GLOBAL EDITION

Principles of Human Physiology

SIXTH EDITION

Cindy L. Stanfield

Pearson

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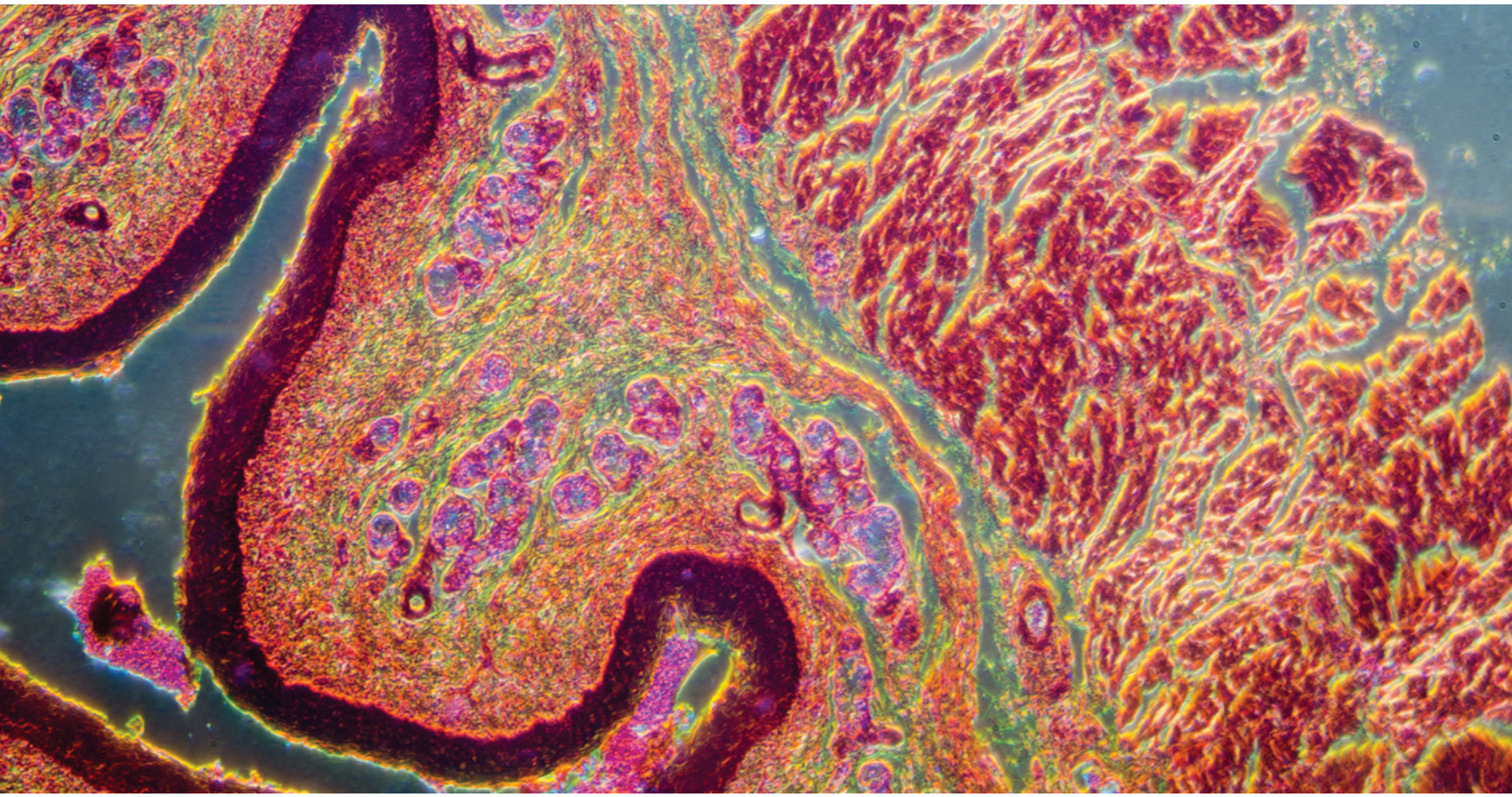

