NERVOUS TISSUE

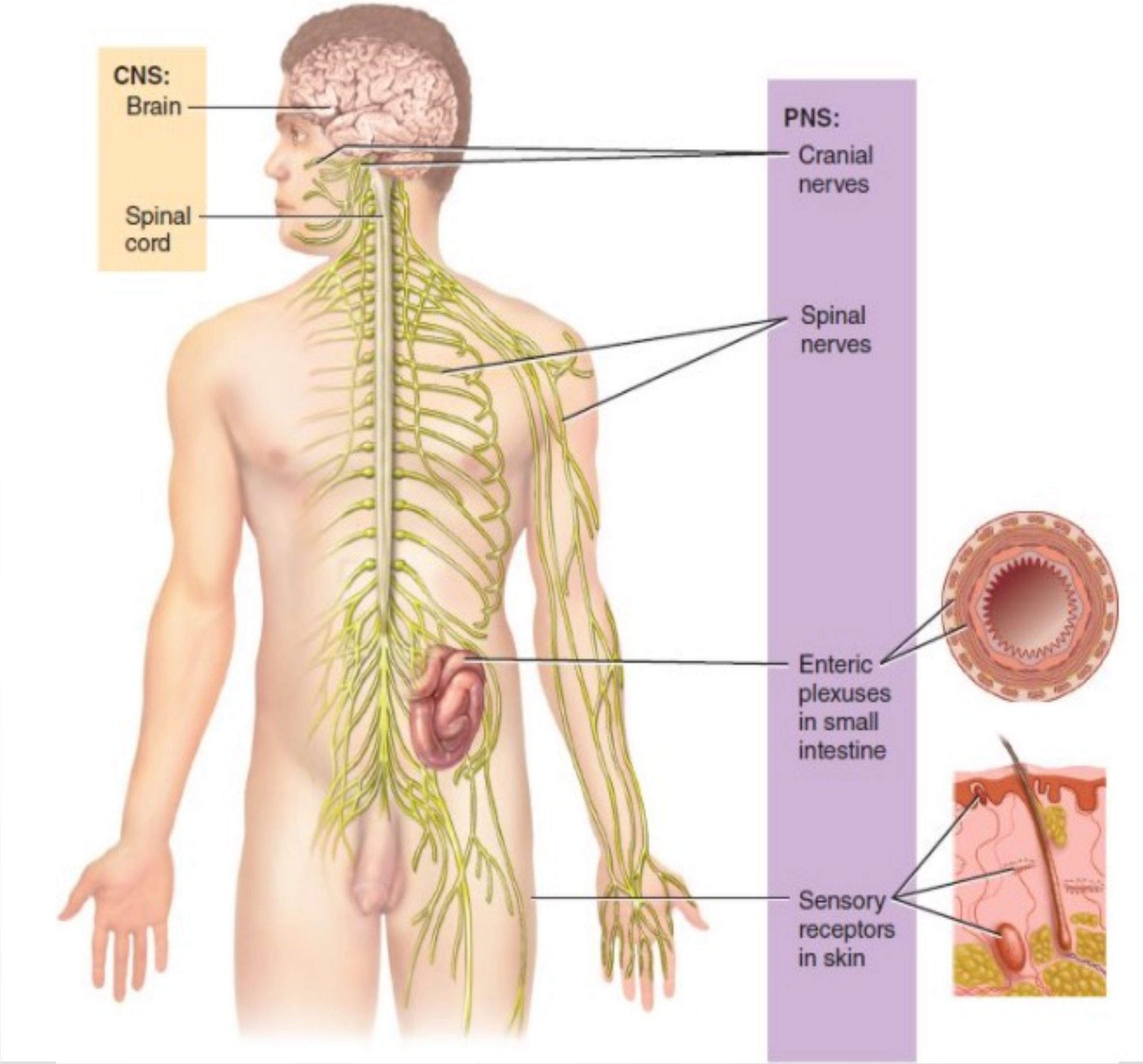
JANQUEIRA'S BASIC HISTOLOY

STRUCTURE AND ORGANIZATION

1. **Central nervous system** (CNS): brain and spinal cord
2. **Peripheral nervous system** (PNS): cranial, spinal, and Ganglia: small aggregates of nerve cells outside the CNS.

<u>Cells in both central and peripheral:</u>

- Neurons: have numerous long processes, responsible for neural synapses
- Glial cells: short processes: support and protect neurons.



SENSORY AND MOTOR

Functionally the nervous system consists of:

1. **Sensory division (afferent)**

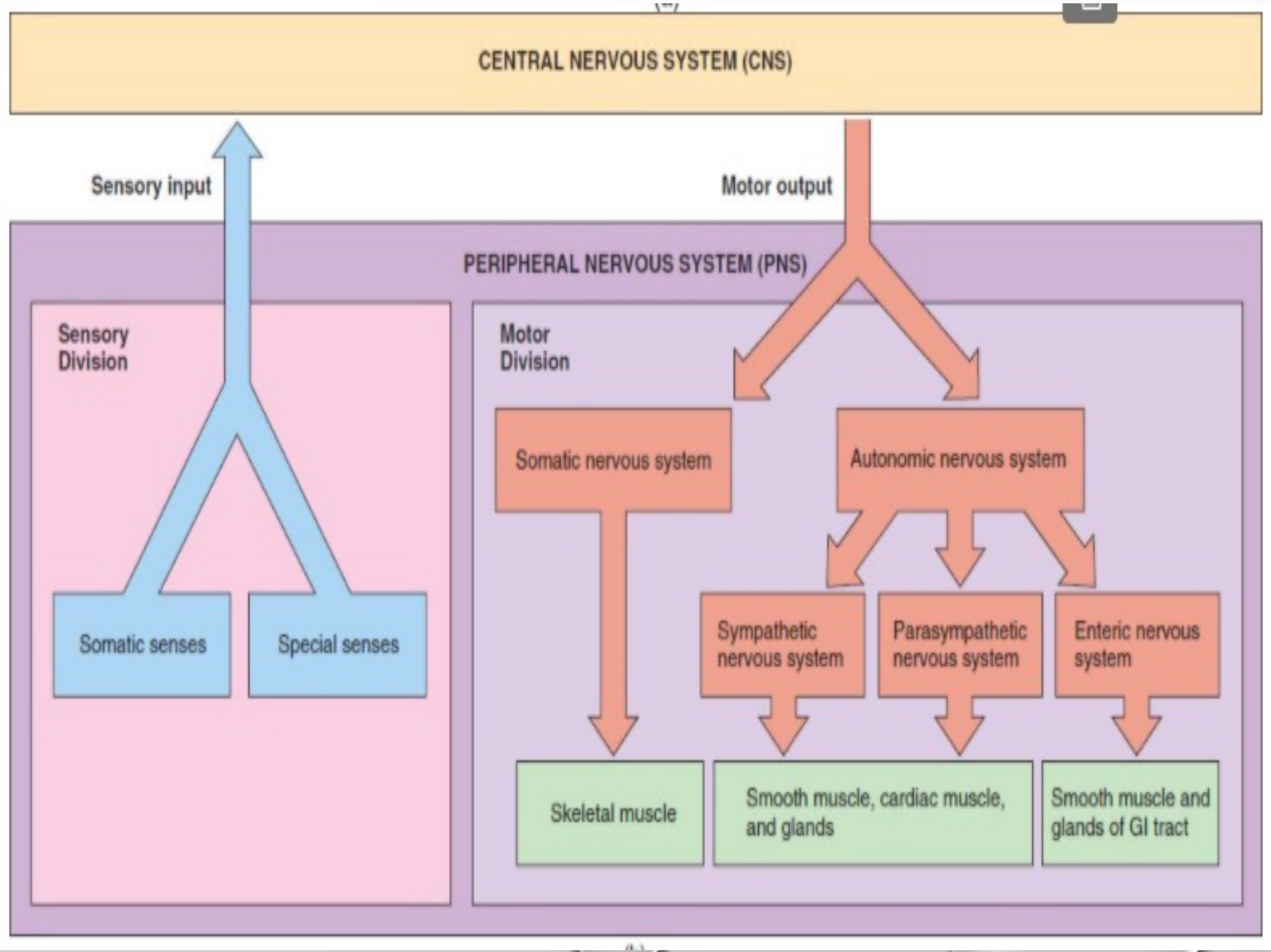
A. Somatic – sensory input perceived consciously (eg, from eyes ears, skin, musculoskeletal structures)

B. Visceral – sensory input not perceived consciously (eg, from Internal organs and cardiovascular structures)

2. **Motor division (efferent)**

A. Somatic – motor output controlled consciously or voluntarily (eg, by skeletal muscle effectors)

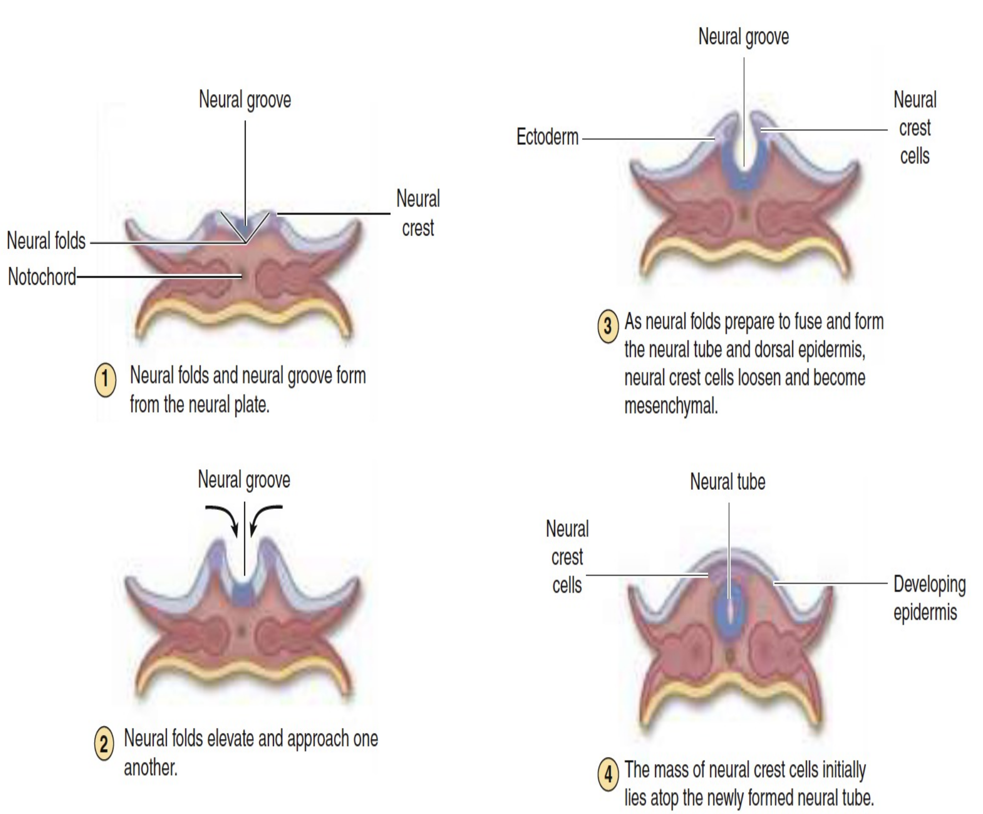
B. Autonomic – motor output not controlled consciously (eg, by heart or gland effectors)



DEVELOPMENT OF NERVE TISSUE

- Nervous tissue develops from the ectoderm.
- Beginning in the third week of development.
- Ectoderm---thickening---epithelial neural plate---folds and forms the **Neural tube–** gives rise to entire CNS (neurons and most glial cells).
- **Neural crest-**--migrate--- gives rise to cells of PNS and several other tissues.

