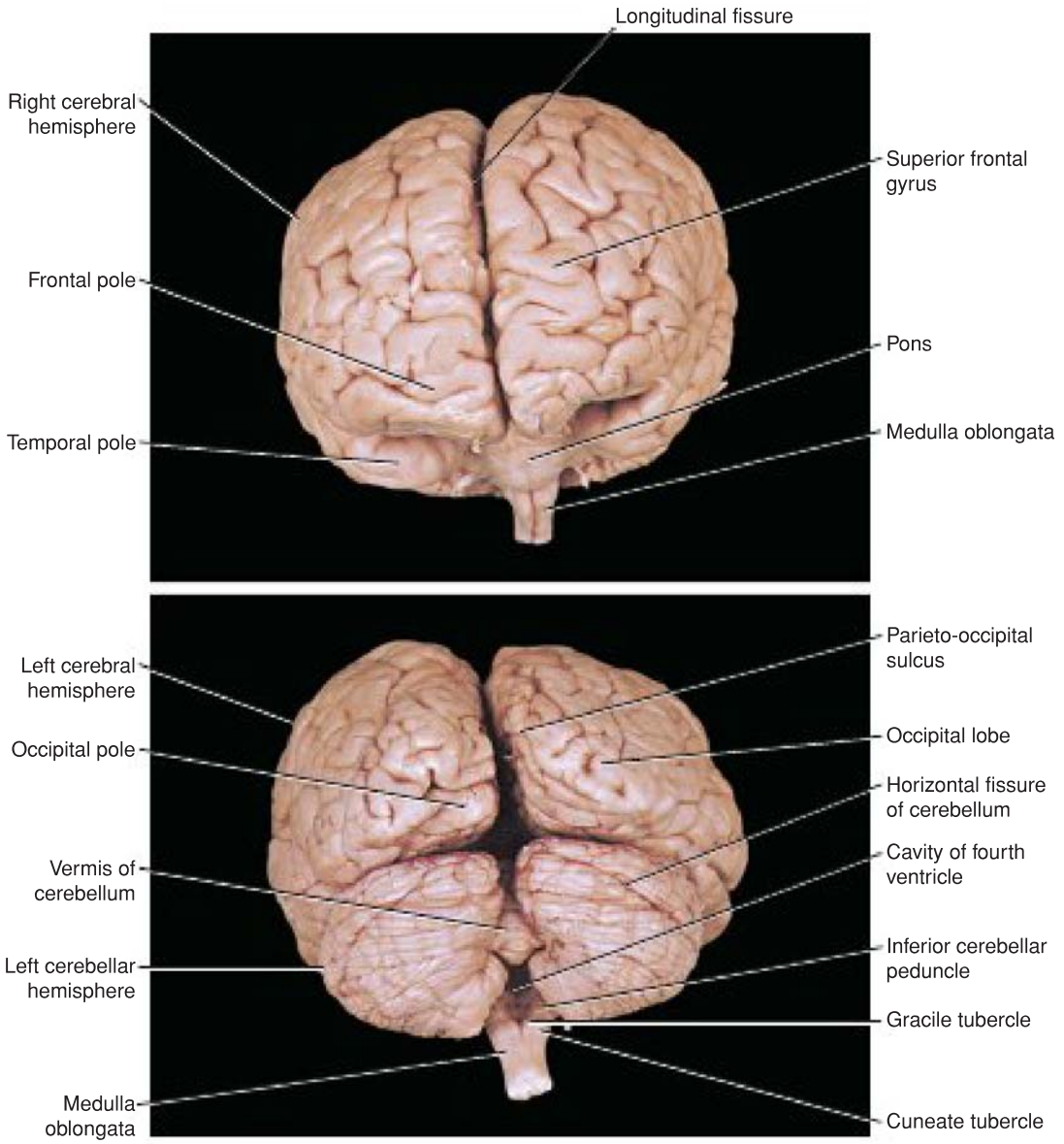

Figure CA-2 **Top:** Anterior view of the brain. **Bottom:** Posterior view of the brain.

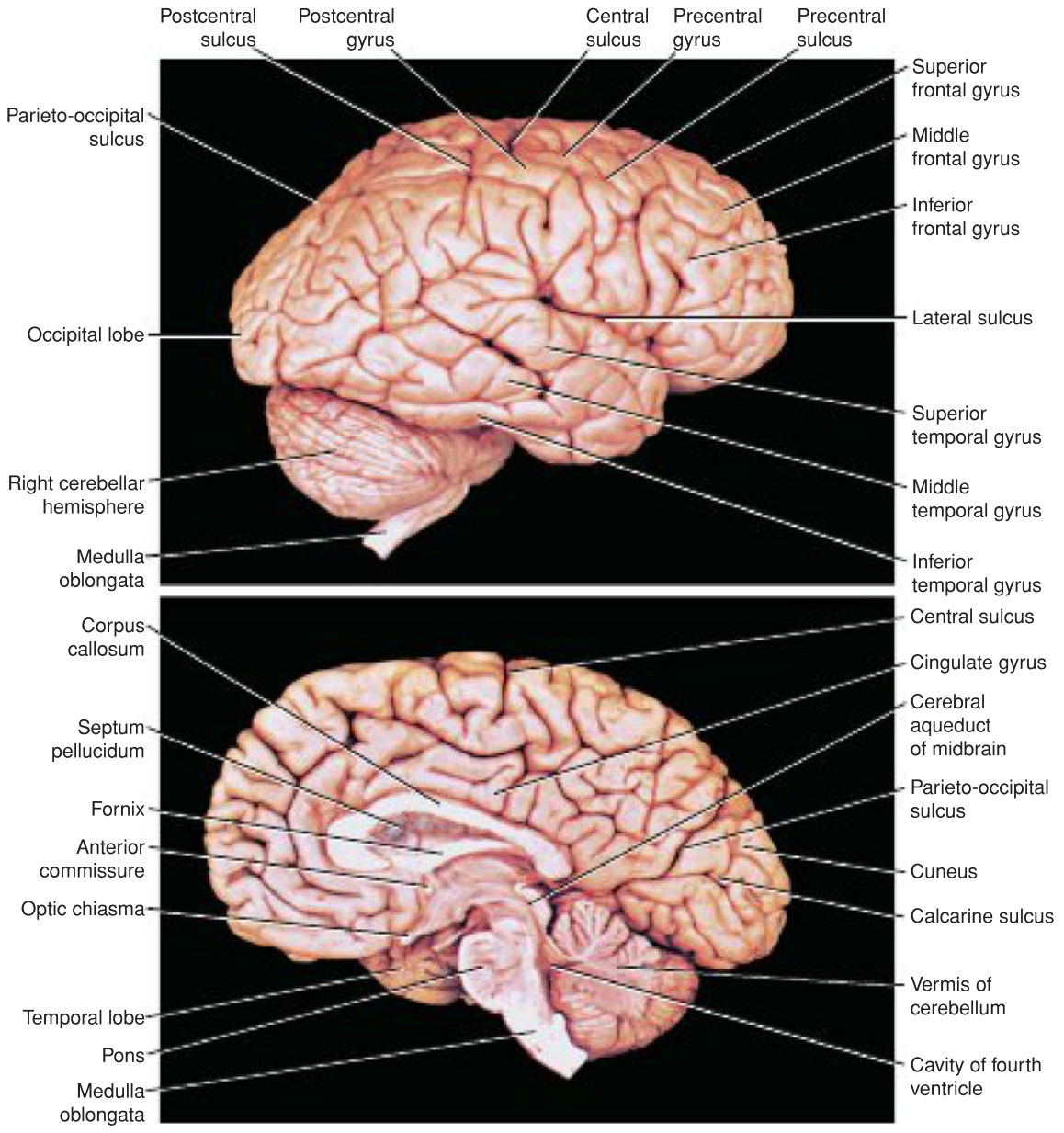

Figure CA-3 **Top:** Right lateral view of the brain. **Bottom:** Medial view of the right side of the brain following median sagittal section.

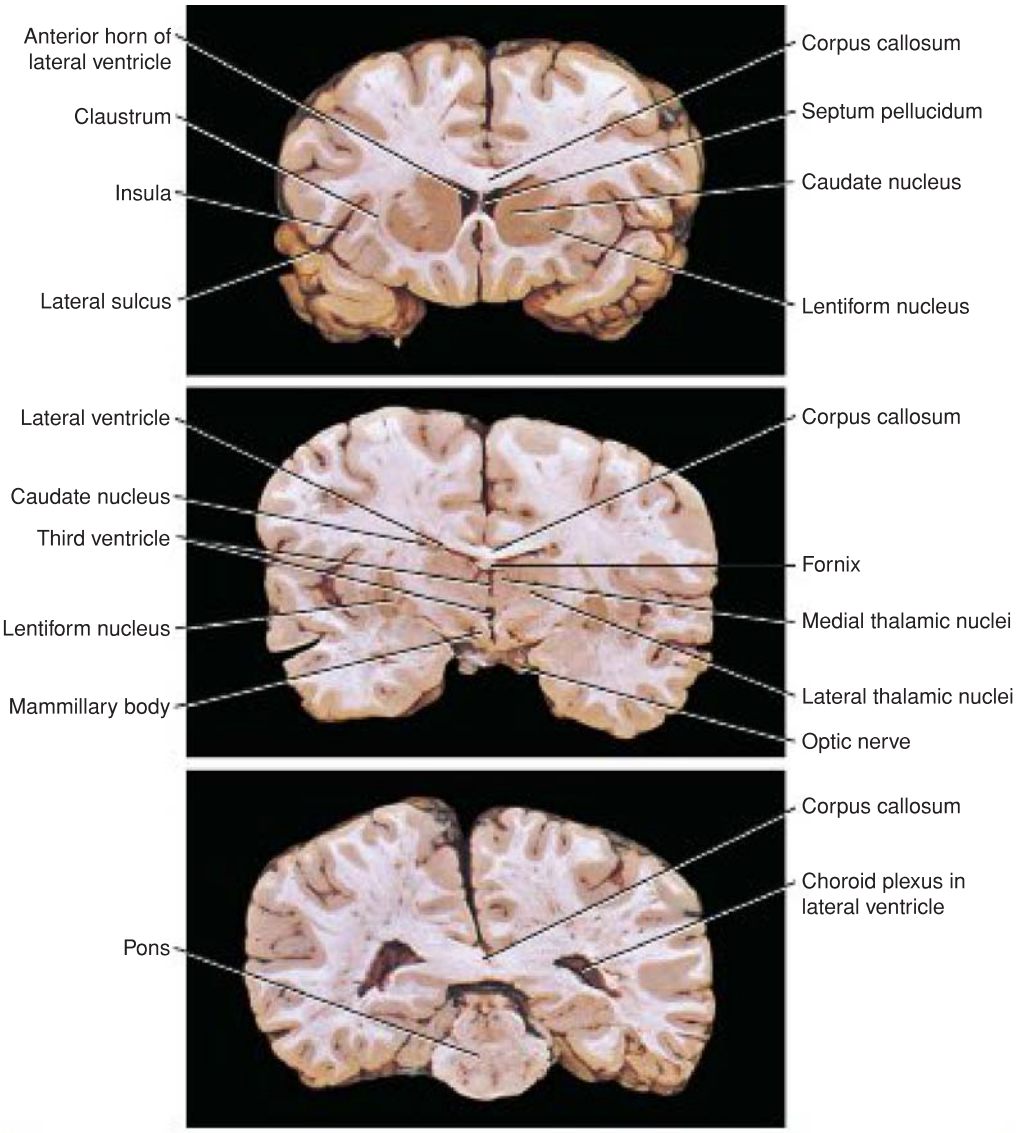

Figure CA-4 Coronal sections of the brain passing through the anterior horn of the lateral ventricle **(top)**, the mammillary bodies **(middle)**, and the pons **(bottom)**.

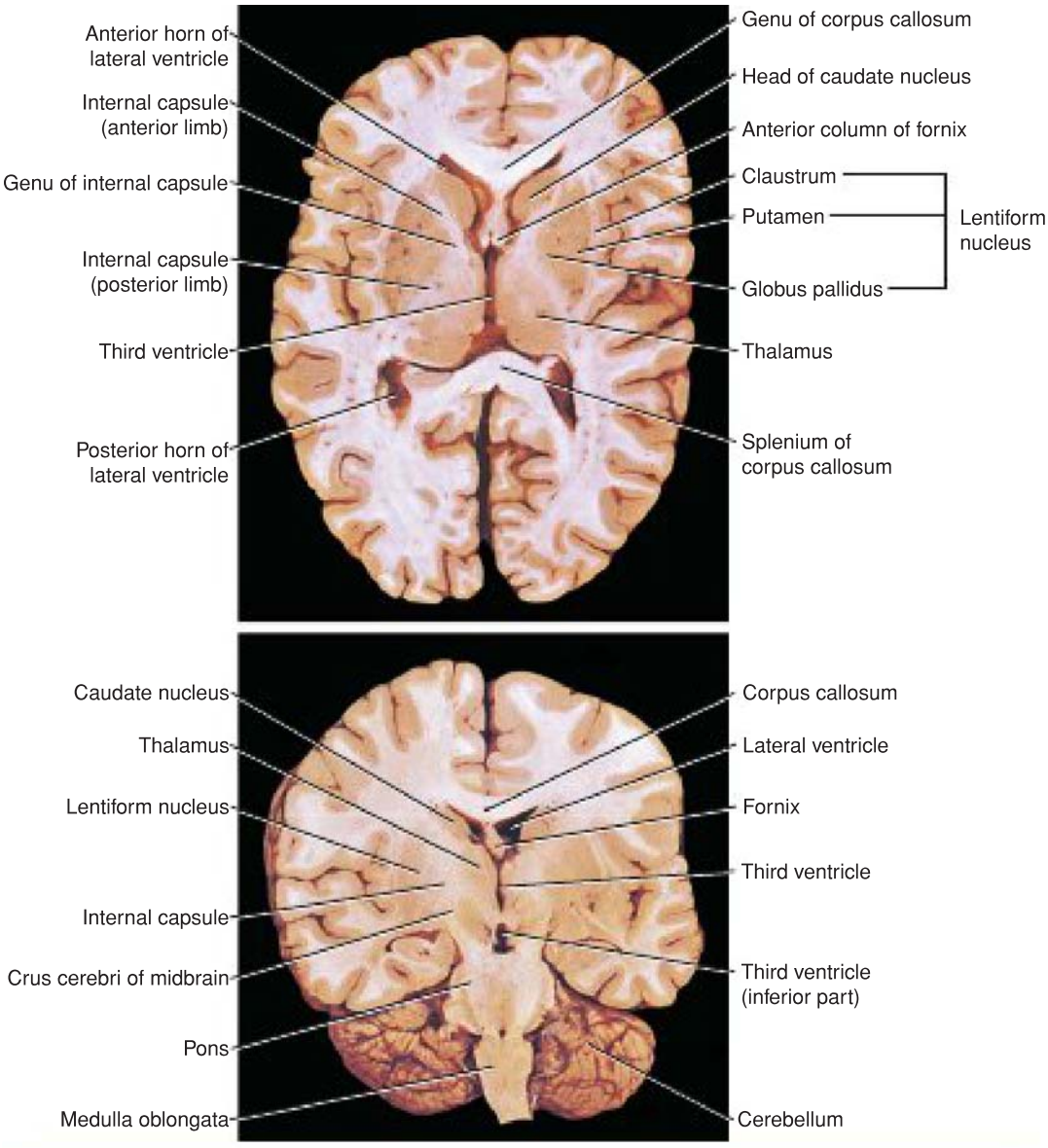

Figure CA-5 **Top:** Horizontal section of the cerebrum showing the lentiform nucleus, the caudate nucleus, the thalamus, and the internal capsule. **Bottom:** Oblique coronal section of the brain.

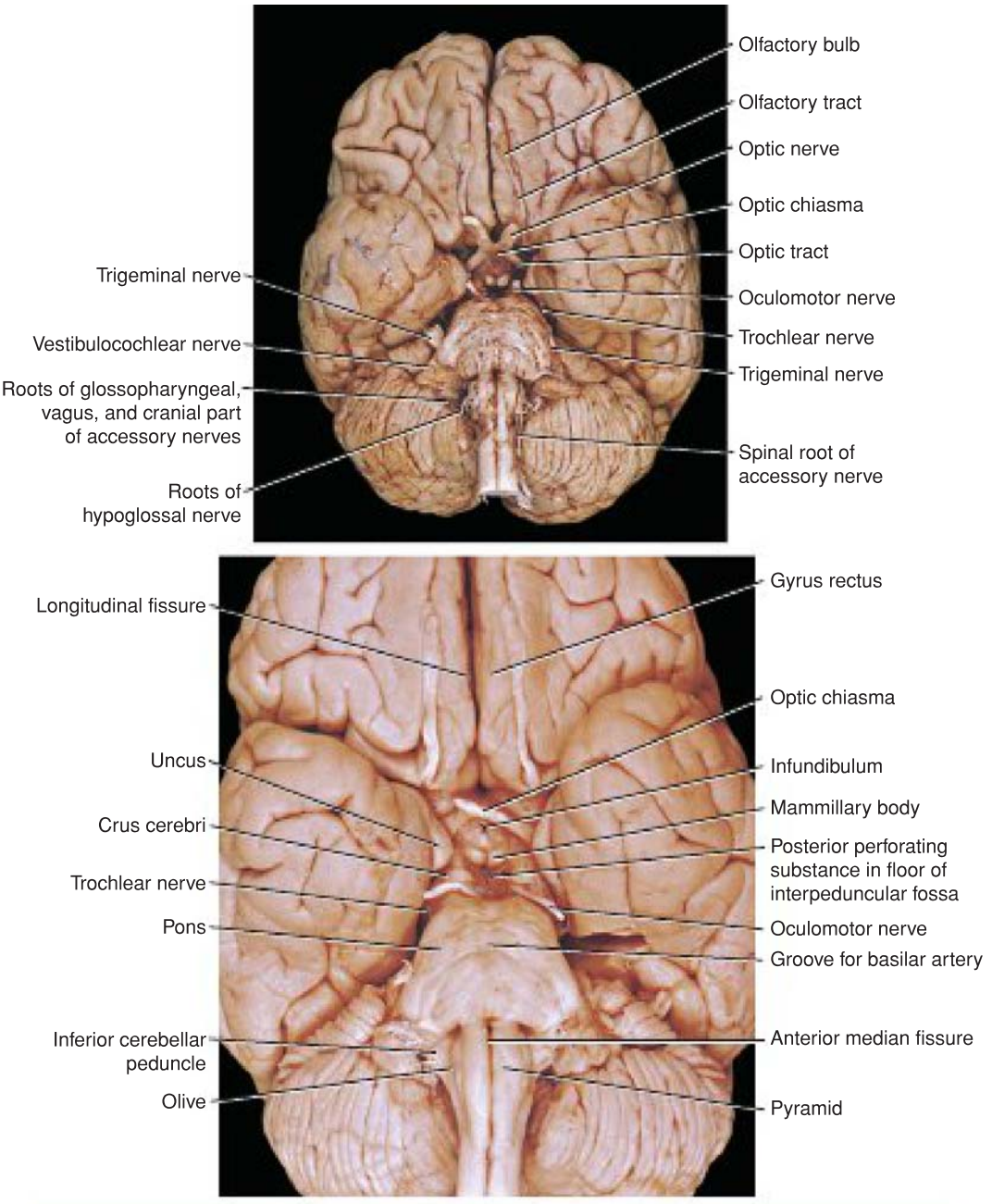

Figure CA-6 **Top:** Inferior view of the brain showing cranial nerves. The abducens and facial nerves cannot be seen. **Bottom:** Enlarged inferior view of the central part of the brain.

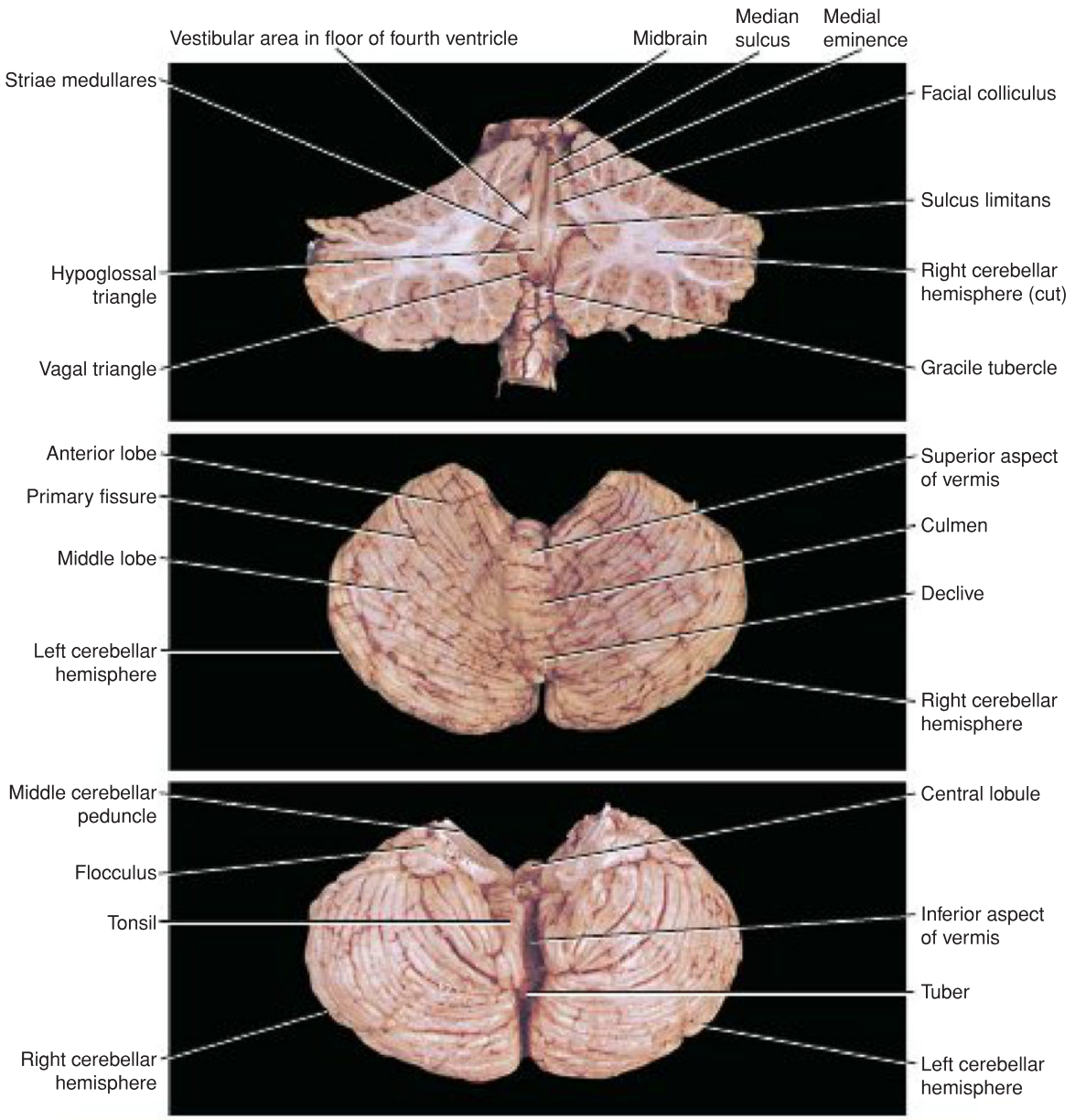

Figure CA-7 **Top:** Posterior view of the brainstem. The greater part of the cerebellum had been removed to expose the floor of the fourth ventricle. **Middle:** Superior view of the cerebellum showing the vermis and right and left cerebellar hemispheres. **Bottom:** Inferior view of the cerebellum showing the vermis and right and left cerebellar hemispheres.

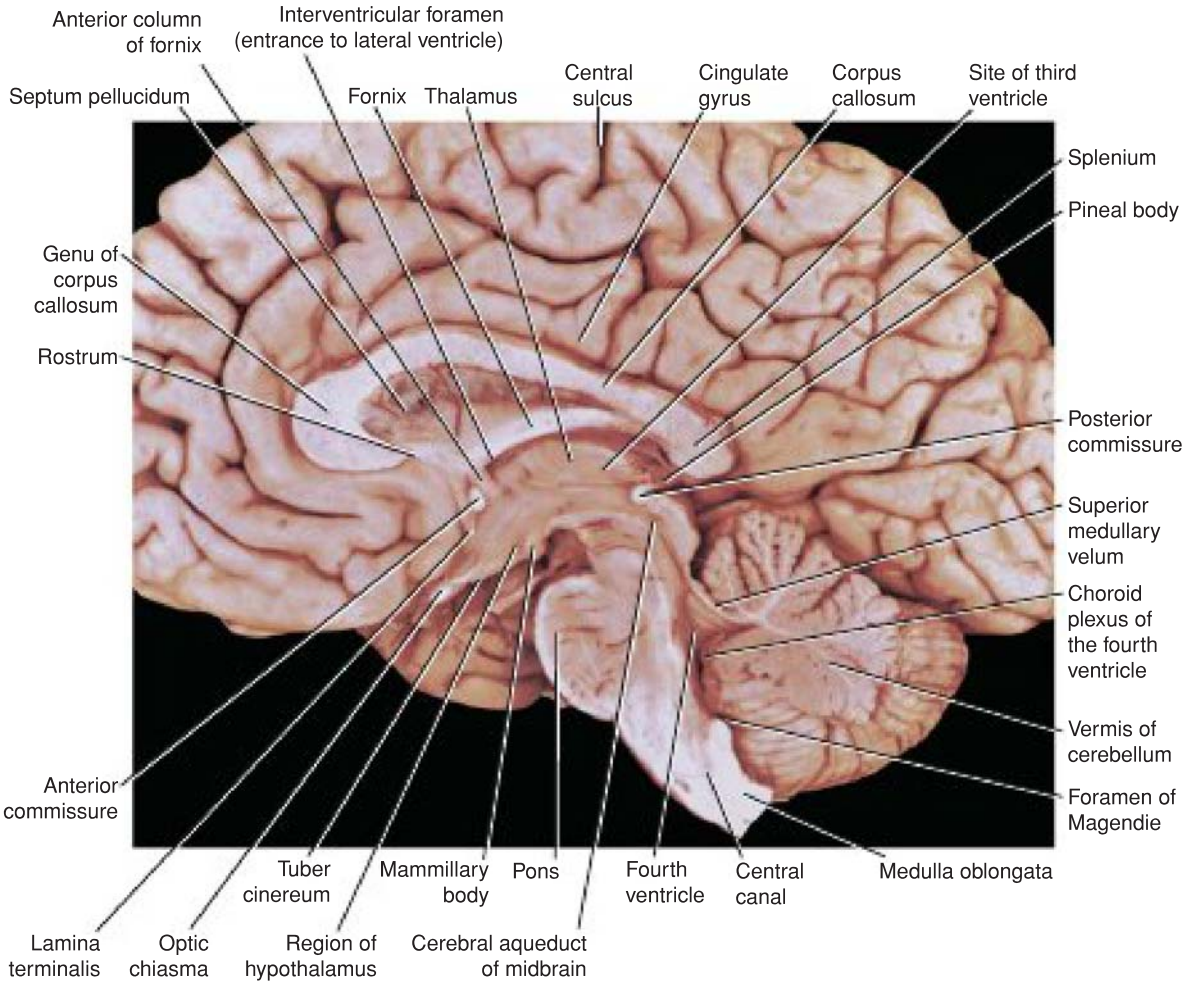

Figure CA-8 Enlarged medial view of the right side of the brain following median sagittal section, showing the continuity of the central canal, fourth ventricle, cerebral aqueduct, and the third ventricle and entrance into the lateral ventricle through the interventricular foramen.

1 Introduction and Organization of the Nervous System

CHAPTER OBJECTIVES

- To understand the basic organization of the main structures that form the nervous system
- To gain a three-dimensional appreciation of the parts of the brain and their relative positions to one another

A 23-year-old student is driving home from a party and crashes his car head-on into a tree. On examination in the emergency department of the local hospital, he has a fracture dislocation of the 7th thoracic vertebra, with signs and symptoms of severe damage to the spinal cord. Later, he is found to have paralysis of the left leg. Testing of cutaneous sensibility reveals a band of cutaneous hyperesthesia (increased sensitivity) extending around the abdominal wall on the left side at the level of the umbilicus. Just below this, he has a narrow band of anesthesia and analgesia. On the right side, he has total analgesia, thermoanesthesia, and partial loss of touch sensation of the skin of the abdominal wall below the level of the umbilicus and involving the whole of the right leg.

With knowledge of anatomy, a clinician knows that a fracture dislocation of the 7th thoracic vertebra can result in severe damage to the 10th thoracic segment of the spinal cord. Because of the small size of the vertebral foramen in the thoracic region, such an injury inevitably results in damage to the spinal cord. Knowledge of the vertebral levels of the various segments of the spinal cord enables the clinician to determine the likely neurologic deficits. The unequal sensory and motor losses on the two sides indicate a left hemisection of the cord. The band of anesthesia and analgesia was caused by the destruction of the cord on the left side at the level of the 10th thoracic segment; all afferent nerve fibers entering the cord at that point were interrupted. The loss of pain and thermal sensibilities and the loss of light touch below the level of the umbilicus on the right side were caused by the interruption of the lateral and anterior spinothalamic tracts on the left side of the cord.

To comprehend what has happened to this patient, the relationship between the spinal cord and its surrounding vertebral column must be understood. The various neurologic deficits will be easier to understand after the reader has learned how the nervous pathways pass up and down the spinal cord. This information will be discussed in Chapter 4.

The nervous system and the endocrine system control the functions of the body. The nervous system is composed basically of specialized cells, whose function is to receive sensory stimuli and to transmit them to effector organs, whether muscular or glandular. The sensory stimuli that arise either outside or inside the body are correlated within the nervous system, and the efferent impulses are coordinated so that the effector organs work harmoniously together for the well-being of the individual. In addition, the nervous system of higher species has the ability to store sensory information received during past experiences. This information, when appropriate, is integrated with other nervous impulses and channeled into the common efferent pathway.

CENTRAL AND PERIPHERAL NERVOUS SYSTEMS

As shown in Figure 1-1, the nervous system is divided into two main parts, for purposes of description: the **central nervous system** (**CNS**), which consists of the brain and spinal cord, and the **peripheral nervous system** (**PNS**), which consists of the cranial and spinal nerves and their associated ganglia.

In the CNS, the brain and spinal cord are the main centers where correlation and integration of nervous information occur. Both the brain and spinal cord are covered with a system of membranes (**meninges**) and are suspended in **cerebrospinal fluid** (**CSF**). Meninges are further protected by the bones of the skull and the vertebral column (Fig. 1-2).

The CNS is composed of large numbers of **neurons**, which are excitable nerve cells, and their processes,

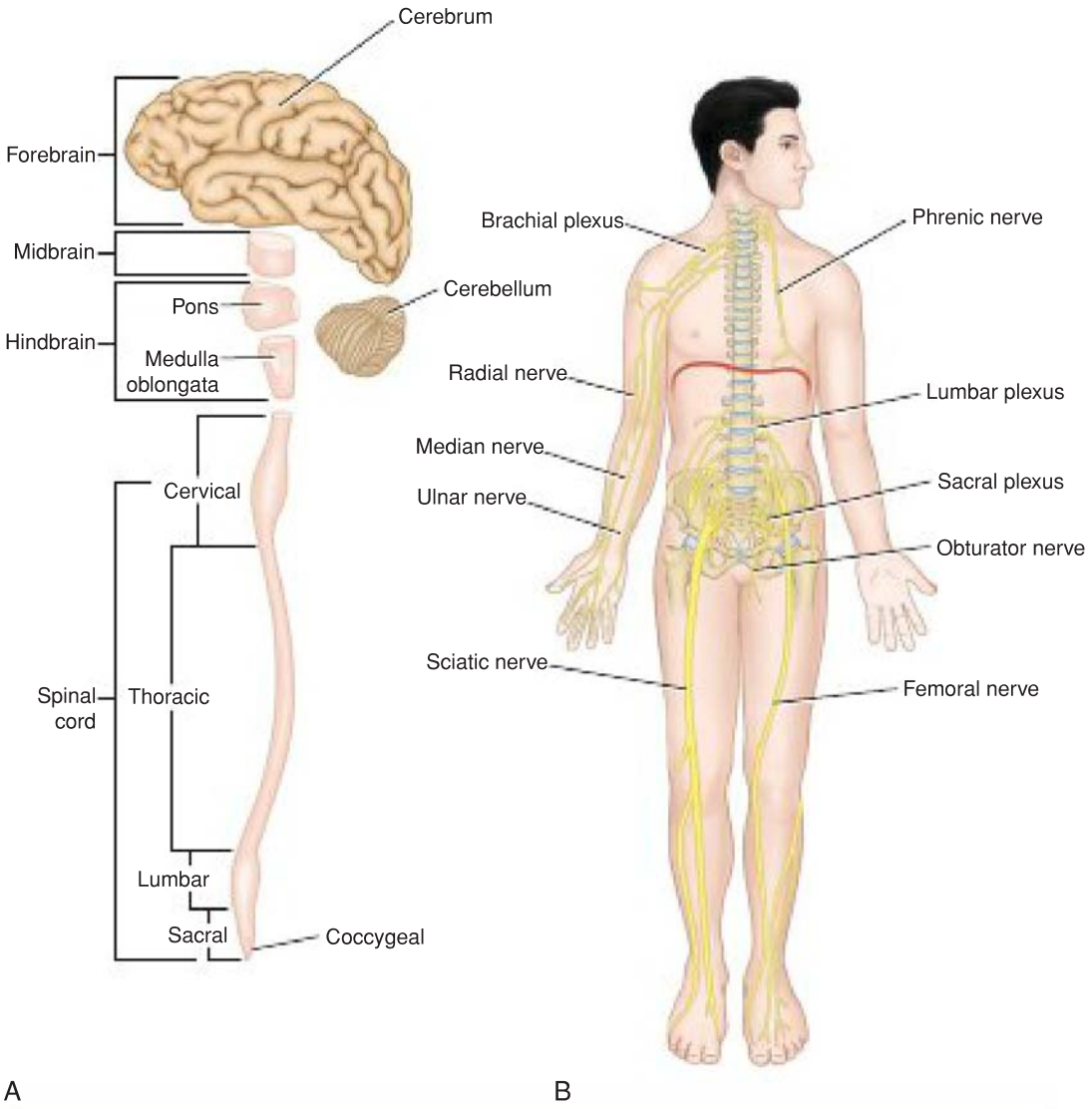

Figure 1-1 **A:** The main divisions of the central nervous system. **B:** The parts of the peripheral nervous system (the cranial nerves have been omitted).

known as **axons** or **nerve fibers**. Neurons are supported by specialized tissue called **neuroglia** (Fig. 1-3).

The CNS interior is organized into gray and white matter. **Gray matter**, which is gray in color, consists of nerve cells embedded in neuroglia. **White matter** consists of nerve fibers embedded in neuroglia and is white in color because of the presence of lipid material in nerve fiber myelin sheaths.

In the PNS, the cranial and spinal nerves, which consist of bundles of nerve fibers (or axons), conduct information to and from the CNS. Although the nerves are surrounded by fibrous sheaths as they run to different parts of the body, they are relatively unprotected and are commonly damaged by trauma.

Autonomic Nervous System

The autonomic nervous system (ANS) is the part of the nervous system that innervates the body's involuntary structures, such as the heart, smooth muscle, and glands. It is distributed throughout the CNS and PNS and is divided into two parts, the **sympathetic** and the **parasympathetic**, both containing afferent and efferent nerve fibers. The activities of the sympathetic part of the ANS prepare the body for an emergency, whereas those of the parasympathetic part are aimed at conserving and restoring energy.

MAJOR DIVISIONS OF THE CENTRAL NERVOUS SYSTEM

Before proceeding to a detailed description of the spinal cord and brain, understanding the main features of these structures and their general relationship to one another is essential (Table 1-1).

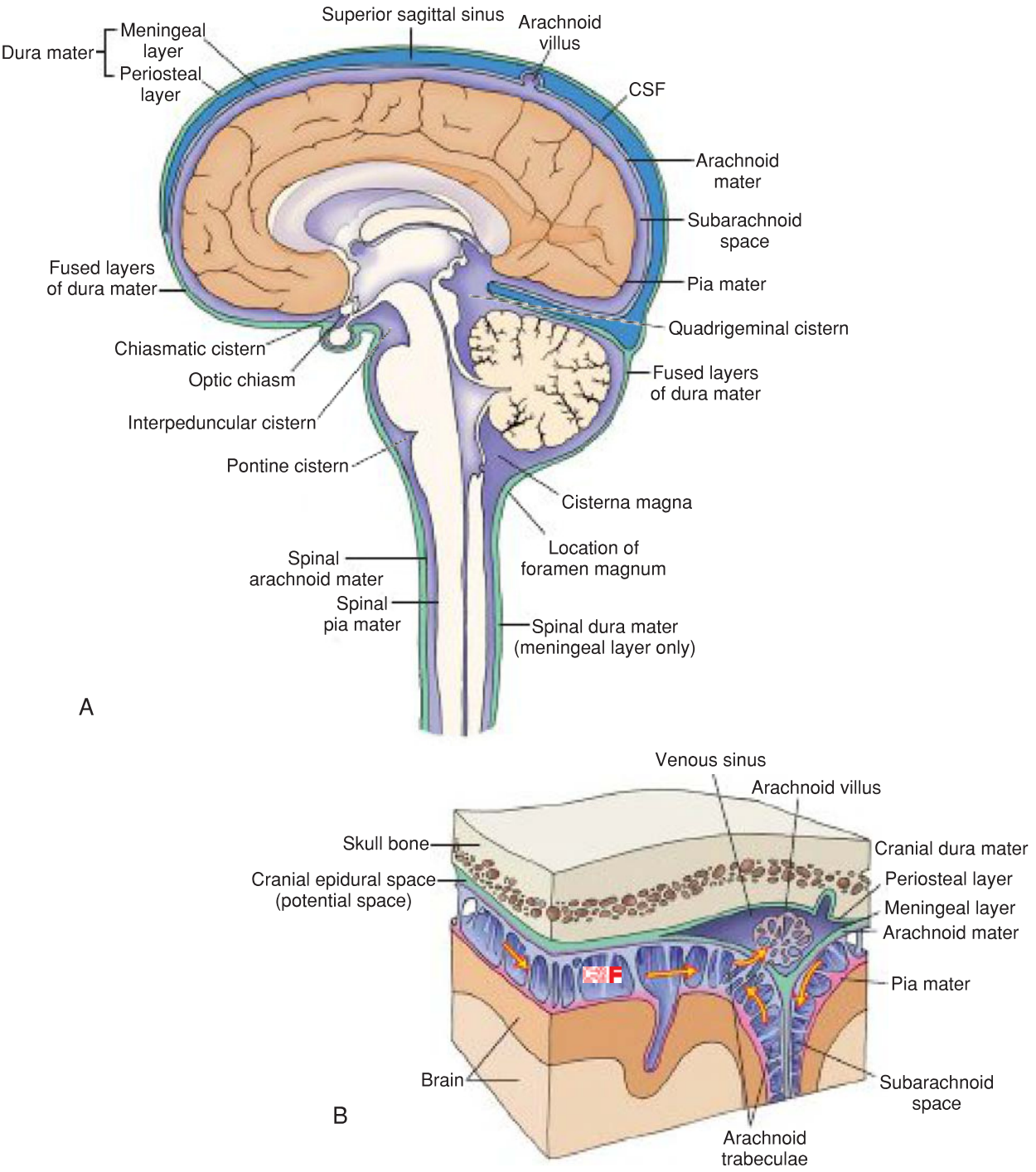

Figure 1-2 **A:** The protective covering of the spinal cord, the meninges, is formed by dura, arachnoid, and pia mater. The space between the arachnoid and pial membranes is called the subarachnoid space and contains cerebrospinal fluid (CSF). The subarachnoid space is enlarged at the cisterna magna and chiasmatic cistern. **B:** In the cranium, the dura consists of fused periosteal and meningeal layers that separate to form dural sinuses. Arachnoid mater projects into the dural venous sinuses to drain CSF from the subarachnoid space. (From Siegel, A., & Sapru, H. N. [2015]. *Essential neuroscience* [3rd ed.]. Baltimore, MD: Wolters Kluwer.)

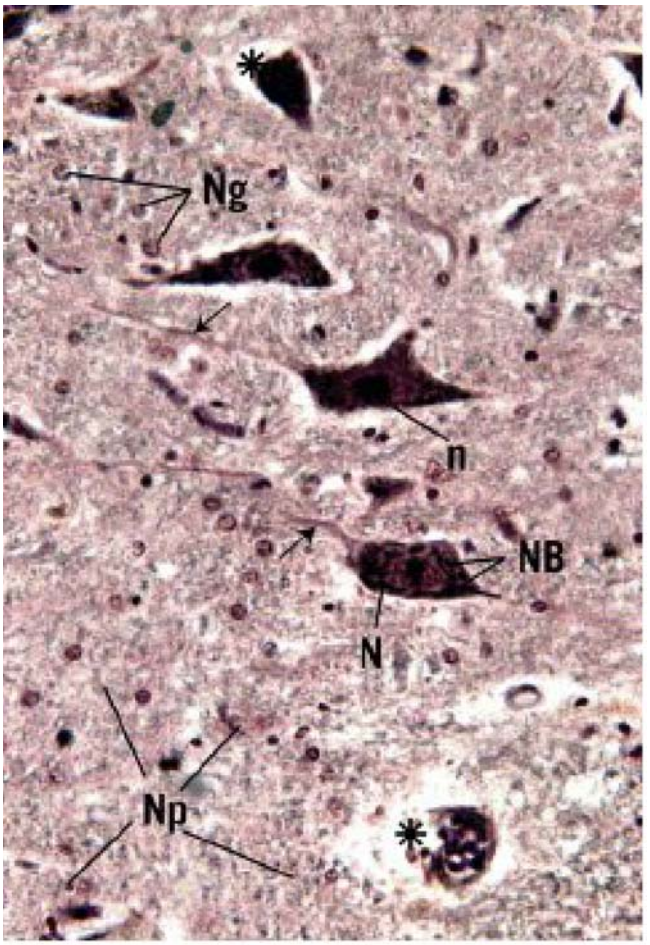

Figure 1-3 Photomicrograph of several large nerve cells with surrounding neuroglia. N, Neuron; n, nucleus; Ng, neuroglia; Np, neuropili; arrows, neurites. (From Gartner, L. P. [2017]. *Color atlas and text of histology* [7th ed.]. Baltimore, MD: Wolters Kluwer.)

Table 1-1 Major Divisions of the Central and Peripheral Nervous Systems

Central Nervous System
Brain
Forebrain
Cerebrum
Diencephalon (between brain)
Midbrain
Hindbrain
Medulla oblongata
Pons
Cerebellum
Spinal cord
Cervical segments
Thoracic segments
Lumbar segments
Sacral segments
Coccygeal segments
Peripheral Nervous System
Cranial nerves and their ganglia—12 pairs that exit the skull through the foramina
Spinal nerves and their ganglia—31 pairs that exit the vertebral column through the intervertebral foramina
8 Cervical
12 Thoracic
5 Lumbar
5 Sacral
1 Coccygeal

Spinal Cord

The spinal cord is situated within the **vertebral canal** of the vertebral column and is surrounded by three meninges (Figs. 1-4 and 1-5): the **dura mater,** the **arachnoid mater,** and the **pia mater.** Further protection is provided by the **CSF**, which surrounds the spinal cord in the **subarachnoid space**.

The spinal cord is roughly cylindrical and begins superiorly at the foramen magnum in the skull, where it is continuous with the **medulla oblongata** of the brain. It terminates inferiorly in the lumbar region. Below, the spinal cord tapers off into the **conus medullaris**, from the apex of which the **filum terminale** (a prolongation of the pia mater) descends to attach to the back of the coccyx (see Fig. 1-4B).

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. 1-6; also see Fig. 1-5). 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**. The gray matter is seen on cross section as an H-shaped pillar with **anterior** and **posterior gray columns**, or **horns**, united by a thin **gray commissure** containing the small **central canal**. The white matter, for purposes of description, is divided into **anterior**, **lateral**, and **posterior white columns** (see Fig. 1-6).

Brain

The brain (Fig. 1-7) lies in the cranial cavity and is continuous with the spinal cord through the foramen magnum (see Fig. 1-5A). As shown in Figure 1-2, it is surrounded by the **dura mater,** the **arachnoid mater**, and the **pia mater**. These three meninges are continuous with the corresponding meninges of the spinal cord. The CSF surrounds the brain in the subarachnoid space.