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Objective Questions

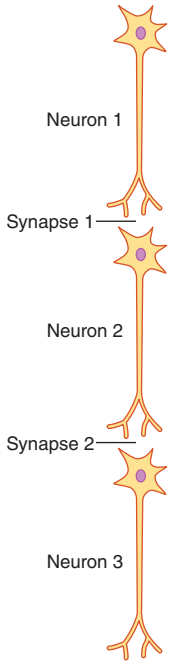
11. At electrical synapses, which type of junction exists between the two cells?
12. Signaling across both chemical and electrical synapses is bidirectional. (true/false)
13. Most of the synapses in the nervous system are (chemical/electrical) synapses.
14. Whether a synapse is excitatory or inhibitory is determined by the mechanism of coupling between the neurotransmitter receptor and ion channels in the postsynaptic cell. (true/false)
15. The synaptic delay includes the time it takes for an action potential to travel from the trigger zone of a presynaptic cell to the axon terminal. (true/false)
16. A given neurotransmitter might be excitatory at one synapse and inhibitory at another synapse. (true/false)
17. Given that release of an inhibitory neurotransmitter is altered by presynaptic facilitation, the response in the postsynaptic cell will be a (larger/smaller) degree of hyperpolarization.
18. Neurotransmitters are released from axon terminals by (endocytosis/exocytosis).
19. The enzymes that catalyze the degradation of catecholamines are _____ and _____.
20. Adenylate cyclase catalyzes the formation of _____.

Essay Questions

21. Describe the sequence of events occurring at a chemical synapse, starting with an action potential in the presynaptic cell and ending with a response in the postsynaptic cell.
22. Compare the fast and slow responses that can be induced by a neurotransmitter in a postsynaptic neuron.
23. Explain the ionic basis of a fast EPSP.
24. Explain the role of axoaxonic synapses.
25. Describe the steps of the cAMP second messenger system. Explain how cAMP can produce different responses in the many different types of cells that use cAMP as a second messenger.

Critical Thinking

Questions 26–28: The accompanying diagram depicts three neurons in a neural pathway in which neuron 1 synapses on neuron 2, and neuron 2 synapses on neuron 3. Neuron 1 can be artificially activated through a stimulating electrode that passes current across the membrane. The membrane potentials of all three neurons are recorded by an intracellular electrode connected to a voltmeter. The voltage tracings in questions 26 and 28 are of membrane potential (V_{m1} for cell 1, and so on). Action potentials are shown as vertical spikes; the horizontal bar over the voltage tracing indicates the time period during which the stimulating electrode was turned on.

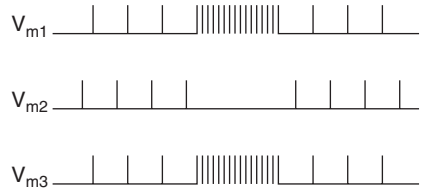


26. From this voltage tracing for cell 1, one can conclude that

a) The stimulation depolarizes the cell membrane.
b) The stimulation hyperpolarizes the cell membrane.
c) The stimulation has no effect on the cell membrane potential.
d) The stimulation mimics the effect of an inhibitory neurotransmitter.

27. If you were to observe an increase in action potential frequency in cell 2 during stimulation of cell 1, you could conclude that
a) Synapse 1 is excitatory.
b) Synapse 1 is inhibitory.
c) The findings are inconclusive.