FIGURE 9–2 Neurulation in the early embryo.



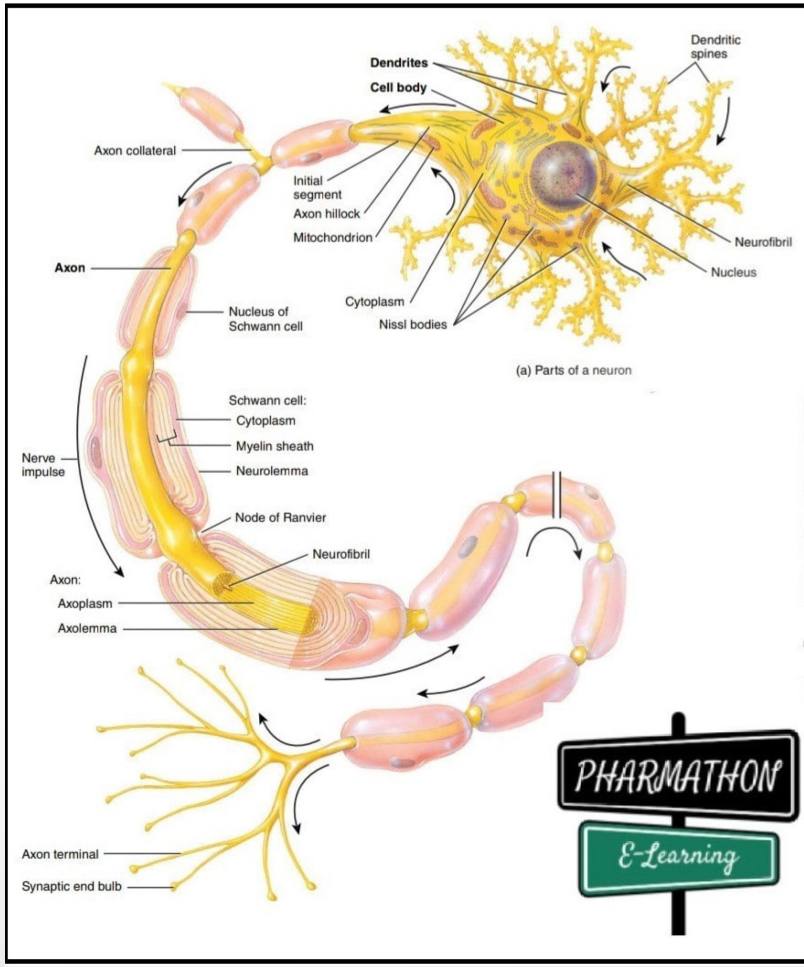
NEURONS

- The functional unit in both the CNS and PNS

<u>Parts of a neuron:</u>

1. Cell body (perikaryon or soma)

- Contains the nucleus and most of the cell's organelles
- The synthetic or trophic center for the entire neuron.



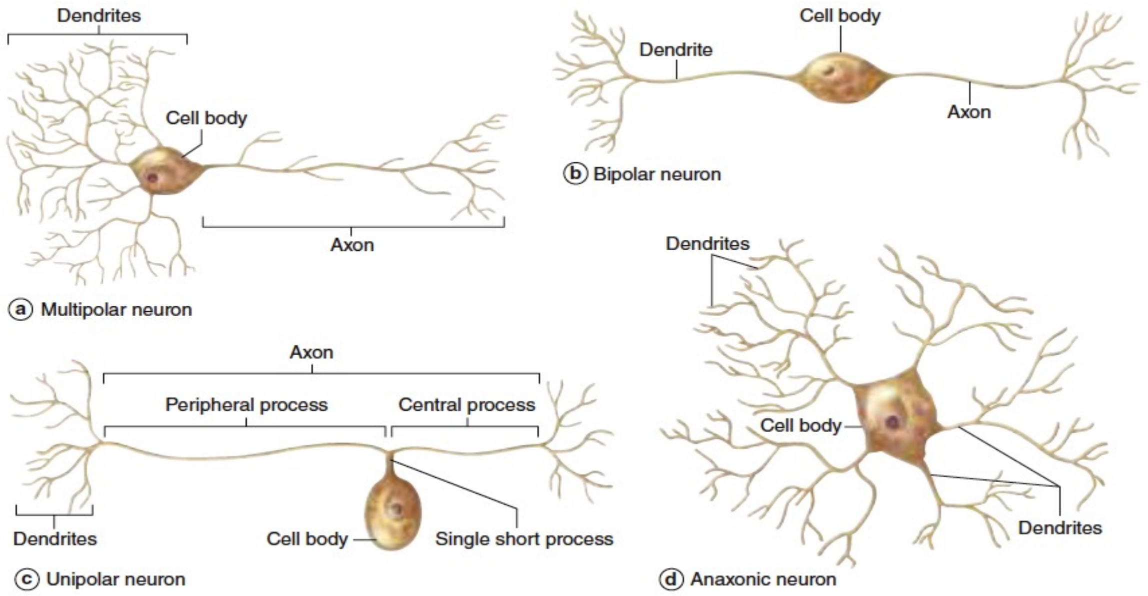
2. Dendrites: numerous elongated processes extending from the perikaryon and specialized to receive stimuli from other neurons.

3. Axon: a single long process ending at synapses specialized to generate and conduct nerve impulses to other cells (nerve, muscle, and gland cells).

NEURON CLASSIFICATION-STRUCTURALLY

1. Multipolar neurons: one axon and two or more dendrites, most common.

2. Bipolar neurons: one dendrite and one axon, sensory neurons of the retina, the olfactory epithelium, and the inner ear.



Shown are the four main types of neurons, with short descriptions. **(a)** Most neurons, including all motor neurons and CNS interneurons, are **multipolar**. **(b) Bipolar neurons** include sensory neurons of the retina, olfactory mucosa, and inner ear. **(c)** All other sensory neurons are **unipolar** or **pseudounipolar**. **(d) Anaxonic** neurons of the CNS lack true axons and do not produce action potentials, but regulate local electrical changes of adjacent neurons.

3. Unipolar or pseudounipolar neurons: single process that bifurcates close to the perikaryon; longer branch extending to a peripheral ending and the other toward the CNS; all other sensory neurons.

4. Anaxonic neurons: many dendrites but no true axon, do not produce action potentials, but regulate electrical changes of adjacent CNS neurons.

NEURON CLASSIFICATION-FUNCTIONALLY

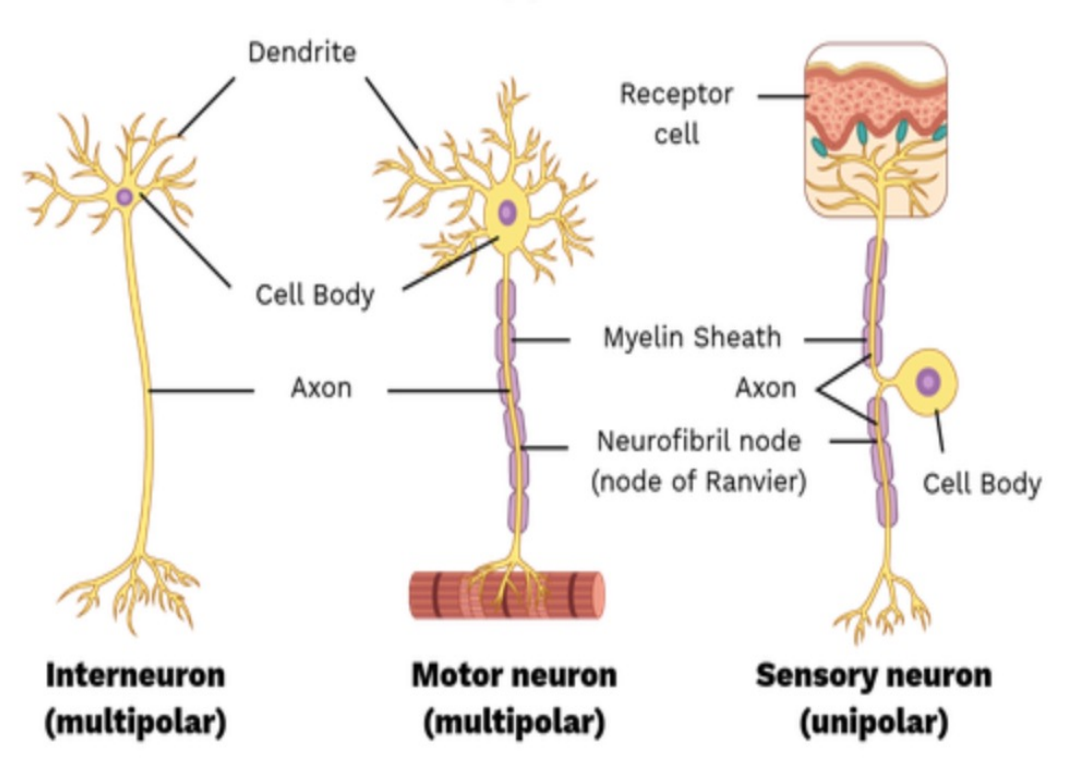
- **Sensory** neurons (afferent):

1. Sensory input perceived consciously (eyes ears, skin, musculoskeletal structures).
2. Visceral – sensory input NOT perceived consciously (Internal organs and cardiovascular structures).