The brain is conventionally divided into three major divisions: the **hindbrain**, the **midbrain**, and the **forebrain** in ascending order from the spinal cord (see Fig. 1-1A). The **brainstem** (a collective term for the

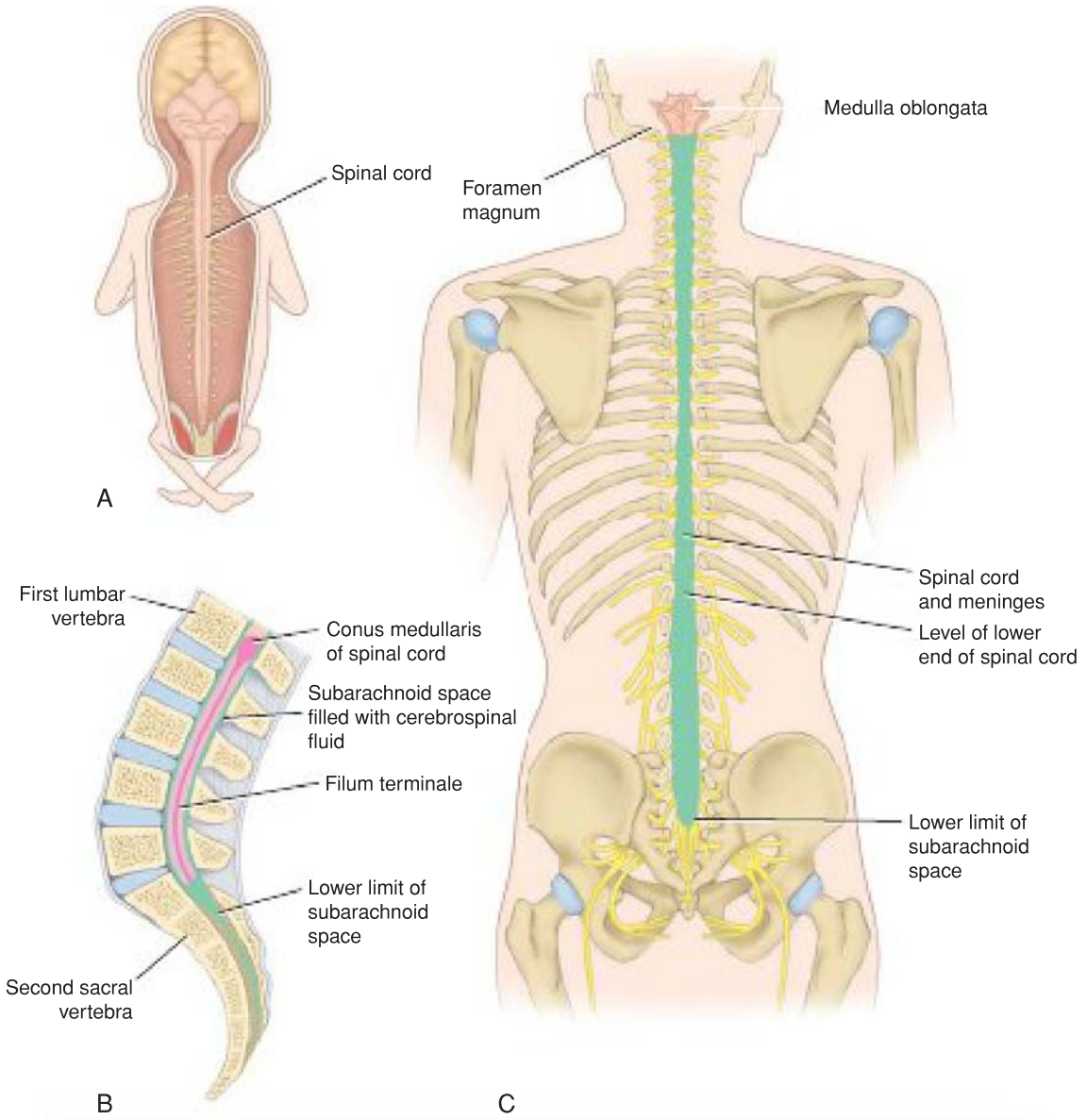

Figure 1-4 **A:** Fetus with the brain and spinal cord exposed on the posterior surface. Note that the spinal cord extends the full length of the vertebral column. **B:** Sagittal section of the vertebral column in an adult showing the spinal cord terminating inferiorly at the level of the lower border of the 1st lumbar vertebra. **C:** Adult spinal cord and covering meninges showing the relationship to surrounding structures.

medulla oblongata, pons, and midbrain) is what remains after the cerebral hemispheres and cerebellum (see below) are removed.

Hindbrain

The hindbrain comprises the **medulla oblongata**, the **pons**, and the **cerebellum**.

Medulla Oblongata

The medulla oblongata is conical in shape and connects the pons superiorly to the spinal cord inferiorly (Fig. 1-8). It contains many collections of neurons, called **nuclei**, and serves as a conduit for ascending and descending nerve fibers.

Pons

The pons is situated on the anterior surface of the cerebellum, inferior to the midbrain and superior to the medulla oblongata (Fig. 1-9; also see Fig. 1-8). The pons, or bridge, derives its name from the large number of transverse fibers on its anterior aspect connecting the two cerebellar hemispheres. It also contains many nuclei and ascending and descending nerve fibers.

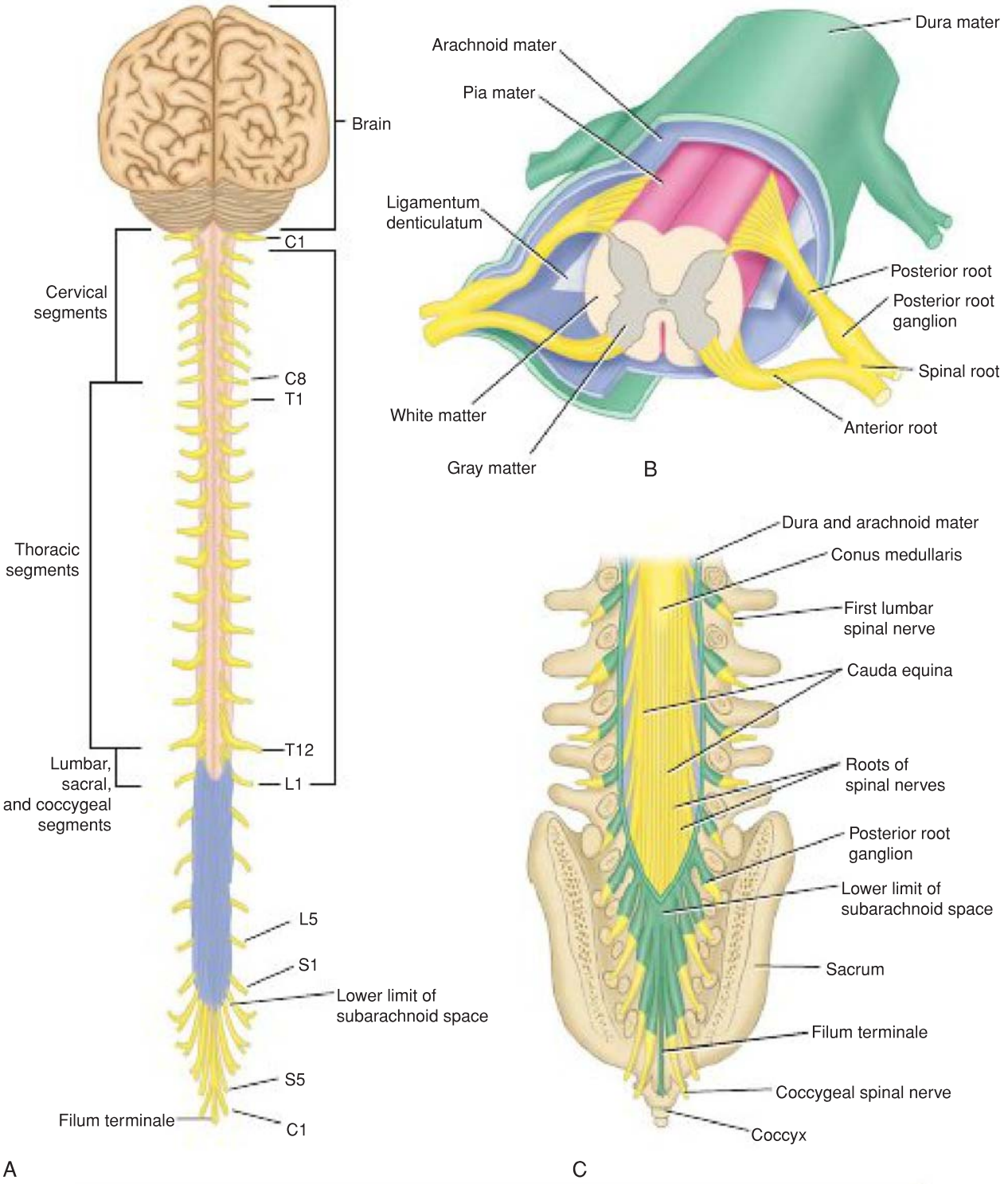

Figure 1-5 **A:** Brain, spinal cord, spinal nerve roots, and spinal nerves as seen on their posterior aspect. **B:** Transverse section through the thoracic region of the spinal cord showing the anterior and posterior roots of a spinal nerve and the meninges. **C:** Posterior view of the lower end of the spinal cord and cauda equina showing their relationship with the lumbar vertebrae, sacrum, and coccyx.

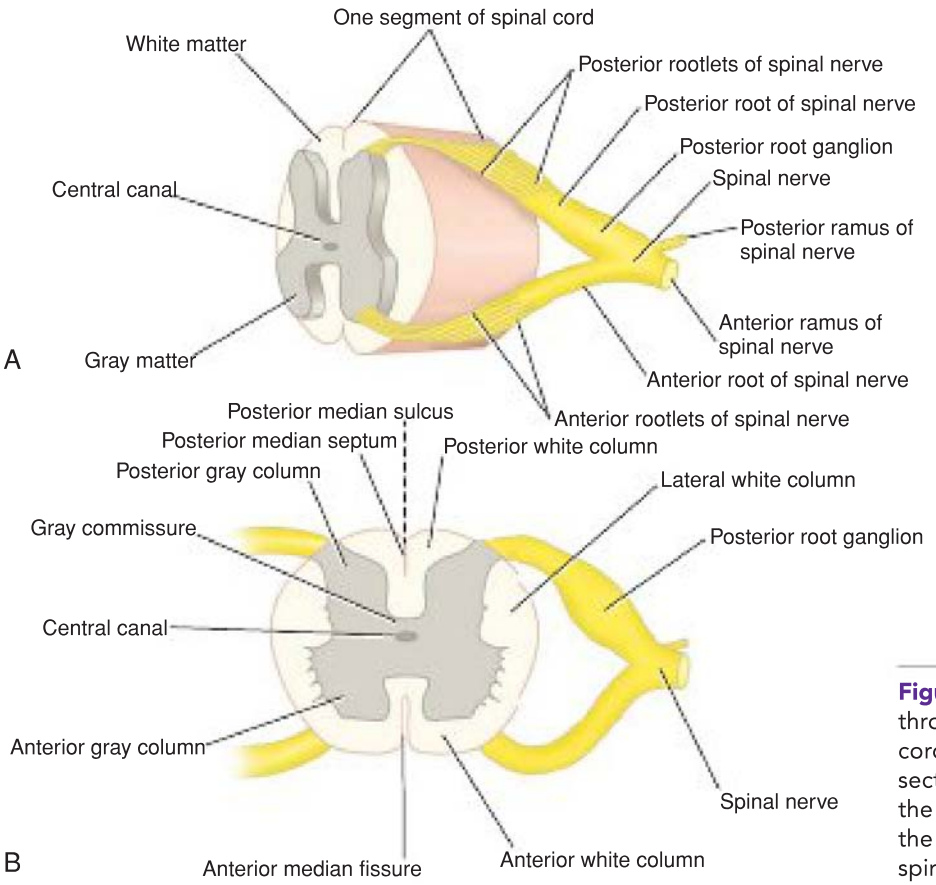

Figure 1-6 **A:** Transverse section through the lumbar part of the spinal cord, oblique view. **B:** Transverse section through the lumbar part of the spinal cord, face view, showing the anterior and posterior roots of a spinal nerve.

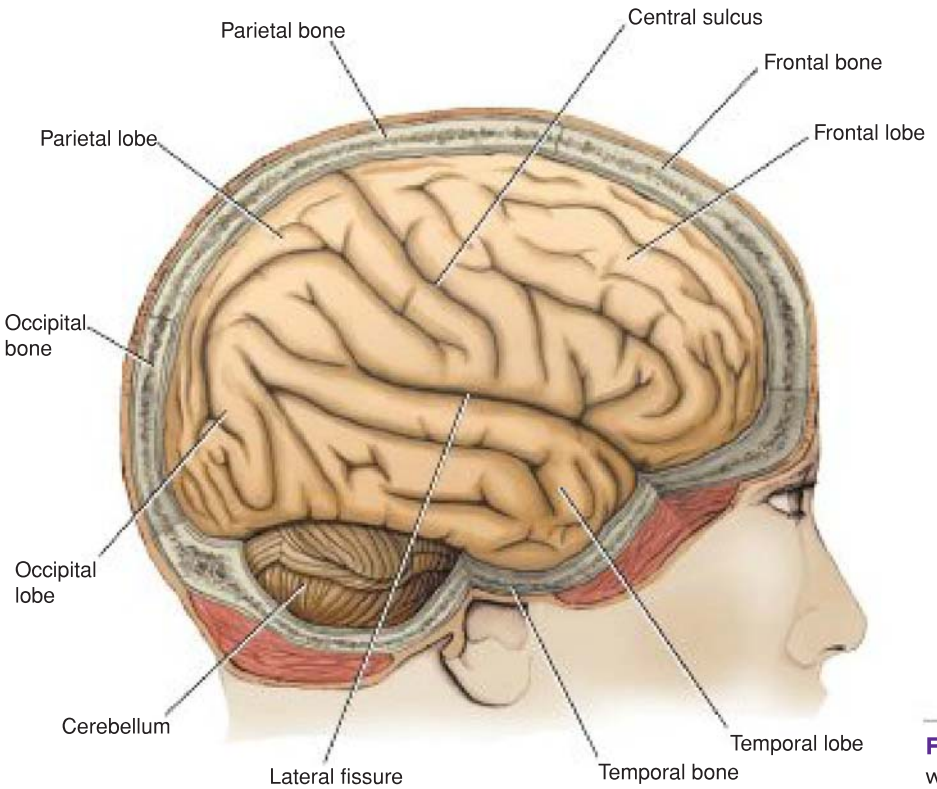

Figure 1-7 Lateral view of the brain within the skull.

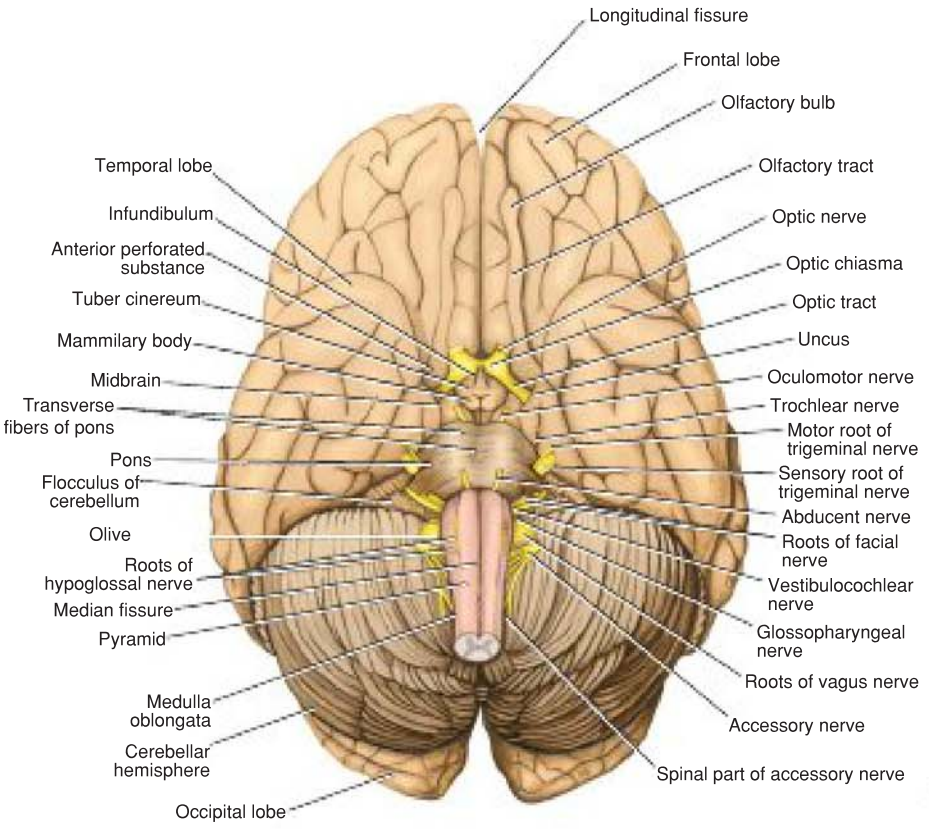

Figure 1-8 Inferior view of the brain.

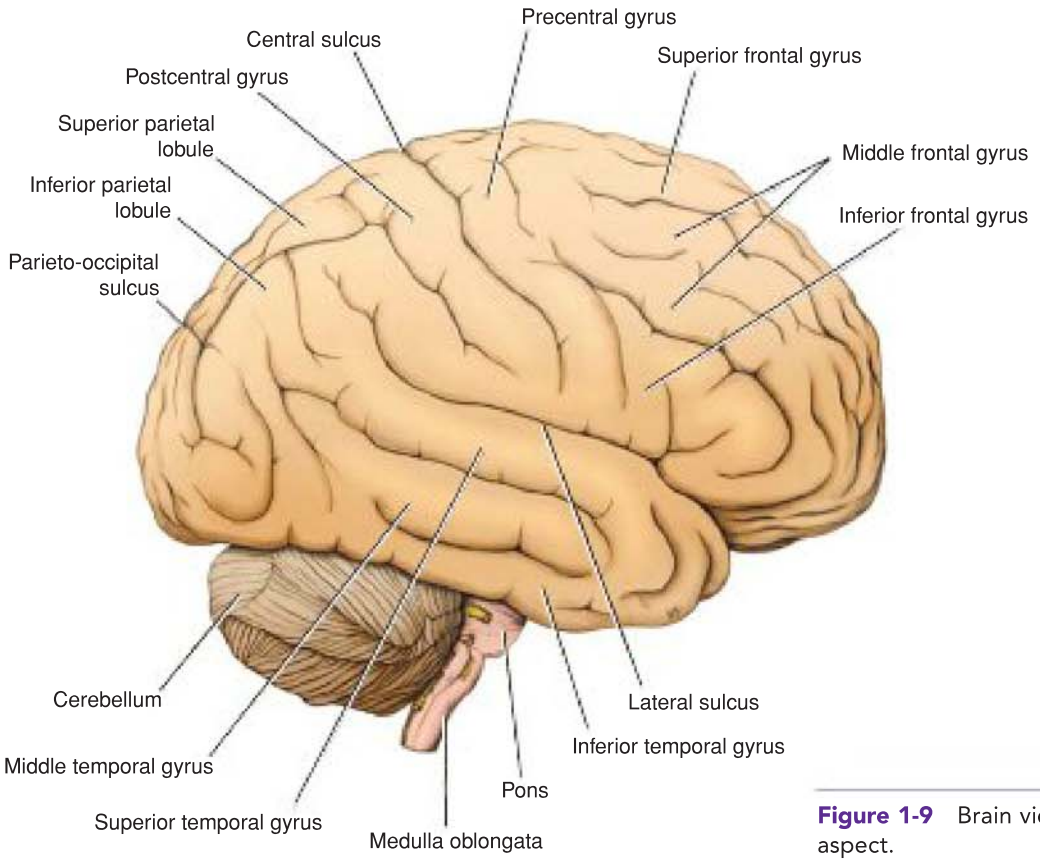

Figure 1-9 Brain viewed from its right lateral aspect.

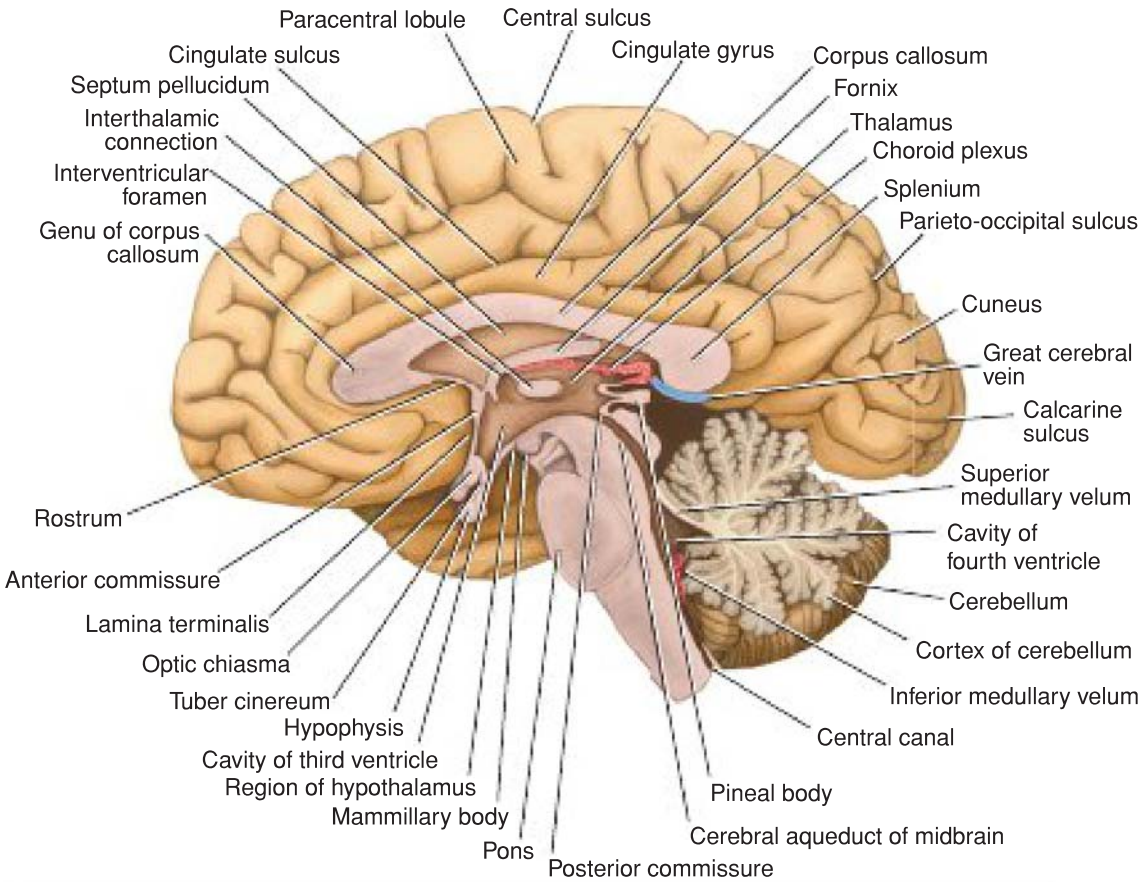

Figure 1-10 Median sagittal section of the brain to show the third ventricle, the cerebral aqueduct, and the fourth ventricle.

Cerebellum

The cerebellum lies within the posterior cranial fossa of the skull (see Figs. 1-7 to 1-9), posterior to the pons and the medulla oblongata. It consists of two laterally placed hemispheres connected by a median portion, the **vermis**. The cerebellum is connected to the midbrain by the **superior cerebellar peduncles**, to the pons by the **middle cerebellar peduncles**, and to the medulla by the **inferior cerebellar peduncles** (see Fig. 6-9). The peduncles are composed of large bundles of nerve fibers connecting the cerebellum to the remainder of the nervous system.

The surface layer of each cerebellar hemisphere is called the **cortex** and is composed of gray matter (Fig. 1-10). The cerebellar cortex is thrown into folds, or folia, separated by closely set transverse fissures. Certain masses of gray matter are found in the interior of the cerebellum, embedded in the white matter; the largest of these is known as the **dentate nucleus** (see Fig. 6-7).

The medulla oblongata, the pons, and the cerebellum surround a cavity filled with CSF, called the **fourth ventricle.** This is connected superiorly to the third ventricle by the **cerebral aqueduct**; inferiorly, it is continuous with the central canal of the spinal cord (Fig. 1-11). It communicates with the subarachnoid space through three openings in the inferior part of the roof. Through these openings, the CSF within the CNS can enter the subarachnoid space.

Midbrain

The midbrain is the narrow part of the brain that connects the forebrain to the hindbrain (see Figs. 1-1A and 1-10). The narrow cavity of the midbrain is the **cerebral aqueduct,** which connects the third and fourth ventricles. The midbrain contains many nuclei and bundles of ascending and descending nerve fibers.

Forebrain

The forebrain comprises the **diencephalon** (between brain), which is the central part of the forebrain, and the **cerebrum**.

Diencephalon

The diencephalon is almost completely hidden from the surface of the brain. It consists of a dorsal **thalamus** and a ventral **hypothalamus** (see Fig. 1-10). The thalamus is a large, egg-shaped mass of gray matter that lies on either side of the third ventricle. The anterior end of the thalamus forms the posterior boundary of the **interventricular foramen**, the

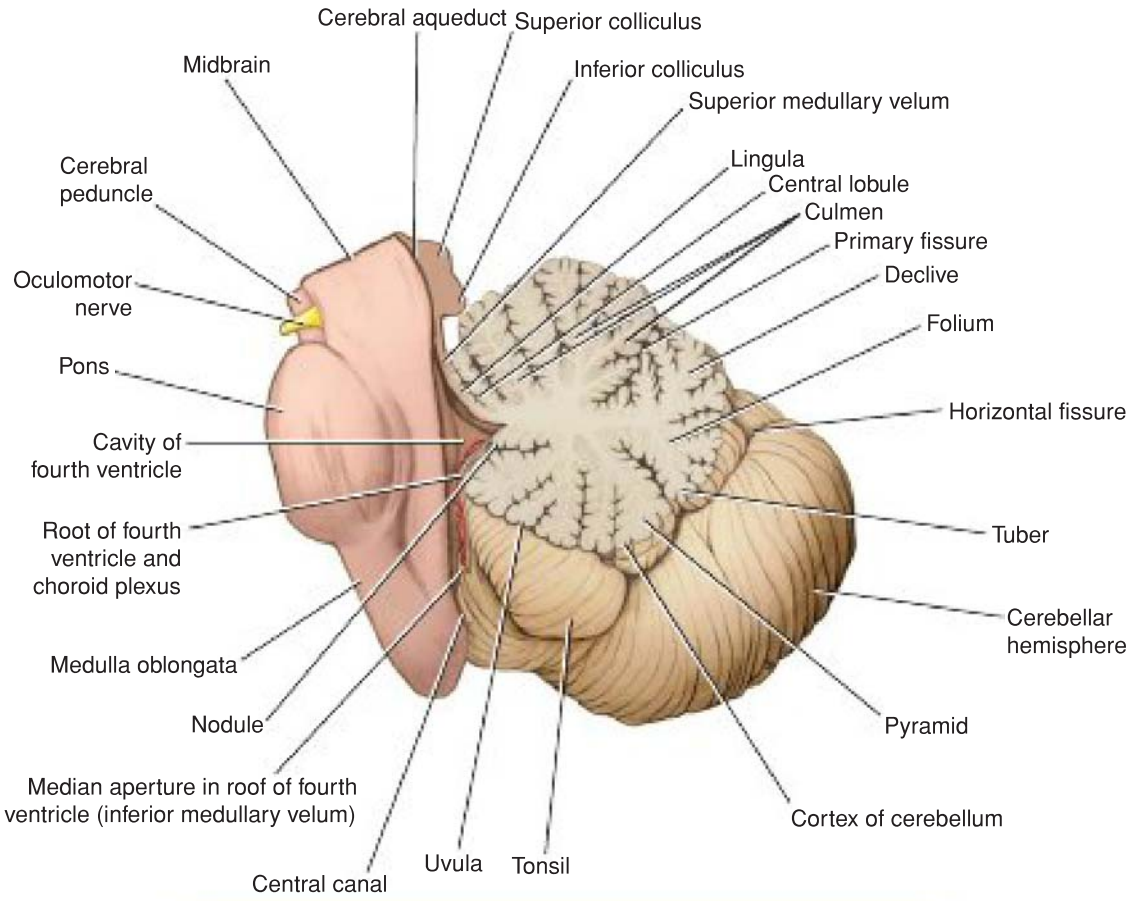

Figure 1-11 Sagittal section through the brainstem and the cerebellum.

opening between the third and lateral ventricles. The hypothalamus forms the lower part of the lateral wall and floor of the third ventricle.

Cerebrum

The cerebrum, the largest part of the brain, consists of two cerebral hemispheres, which are connected by a mass of white matter called the **corpus callosum** (see Figs. 1-9 and 1-10). Each hemisphere extends from the frontal to the occipital bones in the skull, superior to the anterior and middle cranial fossae; posteriorly, the cerebrum lies above the tentorium cerebelli (see Fig. 15-3). The hemispheres are separated by a deep cleft, the **longitudinal fissure**, into which projects the **falx cerebri** (see Fig. 15-1).

The surface layer of each hemisphere, the **cortex**, is composed of gray matter. The cerebral cortex is thrown into folds (**gyri**) separated by fissures, or **sulci** (see Fig. 1-9). This arrangement greatly increases the surface area of the cortex. A number of the large sulci are conveniently used to subdivide the surface of each hemisphere into **lobes**, which are named from the bones of the cranium they lie under.

Within the hemisphere is a central core of white matter containing several large masses of gray matter, the **basal nuclei or ganglia**. A fan-shaped collection of nerve fibers, the **corona radiata** (Fig. 1-12), passes in the white matter to and from the cerebral cortex to the brainstem. The corona radiata converges on the basal nuclei and passes between them as the **internal capsule**. The tailed nucleus situated on the medial side of the internal capsule is the **caudate nucleus** (Fig. 1-13), and the lens-shaped nucleus on the lateral side of the internal capsule is the **lentiform nucleus**.

Within each cerebral hemisphere is a cavity called the **lateral ventricle** (see Figs. 16-2 and 16-3). The lateral ventricles communicate with the third ventricle through the **interventricular foramina**.

During the process of development, the cerebrum becomes enormously enlarged and overhangs the diencephalon, the midbrain, and the hindbrain.

Brain Structure

Unlike the spinal cord, the brain is composed of an inner core of white matter, which is surrounded by an outer covering of gray matter. However, as mentioned previously, certain important masses of gray matter are situated deeply within the white matter: the gray cerebellar nuclei in the cerebellum and the gray thalamic, caudate, and lentiform nuclei in the cerebrum.

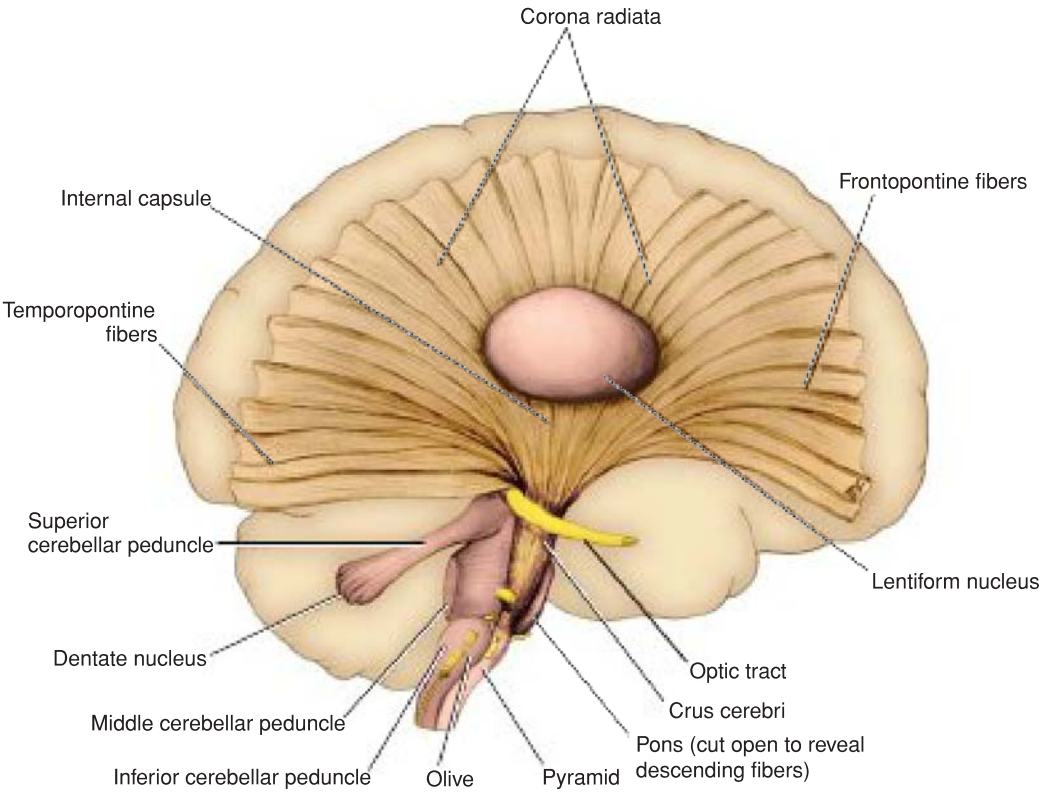

Figure 1-12 Right lateral view showing continuity of the corona radiata, the internal capsule, and the crus cerebri of the cerebral peduncles. Note the position of the lentiform nucleus lateral to the internal capsule.

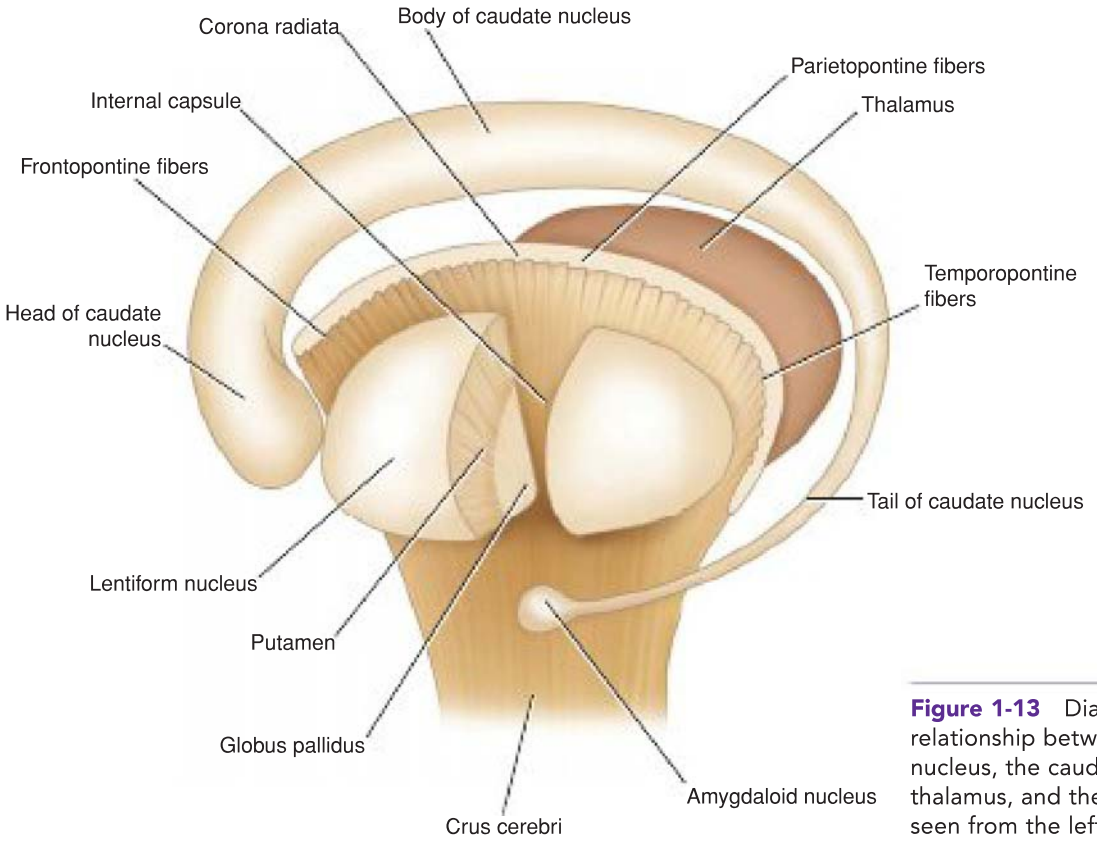

Figure 1-13 Diagram showing the relationship between the lentiform nucleus, the caudate nucleus, the thalamus, and the internal capsule, as seen from the left lateral side.

MAJOR DIVISIONS OF THE PERIPHERAL NERVOUS SYSTEM

The PNS comprises the cranial and spinal nerves and their associated ganglia.

Cranial and Spinal Nerves

The cranial and spinal nerves are made up of bundles of nerve fibers supported by connective tissue.

The 12 pairs of **cranial nerves** (see Fig. 1-8) leave the brain and pass through foramina in the skull. The 31 pairs of **spinal nerves** (see Fig. 1-5) leave the spinal cord and pass through intervertebral foramina in the vertebral column. The spinal nerves are associated with regions of the spinal cord: 8 **cervical**, 12 **thoracic**, 5 **lumbar**, 5 **sacral**, and 1 **coccygeal**. Note that there are 8 cervical nerves yet only 7 cervical vertebrae and that there is 1 coccygeal nerve but 4 coccygeal vertebrae.

Each spinal nerve is connected to the spinal cord by two roots: the **anterior root** and the **posterior root** (see Fig. 1-5B). The anterior root consists of bundles of nerve fibers carrying nerve impulses *away* from the CNS—**efferent fibers**. Those that go to skeletal muscles and cause them to contract are **motor fibers**. Their cells of origin lie in the anterior gray horn of the spinal cord.

The posterior root consists of bundles of **afferent fibers** that carry nervous impulses *to* the CNS. Because these fibers convey information about sensations of touch, pain, temperature, and vibration, 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**.

The spinal nerve roots pass from the spinal cord to the level of their respective intervertebral foramina, where they unite to form a **spinal nerve** (Fig. 1-14). Here, the motor and sensory fibers mix together; thus, a spinal nerve comprises both motor and sensory fibers.

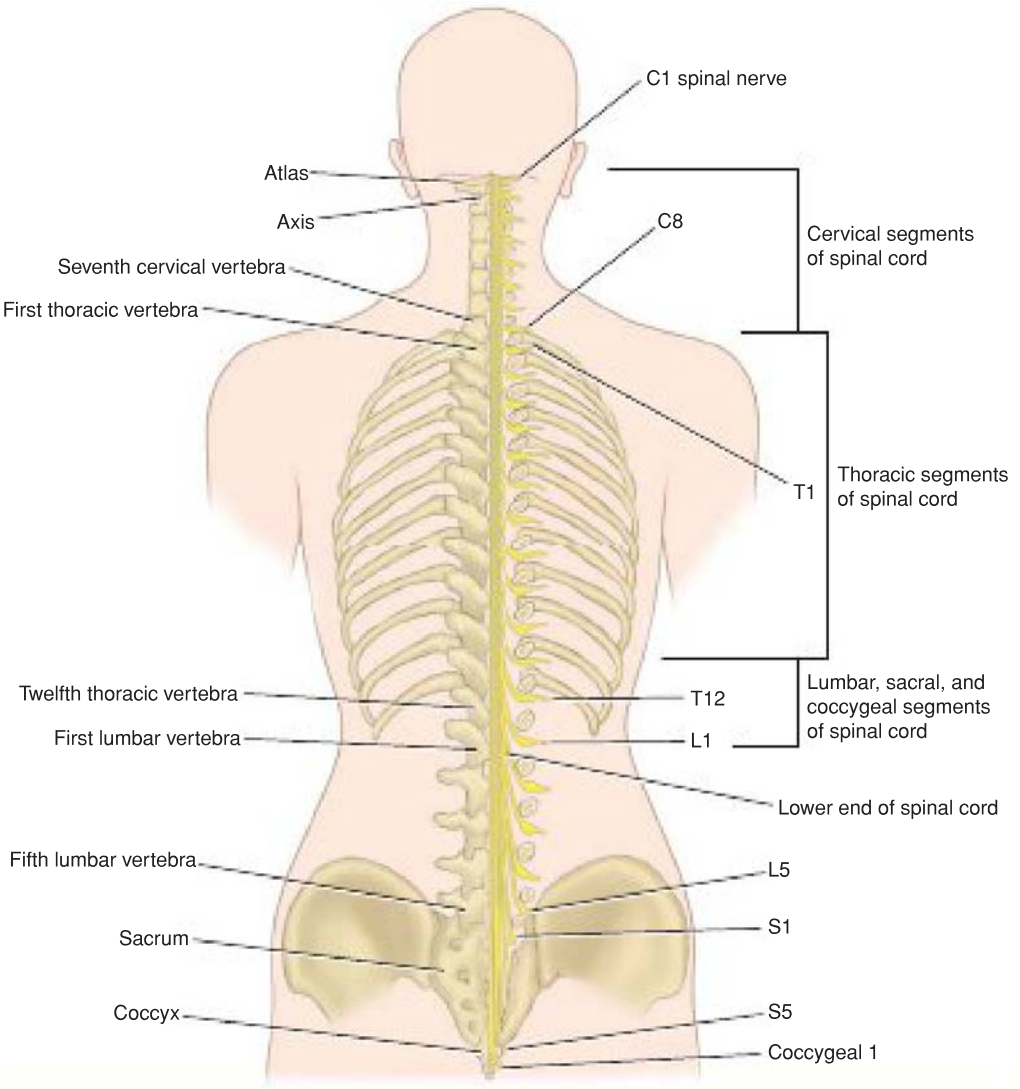

Figure 1-14 Posterior view of the spinal cord showing the origins of the roots of the spinal nerves and their relationship to the different vertebrae. On the right, the laminae have been removed to expose the right half of the spinal cord and the nerve roots.

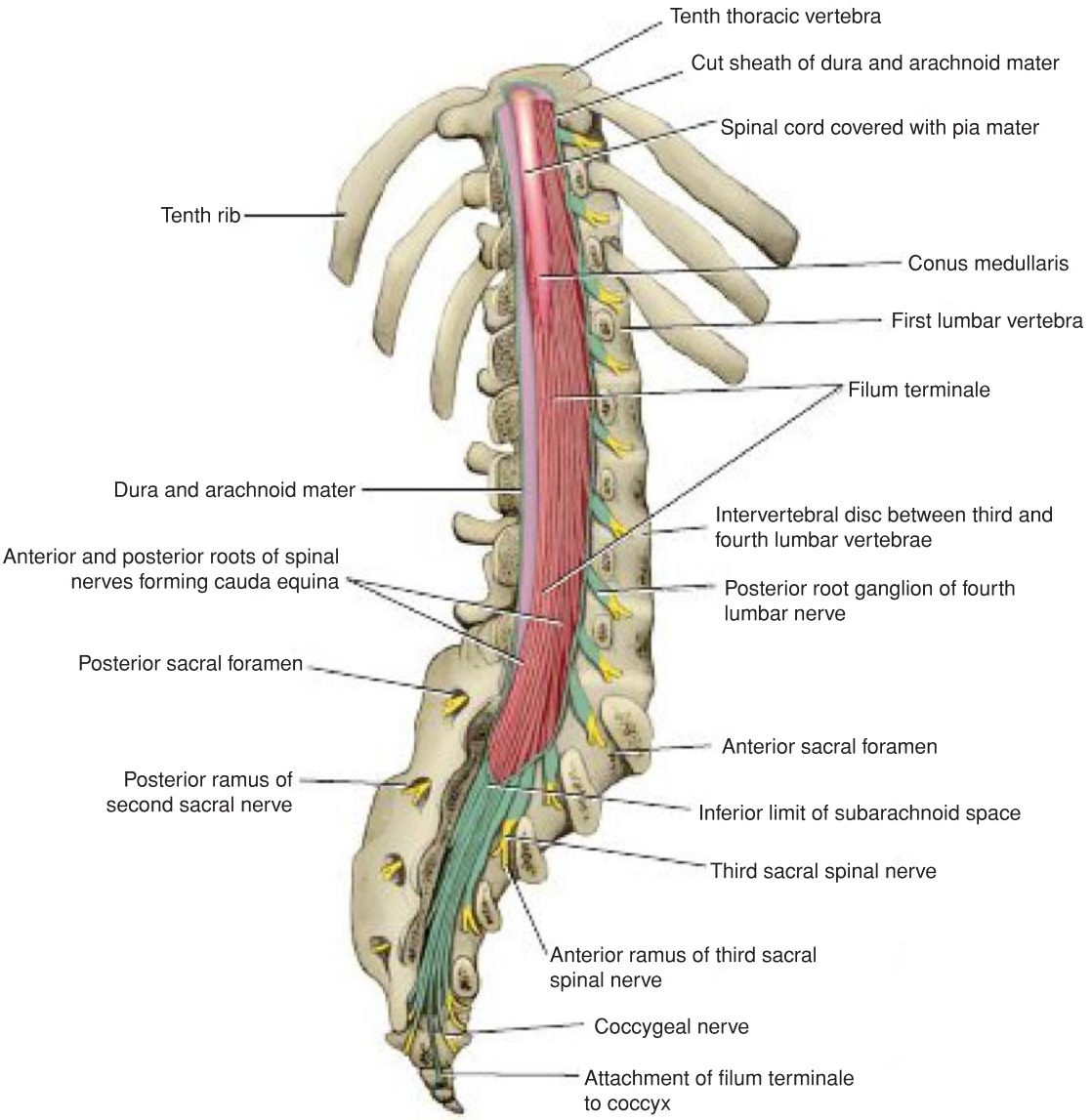

Figure 1-15 Oblique posterior view of the lower end of the spinal cord and the cauda equina. On the right, the laminae have been removed to expose the right half of the spinal cord and the nerve roots.

Because of the disproportionate growth in length of the vertebral column during development, compared with that of the spinal cord, the length of the roots increases progressively from above downward (see Fig. 1-15). In the upper cervical region, the spinal nerve roots are short and run almost horizontally, but the roots of the lumbar and sacral nerves below the level of the termination of the cord (lower border of the 1st lumbar vertebra in the adult) form a vertical leash of nerves around the **filum terminale** (Fig. 1-15). Together, these lower nerve roots are called the **cauda equina**.

After emerging from the intervertebral foramen, each spinal nerve immediately divides into a large **anterior ramus** and a smaller **posterior ramus**, each containing both motor and sensory fibers. The posterior ramus passes posteriorly around the vertebral column to supply the muscles and skin of the back. The anterior ramus continues anteriorly to supply the muscles and skin over the anterolateral body wall and all the muscles and skin of the limbs.

The anterior rami join one another at the root of the limbs to form complicated **nerve plexuses** (see Fig. 1-1B). The **cervical and brachial plexuses** are found at the root of the upper limbs, and the **lumbar and sacral plexuses** are found at the root of the lower limbs.

Ganglia

Ganglia can be divided into sensory ganglia of spinal nerves (posterior root ganglia) and cranial nerves and autonomic ganglia.

Sensory Ganglia

Sensory ganglia are fusiform swellings (see Fig. 1-5) on the posterior root of each spinal nerve just proximal to the root's junction with a corresponding anterior root. They are referred to as **posterior root ganglia**. Similar ganglia found along the course of cranial nerves V, VII, VIII, IX, and X are the **sensory ganglia** of these nerves.

Autonomic Ganglia

Autonomic ganglia, which are often irregular in shape, are situated along the course of efferent nerve fibers of the ANS. They are found in the paravertebral sympathetic chains (see Figs. 14-1 and 14-2) around the roots of the great visceral arteries in the abdomen and close to, or embedded within, the walls of various viscera.