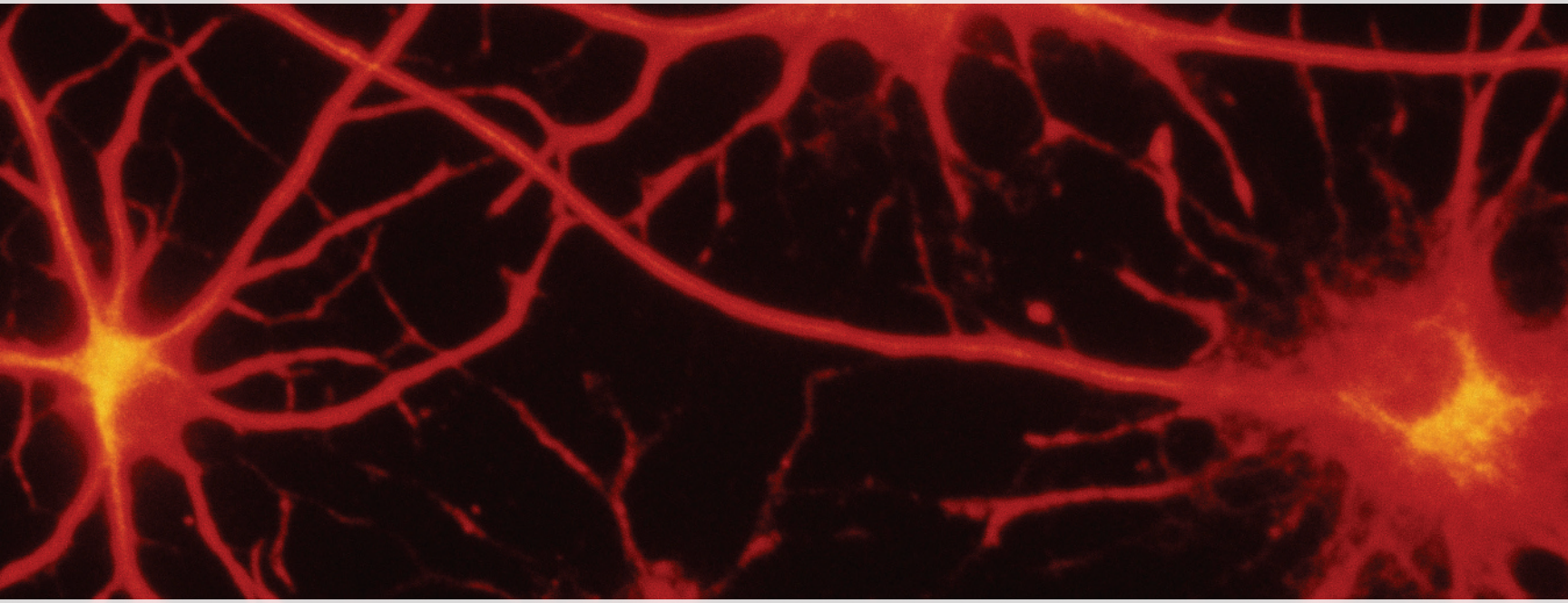
28. Given the following results, what would your conclusion be?



a) Synapse 1 is excitatory, whereas synapse 2 is inhibitory.
b) Synapse 1 is inhibitory, whereas synapse 2 is excitatory.
c) Synapses 1 and 2 are both inhibitory.
d) Synapses 1 and 2 are both excitatory.
e) No definite conclusion is possible.

29. Alzheimer's disease affects memory and cognitive function due to a loss of cholinergic neurons in certain areas of the brain. Propose a treatment strategy based on what you learned in this chapter.

9 The Nervous System: Central Nervous System



Fluorescent micrograph of neurons.

As you read this, your central nervous system is performing many tasks, including perceiving words on the page, comprehending them, and making judgments about their importance and whether they should be stored in memory. As you read further, you may start integrating information with previous memories or thoughts. However, if you are reading this late at night, you might be sleepy and doze off; tomorrow, you may recall little of what you read. In any case, what happens as you read is a consequence of central nervous system processing.

One of the things that makes the nervous system so fascinating is that most of its functions are carried out by neurons. Since all neurons operate according to a small set of principles, how can they be responsible for all of the nervous system's many complexities? How are neurons involved when you feel angry? How can neurons enable you to remember someone's name or how the heart works? One neuron alone can perform none of these functions, but when billions of neurons (and the glial cells associated with them) are organized to form the nervous system, they can handle these and thousands of other functions.