- **Motor** neurons(efferent): sending impulses to effector organs muscle fibers and glands.

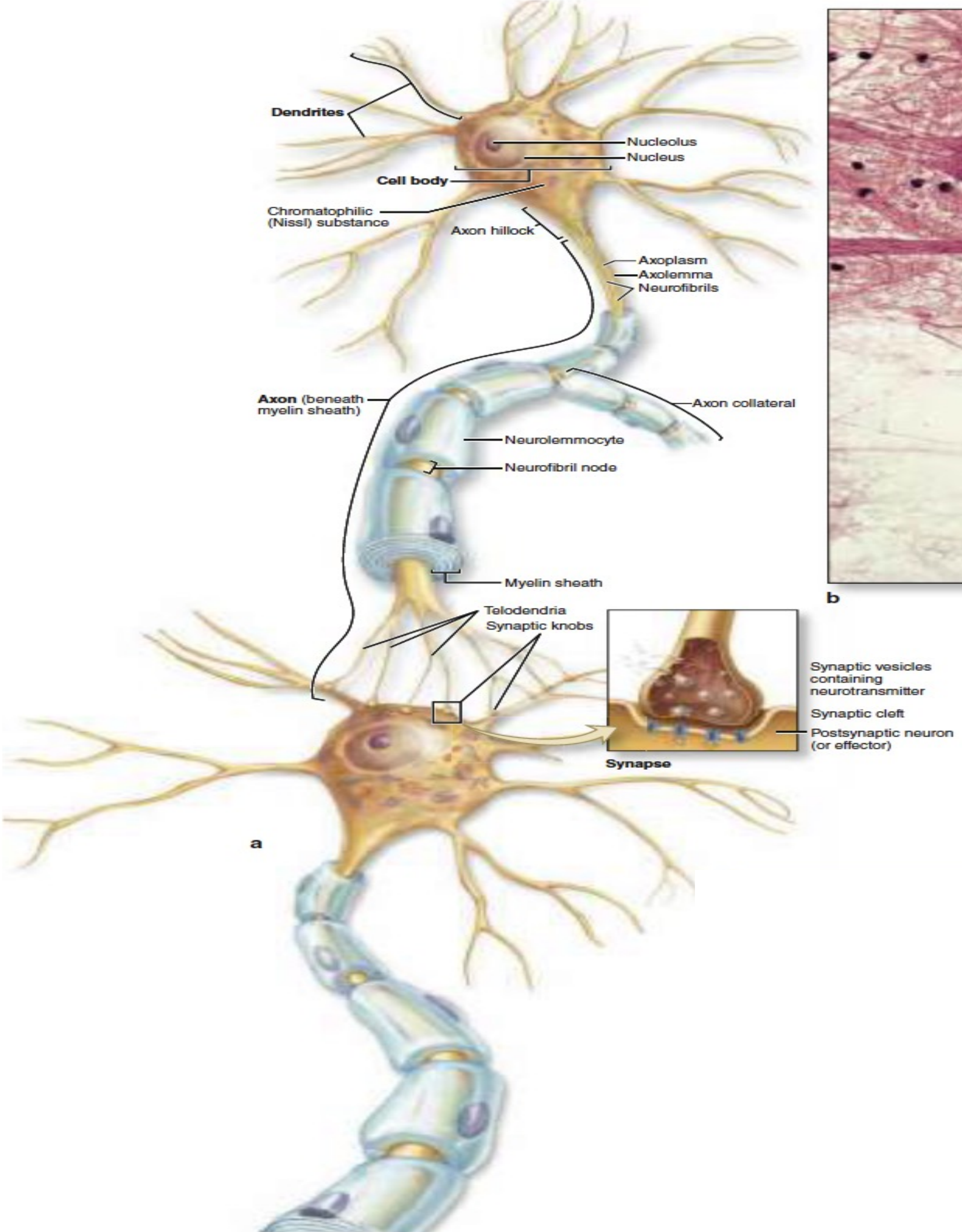
1. Somatic motor nerves--- voluntary -- skeletal muscle.

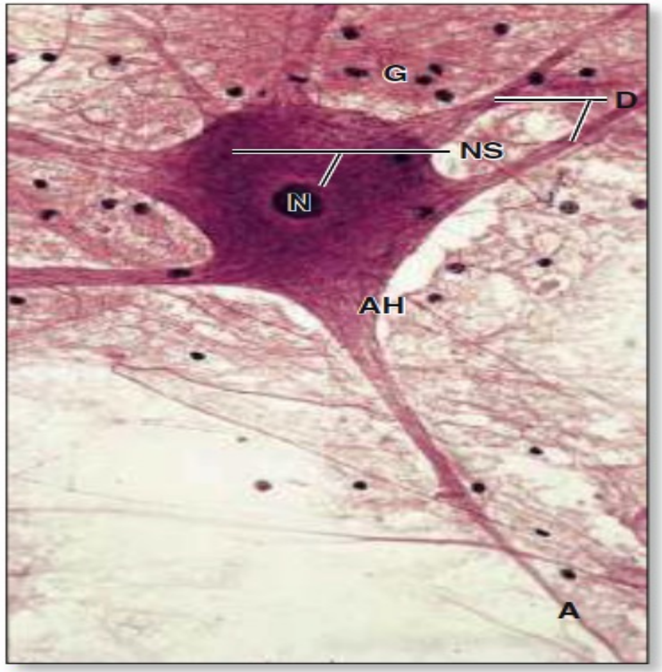
2. Autonomic motor nerves-- involuntary or unconscious--- glands, cardiac muscle, and smooth muscle.



- **Interneurons** establish relationships among other neurons, forming complex functional networks or circuits in the CNS. Interneurons are either multipolar or anaxonic and comprise 99% of all neurons in adults.

NEURON PARTS

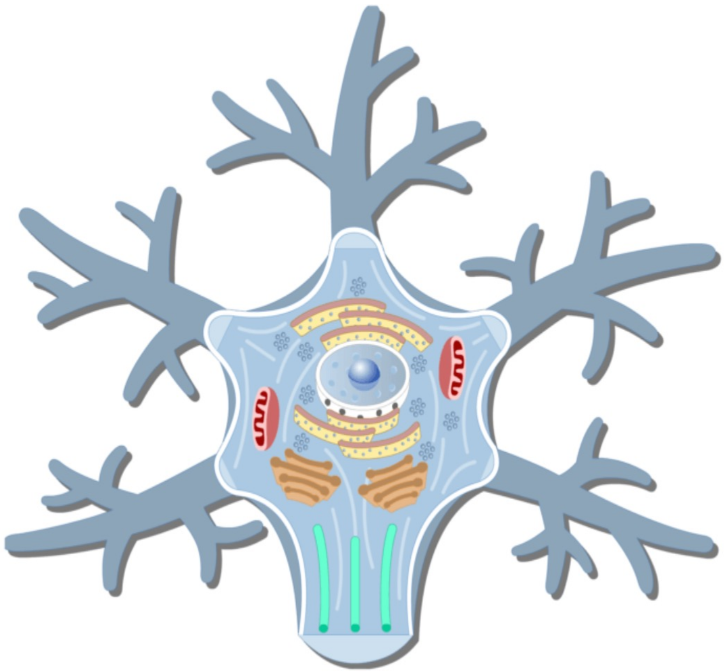


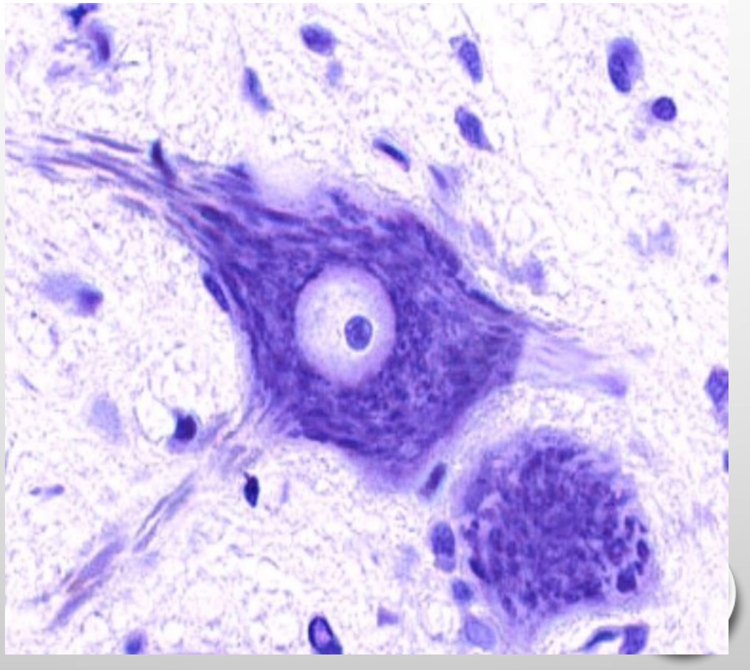


b

CELL BODY (PERIKARYON OR SOMA)

- Contains the nucleus and surrounding cytoplasm.
- It acts as a trophic center.
- Most are in contact with a great number of nerve endings conveying excitatory or inhibitory stimuli.
- Large, euchromatic nucleus with a prominent nucleolus (intense synthetic activity)