EARLY DEVELOPMENT OF THE NERVOUS SYSTEM

Before the formation of the nervous system in the embryo, three main cell layers differentiate. The innermost layer, the **entoderm**, gives rise to the gastrointestinal tract, the lungs, and the liver. The **mesoderm** gives rise to the muscle, connective tissues, and the vascular system. The third and outermost layer, the **ectoderm**, formed of columnar epithelium, gives rise to the entire nervous system.

During the third week of development, the ectoderm on the dorsal surface of the embryo between the primitive knot and the buccopharyngeal membrane thickens to form the **neural plate**. The plate, which is pear shaped and wider cranially, develops a longitudinal **neural groove**. The groove now deepens so that it is bounded on either side by **neural folds** (Fig. 1-16).

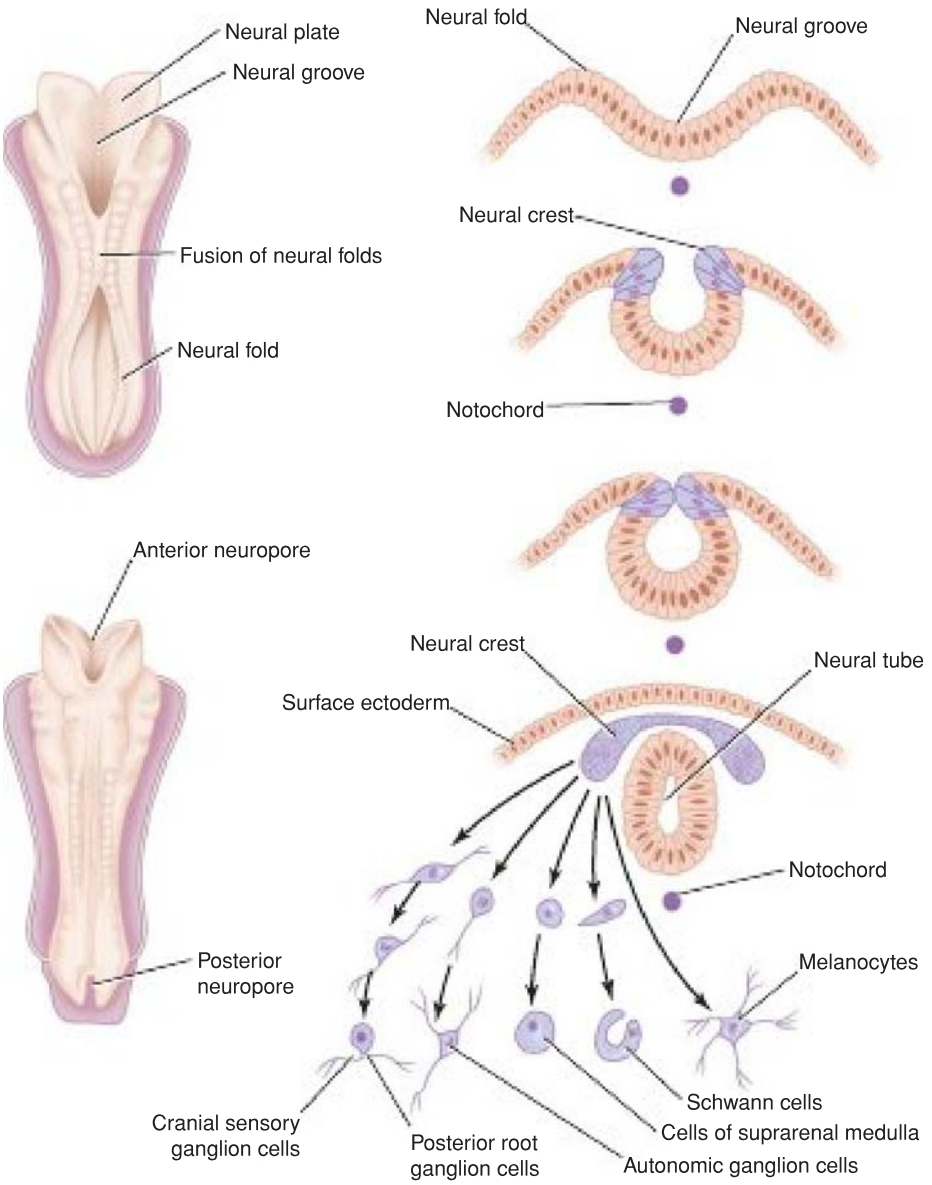

Figure 1-16 Formation of the neural plate, neural groove, and neural tube. The cells of the neural crest differentiate into the cells of the posterior root ganglia, the sensory ganglia of cranial nerves, autonomic ganglia, neurilemmal cells (Schwann cells), the cells of the suprarenal medulla, and melanocytes.

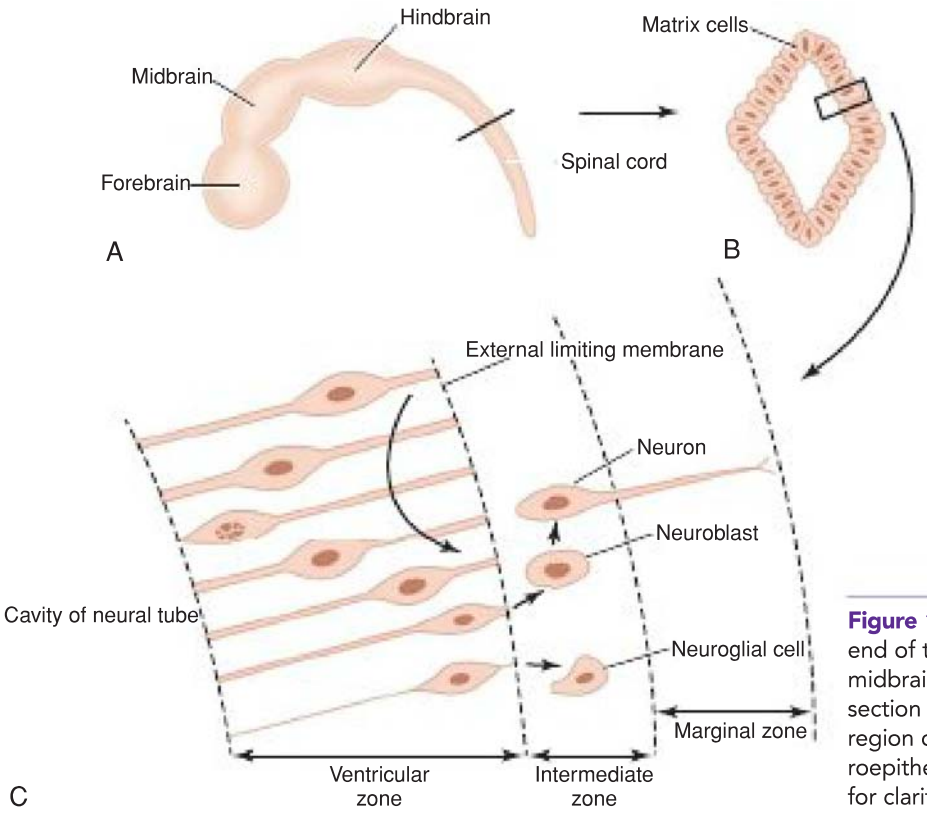

Figure 1-17 **A:** Expansion of the cephalic end of the neural tube to form the forebrain, midbrain, and hindbrain vesicles. **B, C:** Cross section of the developing neural tube in the region of the spinal cord. The cells of the neuroepithelial layer have been widely separated for clarity.

With further development, the neural folds fuse, converting the neural groove into a **neural tube**. Fusion starts at about the midpoint along the groove and extends cranially and caudally so that, in the earliest stage, the cavity of the tube remains in communication with the amniotic cavity through the **anterior** and **posterior neuropores**. The anterior neuropore closes first and the posterior neuropore 2 days later. Thus, normally, the neural tube closure is complete within 28 days. Meanwhile, the neural tube has sunk beneath the surface ectoderm.

During the invagination of the neural plate to form the neural groove, the cells forming the lateral margin of the plate do not become incorporated in the neural tube but instead form a strip of ectodermal cells that lie between the neural tube and the covering ectoderm, the **neural crest** (Fig. 1-16). Subsequently, this group of cells will migrate ventrolaterally on each side around the neural tube. Ultimately, the neural crest cells will differentiate into the cells of the **posterior root ganglia**, the **sensory ganglia of the cranial nerves**, **autonomic ganglia**, the **cells of the suprarenal medulla**, and the **melanocytes**. These cells also probably give rise to mesenchymal cells in the head and neck.

Meanwhile, the proliferation of cells at the cephalic end of the neural tube causes it to dilate and form **three primary brain vesicles**: the **forebrain**, **midbrain**, and **hindbrain vesicles** (Fig. 1-17) (Table 1-2). The rest of the tube elongates and remains smaller in diameter; it will form the **spinal cord.**

Table 1-2 The Primary Divisions of the Developing Brain

Primary Vesicle	Primary Division	Subdivision	Adult Structures
Forebrain vesicle	Prosencephalon (forebrain)	Telencephalon	Cerebral hemisphere, basal ganglia, hippocampus
		Diencephalon	Thalamus, hypothalamus, pineal body, infundibulum
Midbrain vesicle	Mesencephalon (midbrain)	Mesencephalon (midbrain)	Tectum, tegmentum, crus cerebri
Hindbrain vesicle	Rhombencephalon (hindbrain)	Metencephalon	Pons, cerebellum
		Myelencephalon	Medulla oblongata

The subsequent differentiation of cells in the neural tube is brought about by the inductive interactions of one group of cells with another. The inducing factors influence the control of the gene expression in the target cells. Ultimately, the simplest progenitor cell will differentiate into neurons and neuroglial cells. Interestingly, excessive numbers of neurons and neuroglial cells develop, and many (nearly half of the developing neurons) will be programmed to die by a process known as **programmed cell death**. Research into the identification of neurotrophic factors that promote the development and survival of neurons is of great importance, as the results could possibly be applied to the problem of regeneration of the spinal cord neurons following trauma or the inhibition of degenerative diseases such as Alzheimer disease.

The further development of the nervous system will be fully described in Chapter 18 following the description of the different parts of the nervous system and their neuronal connections.

Clinical Notes

Relationship of Spinal Cord Segments to Vertebral Numbers

Because the spinal cord is shorter than the vertebral column, the spinal cord segments do not correspond numerically with the vertebrae that lie at the same level (see Fig. 1-14). The following table will help a clinician determine which spinal segment is related to a given vertebral body (Table 1-3).

Examination of a patient's back shows that the spinous processes lie approximately at the same level as the vertebral bodies. In the lower thoracic region, however, because of the length and extreme obliquity of the spinous processes, the tips of the spines lie at the level of the vertebral body below.

Spinal Cord and Brain Injuries

The spinal cord and brain are well protected. Both are suspended in **cerebrospinal fluid** (**CSF**) and are surrounded by the bones of the vertebral column and skull (see Chapters 4 and 5). However, with enough force, these protective structures can be damaged, with consequent injury to the delicate underlying nervous tissue. Moreover, the cranial and spinal nerves and blood vessels are also likely to be injured.

Spinal Cord Injuries

The degree of spinal cord injury at different vertebral levels is determined largely by anatomical factors. In the cervical region, dislocation or fracture dislocation is common, but the large size of the vertebral canal usually prevents severe injury to the spinal cord. However, with considerable displacement of the bones or bone fragments, the cord is sectioned. Respiration ceases if the cord is completely severed above the segmental origin of the phrenic nerves (C3–C5) because the intercostal muscles and the diaphragm are paralyzed, resulting in death.

In fracture dislocations of the thoracic region, displacement can be considerable. The small size of the vertebral canal results in severe injury to this region of the spinal cord.

In fracture dislocations of the lumbar region, two anatomic facts help prevent substantial nerve injury. First, the spinal cord in the adult extends down only as far as the level of the lower border of the 1st lumbar vertebra (see Fig. 1-15). Second, the large size of the vertebral foramen in this region gives the roots of the cauda equina ample room.

Injury to the spinal cord may produce partial or complete loss of function at the level of the lesion and partial or complete loss of function of afferent and efferent nerve tracts below the level of the lesion. The symptoms and signs of such injuries are discussed after the detailed structure of the spinal cord, and the ascending and descending tracts are discussed in Chapter 4.

Table 1-3 Relationship of Spinal Cord Segments to Vertebral Numbers

Vertebrae	Spinal Segment
Cervical vertebrae	Add 1
Upper thoracic vertebrae	Add 2
Lower thoracic vertebrae (7–9)	Add 3
10th thoracic vertebra	L1–L2 cord segments
11th thoracic vertebra	L3–L4 cord segments
12th thoracic vertebra	L5 cord segment
1st lumbar vertebra	Sacral and coccygeal cord segments

Spinal Nerve Injuries

The intervertebral foramina (Fig. 1-18) transmit the spinal nerves and the small segmental arteries and veins, all of which are embedded in areolar tissue. Each foramen is bounded superiorly and inferiorly by the pedicles of adjacent vertebrae, anteriorly by the lower part of the vertebral body and the intervertebral disc, and posteriorly by the articular processes and the joint between them. In this situation, the spinal nerve is very vulnerable and may be pressed on or irritated by disease of the surrounding structures. Herniation of the intervertebral disc, fractures of the vertebral bodies, and osteoarthritis involving the joints of the articular processes or the joints between the vertebral bodies may all result in pressure, stretching, or edema of the emerging spinal nerve. Such pressure would give rise to dermatomal pain, muscle weakness, and diminished or absent reflexes.

HERNIATED INTERVERTEBRAL DISCS

Herniation of the intervertebral discs occurs most commonly in areas of the vertebral column where a mobile part joins a relatively immobile part—for example, the cervicothoracic and lumbosacral junctions. In these areas, the

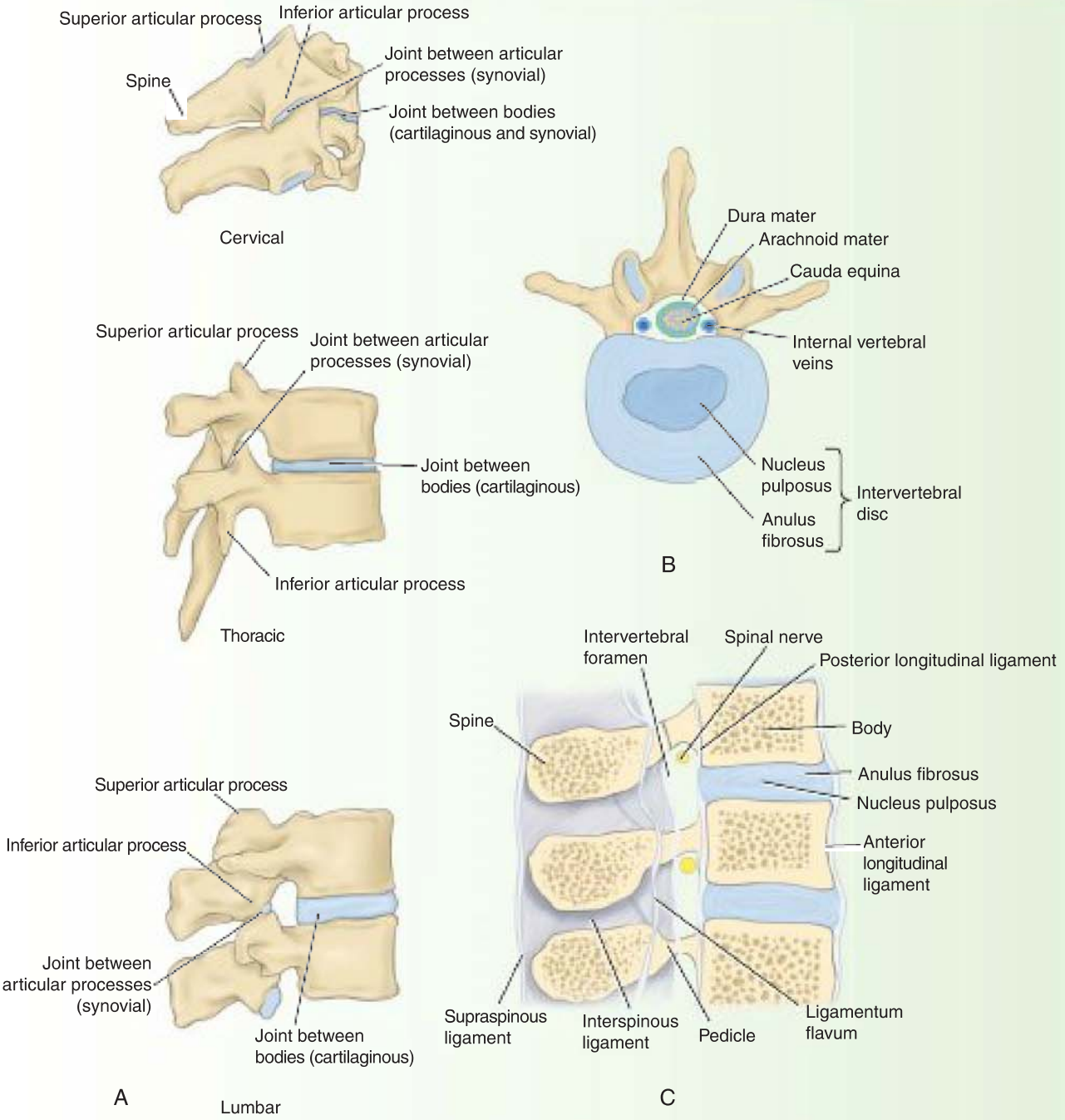

Figure 1-18 **A:** Joints in the cervical, thoracic, and lumbar regions of the vertebral column. **B:** Third lumbar vertebra seen from above showing the relationship between the intervertebral disc and the cauda equina. **C:** Sagittal section through three lumbar vertebrae showing the ligaments and the intervertebral discs. Note the relationship between the emerging spinal nerve in an intervertebral foramen and the intervertebral disc.

posterior part of the anulus fibrosus of the disc ruptures, and the central nucleus pulposus is forced posteriorly like toothpaste out of a tube. This herniation of the nucleus pulposus may result either in a central protrusion in the midline under the posterior longitudinal ligament of the vertebrae or in a lateral protrusion at the side of the posterior ligament close to the intervertebral foramen (Fig. 1-19).

Cervical disc herniations are less common than herniations in the lumbar region. The discs most susceptible are those between the 5th and 6th and the 6th and 7th cervical vertebrae. Lateral protrusions cause pressure on a spinal nerve or its roots. Each spinal nerve emerges above the corresponding vertebra; thus, the protrusion of the disc between the 5th and 6th cervical vertebrae

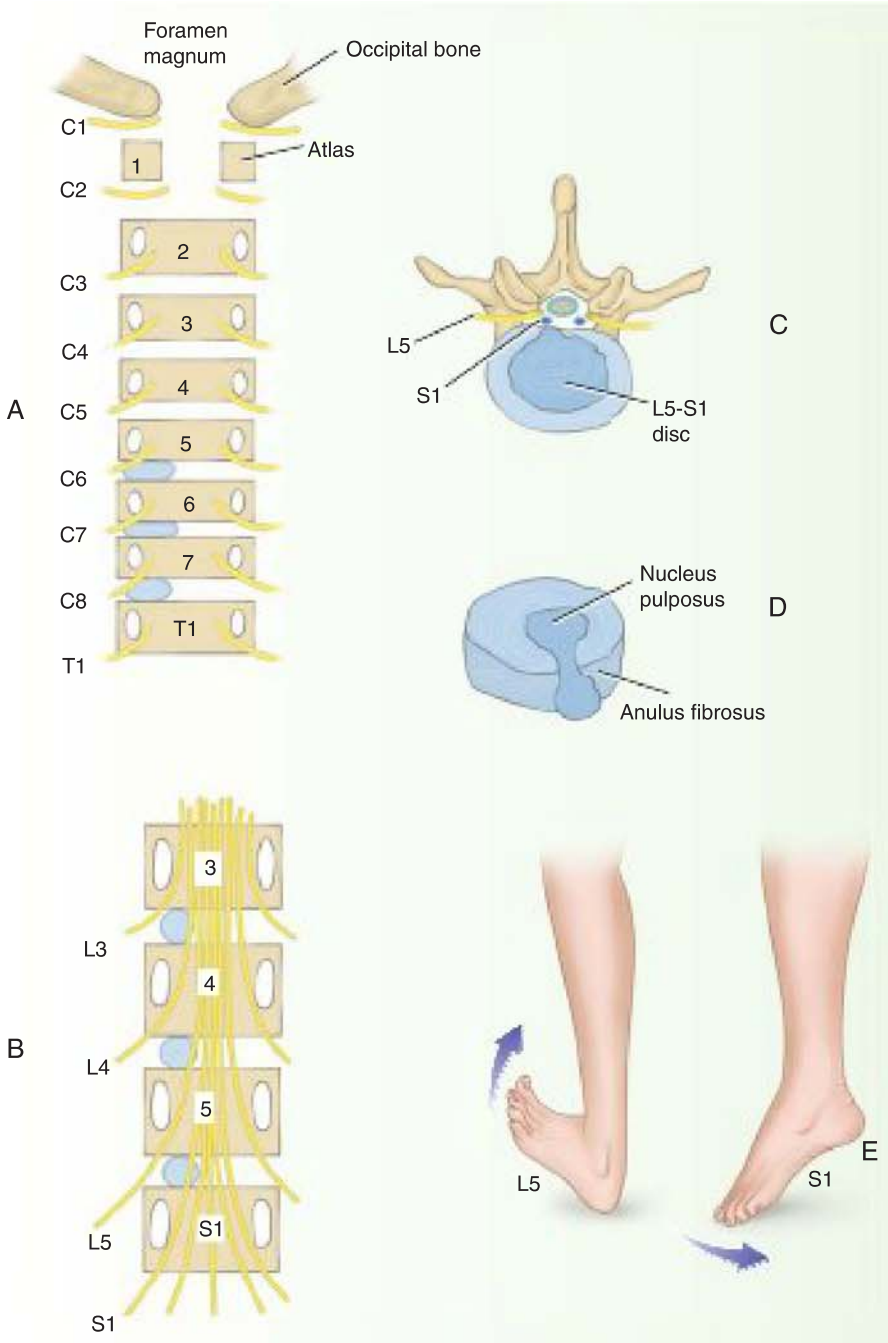

Figure 1-19 **A, B:** Posterior views of the vertebral bodies in the cervical and lumbar regions showing the relationship that might exist between a herniated nucleus pulposus and spinal nerve roots. Note there are eight cervical spinal nerves and only seven cervical vertebrae. In the lumbar region, for example, the emerging L4 nerve roots pass out laterally close to the pedicle of the 4th lumbar vertebra and are not related to the intervertebral disc between the 4th and 5th lumbar vertebrae. **C:** Posterolateral herniation of the nucleus pulposus of the intervertebral disc between the 5th lumbar vertebra and the 1st sacral vertebra showing pressure on the S1 nerve root. **D:** An intervertebral disc that has herniated its nucleus pulposus posteriorly. **E:** Pressure on the L5 motor nerve root produces weakness of dorsiflexion of the ankle; pressure on the S1 motor nerve root produces weakness of plantar flexion of the ankle joint.

may compress the C6 spinal nerve or its roots. Pain is felt near the lower part of the back of the neck and shoulder and along the area in the distribution of the spinal nerve involved. Central protrusions may press on the spinal cord and the anterior spinal artery and involve the various spinal tracts.

Lumbar disc herniations are more common than cervical disc herniations. The discs usually affected are those between the 4th and 5th lumbar vertebrae and between the 5th lumbar vertebra and the sacrum. In the lumbar region, the roots of the cauda equina run posteriorly over a number of intervertebral discs. A lateral herniation may press on one or two roots and commonly involves the nerve root going to the intervertebral foramen just below. The nucleus pulposus occasionally herniates directly backward, and if it is a large herniation, the whole cauda equina may be compressed, causing paraplegia.

In lumbar disc herniations, pain is referred down the leg and foot in the distribution of the affected nerve. Because the sensory posterior roots most commonly pressed on are the 5th lumbar and 1st sacral, pain is usually felt down the back and lateral side of the leg, radiating to the sole of the foot, a condition known as **sciatica**. In severe cases, paresthesia or actual sensory loss may occur.

Pressure on the anterior motor roots causes muscle weakness. Involvement of the 5th lumbar motor root weakens

dorsiflexion of the ankle, whereas pressure on the 1st sacral motor root causes plantar flexion weakness. The ankle jerk reflex may be diminished or absent (see Fig. 1-19E).

A large, centrally placed protrusion may give rise to bilateral pain and muscle weakness in both legs. Acute retention of urine may also occur.

Spinal Tap

Spinal tap (lumbar puncture) may be performed to withdraw a sample of CSF for microscopic or bacteriologic examination or to inject drugs to combat infection or induce anesthesia. Fortunately, the spinal cord terminates inferiorly at the level of the lower border of the 1st lumbar vertebra in adults (in infants, it may reach inferiorly to the 3rd lumbar vertebra). The subarachnoid space extends inferiorly as far as the lower border of the 2nd sacral vertebra. The lower lumbar part of the vertebral canal is thus occupied by the subarachnoid space, which contains the lumbar and sacral nerve roots and the filum terminale (the cauda equina). A needle inserted into the subarachnoid space in this region usually pushes the nerve roots to one side without causing damage.

With the patient lying on his or her side or in the upright sitting position, with the vertebral column well flexed, the space between adjoining laminae in the lumbar region is opened to a maximum (Fig. 1-20). An imaginary line joining the highest points on the iliac crests passes over the 4th lumbar spine. Using a careful aseptic technique and local anesthesia, the clinician passes the lumbar puncture needle fitted with a stylet into the vertebral canal above or below the 4th lumbar spine. The needle will pass through the following anatomical structures before it enters the subarachnoid space: (a) skin, (b) superficial fascia, (c) supraspinous ligament, (d) interspinous ligament, (e) ligamentum flavum, (f) areolar tissue containing the internal vertebral venous plexus, (g) dura mater, and (h) arachnoid mater. The depth to which the needle will have to pass will vary from 1 in (2.5 cm) or less in a child to as much as 4 in (10 cm) in an obese adult.

As the stylet is withdrawn, a few drops of blood may escape. This usually indicates that the point of the needle is in one of the veins of the internal vertebral plexus and has not yet reached the subarachnoid space. If the needle stimulates one of the nerve roots of the cauda equina, the patient will experience a fleeting discomfort in one of the dermatomes or a muscle will twitch, depending on whether a sensory or a motor root was affected.

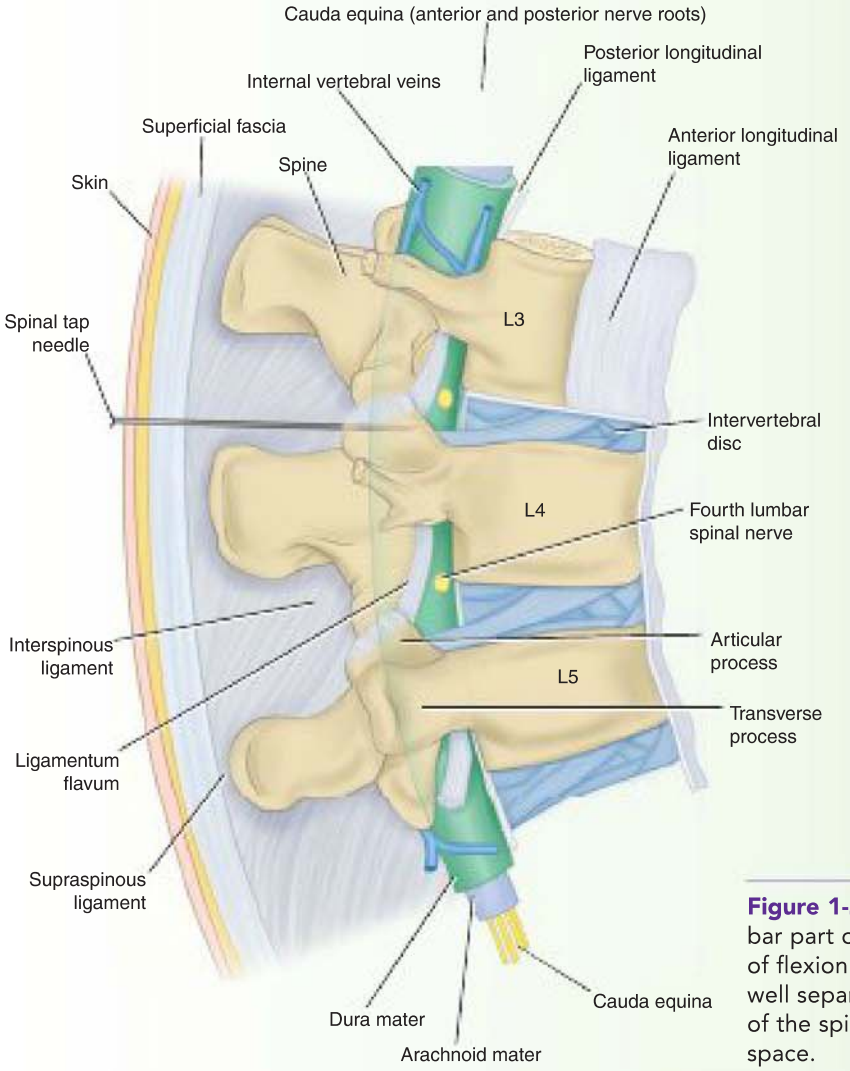

Figure 1-20 Sagittal section through the lumbar part of the vertebral column in a position of flexion. Note that the spines and laminae are well separated in this position allowing insertion of the spinal tap needle into the subarachnoid space.

CSF pressure can be measured by attaching a manometer to the needle. When the patient is in the recumbent position, the **normal pressure is about 60 to 150 mm** of water. The pressure shows oscillations corresponding to the movements of respiration and the arterial pulse.

A block of the subarachnoid space in the vertebral canal, which may be caused by a tumor of the spinal cord or the meninges, can be detected by compressing the internal jugular veins in the neck. This raises the cerebral venous pressure and inhibits the absorption of CSF in the arachnoid granulations, thereby increasing the manometer reading of the CSF pressure. If this rise does not occur, the subarachnoid space is blocked, and the patient exhibits a positive **Queckenstedt sign**.

Caudal Anesthesia

Anesthetic solutions may be injected into the sacral canal through the sacral hiatus. The solutions pass upward in the loose connective tissue and bathe the spinal nerves as they emerge from the dural sheath (Fig. 1-21). Obstetricians use this method of nerve block to relieve the pains of the first and second stages of labor because anesthetic administered by this method does not affect the infant. Caudal anesthesia can also be used in operations in the sacral region, including anorectal surgery.

Head Injuries

A blow to the head may merely bruise the scalp; severe blows may tear or split the scalp. Even if the head is protected by a helmet, the brain can be severely damaged without clinical evidence of scalp injury.

Skull Fractures

Severe blows to the head can change the shape of the skull at the point of impact. Small objects may penetrate the skull and lacerate the brain. Larger objects applied with great force may shatter the skull and drive fragments of bone into the brain at the site of impact.

In the adult, fractures of the skull are common, but they are less common in the young child. In the infant, the skull bones are more resilient, and they are separated by fibrous sutural ligaments. In the adult, the inner table of the skull is particularly brittle. Moreover, the sutural ligaments begin to ossify during middle age.

The type of fracture that occurs in the skull will depend on the age of the patient, the severity of the blow, and the area of the skull receiving the trauma. The **adult skull** resembles an eggshell, with limited resilience. A severe, localized blow will cause a local indentation, commonly with bone splintering. Blows to the vault can result in a series of linear fractures, which radiate out through the thin areas of the bone. The petrous parts of the temporal bones and the occipital crests (see Fig. 5-6) strongly reinforce the base of the skull and tend to deflect linear fractures.

The **young child's skull** resembles a ping-pong ball, because a localized blow produces a depression without splintering. This common type of circumscribed lesion is known as a "pond" fracture.

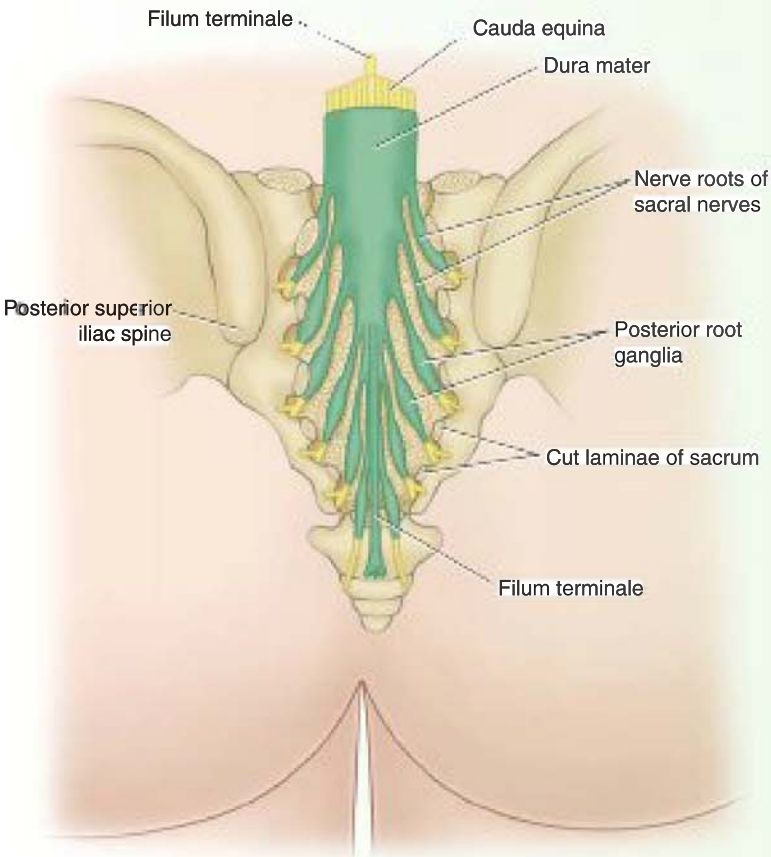

Figure 1-21 Posterior view of the sacrum. Laminae have been removed to show the sacral nerve roots lying within the sacral canal.

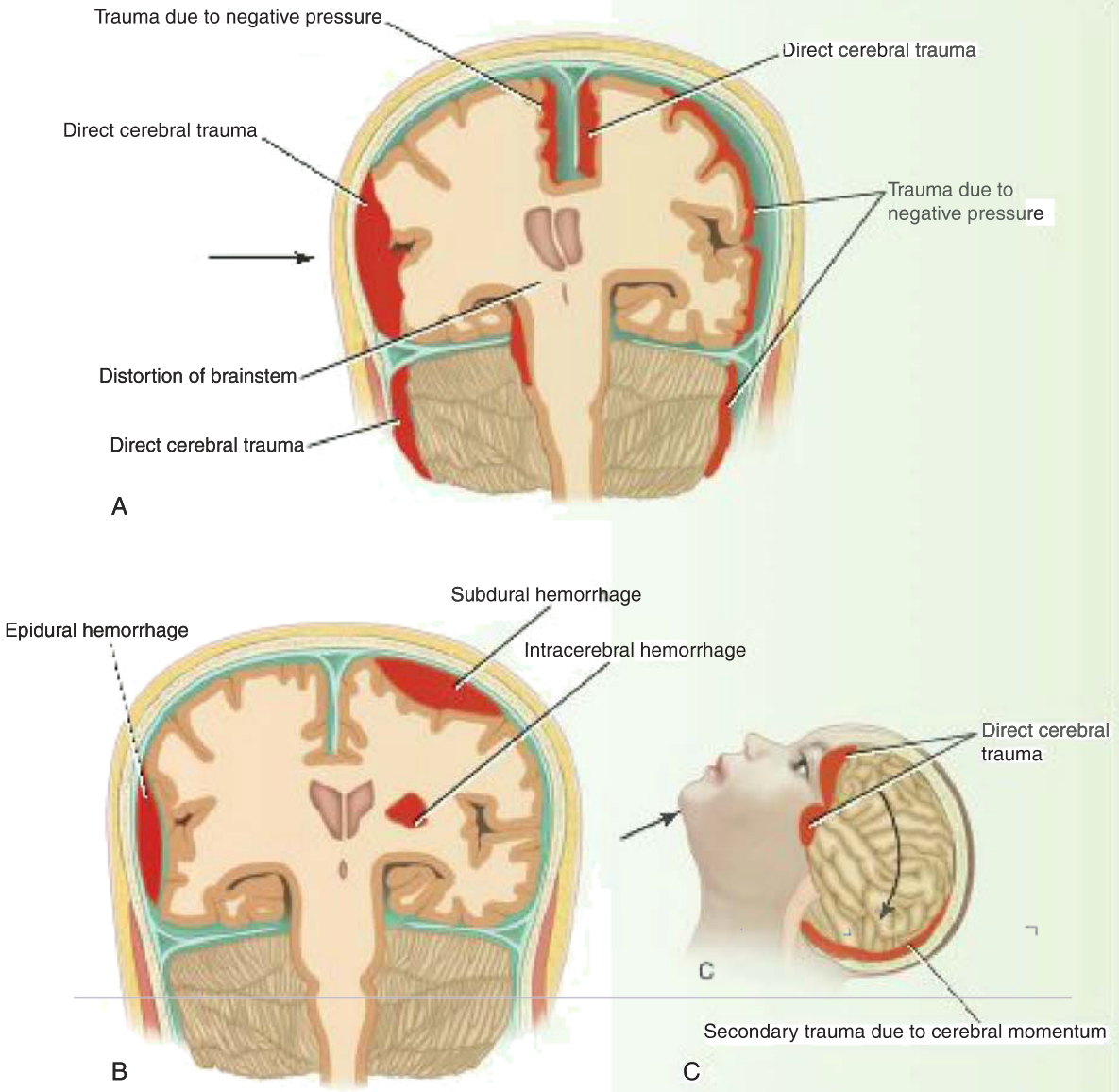

Figure 1-22 **A:** Mechanisms of acute cerebral injury when a blow is applied to the lateral side of the head. **B:** Varieties of intracranial hemorrhage. **C:** Mechanism of cerebral trauma following a blow on the chin. The movement of the brain within the skull can also tear the cerebral veins.

Brain Injuries

Brain injuries are caused by displacement and distortion of the neuronal tissues at the moment of impact (Fig. 1-22). The brain, which is incompressible, is like a water-soaked log suspended in water. The brain is floating in the CSF in the subarachnoid space and is capable of a certain amount of anteroposterior and lateral gliding movement. The anteroposterior movement is limited by the attachment of the superior cerebral veins to the superior sagittal sinus. Lateral displacement of the brain is limited by the falx cerebri. The tentorium cerebelli and the falx cerebelli also restrict displacement of the brain.

Thus, blows on the front or back of the head lead to displacement of the brain, which may cause severe cerebral damage, stretching and distortion of the brainstem, and stretching and even tearing of brain commissures. Blows to the side of the head cause less cerebral displacement, and the injuries to the brain consequently tend to be less severe. However, the falx cerebri is a tough structure and may cause considerable damage to the softer brain tissue in cases of a severe blow to the side of the head. Furthermore, remember that glancing blows to the head may cause considerable brain rotation, with shearing strains and brain distortion, particularly in areas where further rotation is prevented by bony prominences in the anterior and middle cranial fossae. Brain lacerations are very likely to occur when the brain is forcibly thrown against the sharp edges of bone within the skull (see pp. 191–192)—the lesser wings of the sphenoid, for example.

When the brain moves suddenly within the skull, the part of the brain that moves away from the skull wall is subjected to diminished pressure because the CSF has not had time to accommodate to the brain movement. This results in a suction effect on the brain surface, with rupture of surface blood vessels.

A sudden severe blow to the head, as in an automobile accident, may result in damage to the brain at two sites: at the point of impact and at the pole of the brain opposite the point of impact, where the brain is thrown against the skull wall. This is referred to as **contrecoup injury**.

The movement of the brain within the skull at the time of head injuries not only is likely to cause avulsion of cranial nerves but commonly leads to rupture of tethering blood vessels. Fortunately, the large arteries found at the base of the brain are tortuous, and this, coupled with their strength, explains why they are rarely torn. The thin-walled cortical veins, which drain into the large dural venous sinuses, are very vulnerable and can cause severe subdural or subarachnoid hemorrhage.

Traumatic Brain Injury Following an Explosion or Blast

Deployed soldiers are frequently exposed to explosive devices, which may result in extensive injuries to the limbs, eyes, and ears. Open injuries to the skull, where shrapnel has entered the brain, are clearly visible and are dealt with accordingly.

However, in closed injuries, in which the skull remains intact, the underlying brain may be damaged but left untreated. In these cases, the explosion produces a blast of air that strikes the skull and shakes up the brain, resulting in multiple injuries to the soft brain tissue as it is driven against the hard bony projections within the skull. The symptoms and signs will depend on the extent of the neurologic damage and will be mild, moderate, or severe. Although the moderate and severe cases are quickly recognized by medical personnel, the mild cases may be missed, and patients may later develop headaches, nausea, mood changes, and memory loss. Early diagnosis is imperative as studies of these patients have shown that mild neurologic damage can be successfully treated. Individuals who have been exposed to explosive devices should undergo computed tomography (CT) scan or magnetic resonance imaging (MRI) before returning to civilian life.

Intracranial Hemorrhage

Although the brain is cushioned by the surrounding CSF in the subarachnoid space, any severe hemorrhage within the relatively rigid skull will ultimately exert pressure on the brain.

Four types of intracranial hemorrhage may result from trauma or cerebral vascular lesions (see Fig. 1-22).

Epidural (extradural) **hemorrhage** results from injuries to the meningeal arteries (commonly the anterior division of the middle meningeal artery) or veins (see Fig. 15-6). A comparatively minor blow to the side of the head, resulting in fracture of the skull in the region of the anterior–inferior portion of the parietal bone, may sever the artery (see Fig. 1-22). Arterial or venous injury is especially likely to occur if the vessels enter a bony canal in this region. Bleeding occurs and strips the meningeal layer of dura from the internal surface of the skull. The intracranial pressure (ICP) rises, and the enlarging blood clot exerts local pressure on the underlying precentral gyrus (motor area). Blood may also pass laterally through the fracture line to form a soft swelling on the side of the head. To stop the hemorrhage, the torn artery must be ligated or plugged. The burr hole through the skull wall should be placed about 1.5 in (4 cm) above the midpoint of the zygomatic arch.

Subdural hemorrhage results from tearing of the superior cerebral veins where they enter the superior sagittal sinus (see Figs. 15-1 and 17-5). The cause is usually a blow to the front or back of the head resulting in excessive anteroposterior displacement of the brain within the skull. This condition, which is much more common than middle meningeal hemorrhage, can be caused by a sudden minor blow. Once the vein is torn, blood under low pressure begins to accumulate in the potential space between the dura and the arachnoid. The condition is rarely bilateral.

Acute and chronic forms occur depending on the speed of accumulation of fluid in the subdural space. For example, if the patient starts to vomit, the venous pressure will rise as the result of a rise in the intrathoracic pressure. Under these circumstances, the subdural blood clot will rapidly increase in size, causing acute symptoms. In the chronic form, over a course of several months, the small blood clot will attract fluid by osmosis, in which case a hemorrhagic cyst forms and gradually expands, causing pressure symptoms. In both forms, the blood clot must be removed through burr holes in the skull.

Subarachnoid hemorrhage results from nontraumatic leakage or rupture of a congenital aneurysm on the cerebral arterial circle (circle of Willis) or, less commonly, from an arteriovenous malformation. Sudden onset of severe headache, neck stiffness, and loss of consciousness occurs. The diagnosis is established by CT or MRI or by withdrawing heavily blood-stained CSF through a lumbar puncture.

With **cerebral hemorrhage**, **spontaneous intracerebral hemorrhage** (see Fig. 1-22) is most common in patients with hypertension. It is generally due to rupture of the thin-walled **lenticulostriate artery** (see Fig. 17-11), a branch of the middle cerebral artery (see Fig. 17-4). The hemorrhage involves important descending nerve fibers in the internal capsule and causes hemiplegia on the contralateral side. The patient immediately loses consciousness, and paralysis is evident when consciousness is regained. The diagnosis is established by brain CT or MRI.

Shaken Baby Syndrome

Inflicted head injury is the most common cause of traumatic death in infancy. Sudden deceleration, which occurs when an infant is held by the arms or trunk and shaken or the head is forcefully struck against a hard surface, is believed to be responsible for the brain injuries. Biomechanical studies have shown that the rotation of the floating brain around its center of gravity causes diffuse brain injuries, including diffuse axonal injury and subdural hematoma. In shaken baby syndrome, major rotational forces have to occur that clearly exceed those encountered in normal child play activities.

Most cases of shaken baby syndrome take place during the first year of life, and they are usually restricted to infants under 3 years of age. Common symptoms include lethargy, irritability, seizures, altered muscle tone, and symptoms indicating raised ICP, such as impaired consciousness, vomiting, breathing abnormalities, and apnea. In severe cases, the baby may be unresponsive, the fontanelles are bulging, and the child may have retinal hemorrhages. Spinal tap may reveal blood in the CSF. Subdural or subarachnoid hemorrhages can be readily detected on CT

or MRI scans. Autopsy findings commonly include localized subdural hemorrhage in the parietal–occipital region and subarachnoid blood, associated with massive cerebral swelling and widespread neuronal loss.

Space-Occupying Lesions Within the Skull

Space-occupying or expanding lesions within the skull include tumor, hematoma, and abscess. Because the skull is a rigid container of fixed volume, these lesions will add to the normal bulk of the intracranial contents.

An expanding lesion is first accommodated by the expulsion of CSF from the cranial cavity. Later, the veins become compressed, interference with the circulation of blood and CSF begins, and the ICP starts to rise. The venous congestion results in increased production and diminished absorption of CSF, the CSF volume begins to rise, and thus, a vicious circle is established.

The position of the tumor within the brain may have a dramatic effect on the signs and symptoms. For example, a tumor that obstructs the outflow of CSF or directly presses on the great veins will cause a rapid increase in ICP. The signs and symptoms that enable the clinician to localize the lesion will depend on the degree of interference with brain function and nervous tissue destruction. Severe headache, possibly due to the stretching of the dura mater, and vomiting, due to pressure on the brainstem, are common complaints.

A spinal tap should not be performed in patients with suspected intracranial tumor. The withdrawal of CSF may lead to a sudden displacement of the cerebral hemisphere through the notch in the tentorium cerebelli into the posterior cranial fossa (Fig. 1-23) or herniation of the medulla oblongata and cerebellum through the foramen magnum. CT scans or MRIs are used in diagnosis.