CHAPTER OUTLINE

LEARNING OUTCOMES *After studing this chapter, you should be able to:*

- Describe the anatomy of the brain and spinal cord, and relate structure to function.
- Indicate which structures protect the central nervous system and which are involved in neural signaling.
- Describe the anatomy, physiology, and consequences of the blood-brain barrier.
- Describe the energy supplies of the brain, and explain why blood flow is so critical.
- Define *reflex arc*. Describe the following reflex pathways: muscle spindle stretch reflex, withdrawal reflex, and crossed-extensor reflex.
- Describe the areas of the brain that contribute to voluntary control of skeletal muscles, and the basic roles these areas play.
- Describe the different functions of the two language centers: Wernicke's area and Broca's area.
- Describe the different stages of sleep, and explain how the brain shifts from the sleep state to the conscious state.
- Describe the different types of learning and memory. Define *neural plasticity,* and explain how it contributes to learning and memory.

Before You Begin

Make sure you have mastered the following topics:

- Tight junctions, p. 70
- Organization of the nervous system, p. 197
- Neurotransmitters, p. 237
- Neuron structure, p. 198
- Communication at synapses, p. 227
- Neural integration, p. 233

So far, we have learned about electrical signaling in neurons (in Chapter 7) and chemical signaling from one neuron to another at synapses (in Chapter 8). Amazingly, the nervous system—with all its myriad complexities—functions primarily through these two basic processes. In this chapter, we learn how chains of neuron-to-neuron connections *(neural pathways)* allow the central nervous system to carry out its numerous functions.

The central nervous system is ultimately responsible for everything we perceive, do, feel, and think. It gives each of us our unique personality and sense of self-identity. It also performs many critical functions that typically escape our notice. For example, it coordinates the activities of all our organ systems, a function that is necessary for the maintenance of homeostasis. It is estimated that the central nervous system contains approximately 100 billion (10^{11}) neurons and 100 trillion (10^{14}) synapses, all contained within two remarkable structures, the brain and the spinal cord.

Scientists are continuing to unravel the mysteries of the brain even as you read these words. Because the brain is so complex and its functions so difficult to fathom using current scientific methodology, much of what you will read in this chapter comprises the commonly accepted portions of a constantly developing theory of central nervous system function. Perhaps someday we will understand the brain as well as we understand, say, the lungs or the kidneys. For now, we begin by examining the anatomy of the central nervous system.

9.1 General Anatomy of the Central Nervous System

The central nervous system (CNS) consists of the brain and the spinal cord. Because it is made up of soft tissue, with a consistency much like Jell-O, it is particularly vulnerable to damage by physical trauma. Fortunately, the CNS is protected by glial cells, bone, connective tissue, and cerebrospinal fluid, all of which are described in this section.

Glial Cells

When we think of the nervous system, we think of neurons. In reality, 75–90% of the central nervous system is composed of glial cells (or *neuroglia*), nonexcitable cells that provide support to neurons. The role of glial cells in neural communication, however, may go beyond simple support. For example, the higher up the organism is on the evolutionary scale, the more glial cells in the brain. Thus humans have more glial cells than any other animal.

There are four types of glial cells: Schwann cells, oligodendrocytes, microglia, and astrocytes (**Figure 9.1**). Astrocytes are by far the most abundant of the four types. All of the glial cells release growth factors necessary for development and maintenance of the nervous system. In addition, recent studies suggest that glial cells, even though they are nonexcitable cells, communicate with neurons and with each other. The myelin-forming function of Schwann cells and oligodendrocytes was described earlier (in Chapter 7). Here we discuss the function of astrocytes and microglia.

Astrocytes

Astrocytes, which are so named because of their star-like appearance, are the most diverse and numerous of the glial cells. Although astrocytes surround neurons with gaps of only 20 nm between cells, they do not overlap one another; that is, each cell remains in its own "territory." Some astrocytes, however, are connected by gap junctions, which can facilitate protection of neural tissue as described below. In disease states, however, gap junctions can enhance the spread of the disease. Astrocytes form a structural and functional link between neurons and non-nervous tissue and extracellular fluid. They direct the development of special capillaries that restrict the movement of certain molecules between blood and the CNS, called the *blood-brain barrier*. Astrocytes guide developing neurons, especially neurites, to their correct destination and regulate the development and maintenance of synapses. They may also support the regeneration of damaged axons.