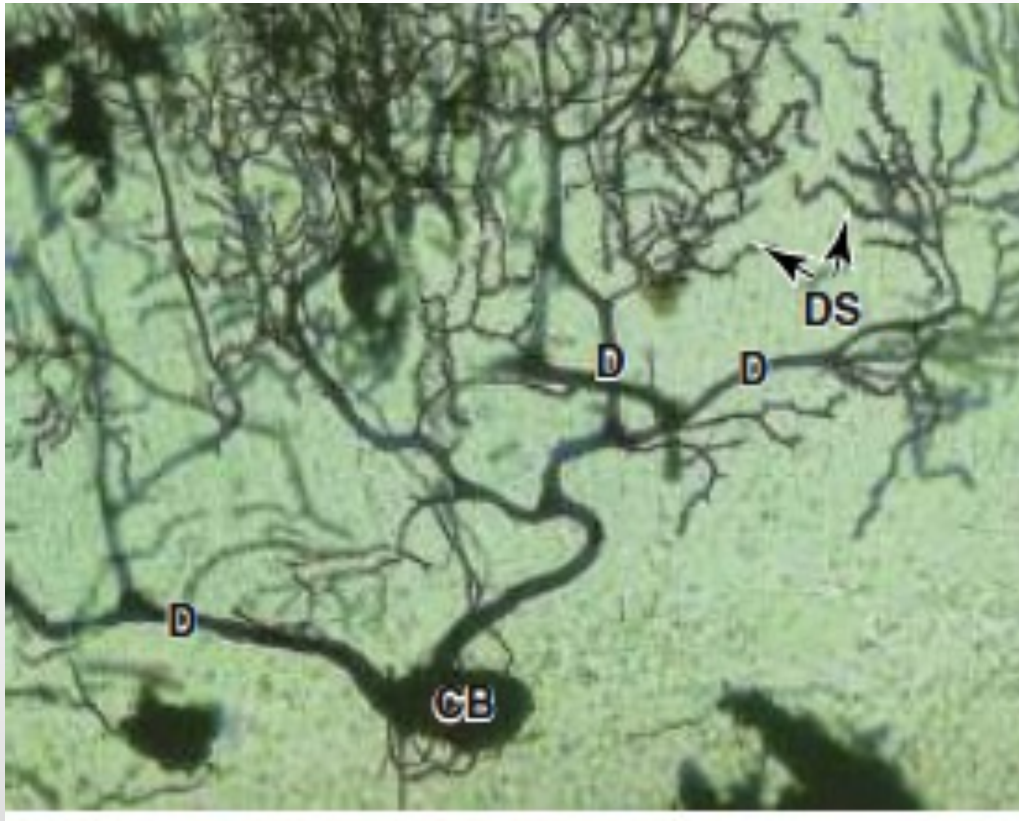




- **Nissl bodies** NB (Nissl substance, chromatophilic substance): numerous free polyribosomes and highly developed RER.
- The amount of NB varies with the type and functional state of the neuron---abundant in large motor neurons.
- The Golgi apparatus is located only in the cell body.
- Mitochondria can be found throughout the cell and are usually abundant in the axon terminals.

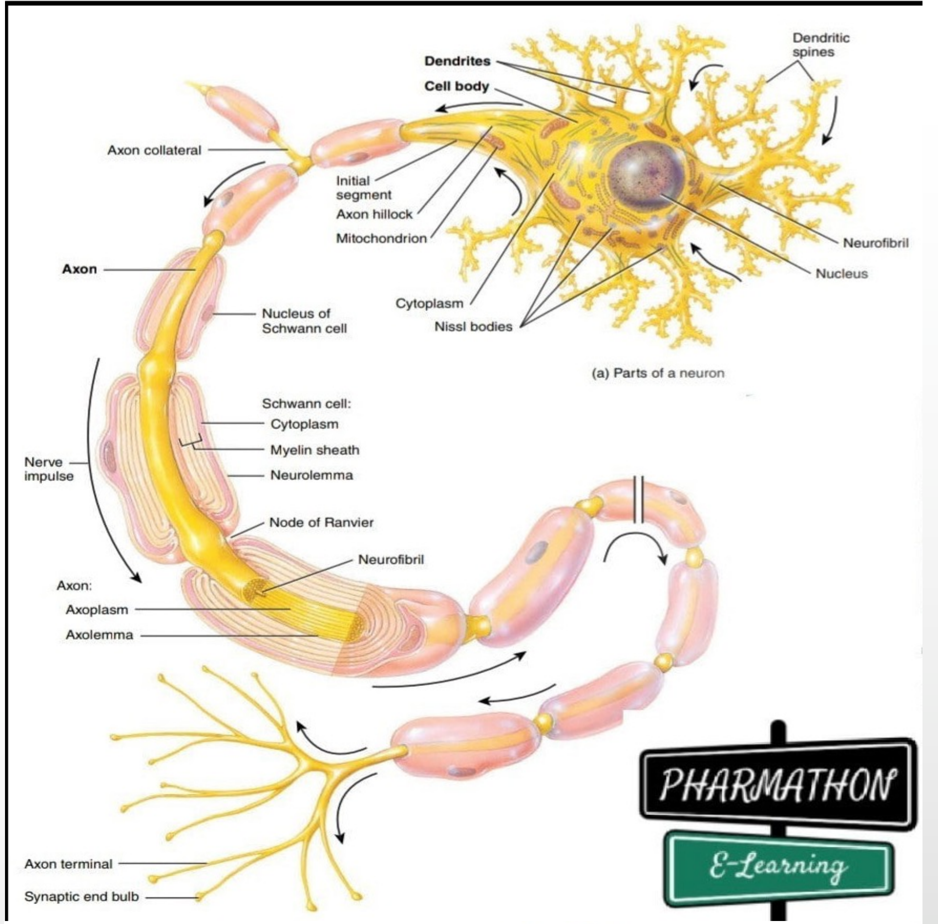
DENDRITES

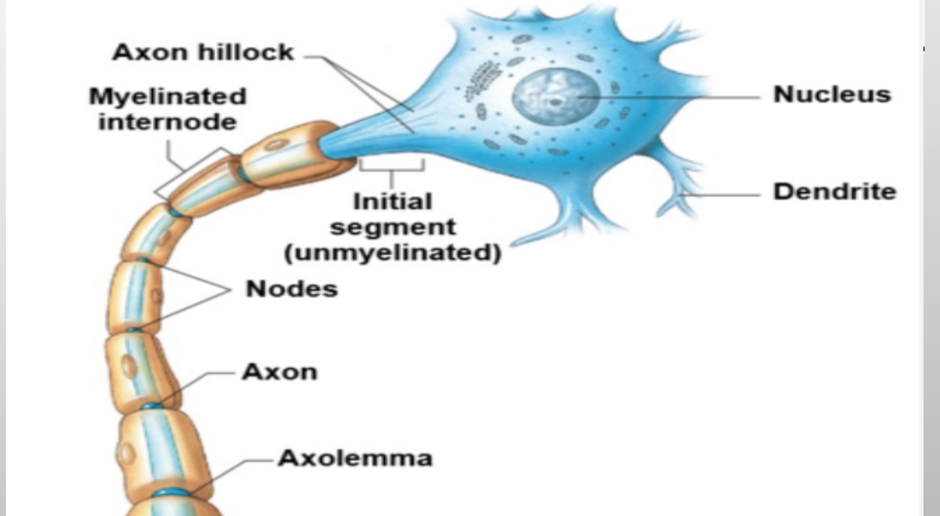
- Short, small processes emerging and branching off the soma.
- Covered with many synapses.
- Are the principal signal reception and processing sites on neurons.
- The large number and extensive arborization---signals from many other nerve cells.
- Dendrites become much thinner as they branch.
- Dendritic spines: dynamic membrane protrusions along the dendritic branches



AXONS

- Most neurons have only one axon.
- Axonal processes vary in length and diameter ---type of neuron.
- Axolemma: plasma membrane.
- Axoplasm: contents of axon.
- Axon hillock: pyramid-shaped region of the perikaryon where axons originate from.
- Initial segment: concentrated ion channels which generate the action potential
- Axons branch less than dendrites---but undergo terminal arborization.



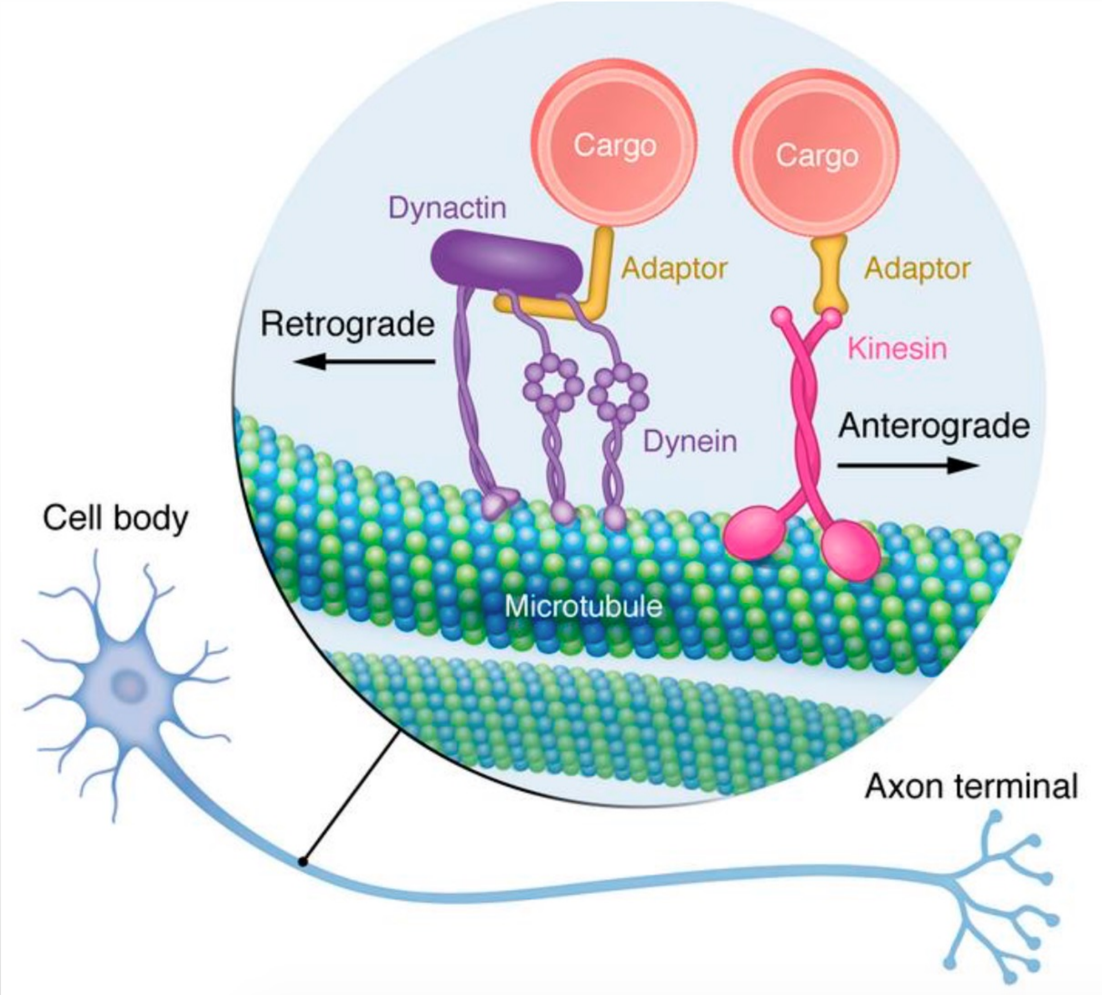


AXONS

- Axons of interneurons and some motor neurons also have major branches called collaterals that end at smaller branches with synapses influencing the activity of many other neurons.
- Terminal bouton: Small axonal branch ends with a dilation-- contacts another neuron or non-nerve cell.
- **Axoplasm** contains mitochondria, microtubules, neurofilaments, and transport vesicles, but very few polyribosomes or cisternae of RER (dependence of axoplasm on the perikaryon).