Computed Tomography

CT is used for the detection of intracranial lesions. The procedure is quick, safe, and accurate. The total dose of irradiation is no greater than for a conventional skull radiograph.

CT relies on the same physics as conventional radiographs, in that structures are distinguished from one another by their ability to absorb energy from x-rays. The x-ray tube emits a narrow beam of radiation as it passes in a series of scanning movements through an arc of 180 degrees around the patient's head. The x-rays having passed through the head are collected by a special x-ray detector. The information is fed to a computer that processes the information, which is then displayed as a reconstructed picture on a screen. Essentially, the observer sees an image of a thin slice through the head, which may then be photographed for later examination (Fig. 1-24).

The sensitivity is such that small differences in x-ray absorption can be easily displayed. The gray matter of the cerebral cortex, white matter, internal capsule, corpus callosum, ventricles, and subarachnoid spaces can all be recognized. An iodine-containing medium can be injected intravascularly, which enhances greatly the contrast between tissues having a different blood flow.

Because a CT scan can be performed in 5 to 10 minutes, it is the method of choice in an emergency situation with patients with head trauma or suspected intracranial hemorrhage.

Magnetic Resonance Imaging

MRI uses the magnetic properties of the hydrogen nucleus excited by radiofrequency radiation transmitted by a coil surrounding the head. The excited hydrogen nuclei emit a signal that is detected as induced electric currents in a receiver coil. MRI is absolutely safe to the patient, and

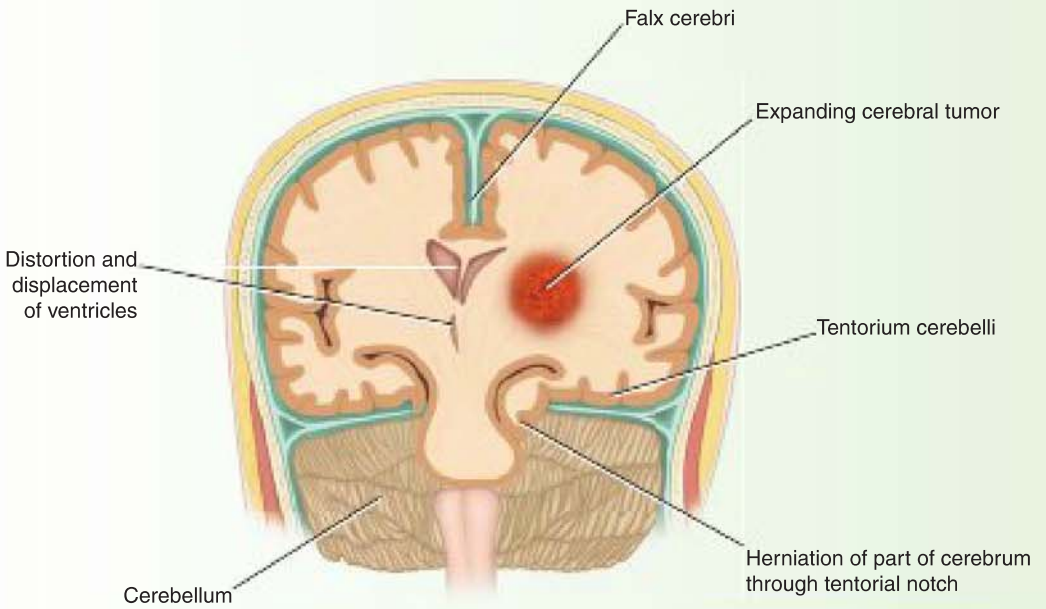

Figure 1-23 Sudden displacement of the cerebral hemispheres through the tentorial notch into the posterior cranial fossa following a lumbar puncture; the cerebral tumor is situated in the right cerebral hemisphere. CT or MRI should be used rather than lumbar puncture when investigating a cerebral tumor.

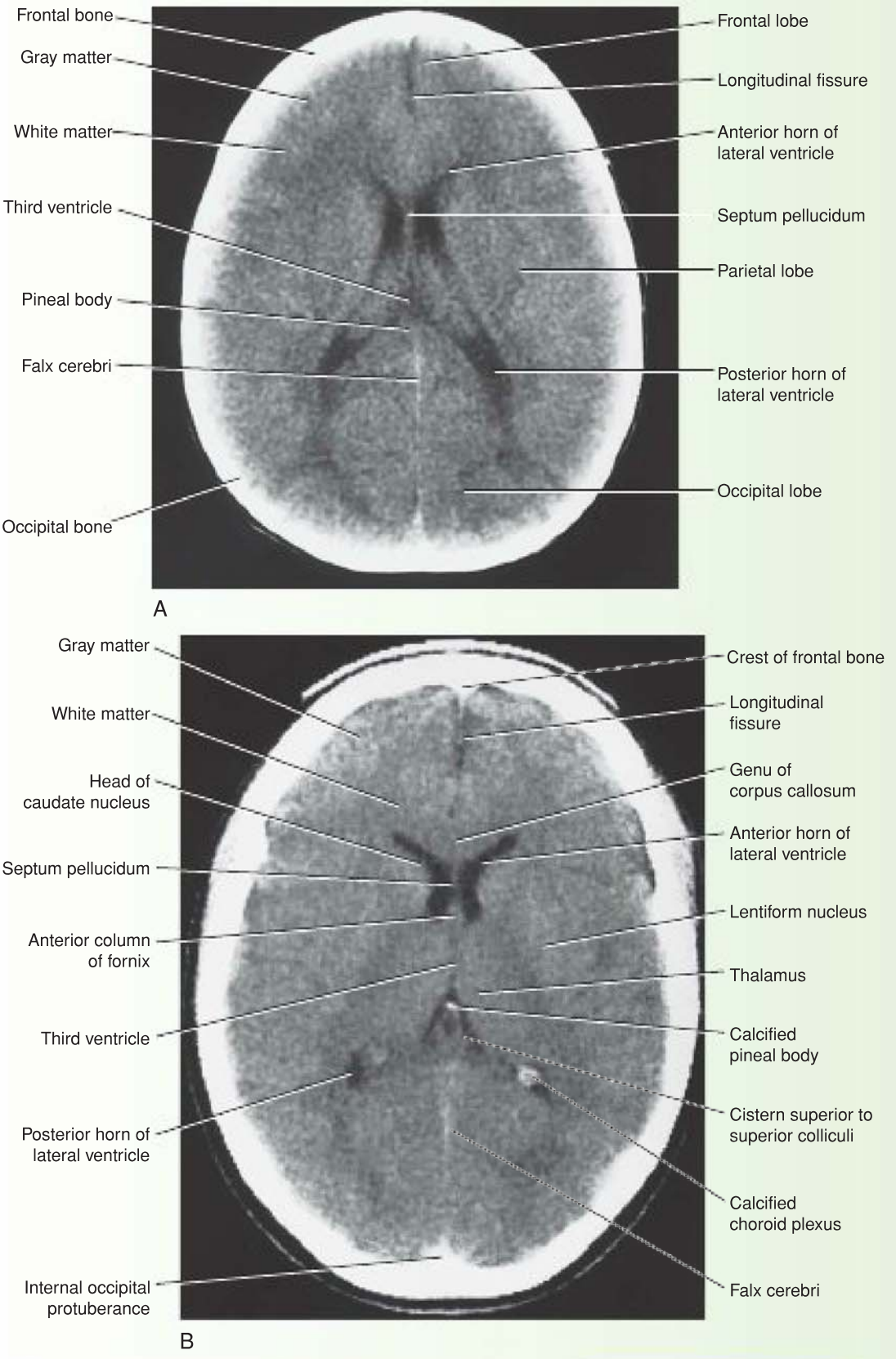

Figure 1-24 CT scan showing the structure of the brain. **A, B:** Horizontal cuts (axial sections).

because it provides better differentiation between gray and white matter, MRI can be more revealing than CT. The reason for this is that gray matter contains more hydrogen in the form of water than white matter, and the hydrogen atoms are less bound in fat (Fig. 1-25). MRI is the best imaging method for detecting low-contrast lesions such as brain tumors or small multiple sclerosis plaques. It is also capable of showing clear images of the brainstem, cerebellum, and the pituitary fossa, which, in the case of a CT scan, are overshadowed by the dense bones of the base of the skull.

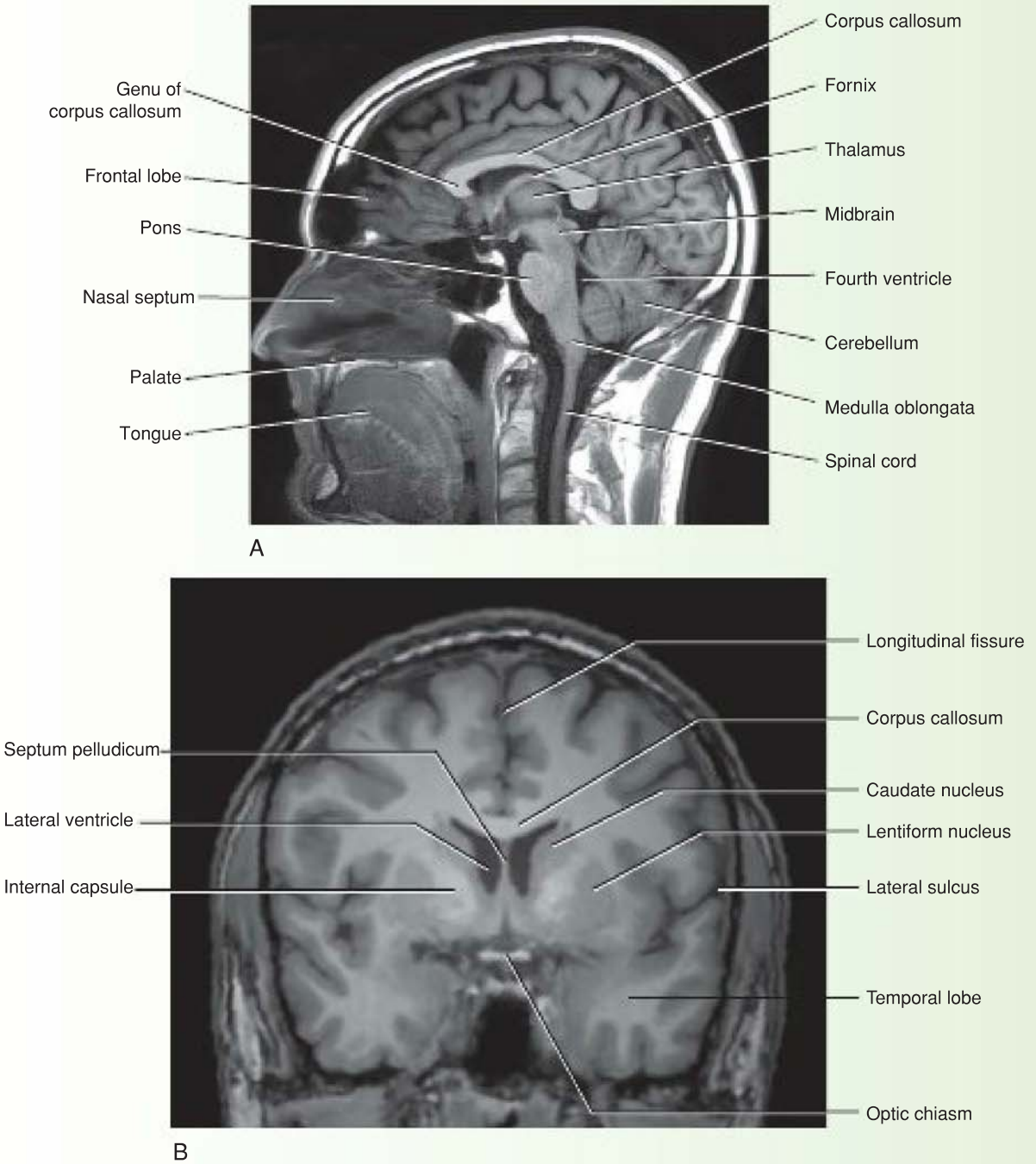

Figure 1-25 MRI showing the structure of the brain. **A:** Sagittal. **B:** Coronal. Compare with Figure 1-24. Note the better differentiation between gray and white matter.

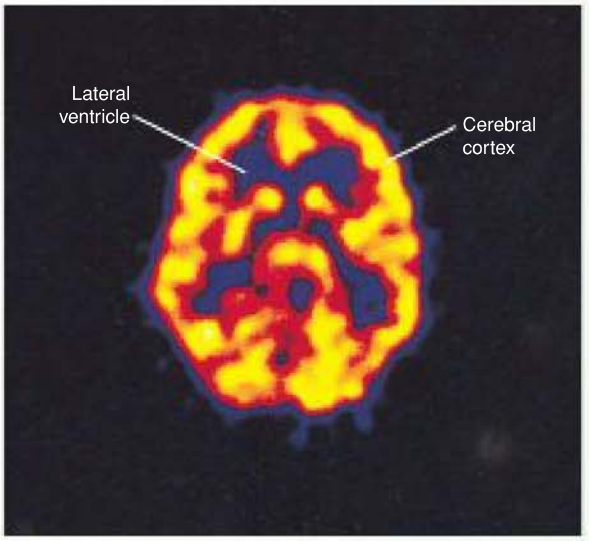

Figure 1-26 Axial (horizontal) PET scan of a normal brain following the injection of 18-fluorodeoxyglucose. Regions of active metabolism (*yellow areas*) are seen in the cerebral cortex. The lateral ventricles are also demonstrated. (Courtesy Dr. Holley Dey.)

The spinal cord structure is much more clearly visualized with MRI.

Unfortunately, an MRI takes longer and costs two-thirds more than a CT scan.

Positron Emission Tomography

Positron emission tomography (PET) uses radioactive isotopes that decay with the emission of positively charged electrons (positrons) to map the biochemical, physiologic, and pharmacologic processes taking place in the brain.

The appropriate isotope is incorporated into molecules of known biochemical behavior in the brain and then is injected into the patient. The metabolic activity of the compound can then be studied by making cross-sectional tomographic images of the brain using the same principles as in CT (Fig. 1-26). Making a series of time-lapse images at different anatomical sites allows variations in brain metabolism to be studied at these sites. This technique has been used to study the distribution and activity of neurotransmitters, variations in oxygen utilization, and cerebral blood flow.

PET has been successfully used in the evaluation of patients with brain tumors (Figs. 1-27 and 1-28), movement disorders, seizures, and schizophrenia.

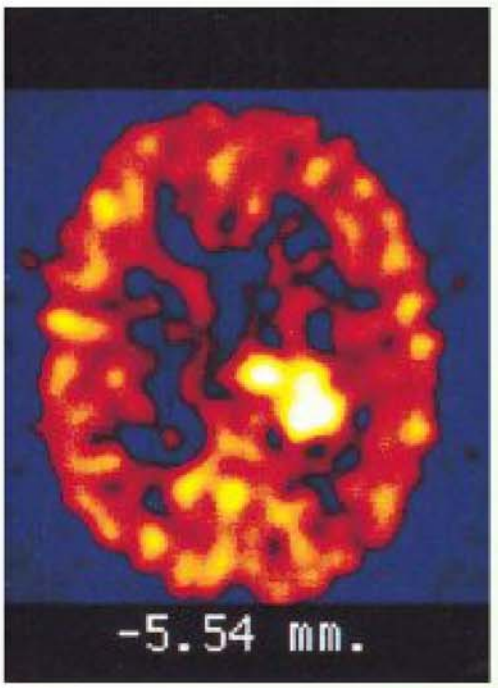

Figure 1-27 Axial (horizontal) PET scan of a 62-year-old male patient with a malignant glioma in the left parietal lobe following the injection of 18-fluorodeoxyglucose. A high concentration of the compound (*circular yellow area*) is seen in the region of the tumor. (Courtesy Dr. Holley Dey.)

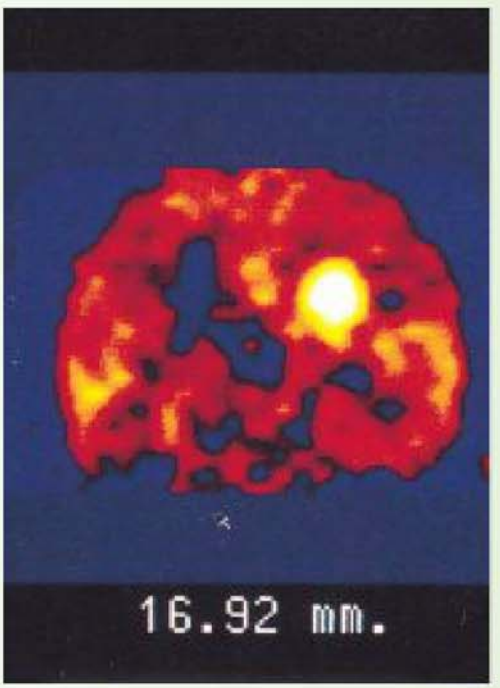

Figure 1-28 Coronal PET scan of a 62-year-old male patient with a malignant glioma in the left parietal lobe following the injection of 18-fluorodeoxyglucose (same patient as in Fig. 1-25). A high concentration of the compound (*circular yellow area*) is seen in the region of the tumor. (Courtesy Dr. Holley Dey.)

Key Concepts

Central and Peripheral Nervous Systems

- The nervous system comprises the central nervous system (CNS) and peripheral nervous system (PNS).
- The CNS consists of the brain and the spinal cord, both of which are surrounded by the meninges and the cerebrospinal fluid (CSF).
- The PNS consists of all other nerves in the body.
- The autonomic nervous system (ANS) is concerned with involuntary structures and distributed throughout both CNS and PNS.

Major Divisions of the Central Nervous System

- The brain has three major divisions: hindbrain, midbrain, and forebrain.
- The hindbrain can be subdivided into the medulla oblongata, the pons, and the cerebellum; the forebrain into the diencephalon and the cerebrum.
- The cerebrum is the largest component of the brain and consists of two hemispheres, covered by cerebral cortex, which is made up of a series of folds and fissures called gyri and sulci.
- The spinal cord is a cylindrical structure continuous with the medulla oblongata of the brainstem.
- Along the length of the spinal cord, 31 pairs of spinal nerves are attached.

Major Divisions of the Peripheral Nervous System

- Motor and sensory roots connect the spinal nerve to the spinal cord.
- The spinal nerves divide into anterior and posterior rami, both containing motor and sensory fibers.
- The posterior rami are distributed to the muscles and skin of the back.
- Anterior rami supply the muscles and skin of the limbs and the anterolateral body wall.
- Ganglia are collections of neuronal cell bodies that result in fusiform swellings within the dorsal roots, or as irregular swellings within the ANS.

Early Development of the Nervous System

- During development, the embryo differentiates into three layers, entoderm, mesoderm, and ectoderm.
- The ectoderm gives rise to the entire nervous system, initially forming the neural plate, then neural folds, and subsequently fusing into the neural tube.
- The leading edge of the neural folds contains neural crest cells which differentiate into ganglion cells, Schwann cells, melanocytes, and cells of the suprarenal medulla.

Clinical Problem Solving

1. A 45-year-old woman is examined by her physician and found to have carcinoma of the thyroid gland. Apart from swelling in the neck, the patient also complains of back pain in the lower thoracic region, with a burning soreness radiating around the right side of her thorax over the 10th intercostal space. Although the back pain can be relieved by changing posture, it is worsened by coughing and sneezing. A lateral radiograph of the thoracic part of the vertebral column reveals a secondary carcinomatous deposit in the 10th thoracic vertebral body. Further physical examination reveals muscular weakness of both legs. Using your knowledge of neuroanatomy, explain the following: (a) the pain in the back, (b) the soreness over the right 10th intercostal space, (c) the muscular weakness of both legs, and (d) which segments of the spinal cord lie at the level of the 10th thoracic vertebral body.
2. A 35-year-old coal miner is crouching down at the mine face to inspect a drilling machine. A large rock suddenly dislodges from the roof of the mine shaft and strikes the miner on the upper part of his back. Examination shows an obvious forward displacement of the 8th thoracic vertebra. What anatomical factors in the thoracic region determine the degree of injury that may occur to the spinal cord?
3. A 20-year-old man with a long history of tuberculosis of the lungs is examined by an orthopedic surgeon because of the sudden development of a humpback (kyphosis). He also has symptoms of a stabbing pain radiating around both sides of

his thorax intensified by coughing or sneezing. A diagnosis of tuberculous osteitis of the 5th thoracic vertebra is made, with the collapse of the vertebral body responsible for the kyphosis. Using your knowledge of neuroanatomy, explain why the collapse of the 5th thoracic vertebral body should cause pain in the distribution of the 5th thoracic segmental nerve on both sides.

4. A 50-year-old man wakes up one morning with a severe pain near the lower part of the back of his neck and left shoulder. The pain is also referred along the outer side of the left upper arm. Movement of the neck causes an increase in the intensity of the pain, which is also accentuated by coughing. A lateral radiograph of the neck shows a slight narrowing of the space between the 5th and 6th cervical vertebral bodies. A magnetic resonance imaging (MRI) shows disruption of the intervertebral disc between the 5th and 6th cervical vertebrae. Using your knowledge of anatomy, state which nerve root was involved. Also, state the nature of the disease.
5. A medical student offers to help a fellow student straighten out the bumper of a car. He has just finished his course in neuroanatomy and is in poor physical shape. Undaunted, he attempts to lift the end of the bumper while his friend stands on the other end. Suddenly, he feels an acute pain in the back that extends down the back and outer side of his right leg. Later, he is examined by an orthopedic surgeon, who finds that the pain is accentuated by coughing. A lateral radiograph of the lumbar vertebral column reveals nothing abnormal. A magnetic resonance imaging (MRI) taken in the sagittal plane shows a small posterior prolapse of the nucleus pulposus in the disc between the 5th lumbar and the 1st sacral vertebrae. A diagnosis of herniation of the intervertebral disc between the 5th lumbar and 1st sacral vertebrae is made. Using your knowledge of neuroanatomy, explain the symptoms of this disease. Which spinal nerve roots were pressed on?
6. A 5-year-old child is seen in the emergency department, and a diagnosis of acute meningitis is made. The resident decides to perform a lumbar puncture in order to confirm the diagnosis. Using your knowledge of neuroanatomy, where would you perform a lumbar puncture? Name, in order, the structures pierced when a lumbar puncture needle is inserted into the subarachnoid space.
7. A pregnant young woman tells her friends that she hates the idea of going through the pain of childbirth but that she equally detests the thought of having a general anesthetic. Is there a specialized local analgesic technique that will alleviate labor pains?
8. While crossing the road, a pedestrian is struck on the right side of his head by a passing car. He falls to the ground but does not lose consciousness. After resting for an hour and then getting up, he appears to be confused and irritable. Later, he staggers and falls to the floor. On questioning, he is seen to be drowsy, and twitching of the lower left half of his face and left arm is noted. A diagnosis of epidural hemorrhage is made. Which artery is likely to have been damaged? What is causing the drowsiness and muscle twitching?
9. A 45-year-old woman is examined by a neurologist and found to have an intracranial tumor. She complains of severe headaches, which occur during the night and early morning. She describes the pain as "bursting" in nature, and although at first, 6 months ago, the headaches were intermittent, they are now more or less continuous. Coughing, stooping, and straining during defecation make the pain worse. The pain is accompanied by vomiting on three recent occasions. What is the sequence of events that occurs within the skull as the intracranial pressure (ICP) rises? Would you perform a routine lumbar puncture on every patient you suspected of having an intracranial tumor?
10. While examining an unconscious 18-year-old man admitted to the emergency room following a motorcycle accident, the neurosurgeon asks the attending medical student what happens to the brain in an accident in which it is suddenly decelerated within the skull. How would you answer the inquiry? What is the value of wearing a helmet?

Answers and Explanations to Clinical Problem Solving

1. Carcinoma of the thyroid, breast, kidney, lung, and prostate commonly gives rise to metastases in bone. (a) The pain in the back was caused by the carcinoma invading and destroying the 10th thoracic vertebral body. (b) Compression of the posterior nerve root of the 10th thoracic spinal nerve by the carcinoma of the vertebral column caused the hyperesthesia and hyperalgesia over the right 10th intercostal space. (c) Muscular weakness of the legs was caused by pressure on the descending motor nerve fibers in the spinal cord by the carcinoma's invasion of the vertebral canal. (d) Although disproportionate growth in length of the vertebral column occurs during development compared with that of the spinal cord, the upper cervical segments of the spinal cord still lie posterior to the vertebral bodies of the same number. However, the spinal cord in the adult terminates inferiorly at the level of the lower border of the 1st lumbar vertebra, and therefore, the 1st and 2nd lumbar segments of the spinal cord lie at the level of the 10th thoracic vertebral body.
2. This patient had a severe fracture dislocation between the 7th and 8th thoracic vertebrae. The vertical arrangement of the articular processes and the low mobility of this region because of the thoracic cage mean that a dislocation can occur in this region only if the articular processes are fractured by a great force. The small circular vertebral canal

leaves little space around the spinal cord; thus, severe cord injuries are certain.

3. Each spinal nerve is formed by the union of a posterior sensory root and an anterior motor root and leaves the vertebral canal by traveling through an intervertebral foramen. Each foramen is bounded superiorly and inferiorly by the pedicles of adjacent vertebrae, anteriorly by the lower part of the vertebral body and by the intervertebral disc, and posteriorly by the articular processes and the joint between them. In this patient, the 5th thoracic vertebral body had collapsed and the intervertebral foramina on both sides had been considerably reduced in size, causing compression of the posterior sensory roots and the spinal nerves. The consequent irritation of the sensory fibers was responsible for the pain.
4. This patient had symptoms suggestive of irritation of the left 6th cervical posterior nerve root. The radiograph revealed narrowing of the space between the 5th and 6th cervical vertebral bodies, suggesting a herniation of the nucleus pulposus of the intervertebral disc at this level. MRI showed the nucleus pulposus extending posteriorly beyond the anulus fibrosus, thus confirming the diagnosis.
5. The herniation occurred on the right side and was relatively small. The pain occurred in the distribution of the 5th lumbar and 1st sacral segments of the spinal cord, and the posterior sensory roots of these segments of the cord were pressed on the right side.
6. In a 5-year-old child, the spinal cord terminates inferiorly at about the level of the 2nd lumbar vertebra (certainly no lower than the 3rd lumbar vertebra). With the child lying on his side and with the operator using an aseptic technique, the skin is anesthetized in the midline just below the 4th lumbar spine. The 4th lumbar spine lies on an imaginary line joining the highest points on the iliac crests. The lumbar puncture needle fitted with a stylet is then passed carefully into the vertebral canal. The needle will pass through the skin, superficial fascia, supraspinous and interspinous ligaments, ligamentum flavum, areolar tissue containing the internal vertebral venous plexus, and the dura and arachnoid mater before entering the subarachnoid space.
7. Caudal analgesia (anesthesia) is very effective in labor if it is performed skillfully. The anesthetic solutions are introduced into the sacral canal through the sacral hiatus. Sufficient solution is given so that the nerve roots up as far as T11–T12 and L1 are blocked. This will make the uterine contractions painless during the first stage of labor. If the nerve fibers of S2–S4 are also blocked, the perineum will be anesthetized.
8. A blow on the side of the head can fracture the thin anterior part of the parietal bone. The anterior branch of the middle meningeal artery commonly enters a bony canal in this region and is sectioned at the time of the fracture. The resulting hemorrhage causes gradual accumulation of blood under high pressure outside the meningeal layer of the dura mater. The pressure is exerted on the underlying brain as the blood clot enlarges, and the symptoms of confusion and irritability become apparent. This is followed later by drowsiness. Pressure on the lower end of the motor area of the cerebral cortex (the right precentral gyrus) causes facial muscle twitching and, later, left arm muscle twitching. As the blood clot progressively enlarges, the intracranial pressure (ICP) rises and the patient's condition deteriorates.
9. A detailed account of the various changes that occur in the skull in patients with an intracranial tumor is given on page 23. A patient suspected of having an intracranial tumor should *not* undergo a spinal tap. The withdrawal of cerebrospinal fluid (CSF) may lead to a sudden displacement of the cerebral hemisphere through the opening in the tentorium cerebelli into the posterior cranial fossa or herniation of the medulla oblongata and cerebellum through the foramen magnum. CT scans or MRIs are now used in making the diagnosis.
10. The brain is floating in the cerebrospinal fluid (CSF) within the skull, so a blow to the head or sudden deceleration leads to displacement of the brain. This may produce severe cerebral damage; stretching or distortion of the brainstem; avulsion of cranial nerves; and, commonly, rupture of tethering cerebral veins. A helmet helps to protect the brain by cushioning the blow and thus slowing the rate of brain deceleration.

Review Questions

Directions: Each of the incomplete statements in this section is followed by completions of the statement. Select the ONE lettered completion that is BEST in each case.

1. The spinal cord has
   (a) an outer covering of gray matter and an inner core of white matter.
   (b) an enlargement below that forms the conus medullaris.
   (c) anterior and posterior roots of a single spinal nerve attached to a single segment.
   (d) cells in the posterior gray horn that give rise to efferent fibers that supply skeletal muscles.
   (e) a central canal that is situated in the white commissure.

2. The medulla oblongata has
   (a) a tubular shape.
   (b) the fourth ventricle lying posterior to its lower part.
   (c) the midbrain directly continuous with its upper border.
   (d) no central canal in its lower part.
   (e) the spinal cord directly continuous with its lower end in the foramen magnum.
3. The midbrain has
   (a) a cavity called the cerebral aqueduct.
   (b) a large size.
   (c) no cerebrospinal fluid (CSF) around it.
   (d) a cavity that opens above into the lateral ventricle.
   (e) a location in the middle cranial fossa of the skull.

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

4. The following statements concern the cerebellum:
   (a) It lies within the middle cranial fossa.
   (b) The cerebellar cortex is composed of white matter.
   (c) The vermis is the name given to that part joining the cerebellar hemispheres together.
   (d) The cerebellum lies anterior to the fourth ventricle.
   (e) The dentate nucleus is a mass of white matter found in each cerebellar hemisphere.
5. The following statements concern the cerebrum:
   (a) The cerebral hemispheres are separated by a fibrous septum called the tentorium cerebelli.
   (b) The bones of the vault of the skull are named for the lobes of the cerebral hemisphere they lie over.
   (c) The corpus callosum is a mass of gray matter lying within each cerebral hemisphere.
   (d) The internal capsule is an important collection of nerve fibers, which has the caudate nucleus and the thalamus on its medial side and the lentiform nucleus on its lateral side.
   (e) The cavity present within each cerebral hemisphere is called the cerebral ventricle.
6. The following statements concern the peripheral nervous system:
   (a) There are 10 pairs of cranial nerves.
   (b) There are 8 pairs of cervical spinal nerves.
   (c) The posterior root of a spinal nerve contains many efferent motor nerve fibers.
   (d) A spinal nerve is formed by the union of an anterior and a posterior ramus in an intervertebral foramen.
   (e) A posterior root ganglion contains the cell bodies of autonomic nerve fibers leaving the spinal cord.
7. The following statements concern the central nervous system:
   (a) A computed tomography (CT) brain scan cannot distinguish between white matter and gray matter.
   (b) The lateral ventricles are in direct communication with the fourth ventricle.
   (c) A magnetic resonance imaging (MRI) of the brain uses the magnetic properties of the hydrogen nucleus excited by radiofrequency radiation transmitted by a coil surrounding the patient's head.
   (d) Following trauma and sudden movement of the brain within the skull, the large arteries at the base of the brain are commonly torn.
   (e) The movement of the brain at the time of head injuries is unlikely to damage the small 6th cranial nerve.
8. The following statements concern the cerebrospinal fluid (CSF):
   (a) The CSF in the central canal of the spinal cord is unable to enter the fourth ventricle.
   (b) With the patient in the recumbent position, the normal pressure is about 60 to 150 mm of water.
   (c) It plays only a minor role in the protection of the brain and spinal cord from traumatic injury.
   (d) Compression of the internal jugular veins in the neck lowers the CSF pressure.
   (e) The subdural space is filled with CSF.
9. The following statements concern the vertebral levels and the spinal cord segmental levels:
   (a) The 1st lumbar vertebra lies opposite the L3–L4 segments of the cord.
   (b) The 3rd thoracic vertebra lies opposite the 3rd thoracic spinal cord segment.
   (c) The 5th cervical vertebra lies opposite the 7th cervical spinal cord segment.
   (d) The 8th thoracic vertebra lies opposite the 9th thoracic spinal cord segment.
   (e) The 3rd cervical vertebra lies opposite the 4th cervical spinal cord segment.

Directions: Each case history is followed by questions. Select the ONE BEST lettered answer.

A 23-year-old woman was unconscious when admitted to the emergency department. While crossing the road, she had been hit on the side of the head by a bus. Within an hour, she was found to have a large, dough-like swelling over the right temporal region. She also had signs of muscular paralysis on the left side of the body. A lateral radiograph of the skull showed a fracture line running downward and forward across the anterior–inferior angle of the right parietal bone. Her coma deepened, and she died 5 hours after the accident.

10. Select the most likely cause of the swelling over the right temporal region in this patient.
    (a) Superficial bruising of the skin
    (b) Hemorrhage from a blood vessel in the temporalis muscle
    (c) Rupture of the right middle meningeal vessels
    (d) Edema of the skin
    (e) Hemorrhage from a blood vessel in the superficial fascia

11. Select the most likely cause of the muscular paralysis of the left side of the body in this patient.
    (a) Laceration of the right side of the cerebral hemisphere
    (b) Right-sided epidural hemorrhage
    (c) Left-sided epidural hemorrhage
    (d) Injury to the cerebral cortex on the left side of the brain
    (e) Injury to the right cerebellar hemisphere

A 69-year-old man was admitted to the neurology unit complaining of severe discomfort of the lower back. Radiologic examination of the lumbar region of the vertebral column revealed significant narrowing of the spinal canal caused by advanced osteoarthritis.

12. Explain the discomfort in the lower back experienced by this patient.
    (a) Muscle fatigue
    (b) Prolapsed intervertebral disc
    (c) Torn ligament in the joints of the lumbar region of the spine
    (d) Compression of the cauda equina
    (e) Bad posture

Later, in this same patient, the back pain became more severe and now radiated down the back of the left leg; the patient was also experiencing difficulty walking. Examination of the patient revealed weakness and some wasting of the muscles of the left leg. Radiologic examination showed that the osteoarthritic changes had spread to involve the boundaries of many of the lumbar intervertebral foramina.

13. Explain the change in the symptoms and signs found in this patient.
    (a) The sciatic nerve was compressed in the pelvis by a spreading rectal cancer.
    (b) The patient had developed advanced atherosclerosis of the arteries of the right lower limb.
    (c) The osteoarthritic process had produced osteophytes that encroached on the intervertebral foramina, compressing the segmental spinal nerve roots.
    (d) Neuritis had developed in the sciatic nerve trunk.
    (e) The patient was experiencing psychiatric problems.

Answers and Explanations to Review Questions

1. C is correct. Anterior and posterior roots of a single spinal nerve are attached to a single spinal cord segment. A. The spinal cord has an outer covering of white matter and an inner core of gray matter (see Fig. 1-5). B. The spinal cord tapers off below to form the conus medullaris. D. The cells in the posterior gray horn of the spinal cord are associated with sensory function (see p. 139). E. The central canal of the spinal cord is situated in the gray commissure (see Fig. 1-6).
2. E is correct. The lower end of the medulla oblongata is directly continuous with the spinal cord in the foramen magnum (see Fig. 1-4). A. The medulla oblongata is conical in shape (see Fig. 1-8). B. The medulla oblongata has the fourth ventricle lying posterior to its upper part. C. The medulla oblongata has the pons directly continuous with its upper border. D. The medulla oblongata has a central canal in its lower part that is continuous with that of the spinal cord.
3. A is correct. The midbrain has a cavity called the cerebral aqueduct. B. The midbrain is of small size (see Fig. 1-1). C. The midbrain is completely surrounded with CSF in the subarachnoid space (see Fig. 1-2A). D. The midbrain has a cavity called the cerebral aqueduct, which opens above into the third ventricle (see Fig. 1-10). E. The midbrain is located in the posterior cranial fossa.
4. C is correct. The vermis is the name given to that part of the cerebellum joining the cerebellar hemispheres together (see Fig. 6-2). A. The cerebellum lies in the posterior cranial fossa (see Fig. 1-7). B. The cerebellar cortex is composed of gray matter (see Fig. 1-10). D. The cerebellum lies posterior to the fourth ventricle (see Fig. 1-10). E. The dentate nucleus is a mass of gray matter found in each cerebellar hemisphere (see Fig. 6-7).
5. D is correct. The internal capsule is an important collection of ascending and descending nerve fibers, which has the caudate nucleus and the thalamus on its medial side and the lentiform nucleus on its lateral side (see Fig. 1-13). A. The cerebral hemispheres are separated by a vertical, sagittally placed fibrous septum called the falx cerebri. The tentorium cerebelli is horizontally placed and roofs over the posterior cranial fossa and separates the cerebellum from the occipital lobes of the cerebrum (see Fig. 15-1). B. The lobes of the cerebral hemisphere are named for the skull bones they lie under. C. The corpus callosum is a mass of white matter lying within each cerebral hemisphere (see Fig. 1-10). E. The cavity present within each cerebral hemisphere is called the lateral ventricle.
6. B is correct. There are 8 pairs of cervical spinal nerves (only 7 cervical vertebrae). A. There are 12 pairs of cranial nerves. C. The posterior root of a spinal nerve contains afferent nerve fibers. D. A spinal nerve is formed by the union of an anterior and a posterior root in an intervertebral foramen. E. A posterior root ganglion contains the cell bodies of sensory nerve fibers entering the spinal cord.
7. C is correct. An MRI of the brain uses the magnetic properties of the hydrogen nucleus excited by radiofrequency radiation transmitted by a coil surrounding the patient's head (see p. 23). A. A CT brain

scan can distinguish between white and gray matter (see Fig. 1-22). B. The lateral ventricles communicate indirectly with the fourth ventricle through the interventricular foramen, the third ventricle, and the cerebral aqueduct of the midbrain (see Fig. 1-10). D. Following trauma and sudden movement of the brain within the skull, the large arteries at the base of the brain are rarely torn. E. The movement of the brain at the time of head injuries may stretch and damage the small delicate 6th cranial nerve (the small 4th cranial nerve may also be injured).

8. B is correct. With the patient in the recumbent position, the normal pressure of CSF is 60 to 150 mm of water. A. The CSF in the central canal of the spinal cord is able to enter the fourth ventricle through the central canal of the lower part of the medulla oblongata (see Fig. 1-2A). C. The CSF is important in protecting the brain and spinal cord from traumatic injury by dissipating the force (compare with the role of the amniotic fluid in protecting the fetus in the pregnant uterus). D. Compression of the internal jugular vein in the neck raises the CSF pressure by inhibiting its absorption into the venous system. E. The subarachnoid space is filled with CSF; the potential subdural space contains only tissue fluid.
9. E is correct. The 3rd cervical vertebra lies opposite the 4th cervical spinal cord segment (see Table 1-3, p. 16). A. The 1st lumbar vertebra lies opposite the sacral and coccygeal spinal cord segments. B. The 3rd thoracic vertebra lies opposite the 5th thoracic spinal cord segment. C. The 5th cervical vertebra lies opposite the 6th cervical spinal cord segment. D. The 8th thoracic vertebra lies opposite the 11th thoracic spinal cord segment.
10. C is correct. The swelling over the right temporal region and the radiologic finding of a linear fracture over the anterior–inferior angle of the right parietal bone would strongly suggest that the right middle meningeal artery had been damaged and an epidural (extradural) hemorrhage had occurred. Blood had spread through the fracture line into the overlying temporalis muscle and soft tissue.
11. B is correct. The left-sided paralysis (left hemiplegia) was due to pressure exerted by the right-sided epidural hemorrhage on the precentral gyrus of the right cerebral hemisphere.
12. D is correct. In persons in whom the spinal canal was originally small, significant narrowing of the canal in the lumbar region can lead to neurologic compression of the cauda equina with pain radiating to the back, as in this patient.
13. C is correct. One of the complications of osteoarthritis of the vertebral column is the growth of osteophytes, which commonly encroach on the intervertebral foramina, causing pain along the distribution of the segmental nerve. In this patient, the segmental nerves L4–L5 and S1–S3, which form the important sciatic nerve, were involved. This would explain the pain radiating down the left leg and the atrophy of the leg muscles.

2 Neurons and Neuroglia

CHAPTER OBJECTIVES

- To define the neuron and name its processes
- To learn the varieties of neurons and identify them in different parts of the nervous system
- To review the cell biology of a neuron and understand the function of a nerve cell and its processes
- To review the structure of the plasma membrane as it is related to its physiology
- To learn the transport of materials from the cell body to the axon terminals
- To understand the structure and function of synapses and neurotransmitters
- To review the supporting function of the neuroglial cells for nerve cells and the possible role that they play in neuronal metabolism, function, and neuronal death

A 38-year-old man with a history of involuntary movements, personality changes, and mental deterioration is referred to a neurologist. The symptoms started insidiously 8 years ago and are getting progressively worse. The first symptoms are involuntary, abrupt, and purposeless movements of the upper limbs associated with clumsiness and dropping things. At presentation, the patient has difficulty walking, speaking, and swallowing. Associated with these movement defects are memory impairment and loss of intellectual capacity. Impulsive behavior and bouts of depression also occur. Close questioning of the patient and his wife reveals that the patient's father and his older brother had similar symptoms before they died. A diagnosis of Huntington disease is made.

Huntington disease is an autosomal-dominant disorder with the defect localized to the short arm of chromosome 4. Histologically, the caudate nucleus and the putamen show extensive degeneration, mainly involving the acetylcholine and γ-aminobutyric acid (GABA)-producing neurons; the dopamine neurons are unaffected. Secondary degeneration of the cerebral cortex also occurs. This case is an example of a hereditary disorder that mainly involves a particular group of neurons.

The purpose of this chapter is to help students understand how the basic excitable cell—the neuron—communicates with other neurons. It also considers certain injuries to the neuron and the effects of drugs on the mechanism by which neurons communicate with one another.

NEURONS

Neuron is the name given to the nerve cell and all its processes (Fig. 2-1). Neurons are excitable cells that are specialized for the reception of stimuli and the conduction of the nerve impulse. They vary considerably in size and shape, but each possesses a **cell body** from which one or more processes called **neurites** project (Fig. 2-2). Neurites responsible for receiving information and conducting it toward the cell body are **dendrites**. The single long tubular neurite that conducts impulses away from the cell body is the **axon**. Dendrites and axons are commonly referred to as **nerve fibers**.

Neurons are found in the brain and spinal cord and in ganglia. Unlike most other cells in the body, normal neurons in the mature individual do not undergo division and replication.

Neuron Types

Although the cell body of a neuron may be as small as 5 μm or as large as 135 μm in diameter, the processes or neurites may extend over a distance of more than 1 m. Neurons can be classified morphologically based on the number, length, and mode of branching of their neurites (Fig. 2-3).

Unipolar neurons have a single neurite that divides a short distance from the cell body into two branches, one proceeding to some peripheral structure and the other entering the central nervous system (CNS). The

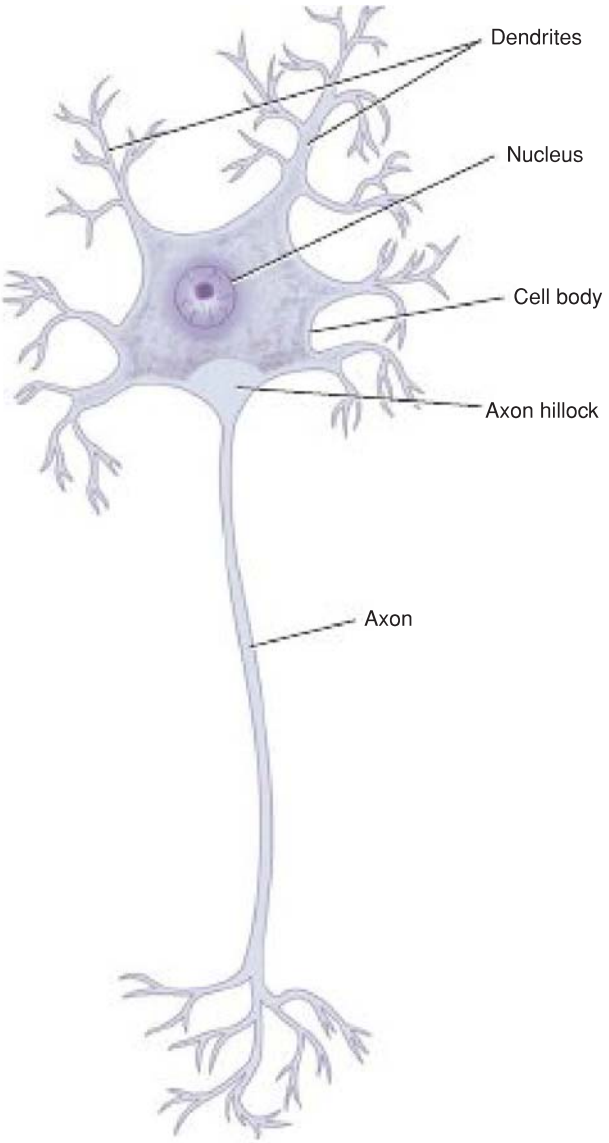

Figure 2-1 A neuron.

branches of this single neurite have the structural and functional characteristics of an axon. In this type of neuron, the fine terminal branches found at the peripheral end of the axon at the receptor site are often referred to as the dendrites. Examples of this form of neuron are found in the posterior root ganglion.

Bipolar neurons have an elongated cell body, with a single neurite emerging from each end. Examples of this type of neuron are found in the retinal bipolar cells and the cells of the sensory cochlear and vestibular ganglia.

Multipolar neurons have a number of neurites arising from the cell body. With the exception of the long process, the axon, the remainder of the neurites are dendrites. Most neurons of the brain and spinal cord are of this type.