Astrocytes are critical to the maintenance of the normal extracellular environment surrounding neurons, especially at synapses. They play an especially important role in maintaining normal extracellular potassium levels—a state that is critical to neuron excitability. Astrocytes also remove certain neurotransmitters,

Functional Fact

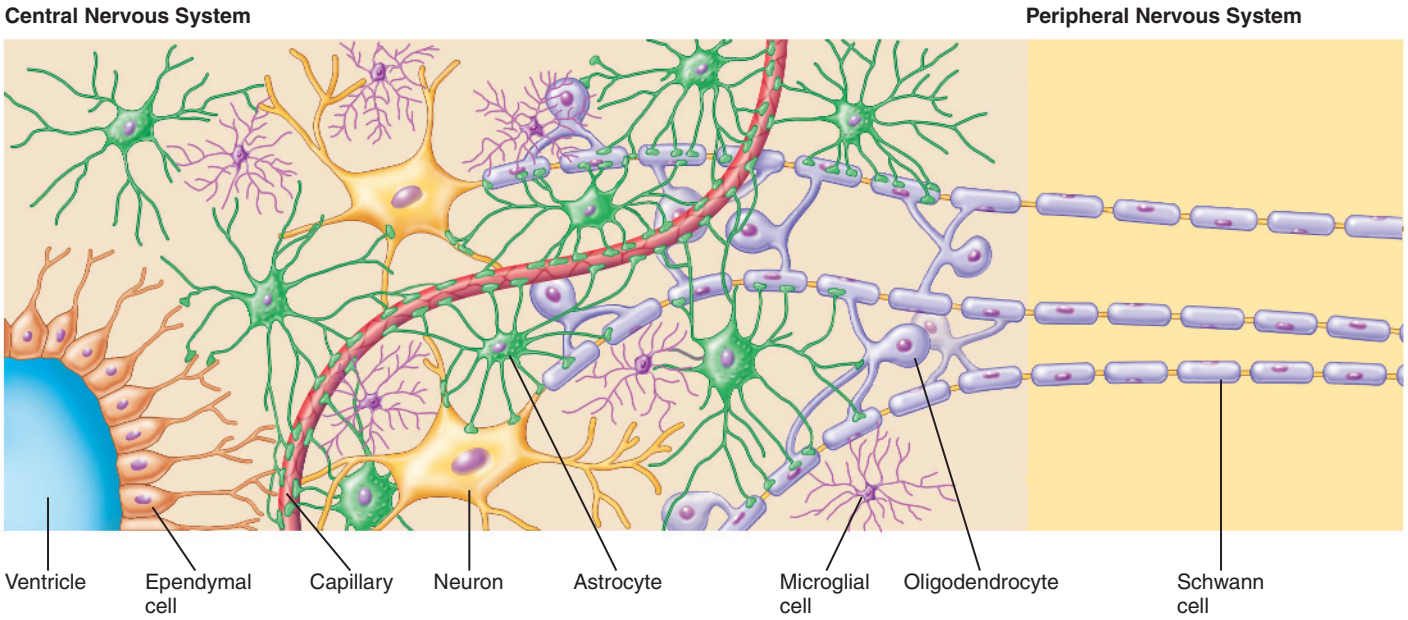


Figure 9.1 Glial cells in the nervous system.

such as glutamate and biogenic amines, from the synaptic cleft. Excess levels of glutamate are toxic and contribute to the spread of neurological damage during a stroke or other types of brain damage.

Astrocytes synthesize and store molecules for use by neurons. For example, they synthesize glutamine, which is then released into the interstitial fluid and picked up by other neurons to form glutamate, an excitatory neurotransmitter. Astrocytes store some glycogen, which can be broken down to lactate; the lactate is then transported to neurons, where it serves as an important energy source for active areas of the brain.