AXON/TRANSPORT

- **Anterograde** transport: away from cell body. Organelles and macromolecules synthesized in the cell body move along axonal microtubules via **kinesin** from the perikaryon to the synaptic terminals.
- **Retrograde** transport: toward cell body. in the opposite direction along microtubules via **dynein** carries certain other macromolecules---endocytosis (including viruses and toxins).
- Anterograde and retrograde transports: 50-400 mm/d.



SYNAPSES

- **Precynaptic cell**

Presynaptic axon terminal (terminal bouton)

Neurotransmotter (synaptic vesicles)

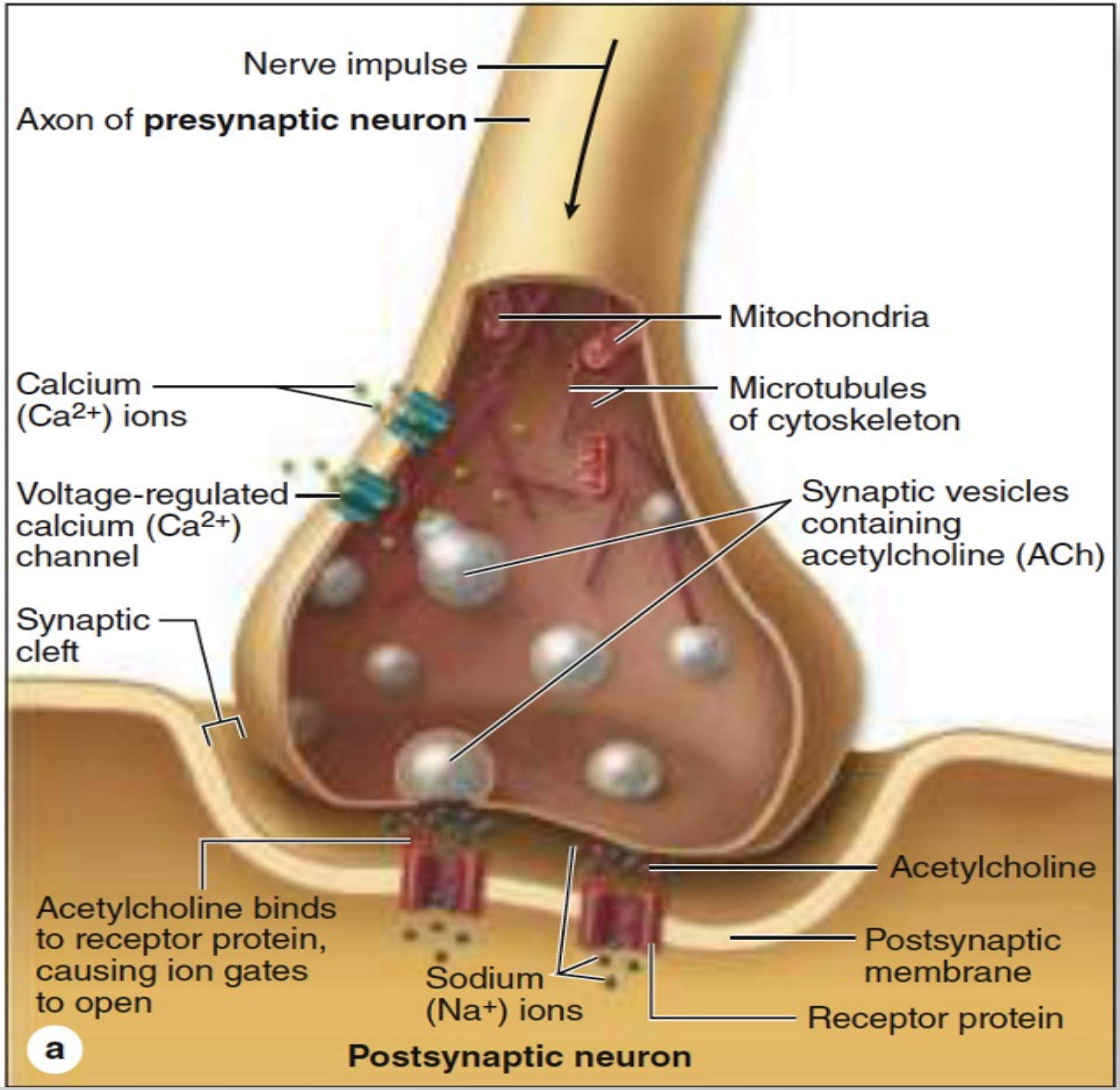
Ca^{2+} !!!

- **Synaptic cleft**

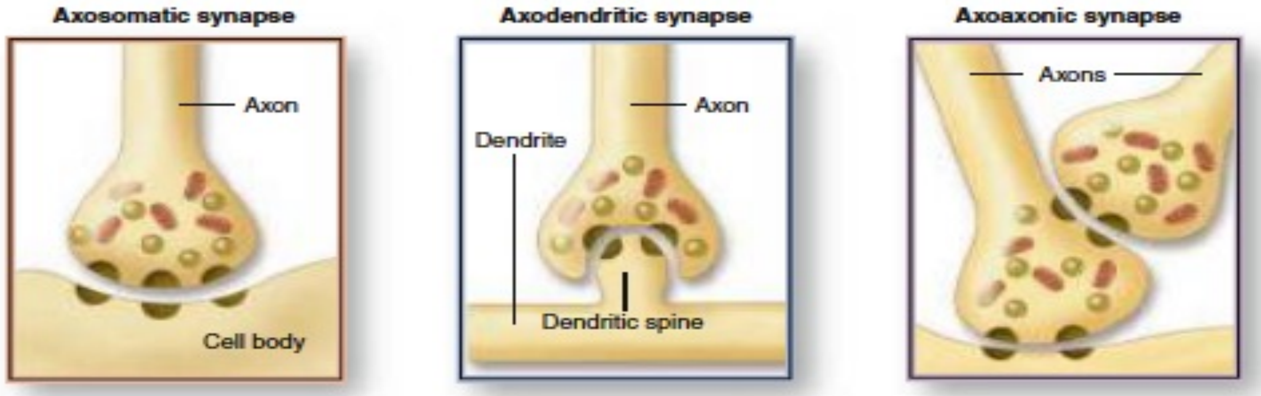
20-30 nm-wide intercellular space called the

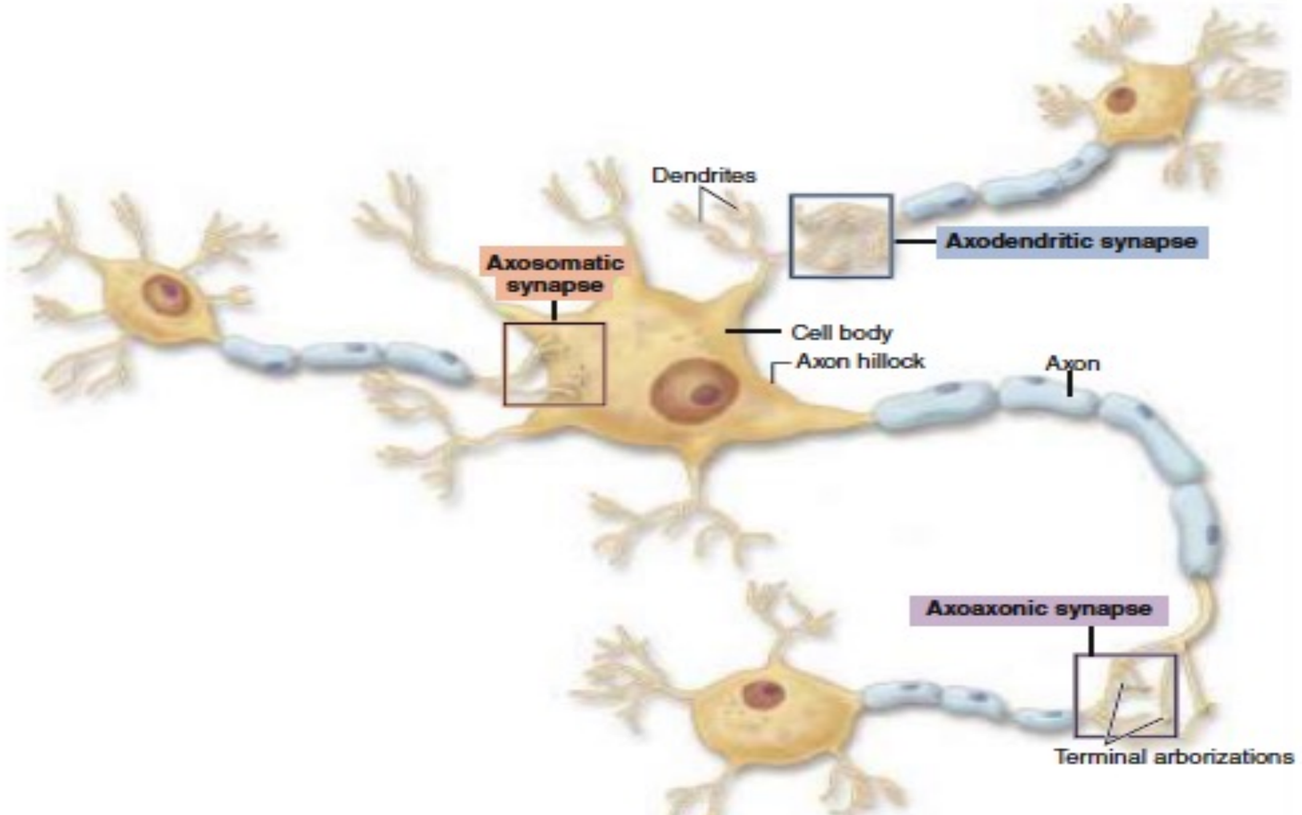
- **Postsynaptic cell**

Postsynaptic cell membrane



TYPES OF SYNAPSES





The diagrams show three common morphologic types of synapses. Branched axon terminals usually associate with and transmit a nerve impulse to another neuron's cell body (or soma) or a dendritic spine. These types of connections are termed an **axosomatic synapse** and an **axodendritic synapse**, respectively. Less frequently, an axon terminal forms a synapse with an axon terminal of another neuron; such an **axoaxonic synapse** functions to modulate synaptic activity in the other two types.