Neurons may also be classified according to size. **Golgi type I neurons** have a long axon that can stretch

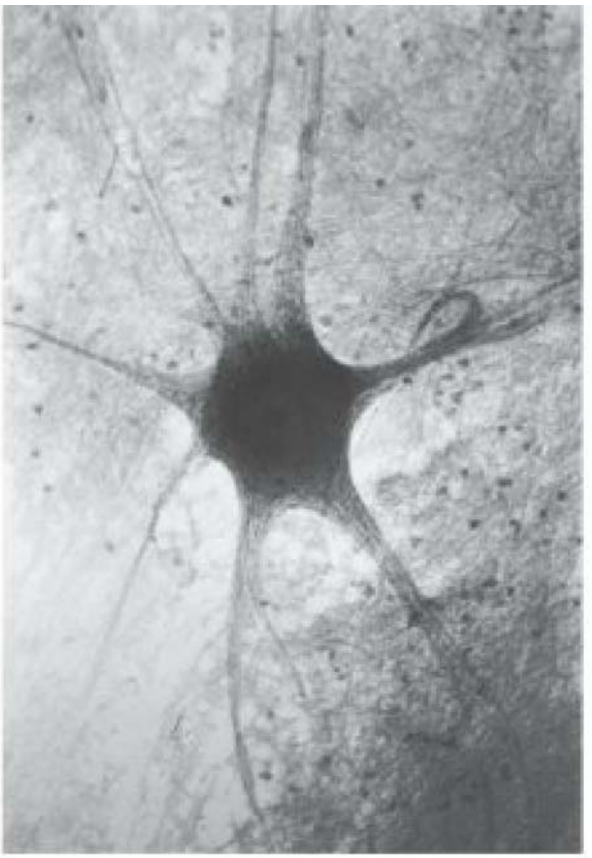

Figure 2-2 Photomicrograph of a smear preparation of the spinal cord showing a neuron with its cell body and its processes or neurites.

1 m or more in length in extreme cases (Figs. 2-4 to 2-6). The axons of these neurons form the long fiber tracts of the brain and spinal cord and the nerve fibers of peripheral nerves. The pyramidal cells of the cerebral cortex, the Purkinje cells of the cerebellar cortex, and the motor cells of the spinal cord are good examples.

Golgi type II neurons have a short axon that terminates in the neighborhood of the cell body or is entirely absent (Figs. 2-5 and 2-6). They greatly outnumber the Golgi type I neurons. The short dendrites that arise from these neurons give them a star-shaped appearance. These neurons are numerous in the cerebral and cerebellar cortex and are often inhibitory in function. Table 2-1 summarizes neuronal classification.

Neuronal Structure

A neuron's cell body, like that of other cells, consists essentially of a mass of cytoplasm in which a nucleus is embedded (Figs. 2-7 and 2-8), bounded externally by a plasma membrane.

Nerve Cell Body

Interestingly, the volume of cytoplasm within the nerve cell body is often far less than the total volume of cytoplasm in the neurites. The cell bodies of the small

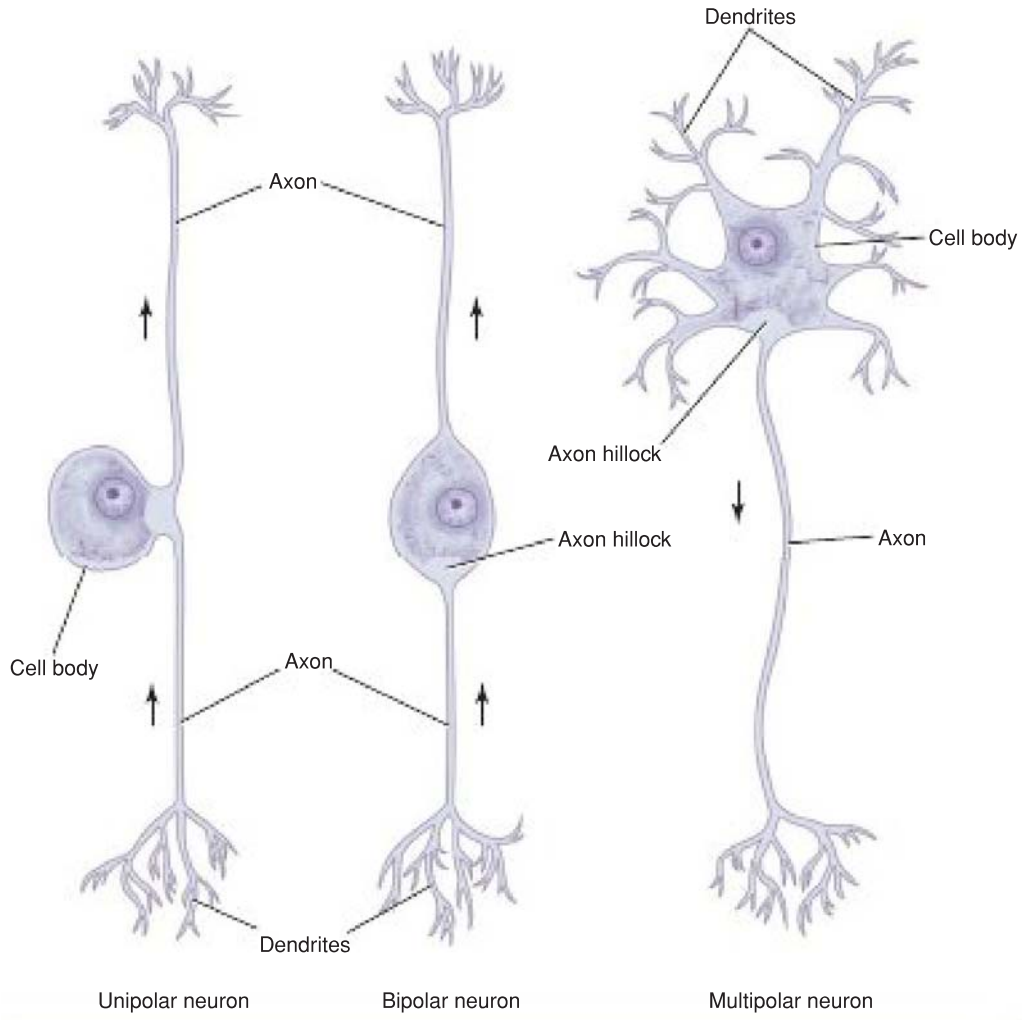

Figure 2-3 The classification of neurons according to the number, length, and mode of branching of the neurites.

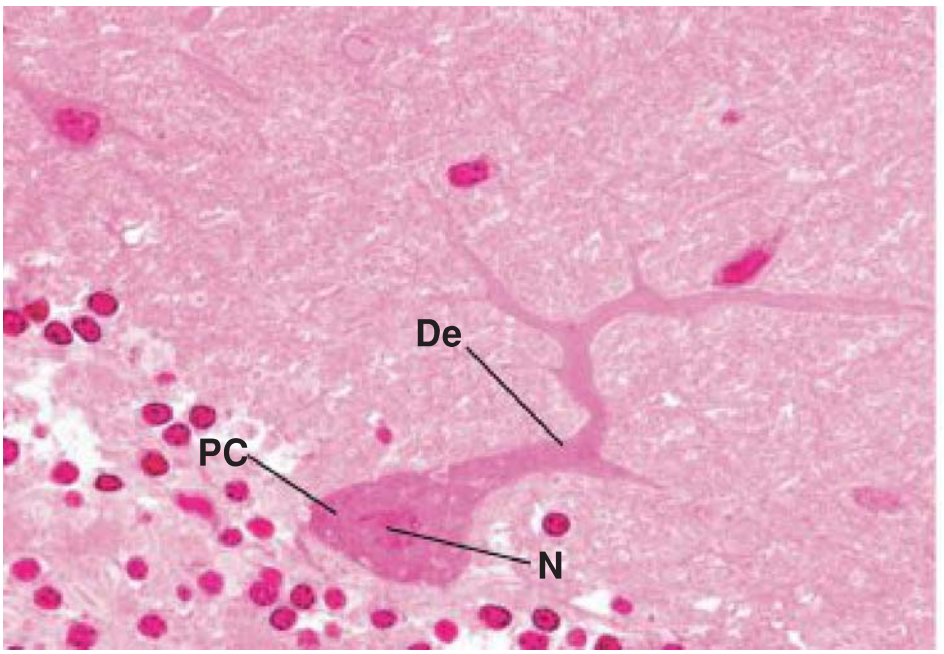

Figure 2-4 Photomicrograph of a silver-stained section of the cerebellar cortex showing two Purkinje cells. These are examples of Golgi type I neurons. De, dendrite; PC, Purkinje cell; N, Nucleus. (From Gartner, L. P. (2018). *Color atlas and text of histology* (7th ed). Baltimore, MD: Wolters Kluwer.)

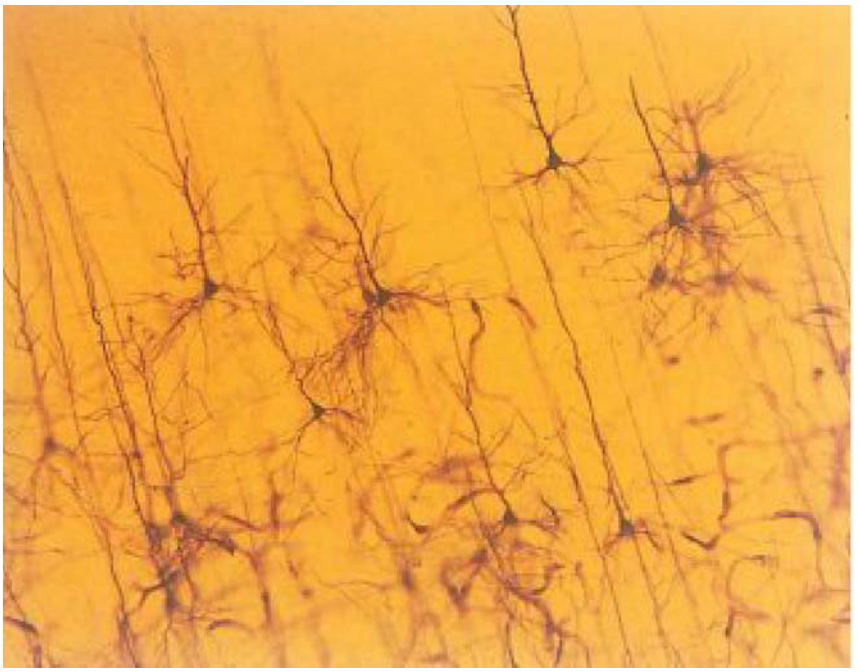

Figure 2-5 Photomicrograph of a silver-stained section of the cerebral cortex. Note the presence of large pyramidal cells, which are examples of Golgi type I neurons, and numerous Golgi type II neurons. (From Bear, M. F., Connors, B. W., & Paradiso, M. A. (2016). *Neuroscience: Exploring the brain* (4th ed). Baltimore, MD: Wolters Kluwer.)

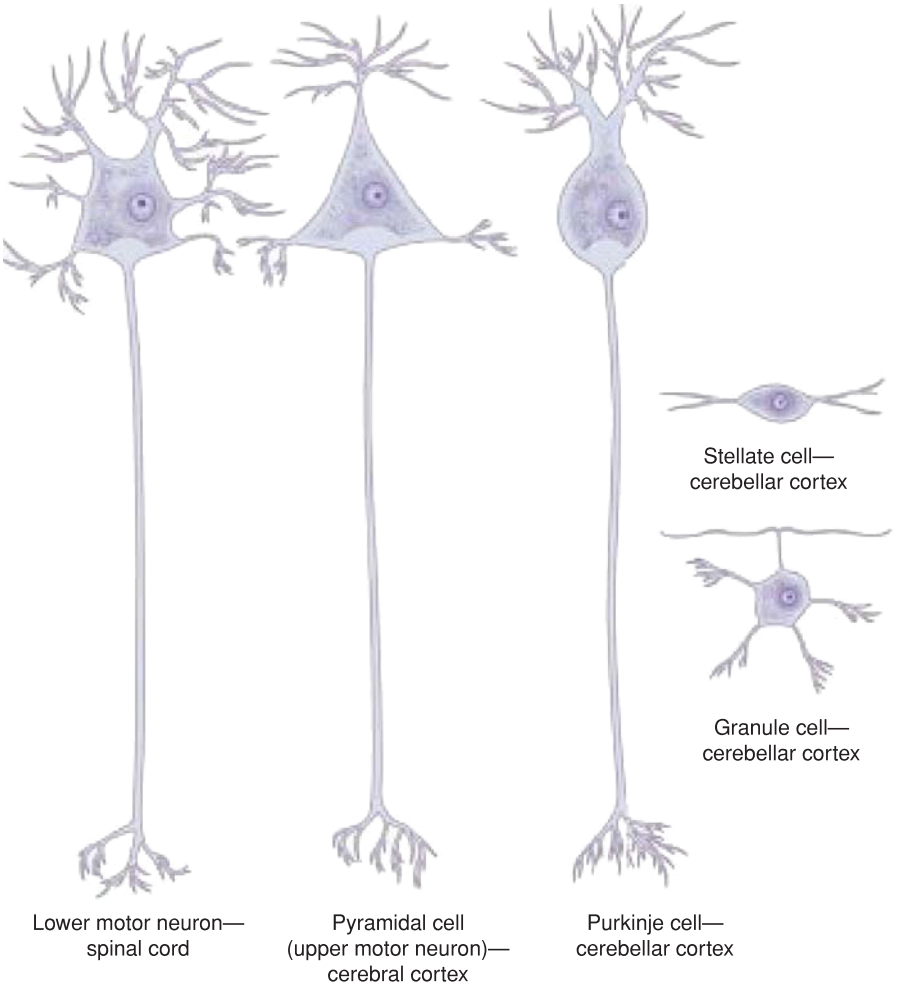

Figure 2-6 Different types of neurons.

Table 2-1 Neuron Classification

Morphologic Classification	Arrangement of Neurites	Location
Number, Length, and Mode of Branching of Neurites		
Unipolar	Single neurite divides a short distance from cell body	Posterior root ganglion
Bipolar	Single neurite emerges from either end of cell body	Retina, sensory cochlea, and vestibular ganglia
Multipolar	Many dendrites and one long axon	Fiber tracts of brain and spinal cord, peripheral nerves, and motor cells of spinal cord
Size of Neuron		
Golgi type I	Single long axon	Fiber tracts of brain and spinal cord, peripheral nerves, and motor cells of spinal cord
Golgi type II	Short axon that with dendrites resembles a star	Cerebral and cerebellar cortex

granular cells of the cerebellar cortex measure about 5 µm in diameter, whereas those of the large anterior horn cells may measure as much as 135 µm in diameter. The main structures of a nerve cell body are summarized in Table 2-2.

Nucleus

The nucleus, which stores the genes, is commonly centrally located within the cell body and is typically large and rounded. Do not confuse the term *nucleus* in cytology with the term *nucleus* in neuroanatomy, which refers to a discrete group of nerve cell bodies in the CNS. In mature neurons, the chromosomes no longer duplicate themselves and function only in gene expression. Therefore, the chromosomes are not arranged as compact structures but exist in an uncoiled state. Thus, the nucleus is pale, and the fine chromatin granules are widely dispersed (Figs. 2-6 and 2-7).

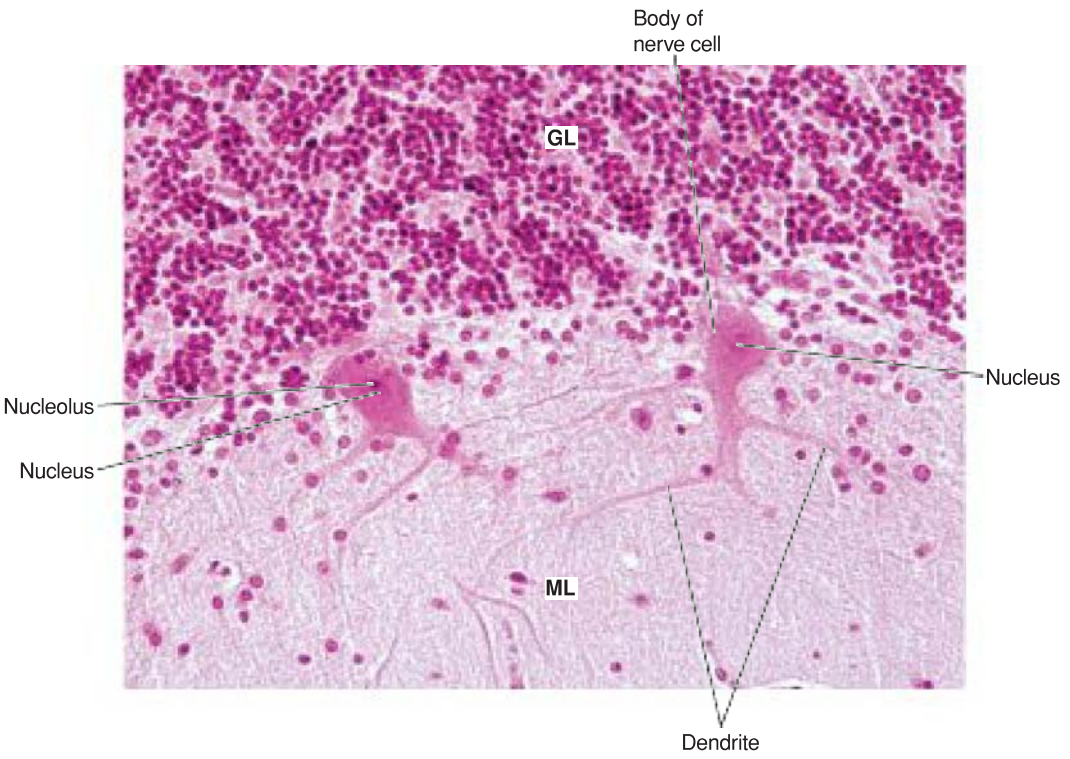

Figure 2-7 Photomicrograph of a section of the anterior gray column of the spinal cord showing two large motor nerve cells with nuclei. Note the prominent nucleolus in one of the nuclei. GL, granular layer; ML, molecular layer.

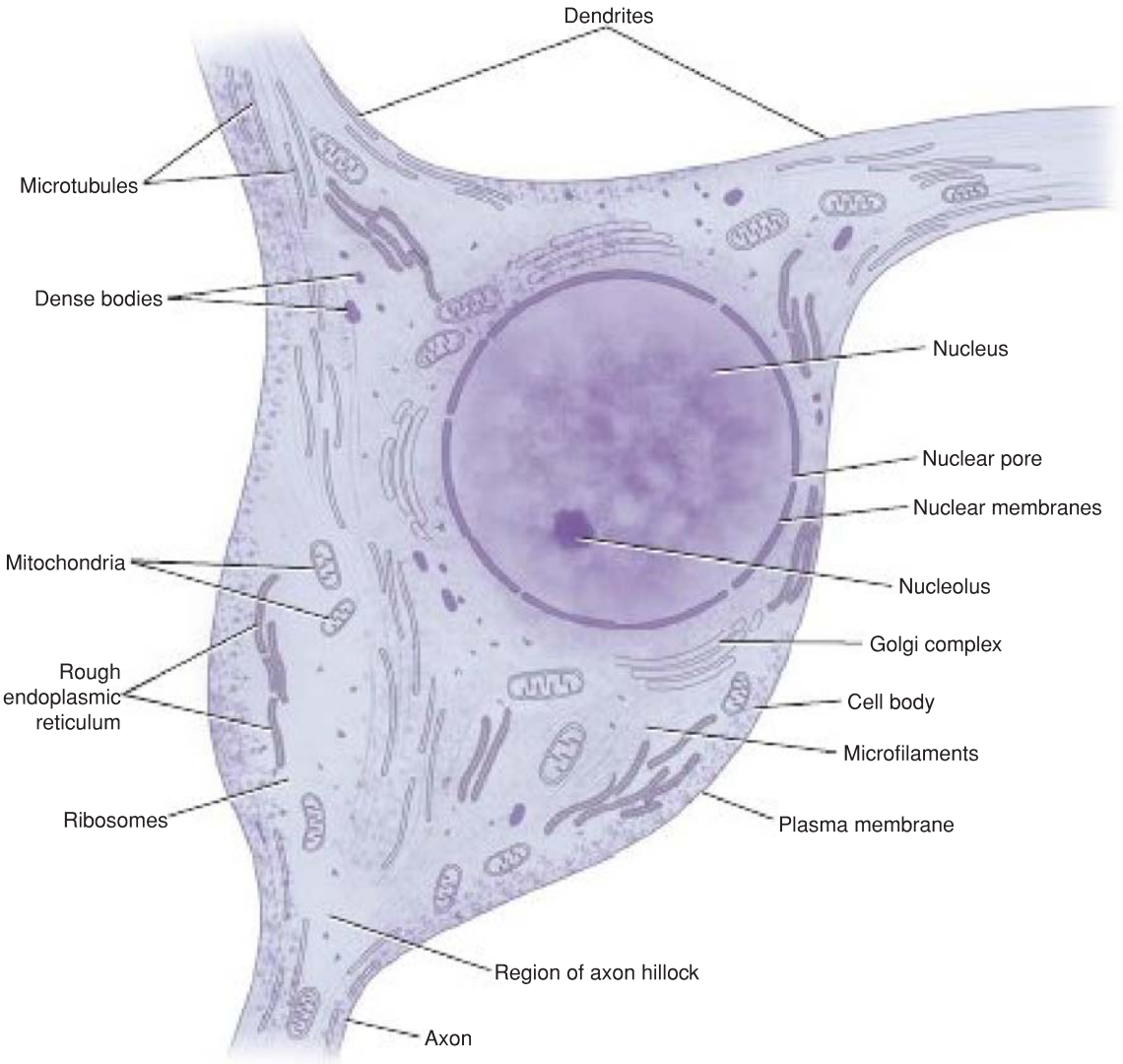

Figure 2-8 Diagrammatic representation of the fine structure of a neuron.

A single prominent nucleolus synthesizes ribosomal ribonucleic acid (rRNA) and assists with ribosome subunit assembly. The large size of the nucleolus probably is due to the high rate of protein synthesis, which is necessary to maintain the protein level in the large cytoplasmic volume that is present in the long neurites as well as in the cell body.

In the female, one of the two X chromosomes is compact and is known as the **Barr body**. It is composed of sex chromatin and sits at the inner surface of the nuclear envelope.

The **nuclear envelope** (Fig. 2-9; also see Fig. 2-8) is continuous with the cytoplasmic rough, or granular, endoplasmic reticulum (RER). The envelope is double layered and possesses fine **nuclear pores**, through which materials can diffuse into and out of the nucleus. Therefore, the substance in the nucleus and the cytoplasm can be considered as functionally continuous. Newly formed ribosomal subunits can be passed into the cytoplasm through the nuclear pores.

Cytoplasm

The cytoplasm is rich in rough (granular) and smooth (agranular) endoplasmic reticulum (Fig. 2-10; also see Fig. 2-9) and contains the following organelles and inclusions: (a) Nissl substance; (b) the Golgi complex; (c) mitochondria; (d) microfilaments; (e) microtubules; (f) lysosomes; (g) centrioles; and (h) lipofuscin, melanin, glycogen, and lipid.

Nissl substance consists of granules that are distributed throughout the cytoplasm of the cell body, except for the region close to the axon, called the **axon hillock** (Fig. 2-11). The granular material also extends into the proximal parts of the dendrites but is not present in the axon.

Electron micrographs show that the Nissl substance is composed of RER (Fig. 2-12) arranged in the form of broad cisternae stacked one on top of the other. Although many of the ribosomes are attached to the surface of the endoplasmic reticulum, many more lie free in the intervals between the cisternae. Because the ribosomes

Table 2-2 Main Structures in a Nerve Cell Body

Structure	Shape	Appearance	Location	Function
Nucleus	Large, rounded	Pale, chromatin widely scattered; single prominent nucleolus; Barr body present in female	Centrally placed, displaced to periphery in cell injury	Controls cell activity
Cytoplasmic organelles Nissl substance	Granules of rough endoplasmic reticulum	Broad cisternae; ribosomes are basophilic	Throughout cytoplasm and proximal part of dendrites, absent from axon hillock and axon, fatigue and injury result in concentration at periphery	Synthesizes protein
Golgi complex	Wavy threads; clusters of flattened cisternae and small vesicles	Smooth endoplasmic reticulum	Close to the nucleus	Adds carbohydrate to protein molecule; packages products for transport to nerve terminals; forms cell membranes
Mitochondria	Spherical, rod shaped	Double membrane with cristae	Scattered	Form chemical energy
Neurofibrils	Linear fibrils	Run parallel to each other; composed bundles of microfilaments, each 10 nm in diameter	Run from dendrites through cell body to axon	Determines the shape of the neuron
Microfilaments	Linear fibrils	Filaments 3–5 nm in diameter	Form a dense network beneath the plasma membrane	Role in formation and retraction of cell processes and in cell transport
Microtubules	Linear tubes	Run between neurofibrils, 25 nm in diameter	Run from dendrites through cell body to axon	Cell transport
Lysosomes	Vesicles	Diameter = 8 nm; three forms: primary, secondary, and residual bodies	Throughout cell	Cell scavengers
Centrioles	Paired hollow cylinders	Wall made up of bundles of microtubules	Confined to cytoplasm of cell body	Take part in cell division; maintain microtubules
Lipofuscin	Granules	Yellowish brown	Scattered through cytoplasm	Metabolic by product
Melanin	Granules	Yellowish brown	Substantia nigra of midbrain	Related to formation of dopamine

contain RNA, the Nissl substance is basophilic and can be well demonstrated by staining with toluidine blue or other basic aniline dyes (Fig. 2-11) and using the light microscope.

The Nissl substance is responsible for synthesizing protein, which flows along the dendrites and the axon and replaces the proteins that are broken down during cellular activity. Fatigue or neuronal damage causes the Nissl substance to move and become concentrated at the periphery of the cytoplasm. This phenomenon, which gives the impression that the Nissl substance has disappeared, is known as **chromatolysis**.

The **Golgi complex**, when seen with the light microscope after staining with a silver-osmium method, appears as a network of irregular wavy threads around the nucleus. In electron micrographs, it appears as clusters of flattened cisternae and small vesicles made up of smooth endoplasmic reticulum (SER) (Figs. 2-8 and 2-9).

The protein produced by the Nissl substance is transferred to the inside of the Golgi complex in transport

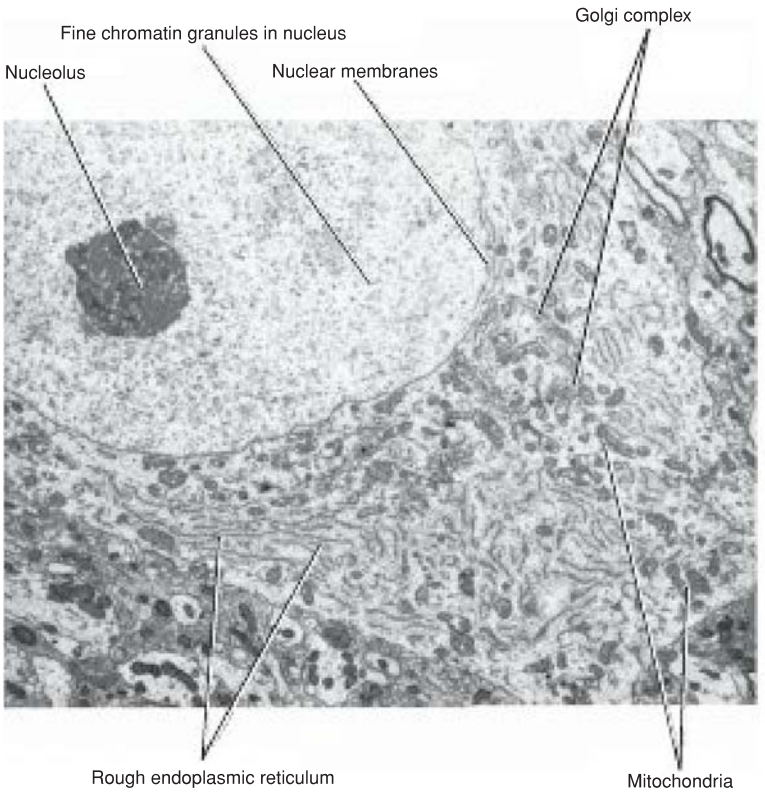

Figure 2-9 Electron micrograph of a neuron showing the structure of the nucleus and a number of cytoplasmic organelles. (Courtesy Dr. J. M. Kerns.)

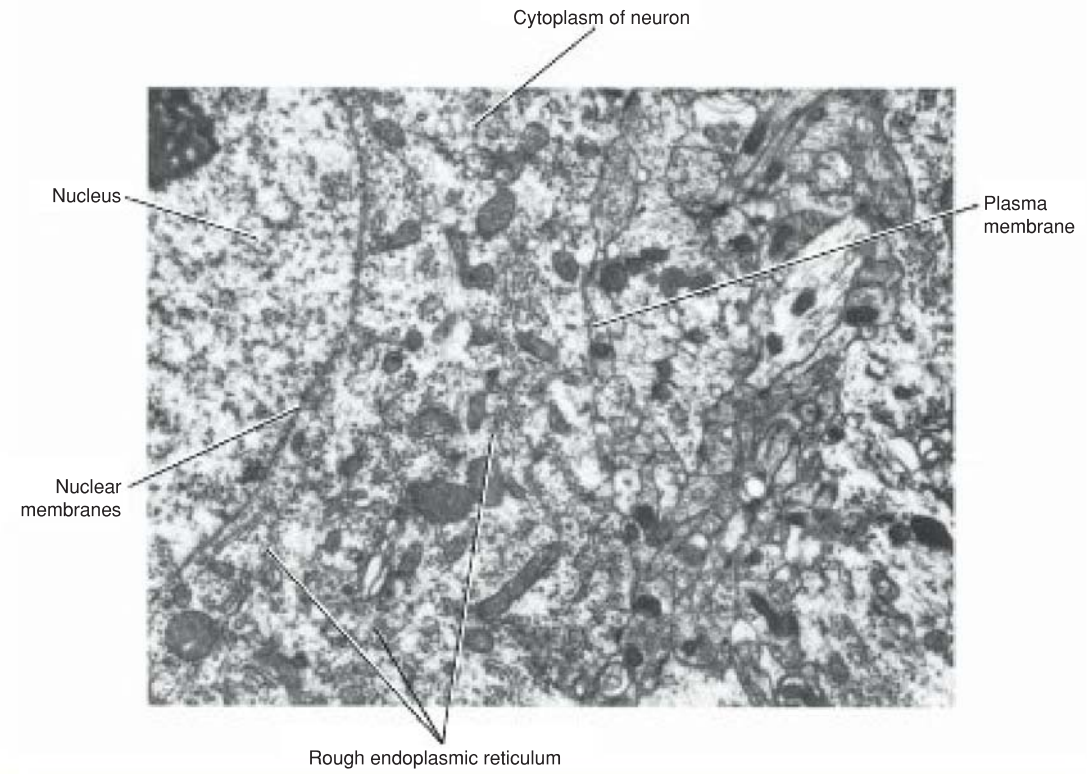

Figure 2-10 Electron micrograph of a neuron showing nuclear and plasma membranes and cytoplasmic organelles. (Courtesy Dr. J. M. Kerns.)

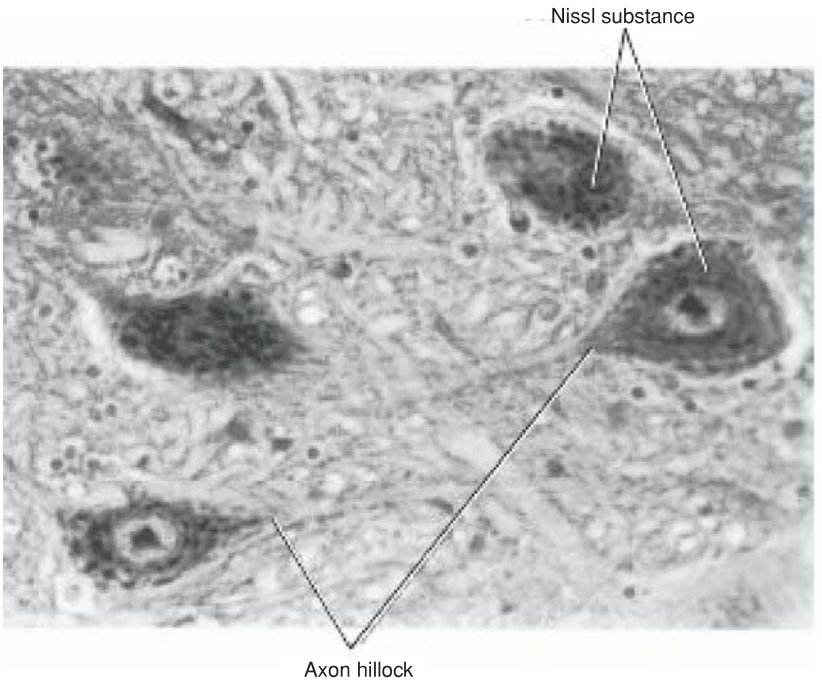

Figure 2-11 Photomicrograph of a section of the anterior gray column of the spinal cord stained with toluidine blue. Note the presence of dark-staining Nissl substance in the cytoplasm of four neurons.

vesicles, where it is temporarily stored and where carbohydrate may be added to the protein to form glycoproteins. The proteins are believed to travel from one cisterna to another via transport vesicles. Each cisterna of the Golgi complex is specialized for different types of enzymatic reaction. At the *trans* side of the complex, the macromolecules are packaged in vesicles for transport to the nerve terminals. The Golgi complex is also thought to be active in lysosome production and in the synthesis of cell membranes. The latter function is particularly important in the formation of synaptic vesicles at the axon terminals.

Mitochondria are found scattered throughout the cell body, dendrites, and axons (Figs. 2-8 and 2-9). They are spherical or rod shaped. In electron micrographs, the walls show a characteristic double membrane. The inner membrane is thrown into folds or cristae that project into the center of the mitochondrion. Mitochondria possess many enzymes, which are localized chiefly on the inner mitochondrial membrane. These enzymes

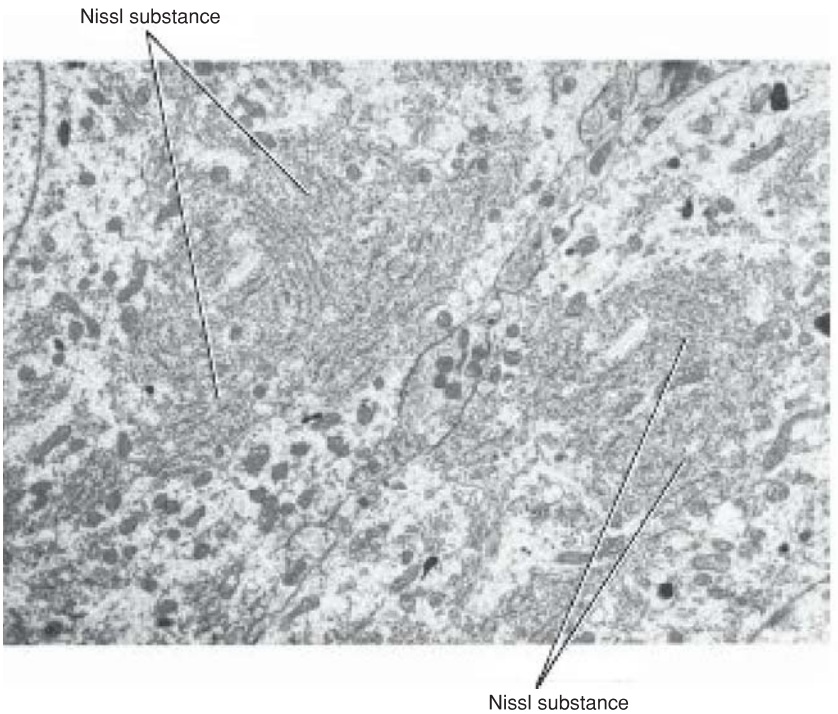

Figure 2-12 Electron micrograph of the cytoplasm of two neurons showing the structure of Nissl bodies (substance). (Courtesy Dr. J. M. Kerns.)

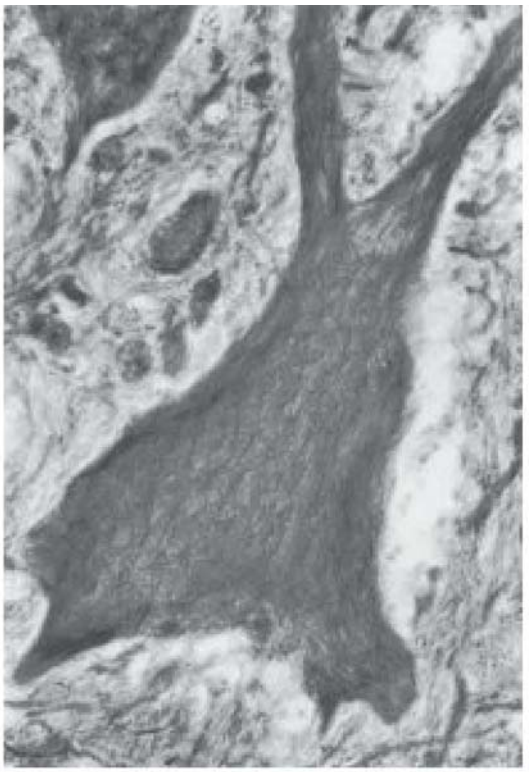

Figure 2-13 Photomicrograph of a silver-stained section of a neuron showing the presence of large numbers of neurofibrils in the cytoplasm of the cell body and the neurites.

take part in the tricarboxylic acid cycle and the cytochrome chains of respiration. Therefore, mitochondria are important in nerve cells, as in other cells, in the production of energy.

Neurofibrils, as seen with the light microscope after staining with silver, are numerous and run parallel to each other through the cell body into the neurites (Fig. 2-13). With the electron microscope, the neurofibrils resolve into bundles of **neurofilaments**—each filament measuring about 10 nm in diameter (Fig. 2-14). The neurofilaments form the main component of the cytoskeleton. Chemically, neurofilaments are very stable and belong to the cytokeratin family.

Microfilaments measure about 3 to 5 nm in diameter and are formed of actin. Microfilaments are concentrated at the periphery of the cytoplasm just beneath the plasma membrane where they form a dense network. Together with microtubules, microfilaments play a key role in the formation of new cell processes and the retraction of old ones. They also assist the microtubules in axon transport.

Microtubules are similar to those seen in other types of cells. They measure about 25 nm in diameter and are found interspersed among the neurofilaments (Fig. 2-14). They extend throughout the cell body and its processes. In the axon, all the microtubules are arranged in parallel, with one end pointing to the cell body and the other end pointing distally away from the cell body.

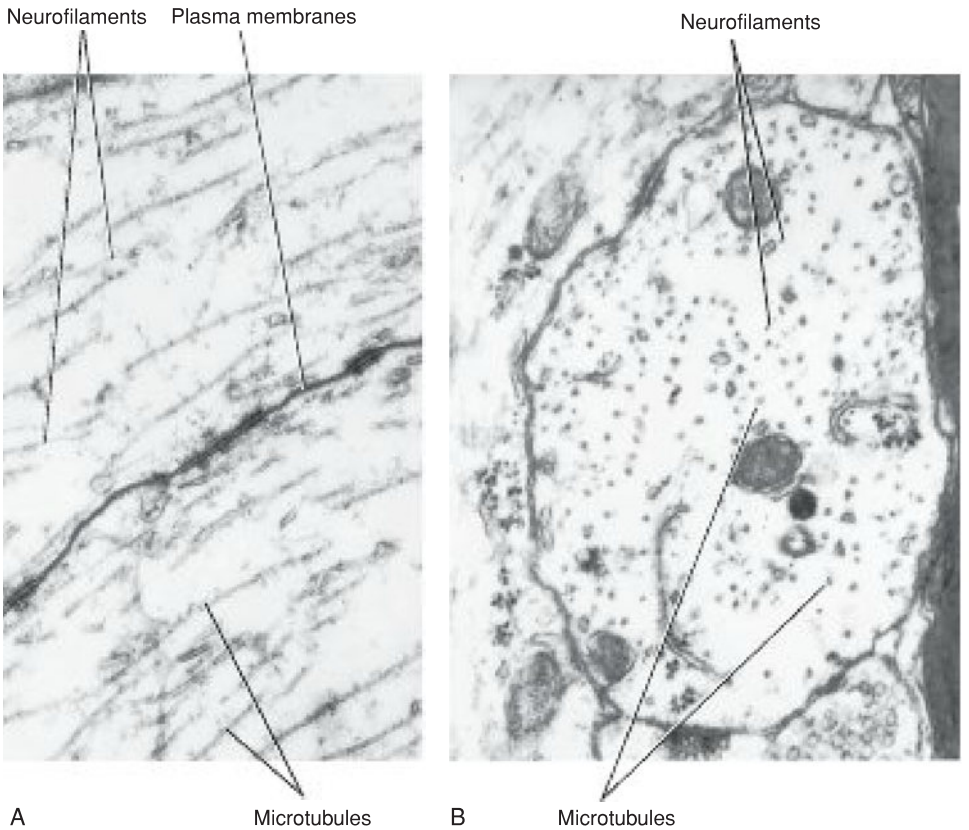

Figure 2-14 Electron micrograph of dendrites showing the presence of neurofilaments and microtubules within their cytoplasm. **A:** Longitudinal section of two adjacent dendrites. **B:** Transverse section of a dendrite. (Courtesy Dr. J. M. Kerns.)

Microtubules and microfilaments provide a stationary track that permits specific organelles to move by molecular motors. The stop-and-start movement is caused by the periodic dissociation of the organelles from the track or the collision with other structures.

Cell transport involves the movement of membrane organelles, secretory material, synaptic precursor membranes, large dense core vesicles, mitochondria, and SER.

Cell transport can take place in both directions in the cell body and its processes. **Rapid transport** (100 to 400 mm/day) is mediated by two motor proteins associated with the microtubule adenosine triphosphate (ATP)-ase sites. In *anterograde* (away from the cell) movement, **kinesin**-coated organelles are thought to move toward one end of the tubule, and, in *retrograde* (toward the cell) movement, dynein-coated organelles are thought to move toward the other end of the tubule. The direction and speed of the movement of an organelle can be brought about by the activation of one of the motor proteins or of both simultaneously.

Slow transport (0.1 to 3.0 mm/day) involves the bulk movement of the cytoplasm and includes the movement of mitochondria and other organelles. Slow axonal transport occurs only in the anterograde direction. The molecular motor has not been identified but is probably one of the kinesin families.

Lysosomes are membrane-bound vesicles measuring about 8 nm in diameter. They serve the cell by acting as intracellular scavengers and contain hydrolytic enzymes. They are formed by the budding off of the Golgi apparatus. Lysosomes exist in three forms: (1) **primary lysosomes**, which have just been formed; (2) **secondary lysosomes**, which contain partially digested material (myelin figures); and (3) **residual bodies**, in which the enzymes are inactive and the bodies have evolved from digestible materials such as pigment and lipid.

Centrioles are small, paired structures found in immature dividing nerve cells. Each centriole is a hollow cylinder whose wall is made up of microtubule bundles. They are associated with the formation of the spindle during cell division and in the formation of microtubules. Centrioles are also found in mature nerve cells, where they are likely involved in the maintenance of microtubules.

Lipofuscin (pigment material) occurs as yellowish-brown granules within the cytoplasm (Fig. 2-15). It probably forms as the result of lysosomal activity, and it represents a harmless metabolic byproduct. Lipofuscin accumulates with age.

Melanin granules are found in the cytoplasm of cells in certain parts of the brain (e.g., the substantia nigra of the midbrain). Their presence may be related to the catecholamine-synthesizing ability of these neurons, whose neurotransmitter is dopamine.

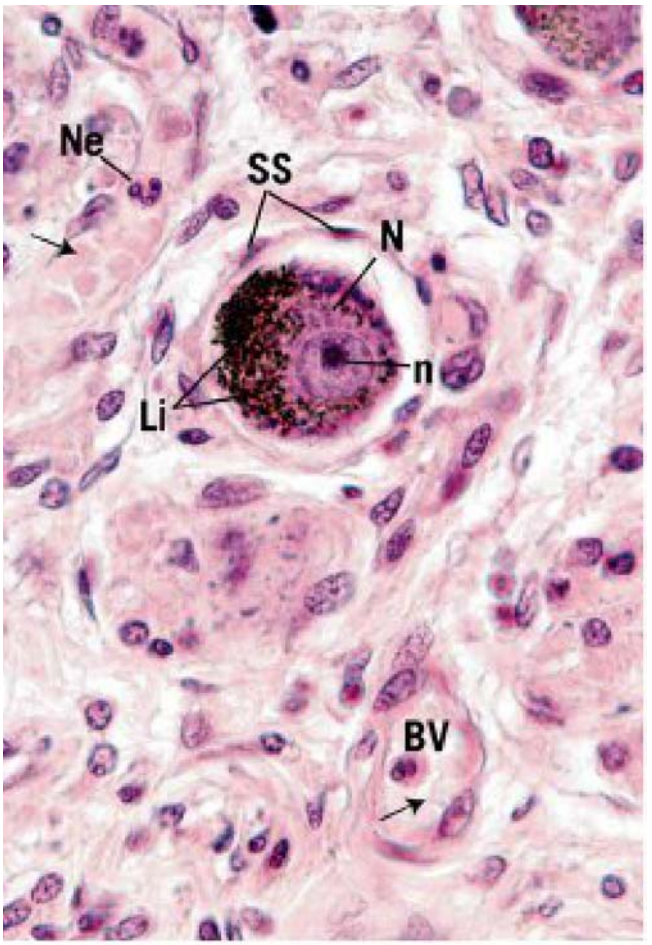

Figure 2-15 Photomicrograph of a longitudinal section of a posterior root ganglion showing the presence of lipofuscin granules within the cytoplasm of sensory neurons. Ne, neutrophil; arrow, red blood cell; SS, satellite cells; N, nucleus; n, nucleolus; Li, lipofuscin; BV, blood vessel.(From Gartner, L. P. (2018). *Color atlas and text of histology* (7th ed). Baltimore, MD: Wolters Kluwer.)

Plasma Membrane

The plasma membrane forms the continuous external boundary of the cell body and its processes, and, in the neuron, it is the site for the initiation and conduction of the nerve impulse (Figs. 2-10 and 2-14). The membrane is about 8 nm thick, which is too thin to be seen with the light microscope. When viewed under the electron microscope, the plasma membrane appears as two dark lines with a light line between them.