Finally, recent studies suggest that astrocytes function in conjunction with *microglia,* described next, to protect neurons from toxic substances. Specifically, astrocytes protect neurons from oxidative stress and help remove cellular debris (see **Clinical Connections: Glial Cells in Neurodegenerative Disorders**).

CLINICAL CONNECTIONS

Glial Cells in Neurodegenerative Diseases MAP

A growing body of evidence suggests that glial cells may contribute to the development of neurodegenerative diseases such as multiple sclerosis, Alzheimer's disease, and Parkinson's disease.

Multiple sclerosis results from the loss of myelin in the central nervous system. Multiple sclerosis is an autoimmune disease, meaning that the immune system attacks a part of the body—in this case, oligodendrocytes. The loss of myelin (and some axons) in the central nervous system slows down or stops communication along certain neural pathways. Symptoms of multiple sclerosis include blurred vision, muscle weakness, and difficulty maintaining balance. (Multiple sclerosis is described in more detail in Chapter 23.)

Alzheimer's disease is caused by the loss of cholinergic neurons in certain brain areas and the replacement of the lost neurons with scar tissue called *plaques*. During the degeneration of cholinergic neurons, astrocytes and microglia become overly active. These glial cells release inflammatory chemicals that enhance further degeneration of cholinergic neurons. Thus a vicious cycle takes place. Early signs of Alzheimer's disease include loss of memory and confusion; later signs include motor dysfunction, loss of communication skills, and decrease in cognitive functions. Treatment options for this disease are limited, chiefly because it is difficult to diagnose the disease before it reaches an advanced stage. Early stages may be treated with acetylcholinesterase inhibitors, but these agents are not effective in advanced Alzheimer's disease.

Parkinson's disease is a degenerative disease involving the loss of dopaminergic neurons. As in Alzheimer's disease, glial cells are thought to enhance neural degeneration through the production of inflammatory agents.

Critical Thinking Questions

1. Describe the symptoms and causes of multiple sclerosis, Alzheimer's disease, and Parkinson's disease.
2. What are the main areas of commonality between these three diseases?
3. What are the key differences between these three diseases?

Microglia

Microglia protect the central nervous system from foreign matter, such as bacteria and remnants of dead or injured cells. They carry out this function through detection of foreign matter, and then by attacking that matter via phagocytosis and the release of certain cytokines, similar to what you will learn about certain white blood cells in chapter 15. Microglia also protect neurons against oxidative stress.

Physical Support of the Central Nervous System

The two outermost structures that protect the soft tissues of the central nervous system are the bony skull, or **cranium,** which surrounds the brain, and the bony **vertebral column,** which surrounds the spinal cord (**Figure 9.2**). Even though these bony structures are clearly beneficial in that they act as rigid armor surrounding delicate nervous tissue, their hardness also poses a potential hazard: What would prevent the soft brain from crashing into the hard inner surface of the skull when, for example, you make a sudden stop in a car moving at freeway speeds? Between the bone and the nervous tissue are a series of three membranes called the meninges and a layer of fluid called cerebrospinal fluid, which provide protection against such impact.

The **meninges** are three connective tissue membranes that separate the soft tissue of the CNS from the surrounding bone (see Figure 9.2). The three meningeal membranes are the **dura mater,** the **arachnoid mater,** and the **pia mater**. *Mater* is Latin for "mother," indicating the protective nature of the meninges. The dura mater is the outermost layer, closest to the bone. *Dura* is Latin for "hard and durable"—an apt name given that the dura mater is a very tough, fibrous tissue that is almost the consistency of leather. The arachnoid mater is the middle layer. *Arachnoid,* Greek for "spider," appropriately describes the arachnoid mater's weblike structure. Normally, no space exists between the dura and the arachnoid. In fact, if a blood vessel passing through the dura ruptures, then blood can accumulate between the dura and arachnoid maters, forming a *subdural hematoma*. The innermost layer of the meninges, the pia mater, is located immediately adjacent to the nervous tissue; *pia* is Latin for "tender and kind." The space between the pia mater and arachnoid mater, called the **subarachnoid space,** is filled with cerebrospinal fluid.