All three morphologic types of synapses have the features of all true synapses: a presynaptic axon terminal that releases a transmitter; a postsynaptic cell membrane with receptors for the transmitter; and an intervening synaptic cleft.

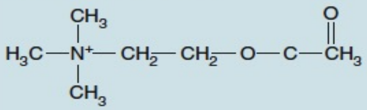
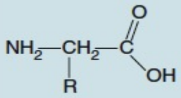
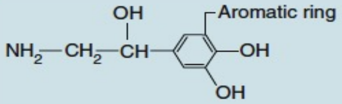
Synaptic structure usually cannot be resolved by light microscopy, although components such as dendritic spines may be shown with special techniques (Figure 9–5).

SYNAPSES

- **Excitatory** synapses cause postsynaptic Na^+ channels to open--- depolarization wave in the postsynaptic neuron (or effector).
- **Inhibitory** synapses neurotransmitters open Cl^- (or other anion), causing ---influx of anions -----hyperpolarization--- membrane potential more negative--- resistant to depolarization.
- <u>The response in postsynaptic neurons is determined by the **summation** of activity at hundreds of synapses on that cell.</u>

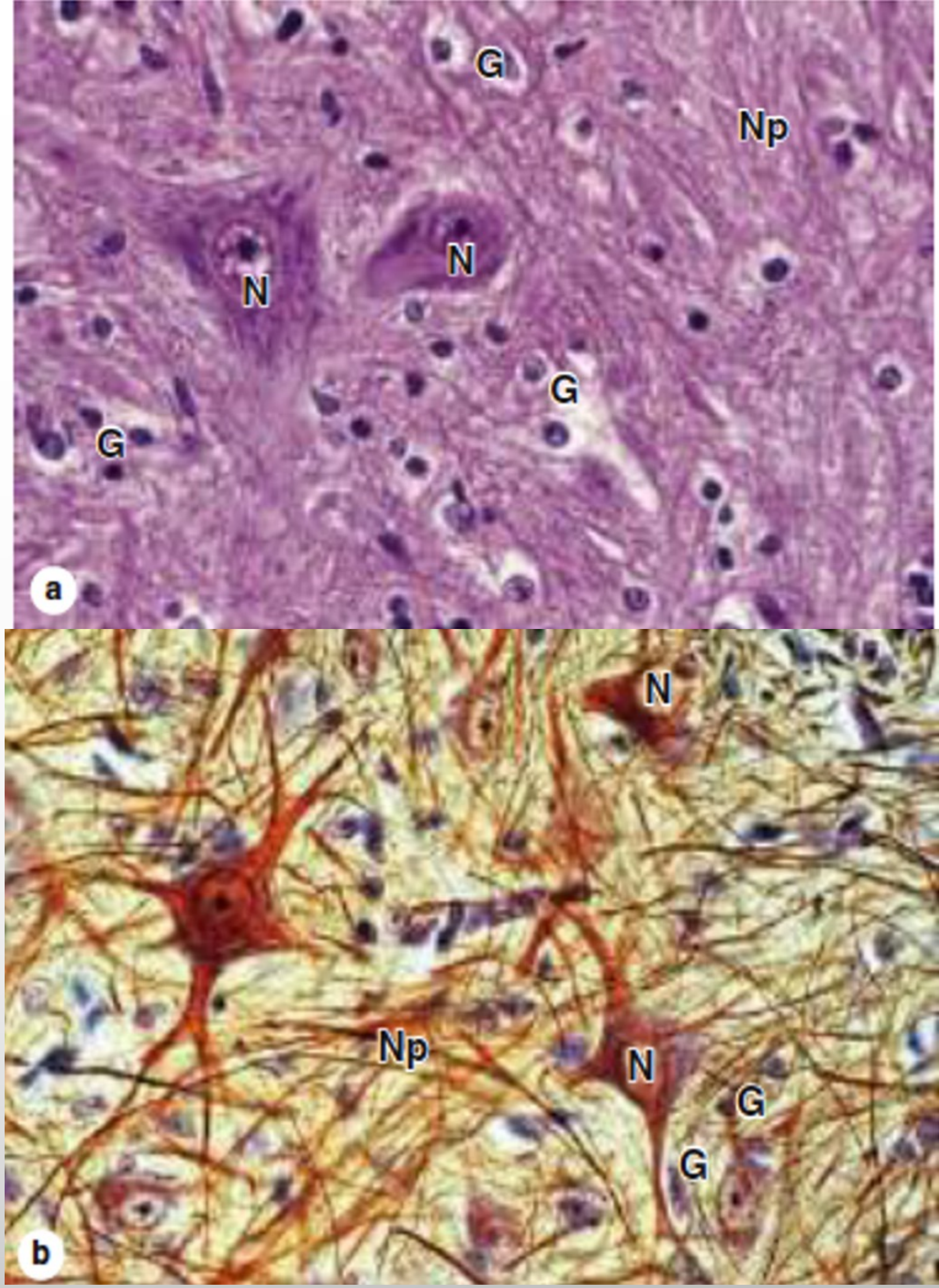
NEUROTRANSMITTERS (READ ONLY)

TABLE 9–1 Common neurotransmitters and their actions.

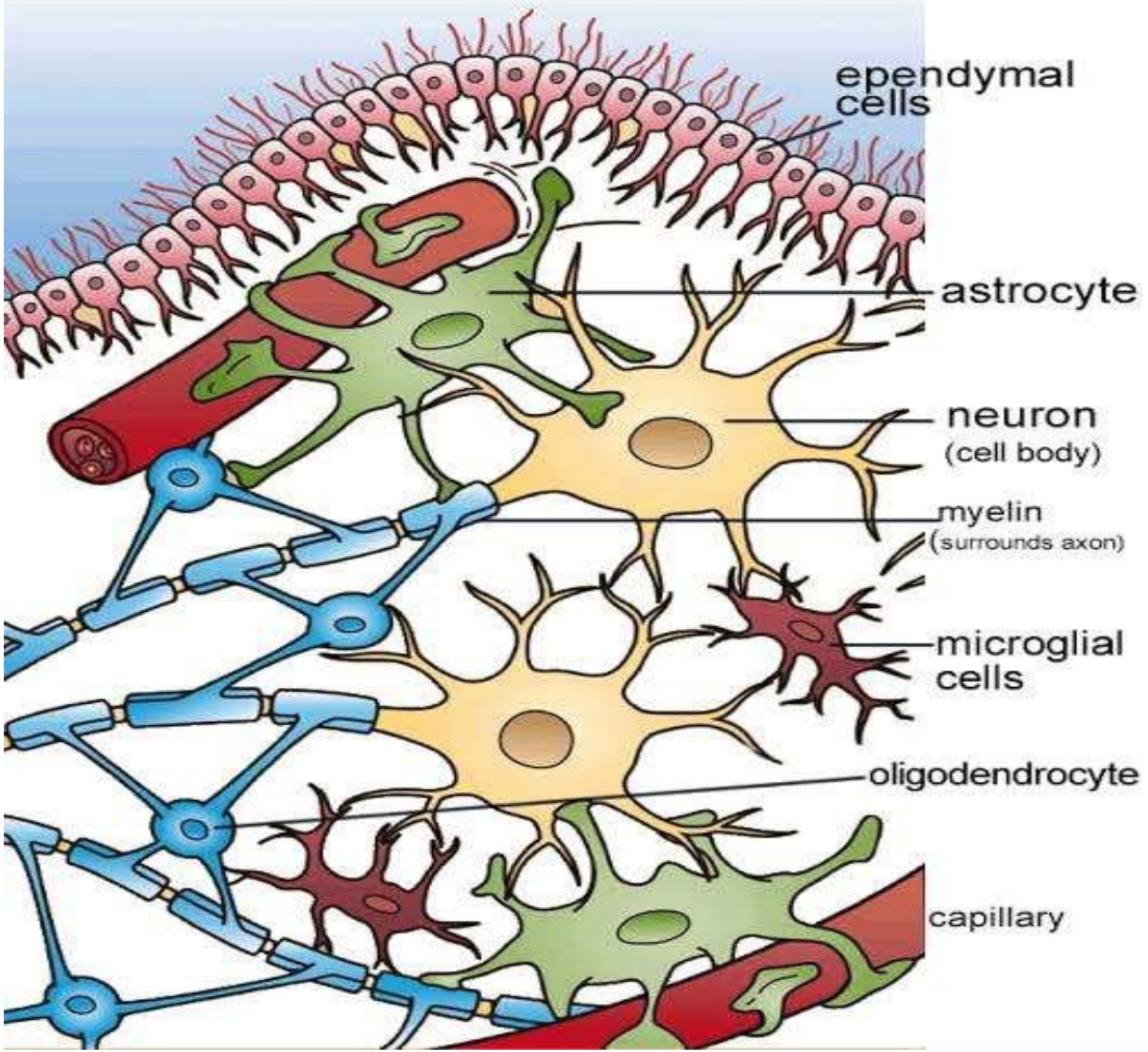
Neurotransmitter	Description/Action
ACETYLCHOLINE (ACh)	
	Chemical structure significantly different from that of other neurotransmitters; active in CNS and in both somatic and autonomic parts of PNS; binds to ACh receptors (cholinergic receptors) in PNS to open ion channels in postsynaptic membrane and stimulate muscle contraction
AMINO ACIDS	
	Molecules with both carboxyl (—COOH) and amine (—NH_2) groups and various R groups; act as important transmitters in the CNS
Glutamate	Excites activity in neurons to promote cognitive function in the brain (learning and memory); most common neurotransmitter in the brain; opens Na^+ channels
Gamma-aminobutyric acid (GABA)	Synthesized from glutamate; primary inhibitory neurotransmitter in the brain; also influences muscle tone; opens or closes various ion channels
Glycine	Inhibits activity between neurons in the CNS, including retina; opens Cl^- channels
MONOAMINES	
	Molecules synthesized from an amino acid by removing the carboxyl group and retaining the single amine group; also called biogenic amines
Serotonin or 5-hydroxytryptamine (5-HT)	Has various functions in the brain related to sleep, appetite, cognition (learning, memory), and mood; modulates actions of other neurotransmitters
Catecholamines	A distinct group of monoamines
Dopamine	Produces inhibitory activity in the brain; important roles in cognition (learning, memory), motivation, behavior, and mood; opens K^+ channels, closes Ca^{2+} channels
Norepinephrine (noradrenaline)	Neurotransmitter of PNS (sympathetic division of autonomic nervous system) and specific CNS regions
Epinephrine (adrenaline)	Has various effects in the CNS, especially the spinal cord, thalamus, and hypothalamus
NEUROPEPTIDES	
	Small polypeptides act as signals to assist in and modulate communication among neurons in the CNS
Enkephalin	Helps regulate response to noxious and potentially harmful stimuli
Neuropeptide Y	Involved in memory regulation and energy balance (increased food intake and decreased physical activity)
Somatostatin	Inhibits activities of neurons in specific brain areas
Substance P	Assists with pain information transmission into the brain
Cholecystokinin (CCK)	Stimulates neurons in the brain to help mediate satiation (fullness) and repress hunger
Beta-endorphin	Prevents release of pain signals from neurons and fosters a feeling of well-being
Neurotensin	Helps control and moderate the effects of dopamine
OTHERS	
Adenosine	Also part of a nucleotide, inhibits activities in certain CNS neurons
Nitric oxide	Involved in learning and memory; relaxes muscle in the digestive tract; important for relaxation of smooth muscle in blood vessels (vasodilation)