The plasma membrane is composed of an inner and an outer layer of very loosely arranged protein molecules, each layer being about 2.5 nm thick, separated by a middle layer of lipid about 3 nm thick. The lipid layer is made up of two rows of phospholipid molecules arranged so that their hydrophobic ends are in contact with each other and their polar ends are in contact with the protein layers. Certain protein molecules lie within the phospholipid layer and span the entire width of the lipid layer. These molecules provide the membrane with hydrophilic channels through which inorganic ions may enter and leave the cell. Carbohydrate molecules are attached to the outside of the plasma membrane and are linked to the proteins or the lipids, forming what is known as the **cell coat** or **glycocalyx**.

The plasma membrane and the cell coat together form a semipermeable membrane that allows diffusion of certain ions through it but restricts others. In the

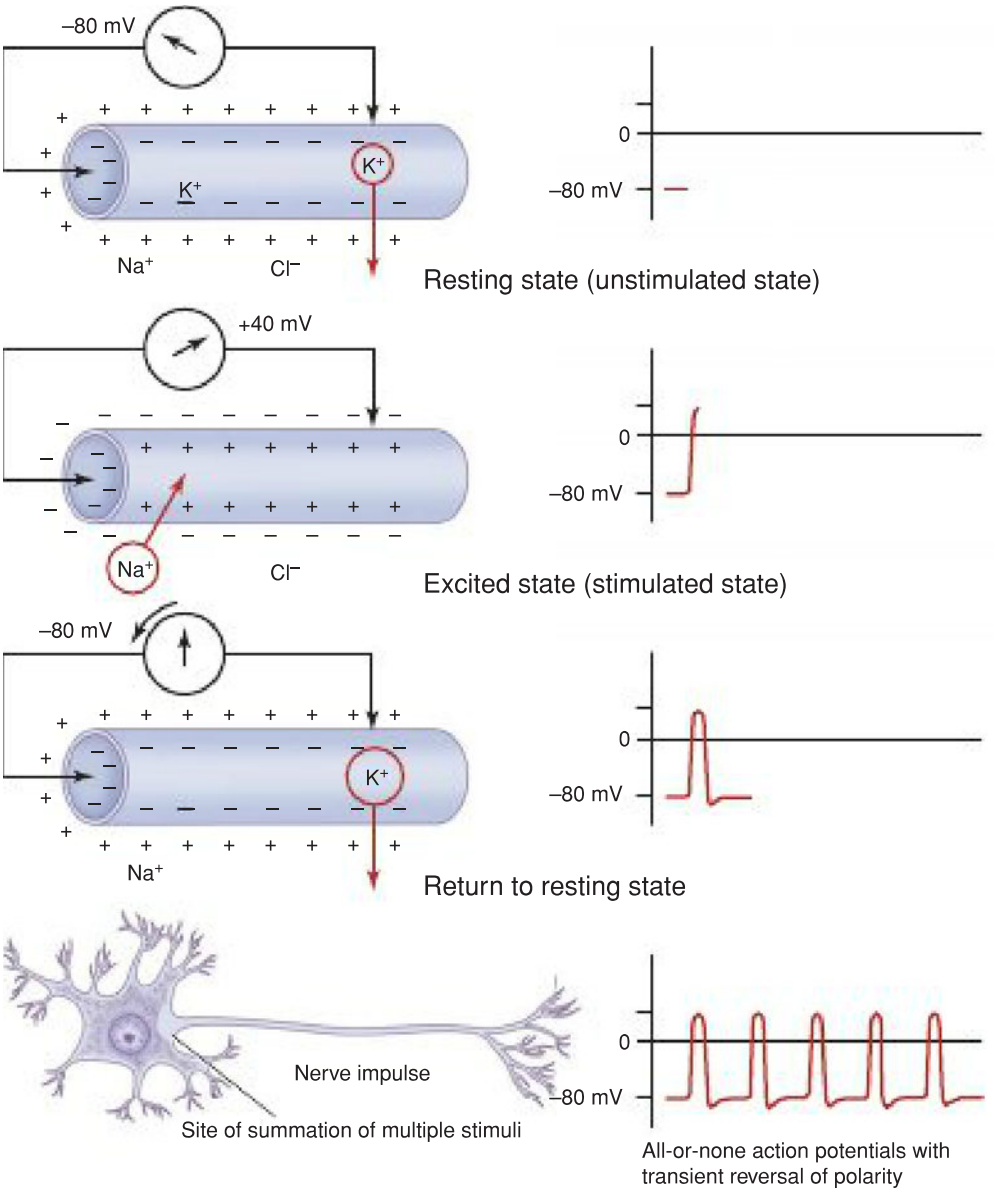

Figure 2-16 Ionic and electrical changes that occur in a neuron when it is stimulated.

resting state (unstimulated state), K^+ ions diffuse through the plasma membrane from the cell cytoplasm to the tissue fluid (Fig. 2-16). The permeability of the membrane to K^+ ions is much greater than that to Na^+ ions; thus, the passive efflux of K^+ is much greater than the influx of Na^+. This results in a steady potential difference of about 280 mV, which can be measured across the plasma membrane because the inside of the membrane is negative with respect to the outside. This potential is known as the **resting potential**.

Membrane Excitation and Conduction

In the resting unstimulated state, a nerve fiber is polarized so that the interior is negative to the exterior; the potential difference across the plasma membrane (axolemma) is about –80 mV and is called the **resting membrane potential** (Fig. 2-17).

When the nerve cell is excited (stimulated) by electrical, mechanical, or chemical means, a rapid change in membrane permeability to Na^+ ions takes place, and Na^+ ions diffuse through the plasma membrane into the cell cytoplasm from the tissue fluid. This results in the membrane becoming progressively depolarized. The sudden influx of Na^+ ions followed by the altered polarity produces an **action potential** (**AP**), which is approximately 140 mV. This potential is very brief, lasting about 5 msec. The increased membrane permeability for Na^+ ions quickly ceases, and membrane permeability for K^+ ions increases. Therefore, K^+ ions start to flow from the cell cytoplasm and return the localized area of the cell to the resting state.

A nerve impulse (**AP**) starts at the initial segment of the axon and is a self-propagating wave of electrical negativity that passes rapidly along the surface of

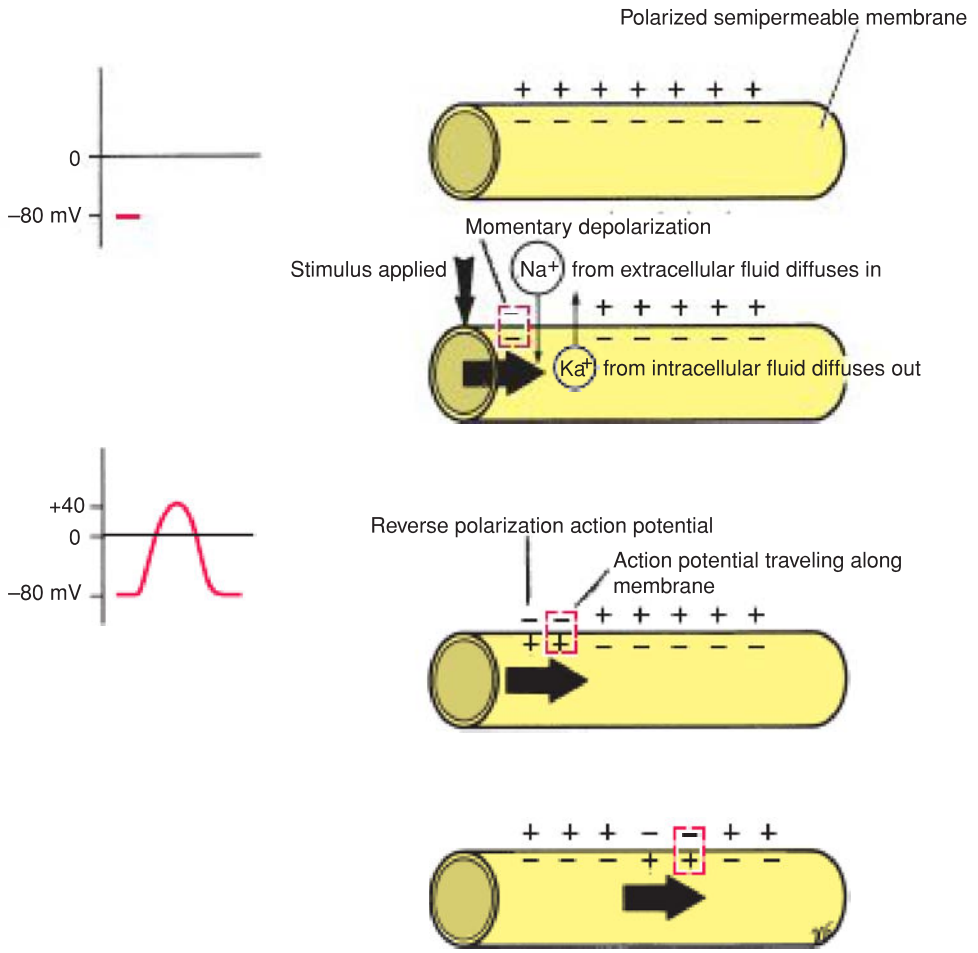

Figure 2-17 Ionic and electrical changes that occur in a nerve fiber when it is conducting an impulse.

the axolemma. Once generated, the AP spreads away from the site of initiation and is conducted along neurites as the **nerve impulse**. The wave of electrical negativity is initiated by an adequate stimulus being applied to the surface of the neuron (Fig. 2-18). Under normal circumstances, this occurs at the initial segment of the axon, which is the most sensitive part of the neuron. The stimulus alters the permeability of the membrane to Na^+ ions at the point of stimulation. Now, Na^+ ions rapidly enter the axon (Fig. 2-17). The positive ions outside the axolemma quickly decrease to zero. Therefore, the membrane potential is reduced to zero and is said to be **depolarized**. A typical resting potential is –80 mV, with the outside of the membrane positive to the inside; the AP is about 140 mV, with the outside of the membrane negative to the inside. In small-diameter axons, the AP may not rise to as much as 40 mV.

The negatively charged point on the outside of the axolemma now acts as a stimulus to the adjacent positively charged axolemma, and, in less than 1 msec, the polarity of the adjacent resting potential is reversed. The AP now has moved along the axolemma from the point originally stimulated to the adjacent point on the membrane. In this manner, the AP travels along the full length of a nerve fiber to its end.

As the AP moves along the nerve fiber, entry of the Na^+ ions into the axon ceases, and the permeability of the axolemma to K^+ ions increases. Now, K^+ ions rapidly diffuse outside the axon because the concentration is much higher within the axon than outside so that the original resting membrane potential is restored. The permeability of the axolemma now decreases, and the status quo is restored by the active transport of the Na^+ ions out of the axon and the K^+ ions into the axon. The outer surface of the axolemma is again electrically positive compared with that of the inner surface. This is a simplistic description of the movements of the Na^+ and K^+ ions. (For further details on the voltage-gated Na^+ and K^+ channels, the Na^+ and K^+ pumps, and the Na^+ and K^+ leak channels, refer to a textbook of physiology.)

For a short time after the passage of a nerve impulse along a nerve fiber, while the axolemma is still depolarized, a second stimulus, however strong, is unable to excite the nerve. This period of time is called the **absolute refractory period**. The underlying reason for the refractory period is that the Na^+ channels become inactivated, and no stimulation, however strong, will

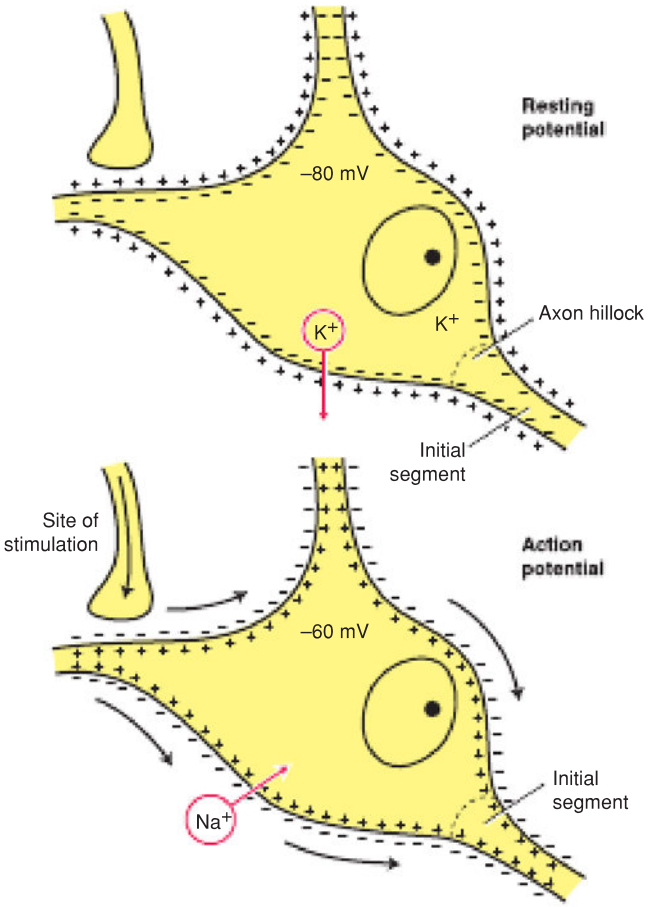

Figure 2-18 Creation of the action potential by the arrival of a stimulus from a single presynaptic terminal. Note that the action potential generated at the initial segment will only occur if the threshold for excitation is reached at the initial segment. (From Snell, R. S. *Clinical neuroanatomy: A review with questions and explanations* (3rd ed., p. 7). Baltimore, MD: Lippincott Williams & Wilkins.)

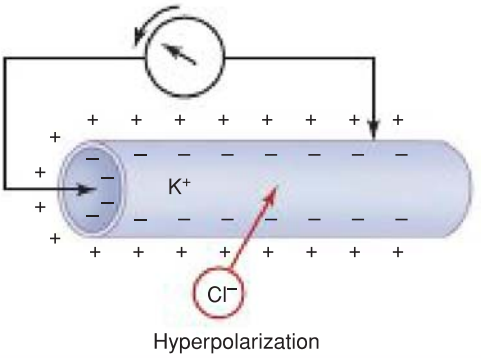

Figure 2-19 Ionic and electrical changes that occur in a neuron during hyperpolarization.

open the Na^+ gates. This period is followed by a further short interval during which the excitability of the nerve gradually returns to normal. This latter period is called the **relative refractory period**. Therefore, the refractory period makes a continuous excitatory state of the nerve impossible and limits the frequency of the impulses.

The greater the strength of the initial stimulus, the larger the initial depolarization and the greater will be the spread into the surrounding areas of the plasma membrane. Multiple excitatory stimuli applied to a neuron's surface result in **summation**. For example, subthreshold stimuli may pass over the surface of the cell body and be summated at the origin of the axon and so initiate an AP. Inhibitory stimuli are believed to produce their effect by causing an influx of Cl^- ions through the plasma membrane into the neuron, thus producing hyperpolarization and reducing the excitatory state of the cell (Fig. 2-19).

The **conduction velocity** of a nerve fiber is proportional to the cross-sectional area of the axon, with the thicker fibers conducting more rapidly than those of smaller diameter. In the large motor fibers (α fibers), the rate may be as high as 70 to 120 m/s; the smaller sensory fibers have slower conduction rates (Table 2-3).

Table 2-3 Classification of Nerve Fibers by Speed of Conduction and Size

Fiber Type	Conduction Velocity (m/s)	Fiber Diameter (μm)	Functions	Myelin	Sensitivity to Local Anesthetics
A Fibers					
α	70–120	12–20	Motor, skeletal muscle	Yes	Least
β	40–70	5–12	Sensory, touch, pressure, vibration	Yes	
γ	10–50	3–6	Muscle spindle	Yes	
δ	6–30	2–5	Pain (sharp, localized), temperature, touch	Yes	
B Fibers	3–15	≤3	Preganglionic autonomic	Yes	
C Fibers	0.5–2.0	0.4–1.2	Pain (diffuse, deep), temperature, postganglionic autonomic	No	Most

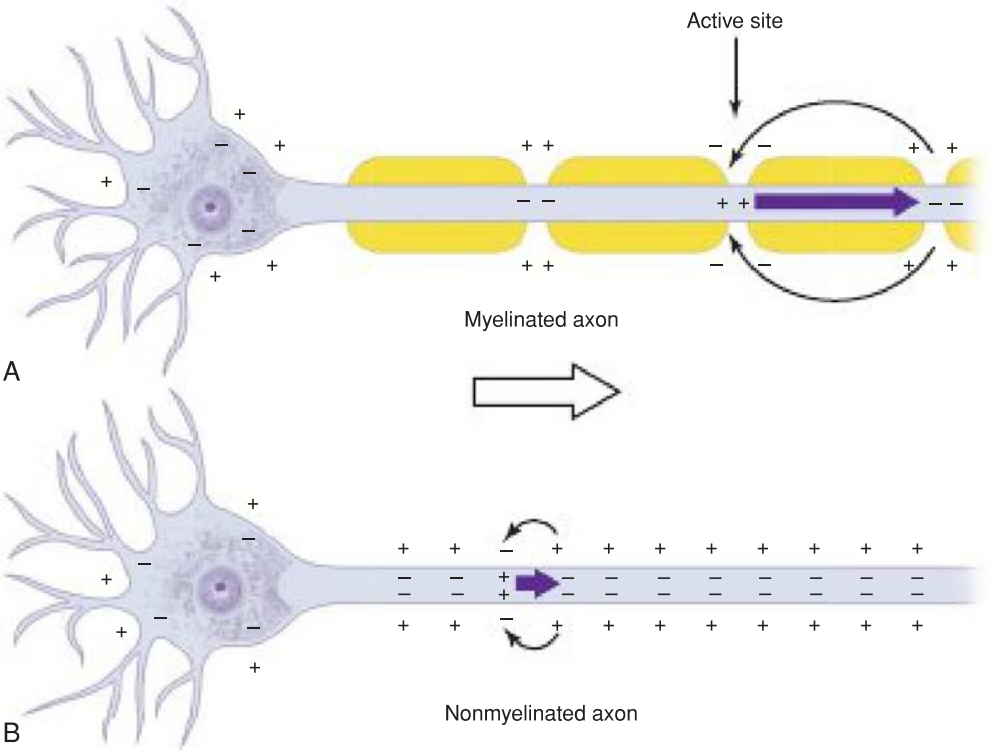

Figure 2-20 Electrical changes that occur in stimulated myelinated axon (saltatory conduction) (**A**) and stimulated nonmyelinated axon (**B**).

In nonmyelinated fibers, the AP passes continuously along the axolemma, progressively exciting neighboring areas of membrane (Fig. 2-20). In myelinated fibers, the presence of a myelin sheath serves as an insulator, and few ions can flow through the sheath. Consequently, a myelinated nerve fiber can be stimulated only at the nodes of Ranvier, where the axon is naked and the ions can pass freely through the plasma membrane between the extracellular fluid and the axoplasm. In these fibers, the AP jumps from one node to the next. The AP at one node sets up a current in the surrounding tissue fluid, which quickly produces depolarization at the next node. This leaping of the AP from one node to the next is referred to as **saltatory conduction**. This is a more rapid mechanism than is found in nonmyelinated fibers (120.0 m/s in a large myelinated fiber compared with 0.5 m/s in a very small unmyelinated fiber).

Sodium and Potassium Channels

Sodium and potassium channels, through which the sodium and potassium ions diffuse through the plasma membrane, are formed of the protein molecules that extend through the full thickness of the plasma membrane (Fig. 2-21). Why a particular channel permits the passage of K^+ ions while excluding Na^+ ions is difficult to explain. The selectivity cannot be due to the diameter of the ions, insofar as the K^+ ion is larger than the Na^+ ion. However, the movement of ions in solution depends not only on the size of the ion but also on the size of the shell of water surrounding it. K^+ ions have weaker electric fields than Na^+ ions; thus, K^+ ions attract less water than Na^+ ions. Therefore, K^+ ions behave as if they are smaller than Na^+ ions. However, this physicochemical explanation does not entirely account for why a channel is selective. The channels may have narrow regions along their length that act as sieves or molecular filters. The ions may also participate in electrostatic interactions with the amino acid residues lining the walls of the channel.

Ion channel proteins are relatively stable, but they exist in at least two conformational states, open and closed functional states. The mechanism responsible for the opening and closing of a channel is not understood but can be thought of as a gate. **Gating** may involve the twisting and distortion of the channel, thus creating a wider or narrower lumen. Gating appears to occur in response to such stimuli as voltage change, the presence of a ligand, or stretch or pressure.

In the nonstimulated state, potassium channel gates are open wider than sodium channel gates, which are nearly closed. This permits the K^+ ions to diffuse out of the cell cytoplasm more readily than the Na^+ ions can diffuse in. In the stimulated state, the sodium channel gates are at first wide open; then, the potassium channel gates are opened, and the sodium channel gates are nearly closed again. The opening and closing of these channels is thought to produce the depolarization and repolarization of the plasma membrane.

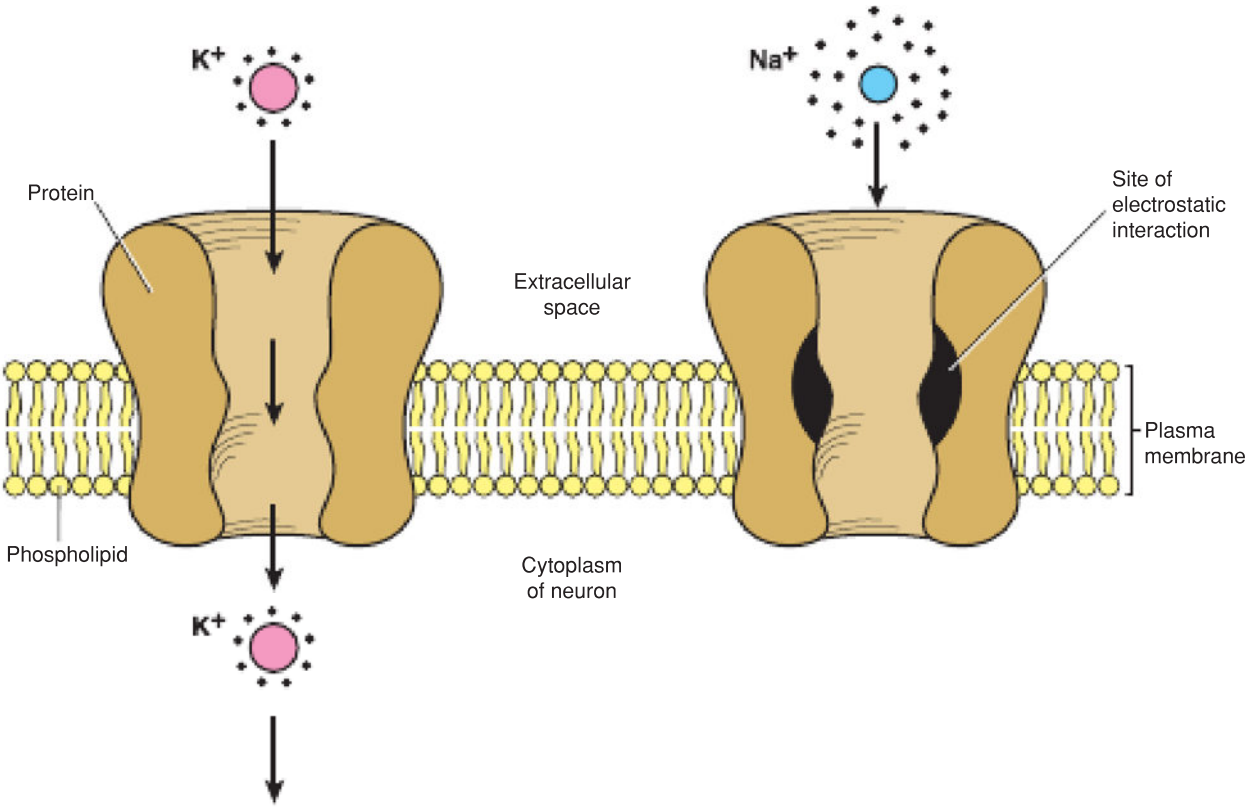

Figure 2-21 Ionic permeability of the plasma membrane. Diagram shows the interactions of the ions with water, the membrane lipid bilayer, and the ion channels.

Nerve Cell Processes

Neurites—the processes of a nerve cell—may be divided into dendrites and an axon.

Dendrites are the short processes of the cell body (Fig. 2-22). Their diameter tapers as they extend from the cell body, and they often branch profusely. In many neurons, the finer branches bear large numbers of small projections called **dendritic spines**. The cytoplasm of the dendrites closely resembles that of the cell body and contains Nissl granules, mitochondria, microtubules, microfilaments, ribosomes, and SER. Dendrites are extensions of the cell body to increase the surface area for the reception of axons from other neurons. Essentially, they conduct the nerve impulse toward the cell body.

During early embryonic development, dendrites are overproduced. Later, they are reduced in number and size in response to altered functional demand from afferent axons. Evidence shows that dendrites remain plastic throughout life and elongate and branch or contract in response to afferent activity.

The **axon** is the longest process of the cell body. It arises from a small conical elevation on the cell body, devoid of Nissl granules, called the **axon hillock** (Fig. 2-23; also see Fig. 2-8). Occasionally, an axon arises from the proximal part of a dendrite. An axon is tubular and is uniform in diameter; it tends to have a smooth surface.

Axons usually do not branch close to the cell body; collateral branches may occur along their length. Shortly before their termination, axons commonly branch profusely. The distal ends of the terminal branches of the axons are often enlarged; they are called **terminals** (Fig. 2-24). Some axons (especially those of autonomic nerves) show a series of swellings resembling a string of beads near their termination; these swellings are called **varicosities**.

Axons may be very short (0.1 mm), as seen in many neurons of the CNS, or extremely long (3.0 m), as seen when they extend from a peripheral receptor in the skin of the toe to the spinal cord and thence to the brain.

Axon diameter varies considerably with different neurons. Those of larger diameter conduct impulses rapidly, and those of smaller diameter conduct impulses very slowly.

The plasma membrane bounding the axon is called the **axolemma**; the cytoplasm of the axon is the **axoplasm**. Unlike the cytoplasm of the cell body, axoplasm lacks Nissl granules and a Golgi complex. The sites for the production of protein, namely RNA and ribosomes, are absent. Thus, axonal survival depends on the transport of substances from the cell bodies.

The **initial segment** of the axon is the first 50 to 100 μm after it leaves the axon hillock of the nerve cell body (Fig. 2-23). This is the most excitable part of the axon and is the site at which an AP originates.

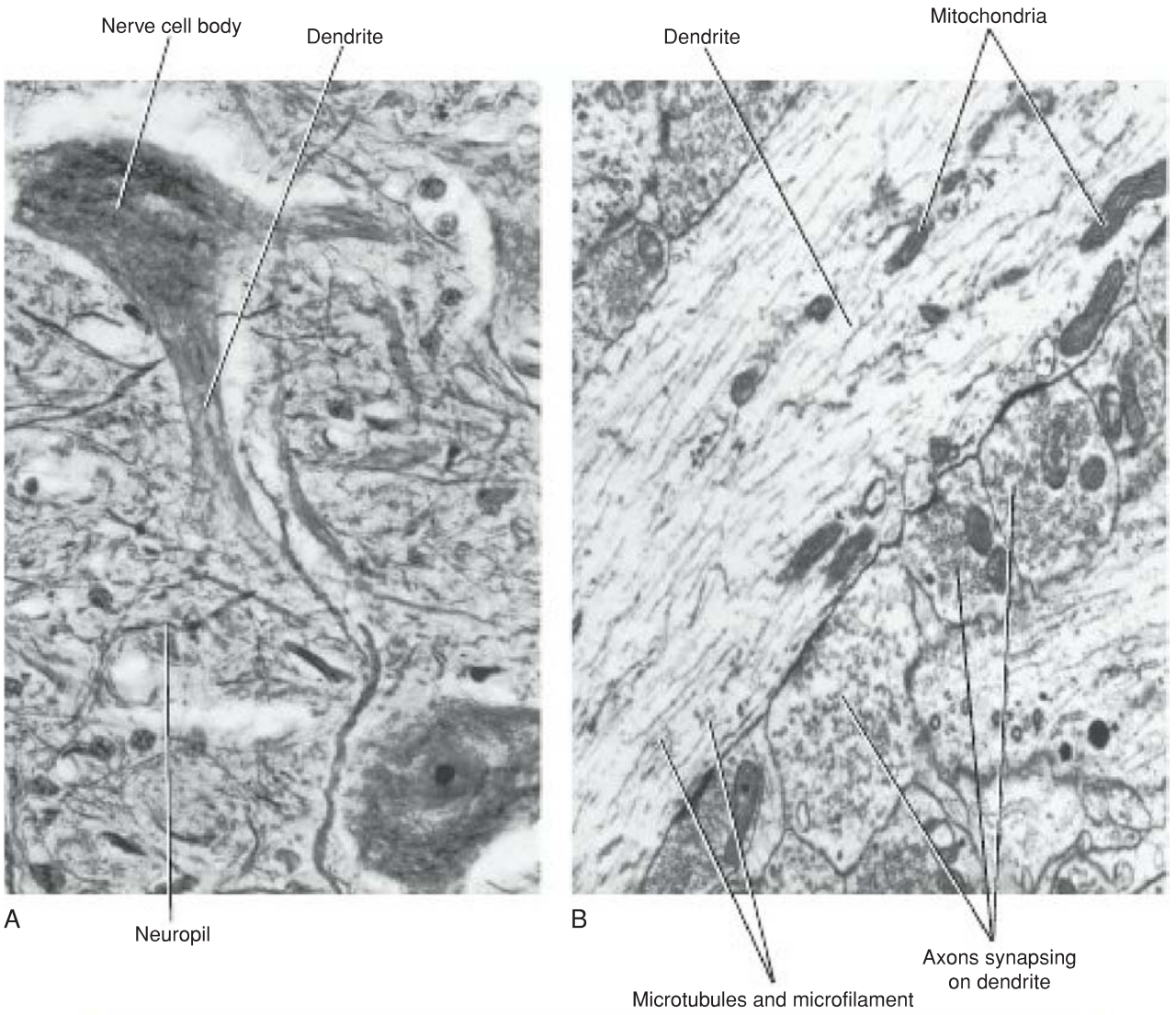

Figure 2-22 **A:** Light photomicrograph of a motor neuron in the anterior gray column of the spinal cord showing the nerve cell body, two dendrites, and the surrounding neuropil. **B:** Electron micrograph of a dendrite showing axodendritic synapses. (Courtesy Dr. J. M. Kerns.)

Remember that, under normal conditions, an AP does not originate on the plasma membrane of the cell body but, instead, always at the initial segment.

An axon always conducts impulses away from the cell body. The axons of sensory posterior root ganglion cells are an exception; here, the long neurite, which is indistinguishable from an axon, carries the impulse toward the cell body. (See unipolar neurons, p. 33.)

Axon Transport

Materials are transported from the cell body to the axon terminals (**anterograde transport**) and to a lesser extent in the opposite direction (**retrograde transport**).

Fast anterograde transport of 100 to 400 mm/day refers to the transport of proteins and transmitter substances or their precursors. **Slow anterograde transport** of 0.1 to 3.0 mm/day refers to the transport of axoplasm and includes the microfilaments and microtubules.

Retrograde transport explains how the cell bodies of nerve cells respond to changes in the distal end of the axons. For example, activated growth factor receptors can be carried along the axon to their site of action in the nucleus. Pinocytotic vesicles arising at the axon terminals can be quickly returned to the cell body. Worn-out organelles can be returned to the cell body for breakdown by the lysosomes.

Axon transport is brought about by microtubules assisted by the microfilaments.

Synapses

The nervous system consists of a large number of neurons that are linked together to form functional

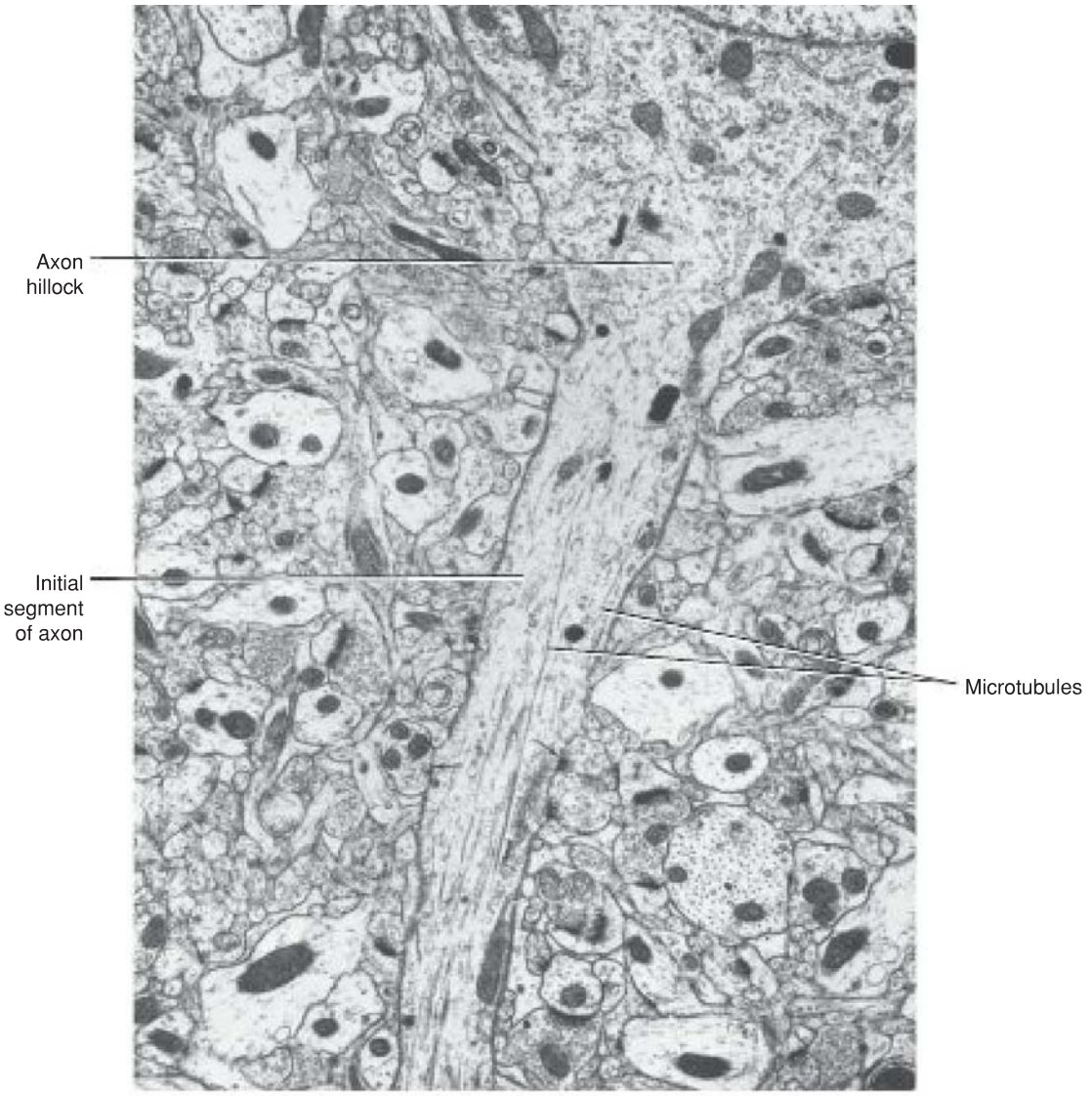

Figure 2-23 Electron micrograph of a longitudinal section of a neuron from the cerebral cortex showing the detailed structure of the region of the axon hillock and the initial segment of the axon. Note the absence of Nissl substance (rough endoplasmic reticulum) in the axon hillock and the presence of numerous microtubules in the axoplasm. Note also the axon terminals (*arrows*) forming axoaxonal synapses with the initial segment of the axon. (Courtesy Dr. A. Peters.)

conducting pathways. The site where two neurons (or a neuron and a skeletal muscle or gland cell) come into close proximity and functional interneuronal communication occurs is referred to as a **synapse** (Fig. 2-25). Most neurons may make synapse with 1,000 or more other neurons and may receive up to 10,000 connections from other neurons. Communication at a synapse, under physiologic conditions, takes place in one direction only. Synapses occur in a number of forms. The most common type is that which occurs between an axon of one neuron and the dendrite or cell body of the second neuron. As the axon approaches the synapse, it may have a terminal expansion (bouton terminal), or it may have a series of expansions (bouton de passage), each of which makes synaptic contact. In other types of synapses, the axon synapses on the initial segment of another axon—that is, proximal to where the myelin sheath begins—or synapses may exist between terminal expansions from different neurons. Depending on the site of the synapse, they are referred to as **axodendritic**, **axosomatic**, or **axoaxonic**.

How an axon terminates varies considerably in different parts of the nervous system. For example, a single axon may terminate on a single neuron, or a single axon may synapse with multiple neurons, as in the case of the parallel fibers of the cerebellar cortex synapsing with multiple Purkinje cells. In the same way, a single neuron may have synaptic junctions with axons of many different neurons. The arrangement of these synapses will determine the means by which a neuron can

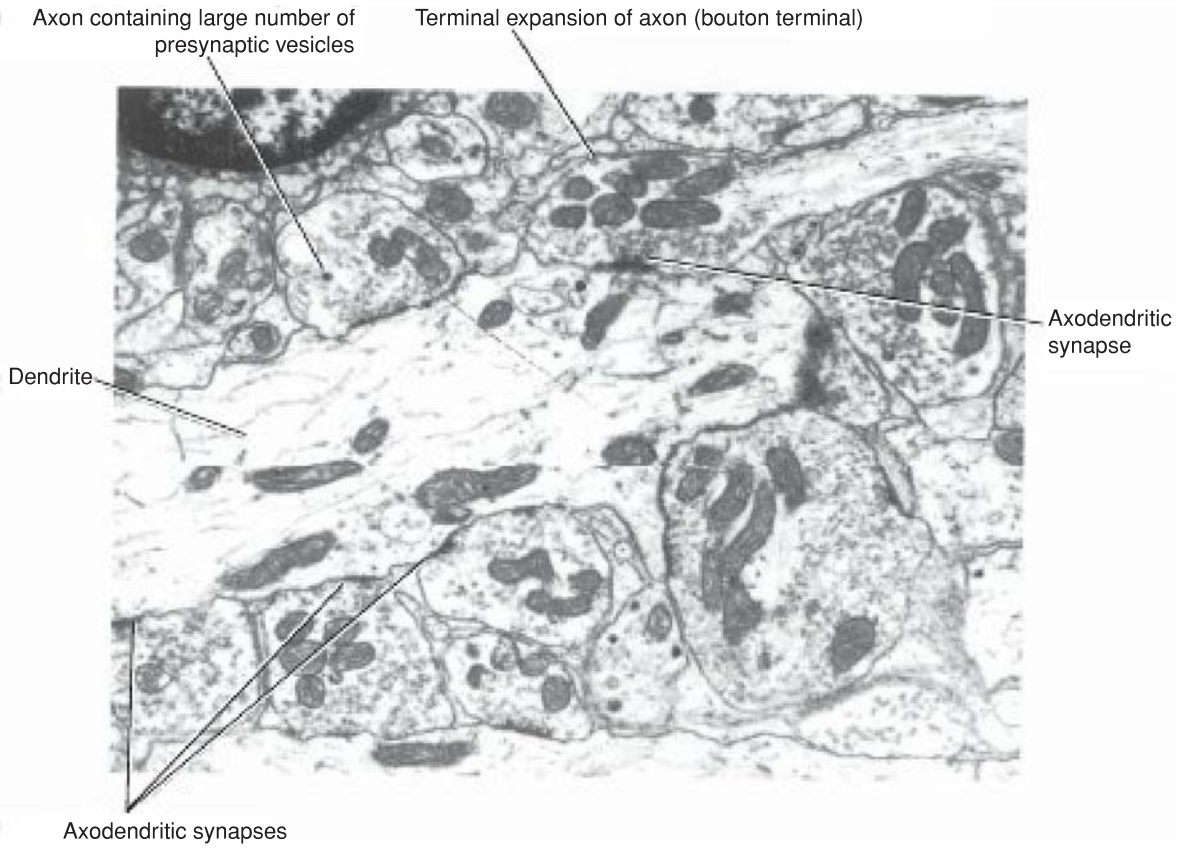

Figure 2-24 Electron micrograph showing multiple axodendritic synapses. Note the presence of large numbers of presynaptic vesicles within the axons. The definition has come to include the site at which a neuron comes into close proximity with a skeletal muscle cell and functional communication occurs. (Courtesy Dr. J. M. Kerns.)

be stimulated or inhibited. **Synaptic spines**, extensions of the surface of a neuron, form receptive sites for synaptic contact with afferent boutons.

Synapses are of two types: chemical and electrical. Most synapses are chemical, in which a chemical substance, the **neurotransmitter**, passes across the narrow space between the cells and becomes attached to a protein molecule in the postsynaptic membrane called the **receptor**.

In most chemical synapses, several neurotransmitters may be present. One neurotransmitter is usually the principal activator and acts directly on the postsynaptic membrane, while the other transmitters function as modulators and modify the activity of the principal transmitter.

Chemical Synapses

On examination with an electron microscope, synapses are seen to be areas of structural specialization (Fig. 2-26; also see Fig. 2-24). The apposed surfaces of the terminal axonal expansion and the neuron are called the **presynaptic** and **postsynaptic membranes**, respectively, and they are separated by a **synaptic cleft** measuring about 20 to 30 nm wide. The presynaptic and postsynaptic membranes are thickened, and the adjacent underlying cytoplasm shows increased density. On the presynaptic side, the dense cytoplasm is broken up into groups; on the postsynaptic side, the density often extends into a **subsynaptic web**. **Presynaptic vesicles**, mitochondria, and occasional lysosomes are present in the cytoplasm close to the presynaptic membrane (see Fig. 2-26). On the postsynaptic side, the cytoplasm often contains parallel cisternae. The synaptic cleft contains polysaccharides.

The presynaptic terminal contains many small presynaptic vesicles that contain the molecules of the neurotransmitter(s). The vesicles fuse with the presynaptic membrane and discharge the neurotransmitter(s) into the synaptic cleft by a process of exocytosis (Fig. 2-27).

When synapses are first formed in the embryo, they are recognized as small zones of density separated by a synaptic cleft. Later, they mature into well-differentiated structures. The presence of simple, undifferentiated synapses in the postnatal nervous system has led to the suggestion that synapses can be developed as required and possibly undergo atrophy when redundant. This plasticity of synapses may be of great importance in the process of learning and in the development and maintenance of memory.

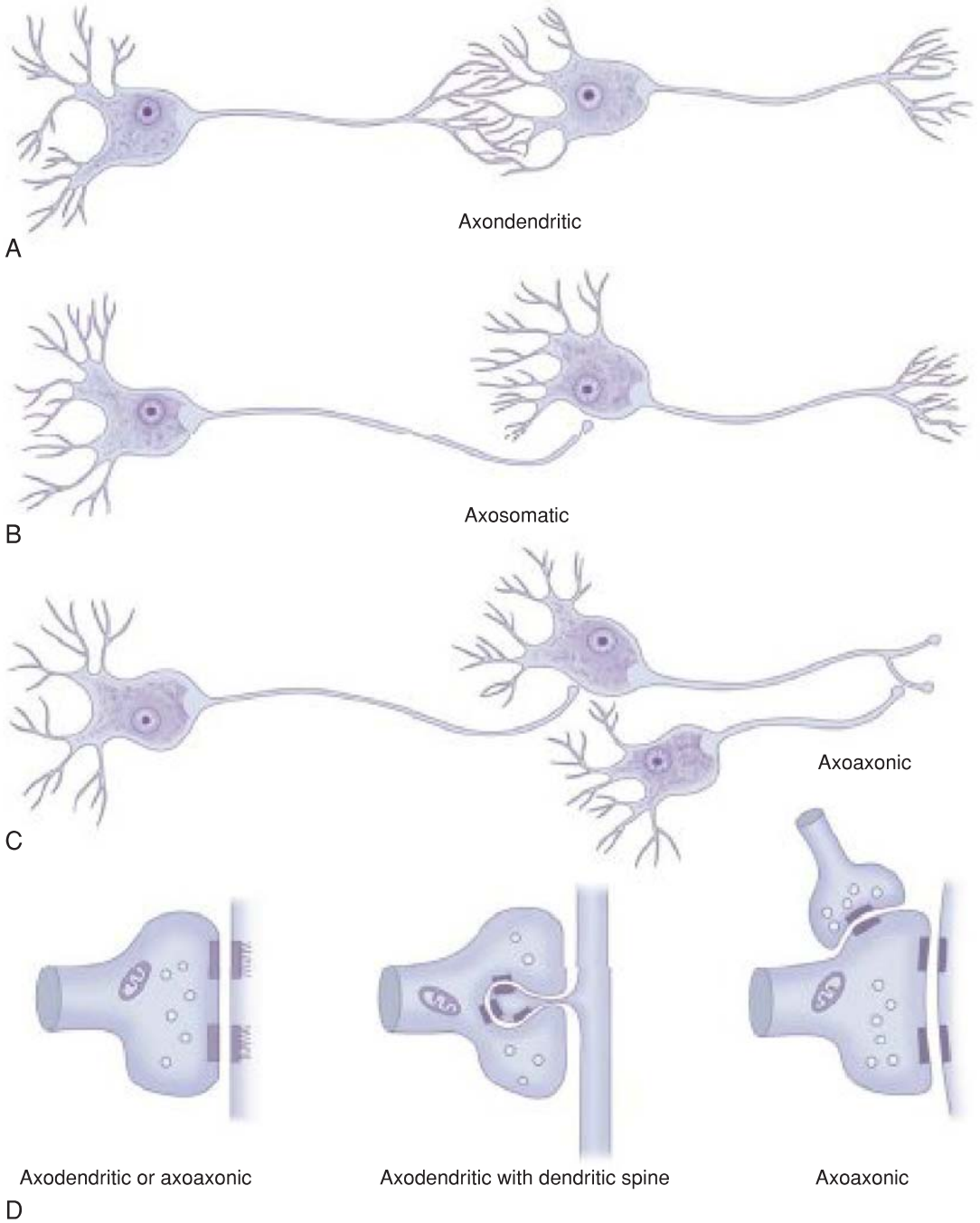

Figure 2-25 **A–D:** Different types of chemical synapses.