Cerebrospinal fluid (CSF) is a clear, watery fluid that bathes the CNS; it is similar (but not identical) in composition to plasma (**Table 9.1**). CSF completely surrounds the CNS and fills a number of cavities located within the brain and spinal cord. The brain contains four such cavities, called **ventricles,** which are continuous with one another. Two C-shaped *lateral ventricles* are connected to a midline *third ventricle* by the *interventricular foramen*. The *cerebral aqueduct* connects the third ventricle to the *fourth ventricle*, which is continuous with the **central canal,** a long thin cylindrical cavity that runs the length of the spinal cord (**Figure 9.3**). The lining of the ventricles and central canal is composed of epithelial cells called **ependymal cells.**

The vascularized lining of the ventricles forms a tissue called the **choroid plexus,** which consists of the pia mater, capillaries, and ependymal cells, and functions in the synthesis of CSF. The total volume of CSF is only 125–150 mL, but because it is recycled approximately three times per day, the choroid plexus must produce 400–500 mL/day. As CSF is produced, it circulates through the ventricular system and enters the subarachnoid space through openings of the fourth ventricle. The CSF in the subarachnoid space is eventually reabsorbed into venous blood through special structures in the arachnoid mater called *arachnoid villi* (singular: *villus;* see Figure 9.2b) located at the top of the brain.

Apply Your Knowledge

Hydrocephalus occurs when an increase in cerebrospinal fluid causes the ventricles to become enlarged. Based on the preceding description of the ventricular system, describe a mechanism whereby CSF levels might increase.

CSF has several functions in the brain. It acts as a shock absorber that prevents the soft nervous tissue from colliding with the hard bone of the skull, because the CNS essentially floats in CSF. CSF also functions as the interstitial fluid that bathes neurons and glial cells, providing these cells with essential nutrients and removing waste products from them. The CSF contributes to the maintenance of normal ionic composition around neurons, which is essential for normal excitability of neurons. For the CSF to carry out its metabolic functions, it must be replenished by the blood supply to the CNS, as described next.

Blood Supply to the Central Nervous System

Although the CNS accounts for only some 2% of body weight (the adult brain and spinal cord weigh approximately 3–4 pounds), it receives almost 15% of the blood that the heart pumps to all of the body's organs and tissues under resting conditions. This large blood supply is necessary because CNS tissue has a high rate of metabolic activity compared to most other body tissues and, therefore, has a high demand for glucose and oxygen to meet its energy needs. Under resting conditions, for example, the brain accounts for approximately 20% of all oxygen that the body consumes, and approximately 50% of all glucose consumed. To ensure delivery of these needed materials, adequate blood flow to the CNS must be maintained at all times. In fact, the CNS is so dependent on this blood supply that disruption of blood flow for even a few minutes can result in irreversible damage to CNS tissue. A reduction of blood flow to a particular area of the CNS can cause deficits in certain functions, such as the ability to speak or move an arm. Such changes in function might occur, for example, following a *stroke*—an event in which blood flow becomes interrupted because of a blocked or ruptured blood vessel in the brain (see **Clinical Connections: Stroke,** p. 251).

Functional Fact

The CNS is particularly sensitive to interruptions in blood flow because cells in the CNS contain very little glycogen (compared to muscle and liver) and, therefore, must obtain glucose directly from the blood. Furthermore, most cells in the CNS do not have access to fatty acids for energy, which increases their demand for glucose. (Recall that oxidation of a single fatty acid molecule can yield as much energy as the oxidation of several molecules of glucose.) Finally, whereas many other tissues can obtain energy from anaerobic metabolism during periods of reduced oxygen