GLIAL CELLS

- Support neuronal survival and activities.
- Ten times more abundant.
- Most glial cells develop from neural plate cells
- In the CNS surrounds both the cell bodies and the processes of axons and dendrites (occupying the spaces between neurons).
- Substitute for cells of connective tissue creating immediately around those cells microenvironments that are optimal for neuronal activity.



NEUROGLIA

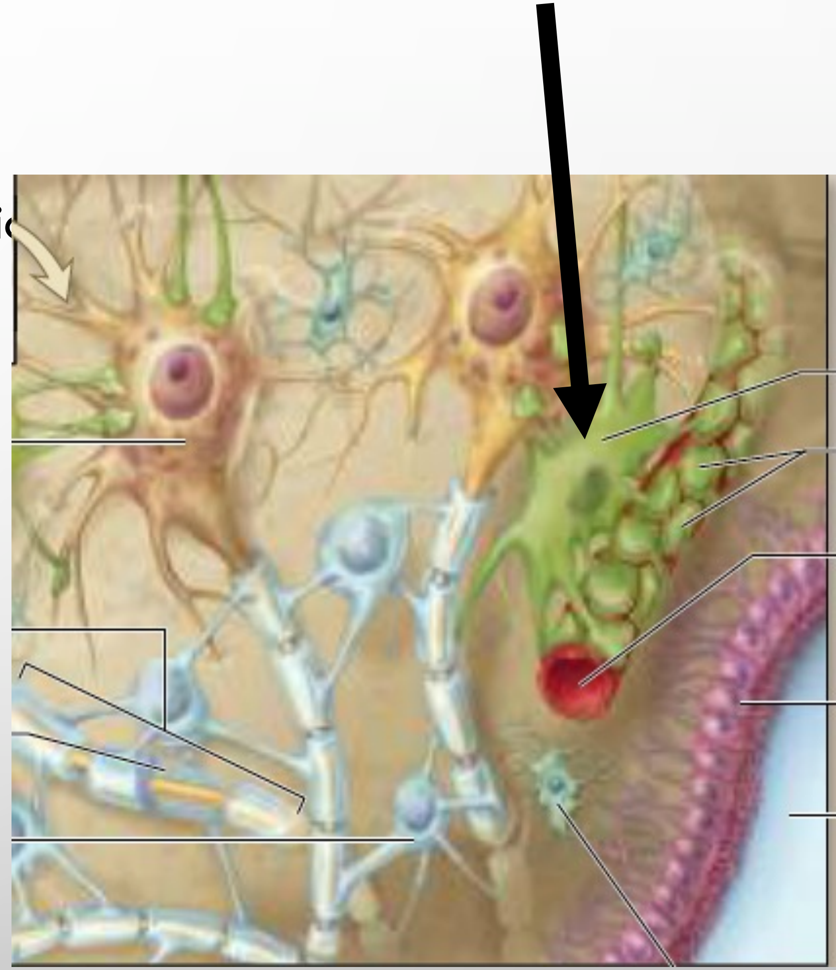


ependymal cells
astrocyte
neuron
(cell body)
myelin
(surrounds axon)
microglial cells
oligodendrocyte
capillary

CENTRAL NEUROGLIA

ASTROCYTES

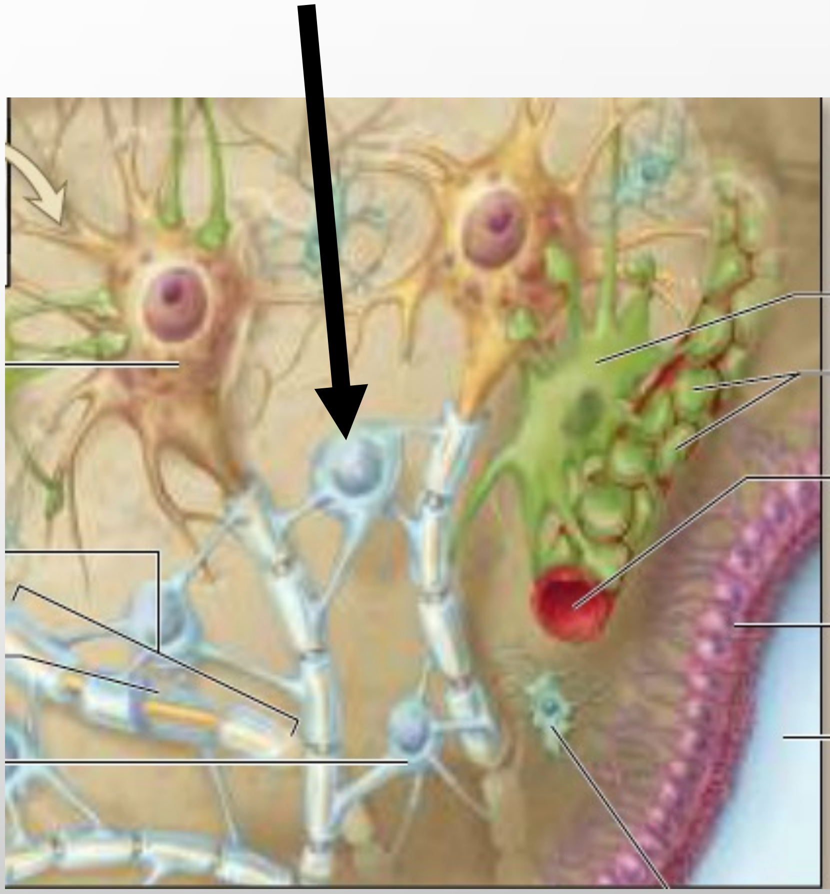
- Have a large number of long radiating, branching processes
- Terminal processes of a single astrocyte associate with over a many synaptic sites.
- Astrocytes originate from neural tube cells.
- Most numerous glial cells of the brain.
- Most diverse structurally and functionally.
- Participate in blood-brain barrier.
- **Fibrous** astrocytes--- white matter ---- long delicate processes
- **Protoplasmic** astrocytes--- gray matter----- shorter processes.
- Communicate directly with one another via gap junctions.



CENTRAL NEUROGLIA

Oligodendrocytes

- Extend many processes---sheet-like and wraps repeatedly around a portion of a nearby CNS axon (myelin: electrical insulation—rabid transmission of impulses).
- Many oligodendrocytes for axon's full length
- Are the predominant glial cells in white matter.
- Appear as small cells with rounded, condensed nuclei and unstained cytoplasm.