Neurotransmitters

Presynaptic vesicles and mitochondria play a key role in the release of neurotransmitter substances at synapses. The vesicles contain the neurotransmitter substance that is released into the synaptic cleft; the mitochondria provide ATP for the synthesis of new transmitter substance.

Most neurons produce and release only one principal transmitter at all their nerve endings. For example, acetylcholine (ACh) is widely used as a transmitter by different neurons in the central and peripheral parts of the nervous system, whereas dopamine is released by neurons in the substantia nigra. Glycine, another transmitter, is found principally in synapses in the spinal cord.

The following chemical substances act as neurotransmitters (many more exist): ACh, norepinephrine, epinephrine, dopamine, glycine, serotonin, GABA, enkephalins, substance P, and glutamic acid.

Note that all skeletal neuromuscular junctions use only ACh as the transmitter, whereas synapses between neurons use a large number of different transmitters.

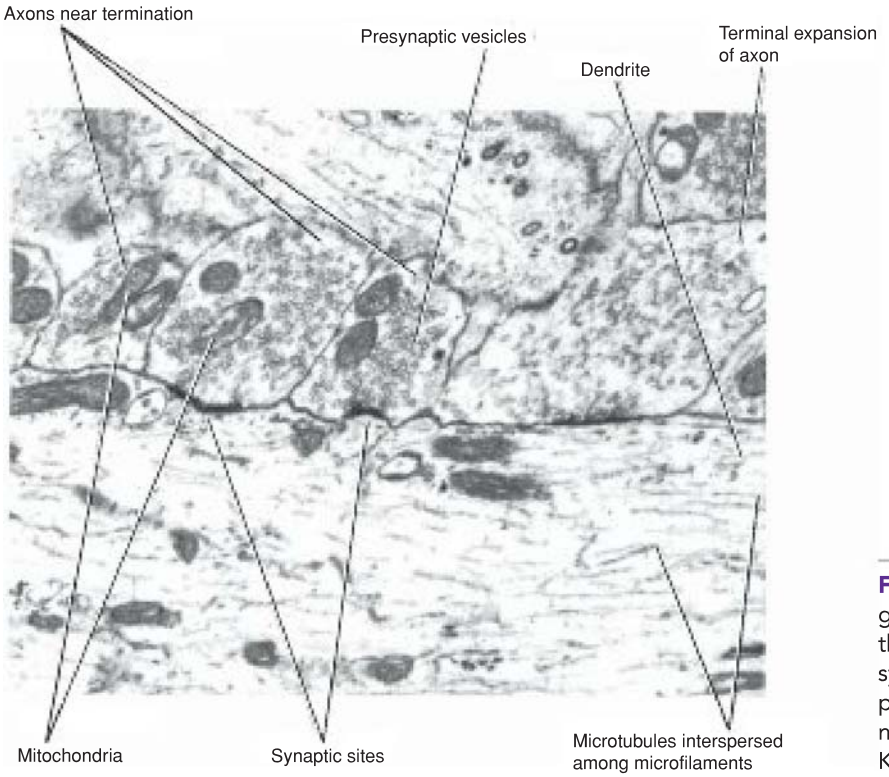

Figure 2-26 High-power electron micrograph of axodendritic synapses showing the thickening of the cell membranes at the synaptic sites, presynaptic vesicles, and the presence of mitochondria within the axons near their termination. (Courtesy Dr. J. M. Kerns.)

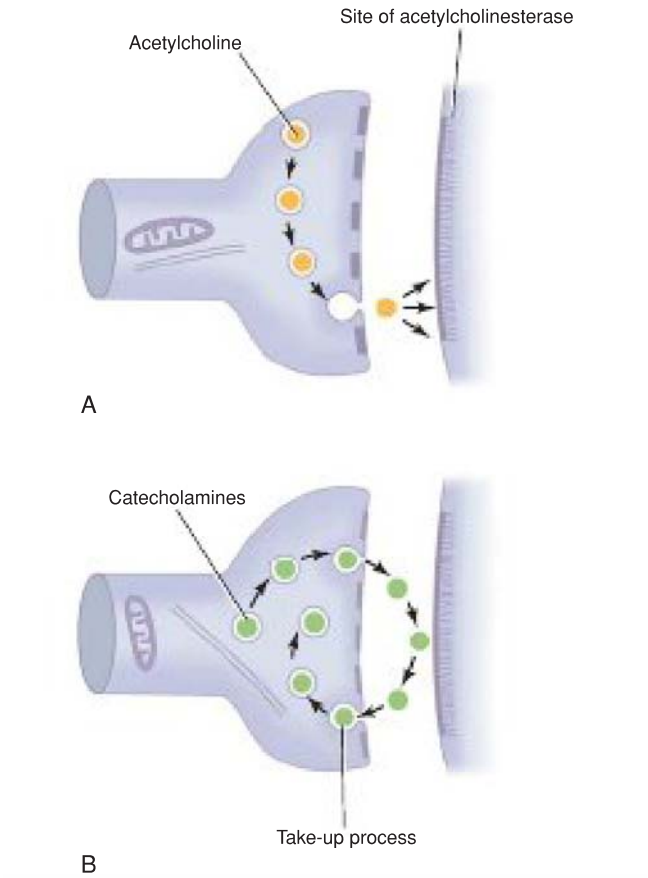

Figure 2-27 Release of neurotransmitters. **A:** Acetylcholine. **B:** Catecholamines.

NEUROTRANSMITTER ACTION

All neurotransmitters are released from their nerve endings by the arrival of the nerve impulse (AP). This results in an influx of Ca^{2+} ions, which causes the synaptic vesicles to fuse with the presynaptic membrane. The neurotransmitters are then ejected into the extracellular fluid in the synaptic cleft. Once in the cleft, they diffuse across the gap to the postsynaptic membrane. There they achieve their objective by raising or lowering the resting potential of the postsynaptic membrane for a brief period of time.

The receptor proteins on the postsynaptic membrane bind the transmitter substance and undergo an immediate conformational change that opens the ion channel, generating an immediate but brief excitatory postsynaptic potential (EPSP) or an inhibitory postsynaptic potential (IPSP). The rapid excitation is seen with ACh (nicotinic) and L-glutamate, or the inhibition is seen with GABA (Table 2-4). Other receptor proteins bind the transmitter substance and activate a second-messenger system, usually through a molecular transducer, a G protein. These receptors have a longer latent period, and the duration of the response may last several minutes or longer. ACh (muscarinic), serotonin, histamine, neuropeptides, and adenosine are good examples of this type of transmitter, which is often referred to as a neuromodulator (see next section, Neuromodulators).

The excitatory and the inhibitory effects on the postsynaptic membrane of the neuron will depend on the summation of the postsynaptic responses at the different synapses. If the overall effect is one of depolarization, the neuron will be excited, an AP will be initiated at the initial segment of the axon, and a

Table 2-4 Examples of Principal (Classic) Neurotransmitters and Neuromodulators at Synapses

Neuromediators[a]	Function	Receptor Mechanism	Ionic Mechanism	Location
Principal Neurotransmitters				
ACh (nicotinic), L-glutamate	Rapid excitation	Ion channel receptors	Opens cation channel (fast EPSP)	Main sensory and motor systems
GABA	Rapid inhibition		Opens anion channel for Cl^- (fast IPSP)	
Neuromodulators				
ACh (muscarinic), serotonin, histamine, adenosine	Modulation and modification of activity	G protein–coupled receptors	Opens or closes K^+ or Ca^{2+} channels (slow IPSP and slow EPSP)	Systems that control homeostasis

[a]Note that these are only a few examples of an ever-increasing number of known neuromediators.
ACh, acetylcholine; GABA, γ-aminobutyric acid; EPSP, excitatory postsynaptic potential; IPSP, inhibitory postsynaptic potential.

nerve impulse will travel along the axon. If, on the other hand, the overall effect is one of hyperpolarization, the neuron will be inhibited and no nerve impulse will arise.

NEUROTRANSMITTER DISTRIBUTION AND FATE

The distribution of the neurotransmitters varies in different parts of the nervous system. **ACh**, for example, is found at the neuromuscular junction, in autonomic ganglia, and at parasympathetic nerve endings. In the CNS, the motor neuron collaterals to the **Renshaw cells** are cholinergic. In the hippocampus, the ascending reticular pathways, and the afferent fibers for the visual and auditory systems, the neurotransmitters are also cholinergic.

Norepinephrine is found at sympathetic nerve endings. In the CNS, it is found in high concentration in the hypothalamus. **Dopamine** is found in high concentration in different parts of the CNS, such as in the basal nuclei (ganglia).

The effect produced by a neurotransmitter is limited by its destruction or reabsorption. For example, in the case of ACh, the effect is limited by the destruction of the transmitter in the synaptic cleft by the enzyme **acetylcholinesterase** (**AChE**) (Fig. 2-27). However, with the **catecholamines**, the effect is limited by the return of the transmitter to the presynaptic nerve ending.

Neuromodulators

Interestingly, in many synapses, certain substances other than the principal neurotransmitters are ejected from the presynaptic membrane into the synaptic cleft. These substances are capable of modulating and modifying the activity of the postsynaptic neuron and are called **neuromodulators**.

NEUROMODULATOR ACTION

Neuromodulators can coexist with the principal neurotransmitter at a single synapse. Usually, but not always, the neuromodulators are in separate presynaptic vesicles. Although the principal neurotransmitters have a rapid, brief effect on the postsynaptic membrane on release into the synaptic cleft, neuromodulators do not have a direct effect on the postsynaptic membrane. Rather, they enhance, prolong, inhibit, or limit the principal neurotransmitter's effect on the postsynaptic membrane. Neuromodulators act through a second-messenger system, usually through a molecular transducer, such as a G protein, and alter the response of the receptor to the neurotransmitter. In a given area of the nervous system, many different afferent neurons can release several different neuromodulators that affect the postsynaptic neuron. Such an arrangement can lead to a wide variety of responses, depending on input from the afferent neurons.

Electrical Synapses

Electrical synapses are gap junctions containing channels that extend from the cytoplasm of the presynaptic neuron to that of the postsynaptic neuron: They are rare in the human CNS. The neurons communicate electrically; a chemical transmitter is not present. The bridging channels permit ionic current flow to take place from one cell to the other with a minimum of delay. In electrical synapses, the rapid spread of activity from one neuron to another ensures that a group of neurons performing an identical function act together. Electrical synapses also have the advantage that they are bidirectional; chemical synapses are not.

NEUROGLIA

The neurons of the CNS are supported by several varieties of nonexcitable cells, which together are called **neuroglia** (Fig. 2-28). Neuroglial cells are generally smaller than neurons and outnumber them by 5 to 10 times; they comprise about half the total volume of the brain and spinal cord.

The four types of neuroglial cells are (1) astrocytes, (2) oligodendrocytes, (3) microglia, and (4) ependyma. A summary of the structural features, location, and functions of the different neuroglial cells is provided in Table 2-5.

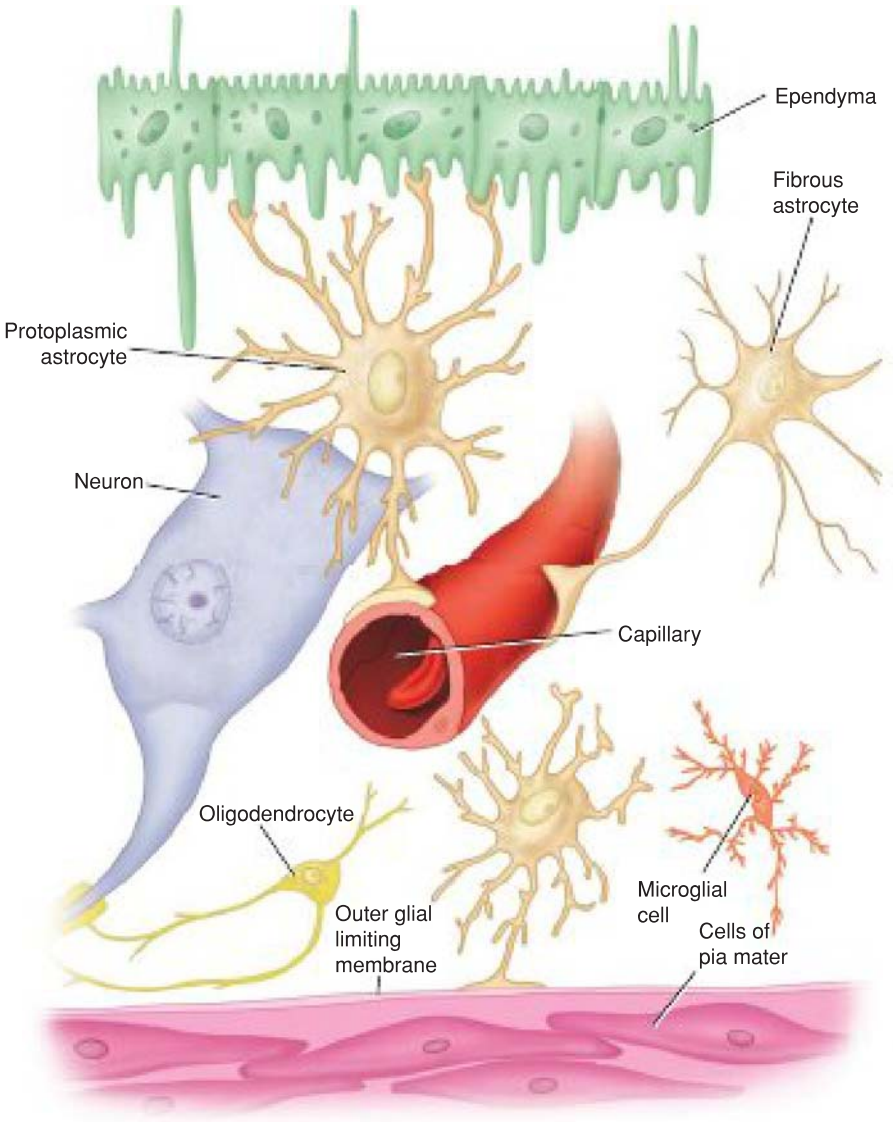

Figure 2-28 Diagrammatic representation of the arrangement of different types of neuroglial cells.

Astrocytes

Astrocytes have small cell bodies with branching processes that extend in all directions. The two types of astrocytes include fibrous and protoplasmic.

Fibrous astrocytes are found mainly in the white matter, where their processes pass between the nerve fibers (Fig. 2-29). Each process is long, slender, smooth, and not much branched. The cell bodies and processes contain many filaments in their cytoplasm.

Protoplasmic astrocytes are found mainly in the gray matter, where their processes pass between the nerve cell bodies (Figs. 2-30 and 2-31). The processes are shorter, thicker, and more branched than those of the fibrous astrocyte, and their cytoplasm contains fewer filaments.

Many of the processes of astrocytes end in expansions on blood vessels (perivascular feet), where they form an almost complete covering on the external surface of capillaries. Large numbers of astrocytic processes are interwoven at the outer and inner surfaces of the CNS, where they form the **outer** and **inner glial limiting membranes**. Thus, the outer glial limiting membrane is found beneath the pia mater, and the inner glial limiting membrane lies beneath the ependyma lining the ventricles of the brain and the central canal of the spinal cord.

Astrocytic processes are also found in large numbers around the initial segment of most axons and in the bare segments of axons at the nodes of Ranvier. Axon terminals at many sites are separated from other nerve cells and their processes by an envelope of astrocytic processes.

Astrocyte Functions

Astrocytes, with their branching processes, form a supporting framework for the nerve cells and nerve fibers. Their processes are functionally coupled at gap junctions. In the embryo, they serve as a scaffolding

Table 2-5 Structural Features, Location, and Functions of Neuroglial Cells

Neuroglial Cell	Structure	Location	Function
Astrocytes			
Fibrous	Small cell bodies, long slender processes, cytoplasmic filaments, perivascular feet	White matter	Provide supporting framework, are electrical insulators, limit spread of neurotransmitters, take up K^+ ions
Protoplasmic	Small cell bodies, short thick processes, many branches, few cytoplasmic filaments, perivascular feet	Gray matter	Store glycogen, have a phagocytic function, take place of dead neurons, are a conduit for metabolites or raw materials, produce trophic substances
Oligodendrocytes	Small cell bodies, few delicate processes, no cytoplasmic filaments	In rows along myelinated nerves, surrounding neuron cell bodies	Form myelin in CNS, influence biochemistry of neurons
Microglia	Smallest of neuroglial cells, wavy branches with spines	Scattered throughout CNS	Are inactive in normal CNS, proliferate in disease and phagocytosis, joined by blood monocytes
Ependyma			
Ependymocytes	Cuboidal or columnar in shape with cilia and microvilli, gap junctions	Line ventricles, central canal	Circulate CSF, absorb CSF
Tanycytes	Long basal processes with end feet on capillaries	Line floor of third ventricle	Transport substances from CSF to hypophyseal–portal system
Choroidal epithelial cells	Sides and bases thrown into folds, tight junctions	Cover surfaces of choroid plexuses	Produce and secrete CSF

CNS, central nervous system; CSF, cerebrospinal fluid.

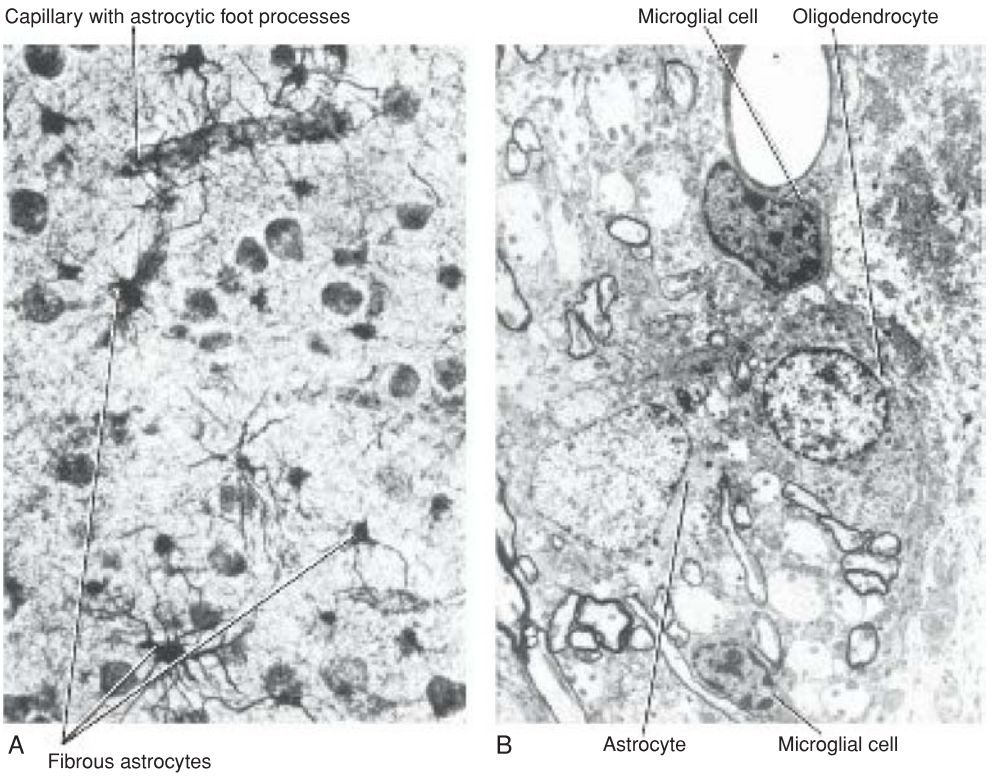

Figure 2-29 **A:** Photomicrograph of a section of the gray matter of the spinal cord showing fibrous astrocytes. **B:** Electron micrograph showing an astrocyte. (Courtesy Dr. J. M. Kerns.)

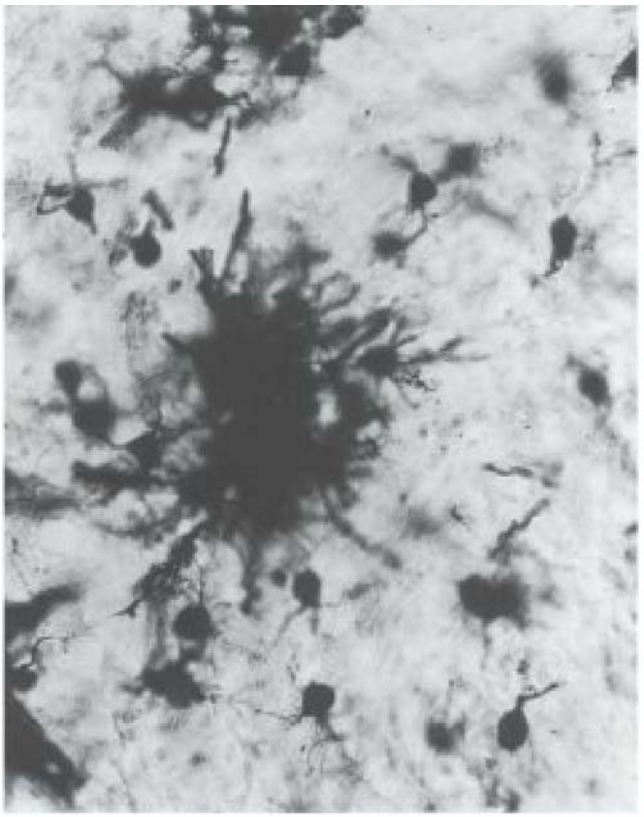

Figure 2-30 Photomicrograph of a protoplasmic astrocyte in the cerebral cortex.

for the migration of immature neurons. By covering the synaptic contacts between neurons, they may serve as electrical insulators preventing axon terminals from influencing neighboring and unrelated neurons. They may even form barriers for the spread of neurotransmitter substances released at synapses. Astrocytes have been shown to be affected by GABA and glutamic acid secreted by the nerve terminals, thereby limiting the influence of these neurotransmitters. Astrocytes appear to be able to take up excess K^+ ions from the extracellular space so that they may have an important function during repetitive firing of a neuron. They store glycogen within their cytoplasm. The glycogen can be broken down into glucose and even further into lactate, both of which are released to surrounding neurons in response to norepinephrine.

Astrocytes may serve as phagocytes by taking up degenerating synaptic axon terminals. Following the death of neurons due to disease, astrocytes proliferate and fill in the spaces previously occupied by the neurons, a process called **replacement gliosis**. Astrocytes possibly serve as a conduit for the passage of metabolites or raw materials from blood capillaries to the neurons through their perivascular feet. Because astrocytes are linked together by gap junctions, they enable ions to pass from one cell to another without entering the extracellular space. Astrocytes may produce substances that have a trophic influence on neighboring neurons. Recent research has suggested that astrocytes secrete cytokines that regulate the activity of immune

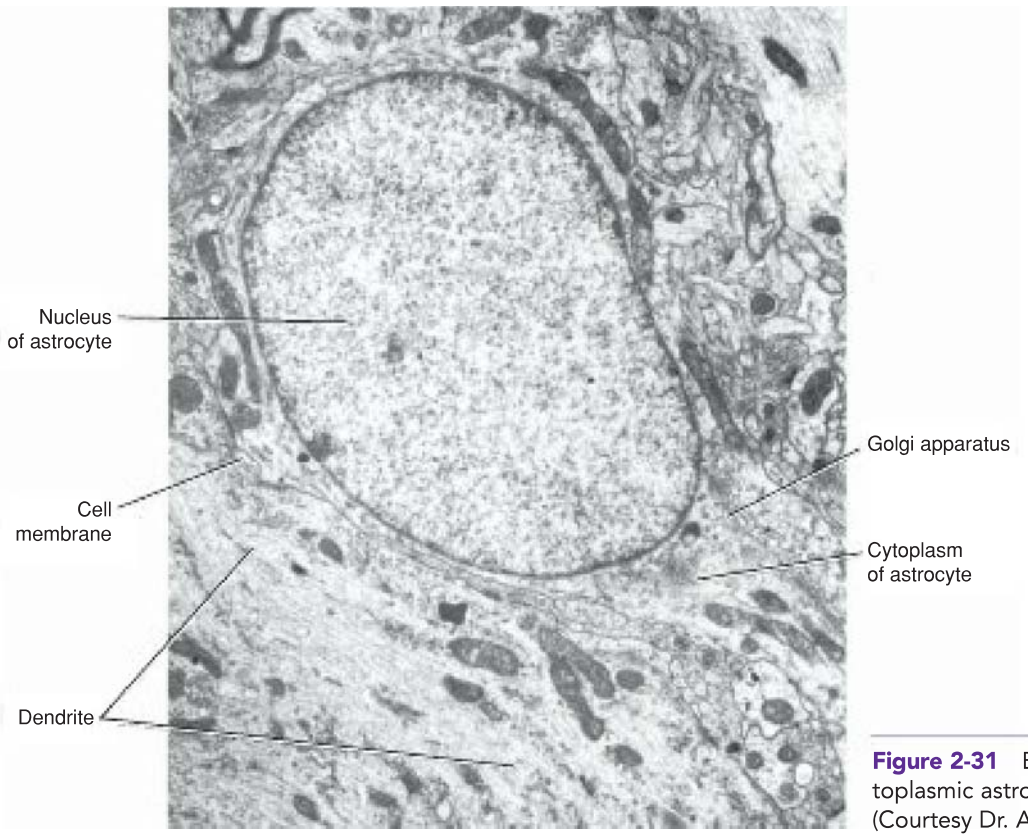

Figure 2-31 Electron micrograph of a protoplasmic astrocyte in the cerebral cortex. (Courtesy Dr. A. Peters.)

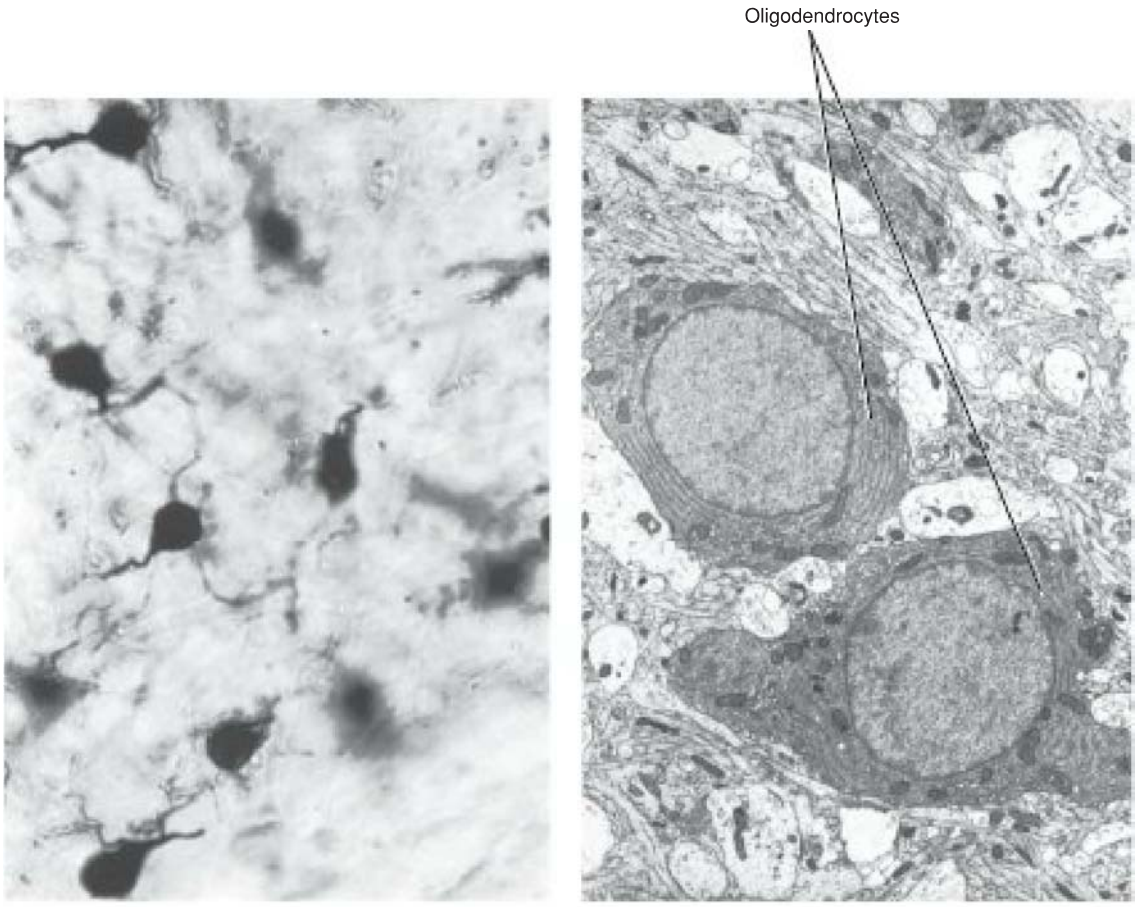

Figure 2-32 **A:** Photomicrograph of a group of oligodendrocytes. **B:** Electron micrograph of two oligodendrocytes. (Courtesy Dr. J. M. Kerns.)

cells entering the nervous system in disease. Finally, astrocytes play an important role in the structure of the blood–brain barrier. Here, the astrocyte processes terminate as expanded feet at the basement membrane of blood vessels.

Oligodendrocytes

Oligodendrocytes have small cell bodies and a few delicate processes; their cytoplasm does not contain filaments. Oligodendrocytes are found in rows along myelinated nerve fibers and surround nerve cell bodies (Fig. 2-32). Electron micrographs show the processes of a single oligodendrocyte joining the myelin sheaths of several nerve fibers (Fig. 2-33). However, only one process joins the myelin between two adjacent nodes of Ranvier.

Oligodendrocyte Functions

Oligodendrocytes are responsible for the formation of the myelin sheath of nerve fibers in the CNS, much as the myelin of peripheral nerves is formed from Schwann cells. This formation and maintenance of myelin around many CNS axons provides them with an insulating coat and greatly increases the speed of nerve conduction along them (see p. 47). Because oligodendrocytes have several processes, unlike Schwann cells, they can each form several internodal segments of myelin on the same or different axons. A single oligodendrocyte can form as many as 60 internodal segments. Note that, unlike Schwann cells in the peripheral nervous system (PNS), oligodendrocytes and their associated axons are *not* surrounded by a basement membrane. Myelination begins at about the 16th week of intrauterine life and continues postnatally until practically all the major nerve fibers are myelinated by the time the child is walking.

Oligodendrocytes also surround nerve cell bodies (satellite oligodendrocytes) and probably have a similar function to the satellite or capsular cells of peripheral sensory ganglia. They are thought to influence the biochemical environment of neurons.

Microglia

The microglial cells are embryologically unrelated to the other neuroglial cells and are derived from macrophages outside the nervous system. They are the

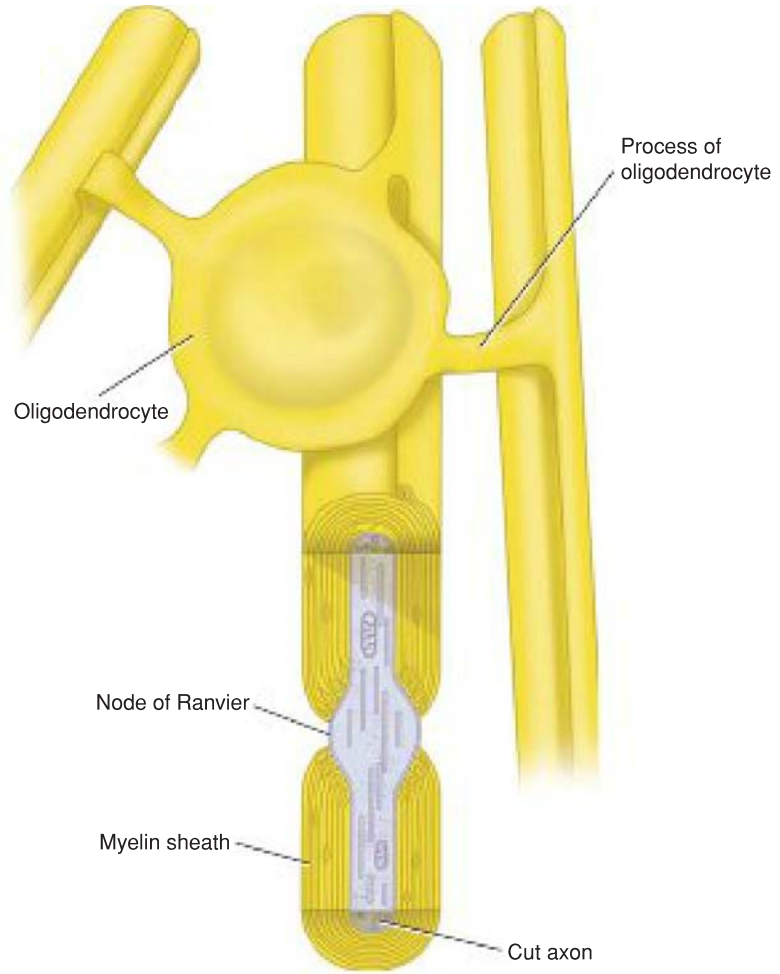

Figure 2-33 A single oligodendrocyte whose processes are continuous with the myelin sheaths of four nerve fibers within the central nervous system.

smallest of the neuroglial cells and are found scattered throughout the CNS (Fig. 2-34). Wavy branching processes arise from their small cell bodies that give off numerous spinelike projections. They closely resemble connective tissue macrophages. They migrate into the nervous system during fetal life. Microglial cells increase in number in the presence of damaged nervous tissue resulting from trauma and ischemic injury and in the presence of diseases including Alzheimer disease, Parkinson disease, multiple sclerosis, and AIDS. Many of these new cells are monocytes that have migrated from the blood.

Microglia Function

Microglial cells in the normal brain and spinal cord appear to be inactive and are sometimes called **resting microglial cells**. In inflammatory disease of the CNS, they become the immune effector cells. They retract their processes and migrate to the site of the lesion. Here, they proliferate and become antigen-presenting cells, which, together with the invading T lymphocytes, confront invading organisms. They are also actively phagocytic; their cytoplasm becomes filled with lipids and cell remnants. The microglial cells are joined by monocytes from neighboring blood vessels.

Ependyma

Ependymal cells line the cavities of the brain and the central canal of the spinal cord. They form a single layer of cells that are cuboidal or columnar in shape and possess microvilli and cilia (Fig. 2-35). The cilia are often motile, and their movements contribute to the flow of the cerebrospinal fluid (CSF). The bases of the ependymal cells lie on the internal glial limiting membrane.

Ependymal cells can be divided into three groups:

1. **Ependymocytes** line the ventricles of the brain and the central canal of the spinal cord and are in contact with the CSF. Their adjacent surfaces have gap junctions, but the CSF is in free communication with CNS intercellular spaces.
2. **Tanycytes** line the floor of the third ventricle overlying the median eminence of the hypothalamus.

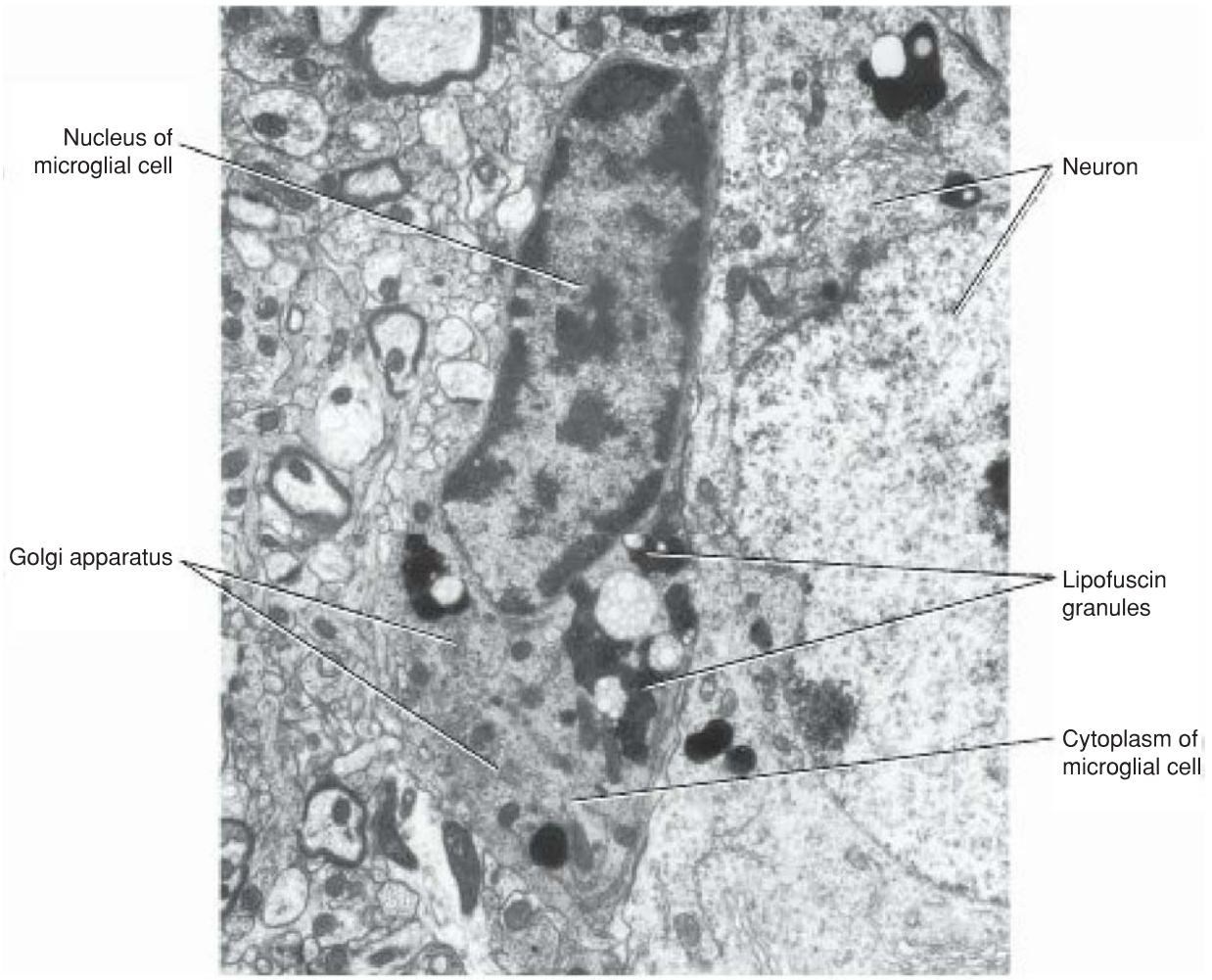

Figure 2-34 Electron micrograph of a microglial cell in the cerebral cortex. (Courtesy Dr. A. Peters.)

These cells have long basal processes that pass between the cells of the median eminence and place endfeet on blood capillaries.

3. **Choroidal epithelial cells** cover the surfaces of the choroid plexuses. The sides and bases of these cells are thrown into folds; near their luminal surfaces, the cells are held together by tight junctions that encircle the cells. The presence of tight junctions prevents the leakage of CSF into the underlying tissues.

Ependymal Cell Functions

Ependymocytes assist in CSF circulation within the cavities of the brain and the central canal of the spinal cord by the movements of the cilia. The microvilli on the free surfaces of the ependymocytes indicate that they also have an absorptive function. Tanycytes are thought to transport chemical substances from the CSF to the hypophyseal portal system. In this manner, they may play a part in the control of the hormone production by the anterior lobe of the pituitary. Choroidal epithelial cells are involved in the production and secretion of CSF from the choroid plexuses.

EXTRACELLULAR SPACE

When nervous tissue is examined under an electron microscope, a very narrow gap separates the neurons and the neuroglial cells. These gaps are linked together and filled with tissue fluid; they are called the **extracellular space**. The extracellular space is in almost direct continuity with the CSF in the subarachnoid space externally and with the CSF in the ventricles of the brain and the central canal of the spinal cord internally. The extracellular space also surrounds the blood capillaries in the brain and spinal cord. (The CNS does not have lymphatic capillaries.)

The extracellular space thus provides a pathway for the exchange of ions and molecules between the blood and the neurons and glial cells. The plasma membrane of the endothelial cells of most capillaries is impermeable to many chemicals, and this forms the blood–brain barrier.

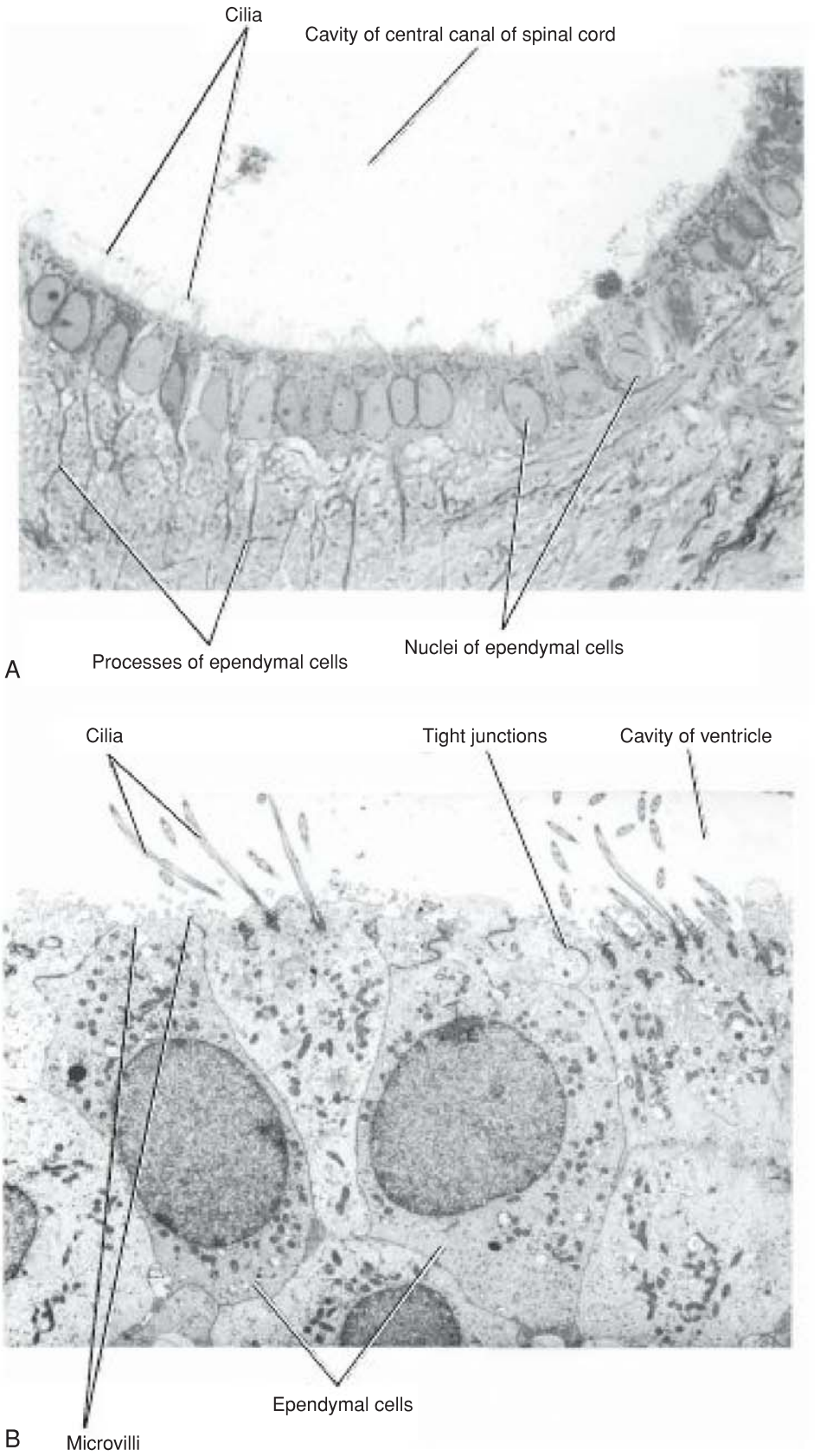

Figure 2-35 **A:** Photomicrograph of ependymal cells lining the central canal of the spinal cord. **B:** Electron micrograph of ependymal cells lining the cavity of the third ventricle. (Courtesy Dr. J. M. Kerns.)

Clinical Notes

General Considerations

The neuron is the basic functional unit of the nervous system. In the mature human, if it is destroyed by trauma or disease, it is not replaced. It is incapable of undergoing cell division.

The neuron consists of the cell body and its processes, the axons, and the dendrites. All three parts are concerned with the process of conduction. The cell body is necessary for the normal metabolism of all its processes. Should these processes become separated from the cell body as the result of disease or simple trauma, they will quickly degenerate. This would explain the necessity for the transport of macromolecules down the axon from the cell body and also emphasizes the dependence of the axon on the cell body. The rate of axoplasmic transport is insufficient to satisfy the release of transmitter substances at the nerve terminals. This problem is resolved in two ways. First, enzymes are present within the nerve terminals in order to synthesize the transmitters from amino acids derived from the extracellular fluid, and second, at some terminals, the transmitter is reabsorbed back into the terminal following its release. Clinically, drugs can influence this reuptake mechanism.

Neuroglial cells, in contrast to neurons, are nonexcitable and do not have axons; furthermore, axon terminals do not synapse on them. They are smaller than neurons and yet outnumber them 5 to 10 times. They comprise about half the total volume of the central nervous system (CNS).

Neuronal Reaction to Injury

The first reaction of a nerve cell to injury is loss of function. Whether the cell recovers or dies will depend on the severity and duration of the damaging agent. If death occurs quickly, such as in a few minutes from lack of oxygen, no morphologic changes will be immediately apparent. Morphologic evidence of cell injury requires a minimum of 6 to 12 hours of survival. The nerve cell becomes swollen and rounded off, the nucleus swells and is displaced toward the cell periphery, and the Nissl granules become dispersed toward the cytoplasm periphery. At this stage, the neuron could recover. If the kind of neuronal injury were not so severe as to cause death, the reparative changes would start to appear. The cell would resume its former size and shape, the nucleus would return to the center of the cell body, and the Nissl granules would take up their normal position.

When cell death is imminent or has just occurred, the cell cytoplasm stains dark with basic dyes (hyperchromatism), and the nuclear structure becomes unclear. The final stage occurs after cell death. The cytoplasm becomes vacuolated, and the nucleus and cytoplasmic organelles disintegrate. The neuron now is dissolved and removed by the activity of the phagocytes. In the CNS, this function is performed by the microglial cells; in the peripheral nervous system (PNS), this function is performed by local members of the reticuloendothelial system.