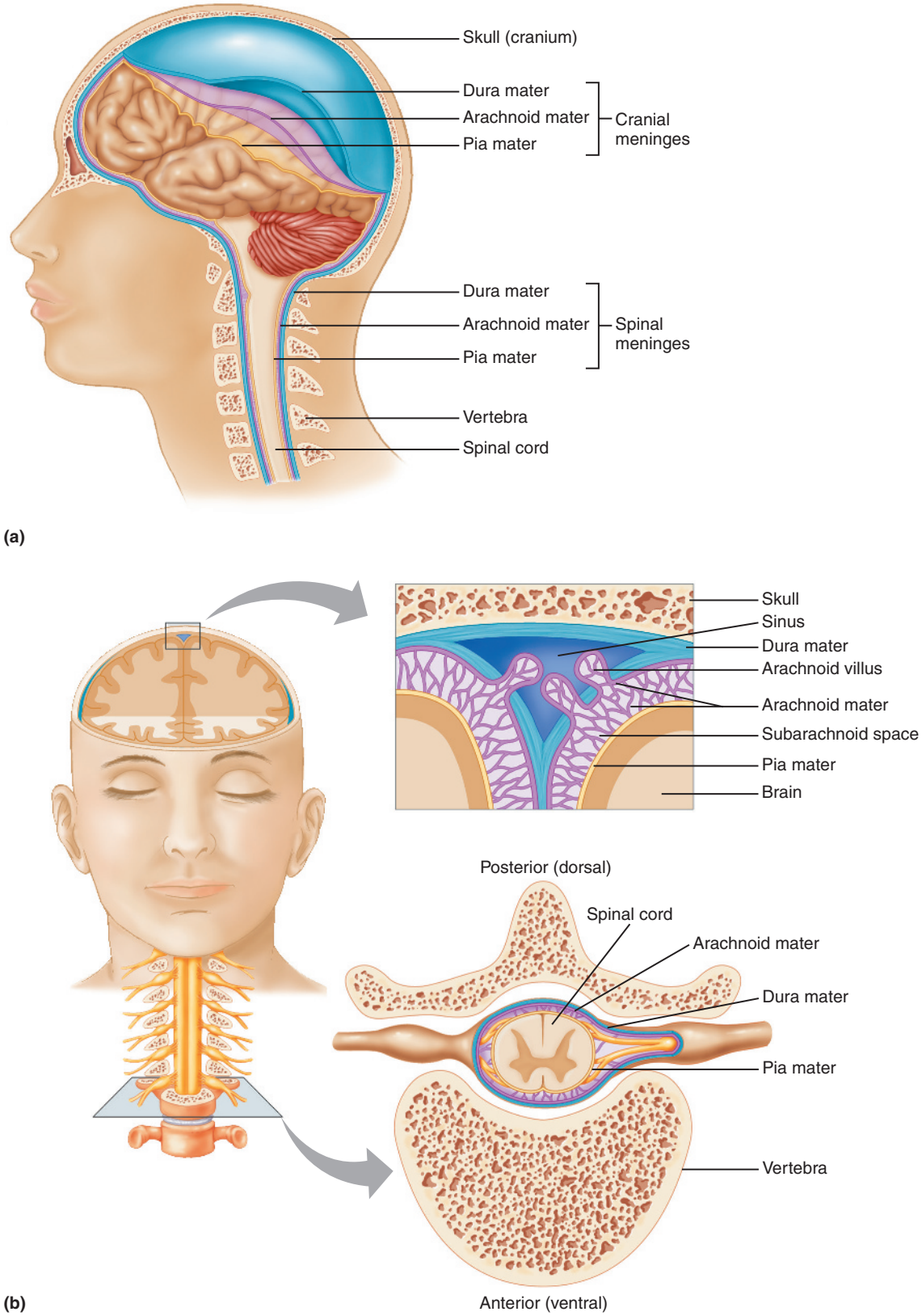


Figure 9.2 **Protective structures of the CNS. (a, b)** Sections of CNS protective structures. Bony outer structures include the cranium and vertebrae. The meninges, which are located between the bony structures and the soft nervous tissue, are composed of three layers: dura mater, arachnoid mater, and pia mater. The cushioning presence of cerebrospinal fluid within the subarachnoid space provides yet another level of protection.