In chronic forms of injury, the size of the cell body is reduced, the nucleus and cytoplasm show hyperchromatism, and the nuclear membranes and those of the cytoplasmic organelles show irregularity.

Axonal Reaction and Axonal Degeneration

Axonal reaction and axonal degeneration are the changes that take place in a nerve cell when its axon is cut or injured. The changes start to appear within 24 to 48 hours after injury; the degree of change will depend on the severity of the injury to the axon and will be greater if the injury occurred close to the cell body. The nerve cell becomes rounded off and swollen, the nucleus swells and becomes eccentrically placed, and the Nissl granules disperse toward the cytoplasm periphery. These changes reach their maximum in about 12 days.

In the PNS, section of an axon is followed by attempts at regeneration, and reparative changes take place in the cell body.

In the CNS, degeneration is not followed by regeneration. If the corticospinal tracts, for example, are destroyed by disease, the nerve cells that give rise to these axons degenerate and disappear completely.

An important exception to the axonal reaction of nerve cells described above occurs in the nerve cells of the posterior root ganglia of the spinal nerves. If the peripheral axons are sectioned, the nerve cells show degenerative changes; if, however, the central axons are sectioned or destroyed by disease, such as tabes dorsalis, the nerve cells show no degenerative changes.

Axonal Transport and Disease Spread

Rabies, which is an acute viral disease of the CNS, is transmitted by the bite of an infected animal. The virus is present in the saliva of the infected animal; following a bite, it travels to the CNS by way of axonal transport in both sensory and motor nerves. The incubation period is related to the length of the peripheral nerve involved. The longer the nerve, the longer the duration of the incubation period. **Herpes simplex** and **herpes zoster** are viral diseases that also involve axonal transport to spread to different parts of the body. Axonal transport is also believed to play a role in the spread of the **poliomyelitis** virus from the gastrointestinal tract to the motor cells of the anterior gray horns of the spinal cord and the brainstem.

Neuron Tumors

Recall that the nervous system is made up of many different types of tissues: neurons, neuroglia, blood vessels, and meninges in the CNS and neurons, Schwann cells, connective tissue, and blood vessels in the PNS. Tumors of neurons in the CNS are rare, but tumors of peripheral neurons are not uncommon.

Neuroblastoma occurs in association with the suprarenal gland; it is highly malignant and occurs in infants and children. **Ganglioneuroma** occurs in the suprarenal medulla or sympathetic ganglia; it is benign and occurs in children and adults. **Pheochromocytoma** occurs in the suprarenal medulla; it is usually benign and gives rise to hypertension because it secretes norepinephrine and epinephrine.

Synaptic Blocking Agents

Transmission of a nervous impulse across a synapse is accomplished by the release of neurotransmitters into the synaptic cleft. Transmission occurs in one direction, and subthreshold stimulation of many synapses leads to summation. The released transmitter then exerts its effect on the postsynaptic membrane by increasing the permeability of the postsynaptic membrane to sodium and causing excitation or by increasing the permeability of the postsynaptic membrane to chloride and causing inhibition.

The synapse is a region in which transmission is easily blocked. As a general rule, long chains of neurons with multiple synapses are more easily blocked than shorter, simpler chains of neurons. General anesthetic agents are effective because they have the ability to block synaptic transmission.

At autonomic ganglia, preganglionic fibers enter the ganglia and synapse with the postganglionic sympathetic or parasympathetic neurons. The nerve impulse, on reaching the termination of the preganglionic nerve, brings about the release of **acetylcholine (ACh)**, which excites a nervous impulse in the postganglionic neuron.

Ganglionic blocking agents may be divided into three groups, depending on their mechanism of action. The first group of agents, which includes the **hexamethonium** and **tetraethylammonium salts**, resembles ACh at the postsynaptic membrane; thus, these agents inhibit transmission across a synapse. The second group of agents, which includes **nicotine**, has the same action as ACh on the postsynaptic membrane, but these agents are not destroyed by the cholinesterase. This results in a prolonged depolarization of the postsynaptic membrane; therefore, it is insensitive to further stimulation by ACh. Unfortunately, this depolarization block is associated with initial stimulation, so these drugs are not suitable for clinical use. The third group of agents, which includes **procaine**, inhibits the release of ACh from the preganglionic fibers.

In the CNS, demonstrating the release of a particular transmitter substance at specific synapses is difficult due to inaccessibility. For example, perfusing specific localized brain areas through their vascular system is impossible, and stimulating an isolated neuronal pathway within the brain or spinal cord is very difficult. The motor neuron collaterals to the Renshaw cells have been shown to liberate ACh at their endings. Many synapses in the CNS are also cholinergic. The development of monoclonal antibody techniques has opened a whole new approach to the identification and localization of chemical mediators in the CNS. Substance P, somatostatin, and cholecystokinin are a few examples of the neuropeptides that have been located here.

The nonuniform concentrations of norepinephrine in the CNS have led many investigators to believe that it might function as a central neurotransmitter. The concentrations are greater in gray matter than in white matter, and the highest concentrations are found in the hypothalamus. Dopamine is found in high concentrations in the CNS and is secreted by neurons that originate in the substantia nigra.

Many of the cholinergic blocking agents used in the PNS have little or no effect on CNS cholinergic synapses because they are unable to cross the blood–brain barrier in significant concentrations. **Atropine, scopolamine,** and **diisopropylphosphorofluoridate** (**DPF**) can effectively cross the barrier, and their effects on human behavior have been extensively studied. Similarly, many psychotropic drugs are believed to affect CNS activities by influencing the release of catecholamines at synaptic sites. The **phenothiazines**, for example, are thought to block dopamine receptors on postsynaptic neurons.

Treatment of Neurologic Disease by Neurotransmitter Manipulation

The increasing numbers of neurotransmitters being discovered in the CNS and the location of their site of action are raising the possibility that certain diseases can be modified by the administration of specific drugs. Huntington chorea, for example, involves loss of neurons that use GABA and ACh as transmitters. GABA is unable to cross the blood–brain barrier, but physostigmine, a cholinesterase inhibitor, can cross the barrier, and its use has brought about some improvement. The use of L-dopa in the treatment of parkinsonism has been most successful; in this disease, it replaces the deficiency of dopamine, which is normally released to the basal ganglia by the neurons of the substantia nigra.

Drugs are now rapidly being developed to modify the process of synaptic transmission in a number of ways: (1) by interfering with the process of neurotransmitter synthesis, (2) by inhibiting the uptake of drugs by the postsynaptic membrane, (3) by binding the neurotransmitter at the receptor site on the postsynaptic membrane, and (4) by terminating the neurotransmitter action.

Neuroglial Reactions to Injury

The reaction of neuroglial cells to injury, whether caused by physical trauma or by vascular occlusion, is characterized by the hyperplasia and hypertrophy of the astrocytes, which become fibrous irrespective of their antecedent morphology. The proliferation of the astrocytes is referred to as **astrocytosis** or **gliosis**. The loss of neuronal tissue is not compensated for in volume by the glial hypertrophy. The cytoplasm of the enlarged astrocytes contains large numbers of fibrils and glycogen granules. The dense feltwork of astrocytic processes that occurs in the areas of neuronal degeneration produces the so-called **gliotic scar**. The degree of gliosis is much greater in the presence of residual damaged neuronal tissue as compared with a clean surgical excision in which no traumatized brain remains. This is why, in patients with focal epilepsy due to a large gliotic scar, the scar is excised surgically, leaving a minimal glial reaction.

Oligodendrocytes respond to injury by expanding and showing vacuolation of their cytoplasm; the nuclei also tend to become pyknotic. Severe damage to oligodendrocytes results in demyelination.

Microglial cells in inflammatory and degenerative lesions of the CNS retract their processes and migrate to the site of the lesion. Here, they proliferate and are actively phagocytic, and their cytoplasm becomes filled with lipids and cell remnants. They are joined in their scavenger activity by monocytes that migrate from the neighboring blood vessels.

Microglial cells are active in a number of diseases including multiple sclerosis, dementia in AIDS, Parkinson disease, and Alzheimer disease.

Neuroglia Neoplasms

Tumors of neuroglia account for 40% to 50% of intracranial tumors. Such tumors are referred to as **gliomas**. Tumors of astrocytes are those most commonly encountered and include **astrocytomas** and **glioblastomas**. Apart from the ependymomas, tumors of the neuroglia are highly invasive. This explains the difficulty in achieving complete surgical removal and the great possibility of recurrence after surgery. Another feature is that as these tumors infiltrate, they often do so without interfering with the function of neighboring neurons. As a result, the tumor can be very much larger than the symptoms and physical signs would indicate.

Multiple Sclerosis

Multiple sclerosis is one of the most common CNS diseases, affecting about 250,000 Americans. It is characterized by the appearance of patches of demyelination in CNS white matter,

generally starting in the optic nerve, spinal cord, or cerebellum. The myelin sheaths degenerate, and the myelin is removed by microglial cells. Astrocytes proliferate, leading to the formation of a gliotic scar. As demyelination occurs, the conduction of the nerve impulses in the axons is impeded. Because raising the temperature shortens the duration of the action potential, one of the early signs of multiple sclerosis is that the symptoms and signs can be improved by cooling and made worse by heating by a hot bath. Most cases occur between the ages of 20 and 40 years. The cause of the disease is unknown, although an interplay between a viral infection and a host immune response may be responsible. For further discussion of this disease, see Chapter 4.

Cerebral Edema

Cerebral edema is a very common clinical condition that can follow head injuries, cerebral infections, or tumors. The resultant swelling of the brain may lead to flattening of the cerebral gyri, herniation of the brain through the tentorial notch or the foramen magnum, and even death.

Cerebral edema is an abnormal increase in the water content of CNS tissues and takes three forms. **Vasogenic edema** is the most common type and is due to the accumulation of tissue fluid in the extracellular space following damage to the vascular capillary walls or the presence of new capillaries without fully formed blood–brain barriers. It can result from infections, trauma, and tumors. **Cytotoxic edema** is due to the accumulation of fluid within the cells of nervous tissue (neurons and glial), resulting in cellular swelling. The cause may be toxic or metabolic and produces a failure in the plasma membrane ATP sodium pump mechanism. **Interstitial edema** occurs in obstructive hydrocephalus when the rise in cerebrospinal fluid (CSF) pressure forces the fluid out of the ventricular system into the extracellular space.

Two anatomical factors must always be remembered in cerebral edema: (1) the brain volume is restricted by the surrounding skull, and (2) the tissue fluid is drained primarily into the venous sinuses via cerebral veins because there is no lymphatic drainage.

Key Concepts

Neurons

- Neuron is the name given to the nerve cell and all its processes, including the cell body, dendrites, and axon.
- The number, length, and mode of branching allows for a morphologic method of classifying neurons.
- Unipolar neurons are those in which the cell body has a single neurite that divides into two branches, one on a peripheral structure and the other ending in the CNS.
- Bipolar neurons are those in which an elongated cell body has two neurites extending from each end.
- Multipolar neurons have many neurites arising from the cell body, only one of which is the axon.
- The neuron cell body is similar to other cells, consisting of a mass of cytoplasm in which a nucleus is embedded.
- The cytoplasm of a neuron contains Nissl substance, rough-surfaced endoplasmic reticulum arranged in the form of broad, stacked cisternae.
- Staining of the Nissl substance is often used to demonstrate neuronal cell bodies in histologic sections.
- Neurofilaments extend throughout the cell and form the cytoskeleton of the neuron.
- Microfilaments and microtubules are interspersed among the cytoskeleton and provide a stationary track for transport of organelles.
- Motor proteins, kinesin and dynein, move organelles through the neuron in a process called rapid transport.
- The plasma membrane of the cell forms a semipermeable membrane that allows diffusion of certain ions but restricts others, resulting in a steady negative potential inside the cell, compared to outside, called the resting potential.
- Excited cells, either by electrical, mechanical, or chemical means, will undergo a rapid change in permeability causing the negative membrane potential to rapidly depolarize, resulting in an action potential.
- The action potential will spread over the plasma membrane, away from the site of initiation, as a nerve impulse.

Neuroglia

- Neuroglia are small nonexcitable cells that greatly outnumber neurons.
- Neuroglia includes astrocytes, oligodendrocytes, microglia, and ependyma.

Astrocytes

- Fibrous and protoplasmic types form a supporting framework for nerve cells and nerve fibers.
- By covering the synaptic contacts between neurons, astrocytes serve as electrical insulators by preventing neighboring axons from influencing unrelated fibers.

Oligodendrocytes

- Oligodendrocytes are responsible for the formation of the myelin sheath of nerve fibers in the CNS.
- They have multiple processes and insulate fiber segments of multiple nerves.

Microglia

- Smallest of all the neuroglial types, microglia act as immune effector cells during inflammatory diseases.

Ependyma

- Ependyma is a single layer of columnar or cuboidal cells that assist in the circulation of the CSF within the cavities of the brain.
- Ependymocytes and tanycytes line the lateral and third ventricles, respectively. Choroidal epithelial cells cover the surface of the choroid plexus.

Clinical Problem Solving

1. During an operation for the repair of a sectioned radial nerve in the arm, the neurosurgeon understands that he is operating on a large bundle of nerve fibers supported by connective tissue. He realizes that the nerve fibers are either axons or dendrites or the nerve is made up of a mixture of axons and dendrites. What is your understanding of the composition of the radial nerve?
2. A well-known textbook of neurosurgery makes the following statements regarding the prognosis following peripheral nerve repair: (a) the younger the patient, the better the return of function; (b) the more distal the injury to a nerve, the more effective the regeneration; (c) the closer a lesion is to the nerve cell body, the more profound the effect on this trophic center; and (d) sensory nerve cells are affected more by this retrograde phenomenon than are motor nerve cells. Comment on these statements.
3. An 18-year-old male patient is examined by a neurosurgeon, 12 months after injury to the right forearm in which the median nerve is severed. At the initial operation, shortly after the injury has occurred, debridement is performed, and the separated nerve ends are tagged with radiopaque sutures. Unfortunately, the wound is infected, and surgical repair of the nerve is deferred. Is it practical to consider repairing a peripheral nerve after a delay of 12 months?
4. While examining a pathology specimen of nervous tissue under a microscope, the pathologist is able to determine the sex of the individual from whom the tissue had been removed. How would you be able to do this?
5. Axoplasmic flow is involved in the transport of certain viruses in the nervous system. What structures present in the cytoplasm of the neuron take part in this process?
6. About 1% of all deaths are due to intracranial tumors. Many different tissues are present within the skull in addition to the nervous system. Moreover, the nervous system itself is composed of many different types of tissues. In fact, tumors that arise as neoplasms of nerve cells and fibers are rare. Name the different types of tissues that are found in the central nervous system (CNS) and in the peripheral nervous system (PNS).
7. When a nerve cell is stimulated, the permeability of the plasma membrane changes, permitting certain ionic movements to take place across the membrane. (a) What is the structure of the plasma membrane? (b) Is the permeability of the plasma membrane increased or decreased when the nerve cell is stimulated? (c) What is the action of local analgesics on the cell membrane?
8. The synapse is a region where nervous transmission is easily blocked. Clinically, the ganglion-blocking drugs used act by competing with acetylcholine (ACh) released from the nerve endings in the ganglia. Name two groups of drugs that have been used for this purpose and indicate the site at which they act.
9. A 2-year-old boy is taken to a pediatrician because his mother has noticed that his right eye is protruding (proptosis). When questioned, the mother states that she had first noticed this protrusion 1 month previously and that it has progressively worsened since that time. The child is otherwise perfectly fit. On physical examination, the child is observed to be healthy in every respect except for the marked proptosis of the right eye. A careful palpation of the abdomen, however, reveals a large, soft mass in the upper part of the abdomen that extends across the midline. X-ray examination, including a computed tomography (CT) body scan, reveal a large, soft tissue mass that displaces the right kidney downward. A diagnosis of malignant tumor of the suprarenal or neighboring sympathetic nervous tissue, with metastases in the right orbital cavity, is made, the latter being responsible for the right-side proptosis. Name a tumor of the suprarenal gland or sympathetic nervous tissue that occurs commonly in children and may metastasize in the bones of the orbit.

10. At an autopsy, a third-year medical student is handed a slice of the cerebrum and is asked what proportion of central nervous tissue is made up by neuroglia. How would you have answered that question? Which cells are present in the largest numbers—neurons or neuroglial cells?
11. A 23-year-old man received a penetrating gunshot wound to the left side of his head while serving in the army. At the operation, the neurosurgeon was able to remove the bullet from the left frontal lobe of his brain. Apart from a slight weakness of his right leg, the patient makes an uneventful recovery. Eighteen months later, the patient starts to have severe generalized attacks of convulsions, during which he loses consciousness. Since this time, the attacks have occurred irregularly at about monthly intervals. Each attack is preceded by a feeling of mental irritability, and twitching of the right leg occurs. A diagnosis of epilepsy is made by the examining neurologist. Is it possible that this patient's attacks of epilepsy are related to his gunshot wound? Is traumatic epilepsy a common condition? What treatment would you recommend?
12. A 42-year-old woman visits her physician because she is suffering from very severe headaches. Until 6 months ago, she experienced only an occasional mild headache. Since that time, her headaches gradually have become more severe, and their duration has increased. They now last 3 to 4 hours and are so intense that she has to lie down. She has felt sick on two occasions, but she vomited only once. The headaches are generalized in nature and are made worse by coughing or straining. A physical examination reveals swelling of both optic discs with congestion of the retinal veins and the presence of multiple retinal hemorrhages. Weakness of the lateral rectus muscle of the right eye also is detected. Anteroposterior (A/P) radiographs of the skull show displacement of the calcified pineal gland to the left side. A/P and lateral radiographs of the skull show some degree of calcification in a localized area in the right cerebral hemisphere. These findings, together with those obtained from CT scans of the brain and magnetic resonance imaging (MRI), make the diagnosis of a right-sided cerebral tumor certain. Surgical exploration confirms the presence of a large infiltrating tumor of the right parietal lobe. What is the most common type of tumor found in such a site in a middle-aged patient? How would you treat such a patient?

Answers and Explanations to Clinical Problem Solving

1. The radial nerve is made up of nerve fibers derived from motor, sensory, and autonomic neurons. By definition, the nerve fibers, or nerve cell processes, are referred to as neurites (short ones are dendrites, and long ones are axons). Customarily, those that conduct the nervous impulse toward the cell body are referred to as the dendrites and those that conduct the impulses away from the cell body as the axons. However, in the case of the unipolar sensory neurons found in the posterior root ganglia, the neurite carrying nervous information toward the cell body has all the structural characteristics of an axon and is referred to as an axon. Thus, the radial nerve, which is composed of sensory and motor fibers, is made up of axons.
2. (a) As a general rule, all reparative phenomena throughout the body occur more readily in the young than in the old. (b) As the distal end of a peripheral nerve is approached, fewer branches remain, and thus there are fewer structures yet to innervate; consequently, fewer possibilities exist of nerve fibers innervating the wrong structure during the process of regeneration. Moreover, the more distal the injury, the less the metabolism of the proximal nerve cell body is affected by the injury. (c) This is a physiologic fact. A very severe nerve injury close to its nerve cell body may result in the death of the entire neuron. (d) The physiology of sensory neurons is more susceptible to change by retrograde phenomena than that of motor neurons.
3. If the wound is not infected, the best time to perform a nerve suture is about 3 weeks after the injury. Satisfactory results have been obtained after a delay of as much as 14 months, provided that paralyzed muscles have not been overstretched and joint adhesions have been avoided by passive movements of the joints. In other words, the neuron still retains the ability to regenerate its processes even after 14 months, but the degree of recovery of function will depend a great deal on the care that the denervated structures receive in the intervening time.
4. In 1949, Barr and Bertram noticed the presence of a small, stainable body of chromatin (Barr body) situated at the inner surface of the nuclear envelope in the female that could not be seen in the cells of the male. It is one of the two X chromosomes present in the female. The presence or absence of the Barr body enables one to readily determine the sex of the individual from whom the tissue was removed.
5. An electron microscope allows visualization of both small tubules that measure about 25 nm in diameter within a neuron's cytoplasm as well as microfilaments measuring about 3 to 5 nm in diameter. The possible role that these structures play in cell transport is discussed on page 43.
6. The CNS comprises (a) neurons, (b) neuroglia, (c) blood vessels, and (d) meninges. The PNS is composed of (a) neurons, (b) Schwann cells, (c) connective tissue, and (d) blood vessels.
7. (a) The structure of the plasma membrane is described on page 43. (b) When a neuron is excited, the permeability of the plasma membrane to Na^+ ions is increased, and these diffuse from the tissue fluid

into the neuron cytoplasm. (c) Local analgesics act as membrane stabilizers and inhibit the increase in permeability to Na^+ ions in response to stimulation. How this stabilization is brought about is not understood. One theory is that the analgesic agent becomes attached to receptor sites on the protein layer of the plasma membrane, reducing the permeability to Na^+ ions and preventing depolarization from taking place. Small-diameter nerve fibers are more readily blocked than large fibers, and nonmyelinated fibers are more readily blocked than myelinated ones. For these reasons, nerve fibers that conduct pain and temperature are most easily blocked, and the large motor fibers are the least easily blocked. The small autonomic nerve fibers are blocked early and account for the rapid appearance of vasodilatation.

8. Tetraethylammonium salts and hexamethonium salts are the two groups of drugs. These salts closely resemble ACh in structure and compete with ACh at the postsynaptic membrane. By this means, they successfully block a ganglion, although the amount of ACh released is unaffected.
9. The neuroblastoma is a tumor of primitive neuroblasts and arises either in the suprarenal medulla or in the upper abdominal sympathetic ganglia. It is malignant and confined to children. The tumor metastasizes early, and the metastasis may be the reason why the child receives medical attention, as in this case. The bones of the orbit are a common site for metastasis of a neuroblastoma.
10. Neuroglia comprises about half the total volume of the central nervous system. Neuroglial cells outnumber neurons by 5 to 10 times.
11. The reaction of tissue of the central nervous system to injury is characterized by astrocyte hyperplasia and hypertrophy. Astrocyte proliferation is referred to as astrocytosis or gliosis. The degree of gliosis is much greater in the presence of residual damaged brain tissue than with a clean surgical incision. The resulting scar tissue, the gliotic scar, in the case of a penetrating gunshot wound, may be extensive and may give rise to focal or generalized epileptic attacks. The majority of such patients who become epileptic do so within 2 years. After careful examination of these patients, including the performance of radiography, CT brain scans, MRIs, and electroencephalography, the trauma site should be explored with a view to removing the gliotic scar. Such a scar will be replaced by a much smaller surgical scar. This operative intervention cures many of these patients.
12. A history of severe headaches and nausea and the finding of a choked optic disc (swelling of the optic disc, congestion of the retinal veins, and retinal hemorrhages) are not always diagnostic of a brain tumor. However, the finding of weakness of the lateral rectus muscle of the right eye owing to compression of the right sixth cranial nerve against the floor of the skull, together with the positive results on radiologic and other laboratory tests, made the diagnosis certain. The glioma (tumor of neuroglia) is the most common type of tumor found in such a patient. Unfortunately, gliomas tend to infiltrate the brain tissue and cannot be completely removed surgically. Biopsy is performed to establish the diagnosis, as much of the tumor is removed as is clinically feasible, and the area is treated by deep x-ray therapy postoperatively. Survival time may also be increased by the use of chemotherapy.

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 the cytology of a neuron:
   (a) A unipolar neuron is one that gives rise to a single neurite that divides a short distance from the cell body into two branches, one proceeding to some peripheral structure and the other entering the central nervous system (CNS).
   (b) A bipolar neuron is one that has two neurites that emerge together from the cell body.
   (c) Nissl substance is found in the axon of a neuron.
   (d) The Golgi complex does not synthesize cell membranes.
   (e) Melanin granules are not found in the neurons of the substantia nigra.
2. The following statements concern the cytology of a neuron:
   (a) The protein molecules projecting from the surface of the microtubules take no part in rapid transport in axoplasm.
   (b) The protein molecules that extend through the full thickness of the plasma membrane of a neuron serve as sodium and potassium channels.
   (c) Strong experimental evidence suggests that the gates of the sodium and potassium channels are formed by actin molecules.
   (d) The size of the nucleolus in a neuron is unrelated to the volume of cytoplasm possessed by neurons.
   (e) A synapse is the site where two neurons come together and their membranes are in contact; interneuronal communication occurs.

3. The following statements concern the axon:
   (a) The initial segment of the axon is the first 500 μm after it leaves the axon hillock.
   (b) The nerve impulse generated by a neuron does not originate at the initial segment of an axon but on the dendrite.
   (c) The action potential is produced by the sudden influx of Na^+ ions into the cytoplasm.
   (d) Following the influx of Na^+ ions in the production of the action potential, the permeability for Na^+ ions increases further, and the permeability for K^+ ions ceases.
   (e) The spread of the action potential along the microtubules of the axon constitutes the nerve impulse.
4. The following statements concern a nerve impulse:
   (a) The refractory period is the duration of the nonexcitable state of the plasma membrane following the passage of a wave of repolarization.
   (b) Subthreshold stimuli, when applied to the surface of a neuron, cannot be summated.
   (c) Inhibitory stimuli are believed to produce their effect by causing an influx of K^+ ions through the plasma membrane of the neuron.
   (d) Hyperpolarization can be produced by causing an influx of K^+ ions through the plasma membrane.
   (e) The axolemma is the site of nerve conduction.
5. The following statements concern the structure of a synapse:
   (a) Synapses may be axodendritic, axosomatic, or axoaxonic.
   (b) The synaptic cleft is the space between the presynaptic and postsynaptic membranes and measures about 200 nm.
   (c) The subsynaptic web lies beneath the presynaptic membrane.
   (d) Presynaptic vesicles do not contain the neurotransmitter substance.
   (e) All neurons produce and release several types of transmitter substances at all their nerve endings.
6. The following statements concern a neuron:
   (a) Nerve fibers are the dendrites and axons of a neuron.
   (b) The volume of cytoplasm within the nerve cell body always far exceeds that found in the neurites.
   (c) Golgi type I neurons have very short axons.
   (d) Golgi type II neurons have very long axons.
   (e) Golgi type II neurons form the Purkinje cells of the cerebellar cortex.
7. The following statements concern the neuron organelles and inclusions:
   (a) Centrioles are not found in mature nerve cells.
   (b) Lipofuscin granules tend to disappear with age.
   (c) The Nissl substance fills the axon hillock but is absent from other areas of the cytoplasm.
   (d) Microfilaments contain actin and do not assist in cell transport.
   (e) Mitochondria are found in the dendrites and axons.
8. The following statements concern dendrites:
   (a) A dendrite conveys a nerve impulse away from the nerve cell body.
   (b) Dendritic spines are small projections of the plasma membrane that increase the receptor surface area of the dendrite.
   (c) The cytoplasm of dendrites does not contain ribosomes and agranular endoplasmic reticulum.
   (d) Most dendrites expand in width as they extend from the nerve cell body.
   (e) Dendrites rarely branch.
9. The following statements concern neuromodulators:
   (a) Neuromodulators may coexist with the principal (classic) transmitter at a single synapse.
   (b) They often diminish and shorten the effect of the principal transmitter.
   (c) They never act through a second messenger.
   (d) They have a brief effect on the postsynaptic membrane.
   (e) Acetylcholine (ACh) (muscarinic) is not a good example of a neuromodulator.
10. The following statements concern the neurobiology of neuron structures:
    (a) A lysosome is a membrane-bound vesicle covered with ribosomes.
    (b) A terminal bouton is the postsynaptic part of an axon.
    (c) A receptor is a protein molecule on the postsynaptic membrane.
    (d) Nissl substance is formed of the smooth-surfaced endoplasmic reticulum.
    (e) Microtubules provide a mobile track that allows specific organelles to move by molecular motors.
11. The following statements concern neuroglia:
    (a) Fibrous astrocytes are located mainly in the gray matter of the central nervous system (CNS).
    (b) Replacement gliosis follows the death of neurons in the CNS and is due to the proliferation of astrocytes.
    (c) Astrocytes are not involved in the absorption of γ-aminobutyric acid (GABA) secreted by the nerve terminals.
    (d) Oligodendrocytes are responsible for the formation of the myelin of nerve fibers in the peripheral nervous system (PNS).
    (e) A single oligodendrocyte can form, by means of its processes, only one internodal segment of myelin on the same axon.
12. The following statements concern the microglial cells:
    (a) Microglial cells resemble connective tissue mast cells.
    (b) Microglial cells are larger than astrocytes or oligodendrocytes.
    (c) Microglial cells migrate into the central nervous system (CNS) during adult life.
    (d) In the presence of damaged neurons, microglial cells become branched.
    (e) In degenerative lesions of the CNS, the circulating blood contributes cells to the population of microglial cells.

13. The following statements concern the ependymal cells:
    (a) Choroidal epithelial cells do not secrete cerebrospinal fluid (CSF).
    (b) Ependymocytes line the ventricular system but do not permit the CSF to enter the extracellular spaces of the nervous tissue.
    (c) Tanycytes have short, unbranched basal processes, many of which have endfeet placed on the capillaries of the median eminence.
    (d) The ependymal cells form a single layer, and many possess microvilli and cilia.
    (e) Ependymal cells are incapable of absorbing substances from the CSF.
14. The following statements concern the extracellular space:
    (a) The space is formed by the gaps between the neurons and not the gaps between the neuroglial cells.
    (b) The space surrounds the lymphatic capillaries present in the brain and spinal cord.
    (c) The space is not continuous with the subarachnoid space.
    (d) The space is filled with tissue fluid.
    (e) The space is not continuous with the synaptic cleft between two neurons.
15. The following statements concern tumors of neuroglia:
    (a) They form about 5% of all intracranial tumors.
    (b) Apart from the ependymomas, tumors of neuroglia grow slowly and are not highly invasive.
    (c) They commonly infiltrate between neurons, causing the minimum disturbance of function.
    (d) They are nonmalignant and easily removed surgically.
    (e) As they expand, they raise the intracranial pressure.
16. The following statements concern neuroglial cells:
    (a) They tend to be larger than nerve cell bodies.
    (b) Heat increases the action potential in an axon and reduces the signs and symptoms in multiple sclerosis.
    (c) Oligodendrocytes are found some distance away from nerve cell bodies and their neurites.
    (d) Multiple sclerosis is a disease involving the oligodendrocyte.
    (e) Like Schwann cells, oligodendrocytes are surrounded by a basement membrane.
17. The following general statements concern the neuroglial cells:
    (a) Microglial cells have straight processes with spinelike projections.
    (b) Astrocytes form a scaffold for developing neurons.
    (c) Oligodendrocyte processes are not continuous with the myelin sheaths.
    (d) Ependymal cells have no cilia on their free borders.
    (e) *Macroglia* is the term used to distinguish the larger oligodendrocytes from the smaller astrocyte.

Answers and Explanations to Review Questions

1. A is correct. A unipolar neuron is one that gives rise to a single neurite that divides a short distance from the cell body into two branches, one proceeding to some peripheral structure and the other entering the CNS (see Fig. 2-3). B. A bipolar neuron is one that gives rise to a neurite that emerges from each end of the cell body. The sensory ganglia of the vestibulocochlear nerve (eighth cranial nerve) possess bipolar neurons. C. Nissl substance is not found in the axon of a neuron but in the cell body of a neuron. D. The Golgi complex is important in the synthesis of cell membranes. E. Melanin granules are found in the neurons of the substantia nigra, and these neurons are responsible for the neurotransmitter dopamine.
2. B is correct. The protein molecules that extend through the full thickness of the plasma membrane of a neuron serve as sodium and potassium channels (see Fig. 2-21). A. The protein molecules projecting from the surface of the microtubules take part in rapid transport in axoplasm. C. The gates of the sodium and potassium channels are formed of protein molecules but not actin molecules. D. The large size of the nucleolus in a neuron is related to the very large volume of cytoplasm possessed by certain neurons. E. A synapse is the site where two neurons come into close proximity and where functional interneuronal communication occurs.
3. C is correct. The action potential within an axon is produced by the sudden influx of Na^+ ions into the cytoplasm (see Fig. 2-17). A. The initial segment of the axon is the first 50 to 100 μm after it leaves the axon hillock. B. The nerve impulse generated by a neuron does originate at the initial segment of an axon but not on the dendrite. D. Following the influx of Na^+ ions in the production of the action potential, the permeability for Na^+ ions ceases, and the permeability for K^+ ions increases; thus K^+ ions start to flow from the cell cytoplasm. E. The spread of the action potential along the plasma membrane of the axon constitutes the nerve impulse.
4. E is correct. The axolemma is the site of nerve conduction. A. The refractory period is the duration of the nonexcitable state of the plasma membrane following the passage of a wave of depolarization (see p. 45). B. Subthreshold stimuli, when applied to the surface of a neuron, can be summated. C. Inhibitory stimuli are believed to produce their effect by causing an influx of Cl^- ions through the plasma membrane of the neuron. D. Hyperpolarization can be produced by causing an influx of Cl^- ions through the plasma membrane.

5. A is correct. The synapses may be axodendritic, axosomatic, or axoaxonic (see Fig. 2-25). B. The synaptic cleft is the space between the presynaptic and postsynaptic membranes and measures about 20 nm. C. The subsynaptic web lies beneath the postsynaptic membrane. D. Presynaptic vesicles may contain the neurotransmitter substance (see Fig. 2-27). E. The majority of neurons produce and release only one principal transmitter at all their nerve endings.
6. A is correct. Nerve fibers are the dendrons and axons of a neuron. B. The volume of cytoplasm within the nerve cell body is often far less than the total volume of cytoplasm in the neurites. C. Golgi type I neurons have very long axons. D. Golgi type II neurons have very short axons. E. Golgi type I neurons form the Purkinje cells of the cerebellar cortex.
7. E is correct. Mitochondria are found in the dendrites and axons. A. Centrioles are found in mature nerve cells as well as in immature dividing nerve cells. B. Lipofuscin granules tend to accumulate with age. C. The Nissl substance is absent from the axon hillock. D. Microfilaments contain actin and probably assist in cell transport (see p. 42).
8. B is correct. Dendritic spines are small projections of the plasma membrane that increase the receptor surface area of the dendrite. A. A dendrite conveys a nerve impulse toward the nerve cell body (see p. 48). C. The cytoplasm of dendrites contains ribosomes and agranular endoplasmic reticulum as well as Nissl granules, microtubules, and microfilaments. D. Most dendrites taper in width as they extend from the nerve cell body. E. Dendrites often branch profusely.
9. A is correct. Neuromodulators may coexist with the principal (classic) transmitter at a single synapse (see p. 54). B. Neuromodulators often enhance and prolong the effect of the principal transmitter. C. Neuromodulators act through a second messenger. D. Neuromodulators may have a prolonged effect on the postsynaptic membrane. E. ACh (muscarinic) is a good example of a neuromodulator.
10. C is correct. A receptor is a protein molecule on the postsynaptic membrane. A. A lysosome is a membrane-bound vesicle that is not covered with ribosomes. B. A terminal bouton is the presynaptic part of an axon. D. Nissl substance is formed of the rough endoplasmic reticulum. E. Microtubules provide a stationary track that allows specific organelles to move by molecular motors.
11. B is correct. Replacement gliosis follows the death of neurons in the CNS and is due to the proliferation of astrocytes (see p. 57). A. Fibrous astrocytes are located mainly in the white matter of the CNS. C. Astrocytes are involved in the absorption of GABA as it is secreted by the nerve terminals. D. Oligodendrocytes are responsible for the formation and maintenance of the myelin of nerve fibers in the CNS (see p. 58). E. Unlike Schwann cells in the PNS, a single oligodendrocyte can form, by means of its many processes, several internodal segments of myelin on the same or different axons.
12. E is correct. In degenerative lesions of the CNS, the circulating blood contributes cells to the population of microglial cells. A. Microglial cells resemble connective tissue macrophages. B. Microglial cells are smaller than astrocytes or oligodendrocytes (Fig. 2-28). C. Microglial cells migrate into the CNS during fetal life. D. In the presence of damaged neurons, microglial cells round off, lose their branches, and increase in number.
13. D is correct. The ependymal cells form a single layer, and many possess microvilli and cilia (see p. 60). A. Choroidal epithelial cells secrete CSF. B. The ependymocytes line the ventricular system but permit CSF to enter the extracellular spaces of the nervous system. C. Tanycytes have long, branching basal processes, many of which have endfeet placed on the capillaries of the median eminence. E. Ependymal cells absorb substances from the CSF.
14. D is correct. The extracellular space is filled with tissue fluid. A. The extracellular space is formed by the gaps between the neurons and the neuroglial cells (see p. 60). B. The central nervous system does not have lymphatic vessels. C. The extracellular space is in almost direct continuity with the subarachnoid space. E. The extracellular space is continuous with the synaptic cleft between two neurons.
15. E is correct. As neuroglial tumors expand, they raise the intracranial pressure. A. Neuroglial tumors form about 40% to 50% of all intracranial tumors. B. Apart from the ependymomas, tumors of neuroglia are highly invasive. C. Neuroglial tumors commonly infiltrate between neurons, initially causing the minimum disturbance of function; later, they completely disrupt neuronal activities. D. Neuroglial tumors, apart from ependymomas, are highly malignant and difficult to remove surgically.
16. D is correct. Multiple sclerosis is a disease involving the oligodendrocyte (see pp. 63–64). A. Neuroglial cells tend to be smaller than nerve cell bodies. B. Heat reduces the action potential in an axon and accentuates the signs and symptoms in multiple sclerosis. C. Oligodendrocytes are found close to nerve cell bodies and their neurites. E. Unlike Schwann cells, oligodendrocytes are not surrounded by a basement membrane.
17. B is correct. Astrocytes form a scaffold for developing neurons. A. Microglial cells have wavy processes with spinelike projections. C. Oligodendrocyte processes are continuous with the myelin sheaths. D. Ependymal cells have cilia on their free borders. E. *Macroglia* is the collective term sometimes used to describe astrocytes and oligodendrocytes as distinct from the smaller microglial cells.

3 Nerve Fibers and Peripheral Innervation

CHAPTER OBJECTIVES

- To consider the basic structure and function of nerve fibers
- To understand the process of nerve degeneration and regeneration
- To review the special organs that lie at the ends of sensory and motor nerves
- To examine the different sensory modalities
- To learn the terms used in assessing skin sensory loss and abnormal muscle activity

A 45-year-old man is recovering from a mild upper respiratory tract infection when he suddenly notices weakness in both legs while walking upstairs. He also develops a numb sensation over the lower part of both legs and feet. Two days later, while shaving, he notices weakness of the muscles on the right side of his face.

On physical examination, the patient does not appear to be ill. He has no pyrexia. Examination of his leg muscles shows obvious signs of muscle weakness involving both legs, especially below the knees. Both ankle reflexes are absent, and the right knee jerk is diminished. He has sensory deficits for touch and pain sensations in the distribution of the stocking area of both feet and lower legs and a mild form of facial nerve palsy involving the right side of the face. Neurologic evidence of loss of function of the brain or spinal cord is not present.

The patient is suspected of having Guillain–Barré syndrome and is admitted to the hospital for observation. The cause of this disease is unknown, although it is believed to be viral and involves the immune system. Histologically, the peripheral nerves show focal scattered areas of demyelination with an accumulation of lymphocytes and macrophages. As the myelin is lost, the axons are left naked, and the Schwann cell bodies remain intact. In the majority of patients, recovery occurs in 2 to 4 weeks with nerve remyelination. Hospitalization is necessary in the early stages because the disease can spread rapidly to involve the intercostal and phrenic nerves, resulting in paralysis of the intercostal muscles and diaphragm. For the same reason, the coughing and swallowing reflexes should be watched carefully. A clinician would find this disease impossible to understand without knowledge of peripheral nerve structure.

In this chapter, the process of nerve degeneration and regeneration is described in detail because nerve lesions are very common in clinical practice and can be caused by a wide variety of diseases, including trauma, neoplasms, infection, metabolic dysfunction (diabetes), and chemical toxins such as lead. The process of nerve degeneration is fast and can take place in nerves in the central and peripheral nervous systems. The regeneration of nerves is slow and confined to the peripheral nervous system (PNS). Because so much research today is being devoted to investigating why regeneration in the central nervous system (CNS) ceases within 2 weeks, the histologic changes that occur must be learned.

The material in this chapter commonly forms the basis for examination questions.

NERVE FIBERS

Nerve fiber is the name given to an axon (or a dendrite) of a nerve cell. The structure of axons and dendrites is described on page 33–34. Bundles of nerve fibers found in the CNS are referred to as **nerve tracts** (Fig. 3-1); bundles of nerve fibers found in the PNS are called **peripheral nerves** (Fig. 3-2).

Two types of nerve fibers are present in the CNS and PNS: myelinated and nonmyelinated.

Myelinated Nerve Fibers

A myelinated nerve fiber is one that is surrounded by a myelin sheath. The myelin sheath is not part of the neuron but is formed by a supporting cell (Fig. 3-3;

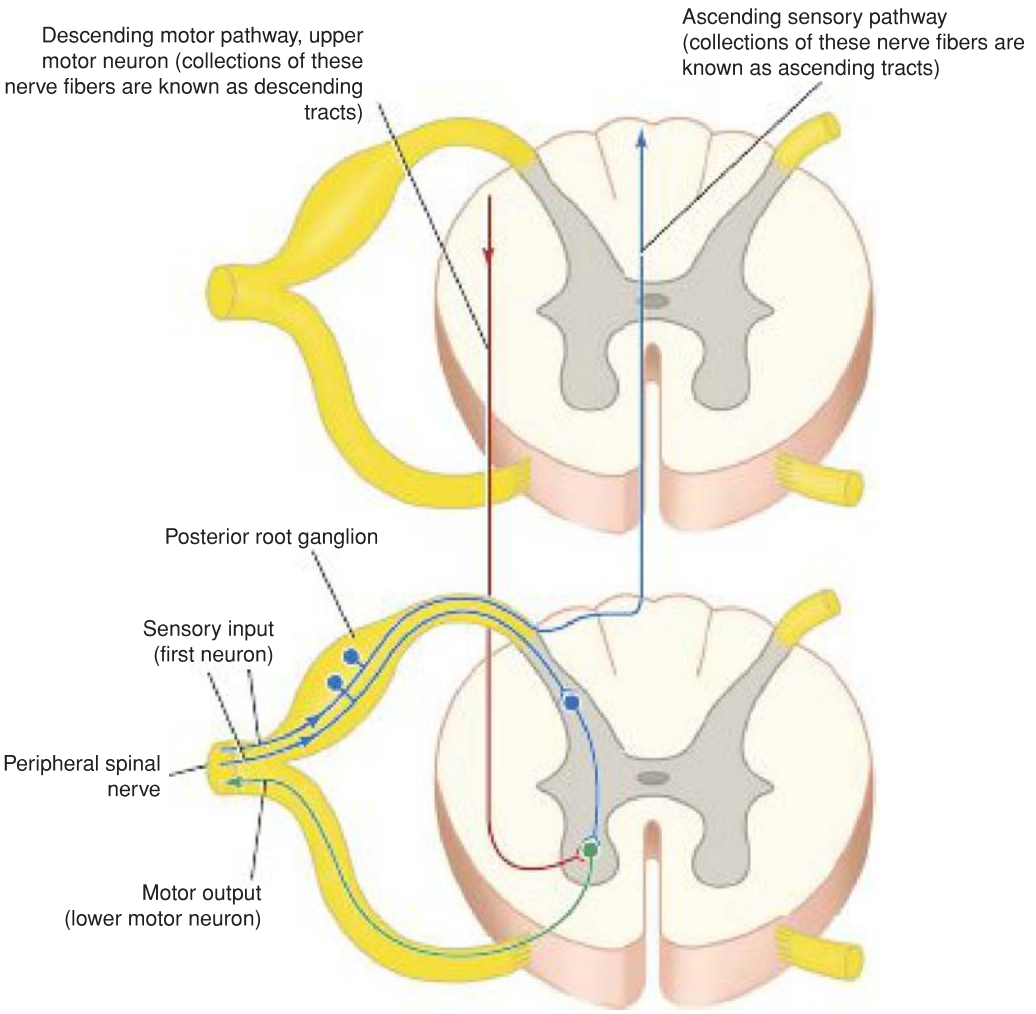

Figure 3-1 Sections through the thoracic region of the spinal cord showing examples of nerve fibers entering or leaving the central nervous system; ascending and descending nerve fibers (tracts or pathways) are also shown.

also see Fig. 3-2). In the CNS, the supporting cell is called the **oligodendrocyte**; in the PNS, it is called the **Schwann cell**.

The myelin sheath is a segmented, discontinuous layer interrupted at regular intervals by the **nodes of Ranvier** (Figs. 3-4 and 3-5). Each segment of the myelin sheath measures approximately 0.5 to 1.0 mm in length. In the CNS, each oligodendrocyte may form and maintain myelin sheaths for as many as 60 nerve fibers (axons). In the PNS, only one Schwann cell maintains each segment of one nerve fiber.

Myelin Formation

Myelin sheaths begin to form before birth and during the first year postnatally. The process has been studied with the electron microscope (Fig. 3-6).

In the **peripheral nervous system** (**PNS**), the nerve fiber or axon first indents the side of a Schwann cell (Fig. 3-4). Later, as the axon sinks farther into the Schwann cell, the external plasma membrane of the Schwann cell forms a **mesaxon**, which suspends the axon within the Schwann cell (Fig. 3-6A). Subsequently, the Schwann cell is believed to rotate on the axon so that the plasma membrane becomes wrapped around the axon in a spiral. The direction of the spiral is clockwise in some segments and counterclockwise in others. To begin with, the wrappings are loose, but gradually the cytoplasm between the layers of the cell membrane disappears, leaving cytoplasm near the surface and in the region of the nucleus. The wrappings become tight with maturation of the nerve fiber. The thickness of the myelin depends on the number of spirals of Schwann cell membrane. Some nerve fibers are surrounded by only a few turns of the membrane, while others have as many as 50 turns. In electron micrographs of cross sections of mature myelinated nerve fibers, the myelin is seen to be laminated. Each lamella measures 13 to 18 nm thick. The dark **major dense line**, about 2.5 nm thick, consists of two inner protein layers