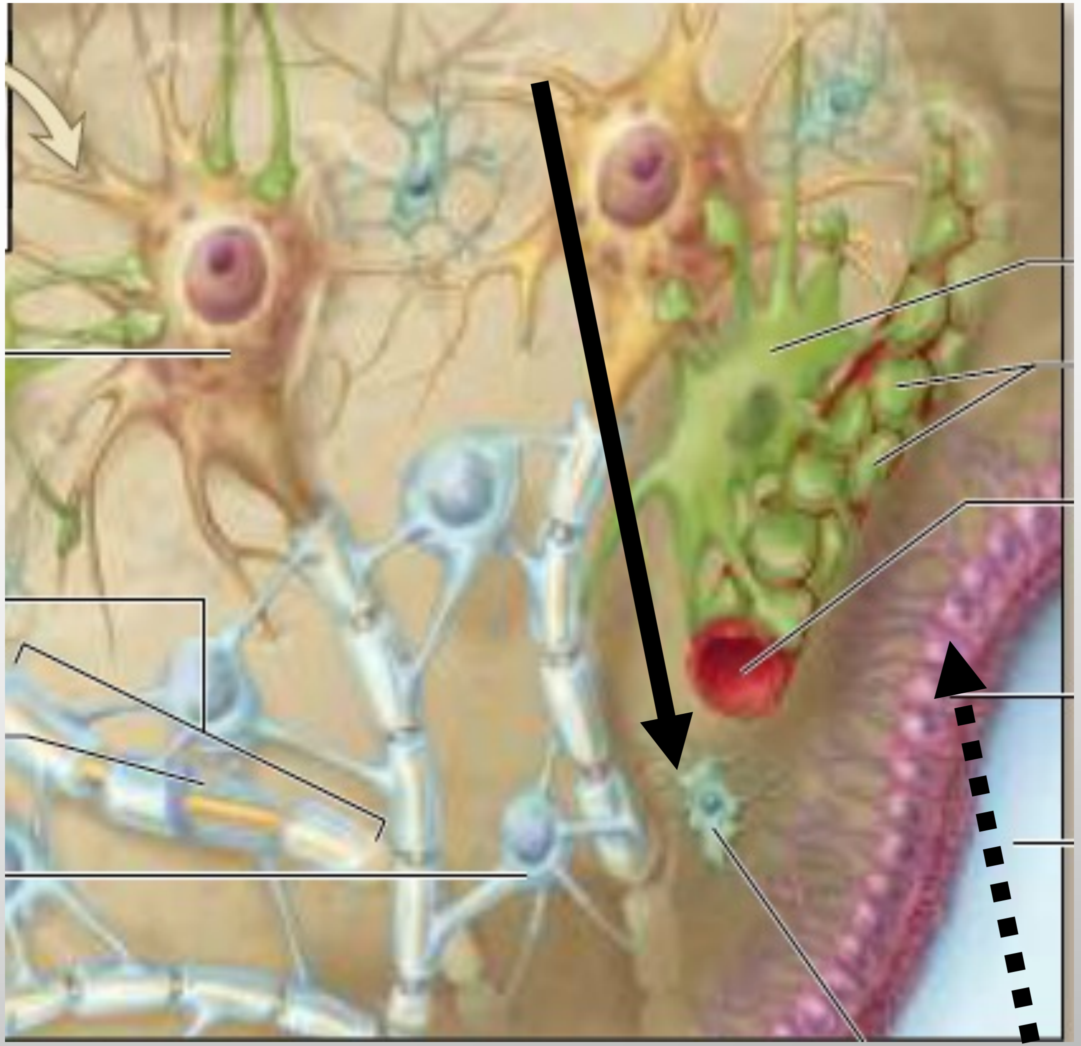
CENTRAL NEUROGLIA

Ependymal cells

- Columnar or cuboidal cells that line the ventricles of the brain and the central canal of the spinal cord.

Microglia

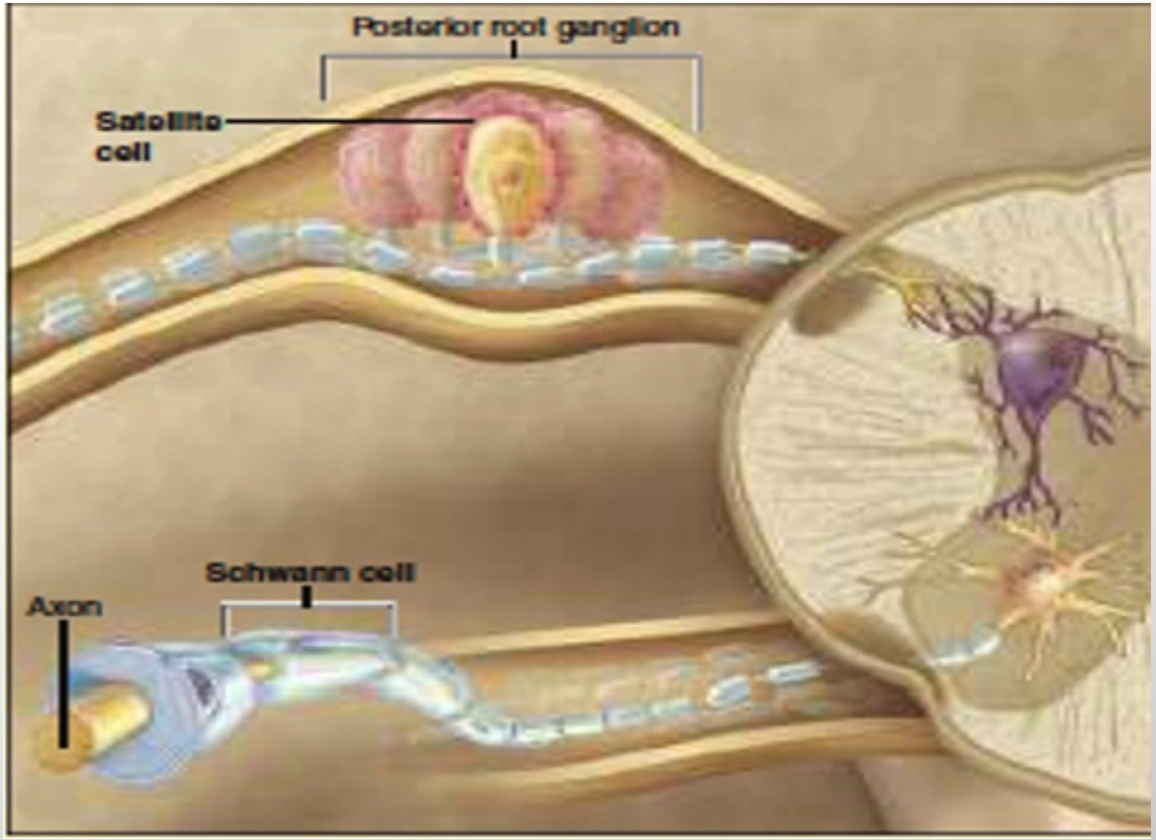
- Less numerous.
- Throughout gray and white matter
- Microglia migrate, with their processes
- Constitute the major mechanism of immune defense in the CNS.
- Originate from circulating blood monocytes.



PERIPHERAL NEUROGLIA

Schwann cells

- Are found only in the PNS
- Differentiate from precursors in the neural crest.
- Are the counterparts to oligodendrocytes of the CNS,
- Having trophic interactions with axons and most importantly forming their myelin sheathes.
- Forms myelin around a portion of only one axon.



Satellite cells of ganglia

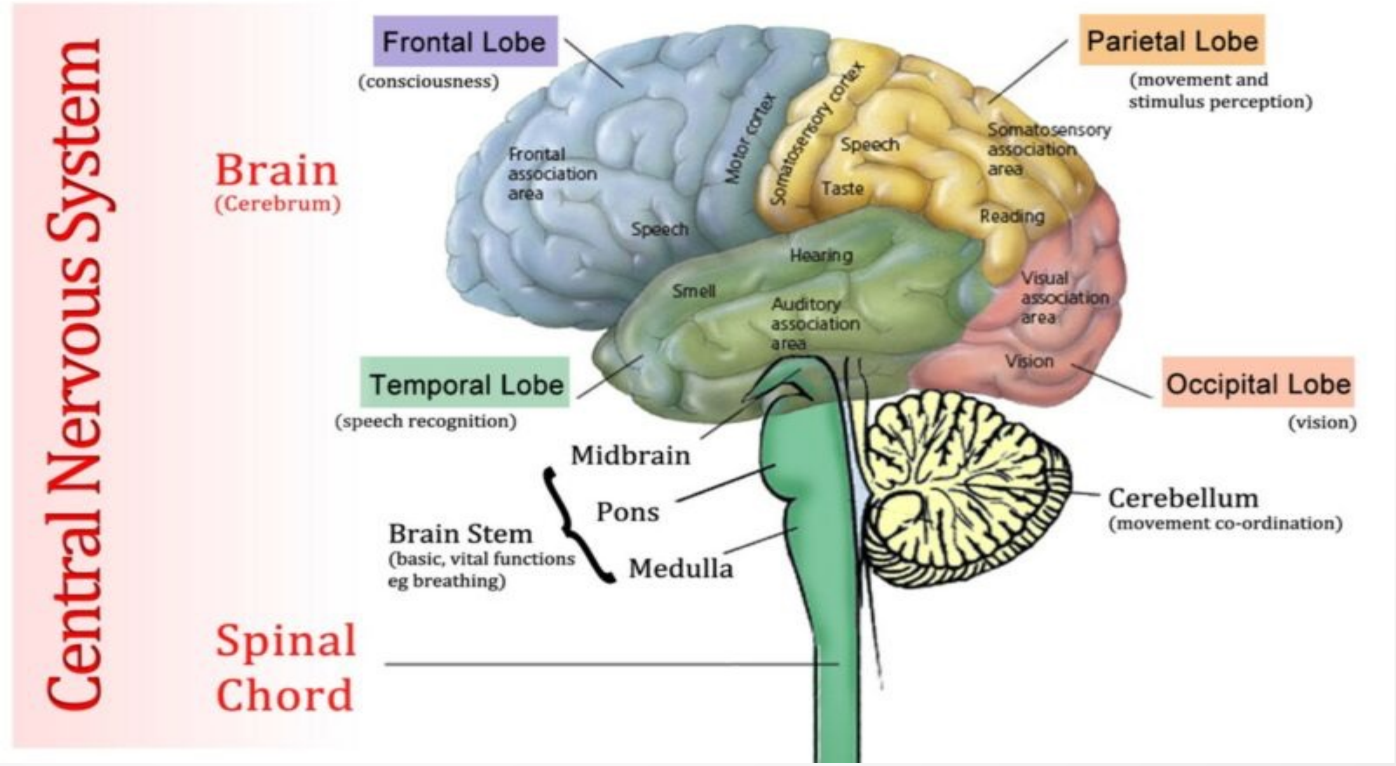
- Derived from the embryonic neural crest.
- Form a thin glial layer around neuronal cell body in the ganglia.

NEUROGLIA (REQUIRED)

Glial Cell Type	Origin	Location	Main Functions
Oligodendrocyte	Neural tube	CNS	Myelin production, electrical insulation
Astrocyte	Neural tube	CNS	Structural and metabolic support of neurons, especially at synapses; repair processes
Ependymal cell	Neural tube	Line ventricles and central canal of CNS	Aid production and movement of CSF
Microglia	Bone marrow (monocytes)	CNS	Defense and immune-related activities
Schwann cell	Neural crest	Peripheral nerves	Myelin production, electrical insulation
Satellite cells (of ganglia)	Neural crest	Peripheral ganglia	Structural and metabolic support for neuronal cell bodies

CNS

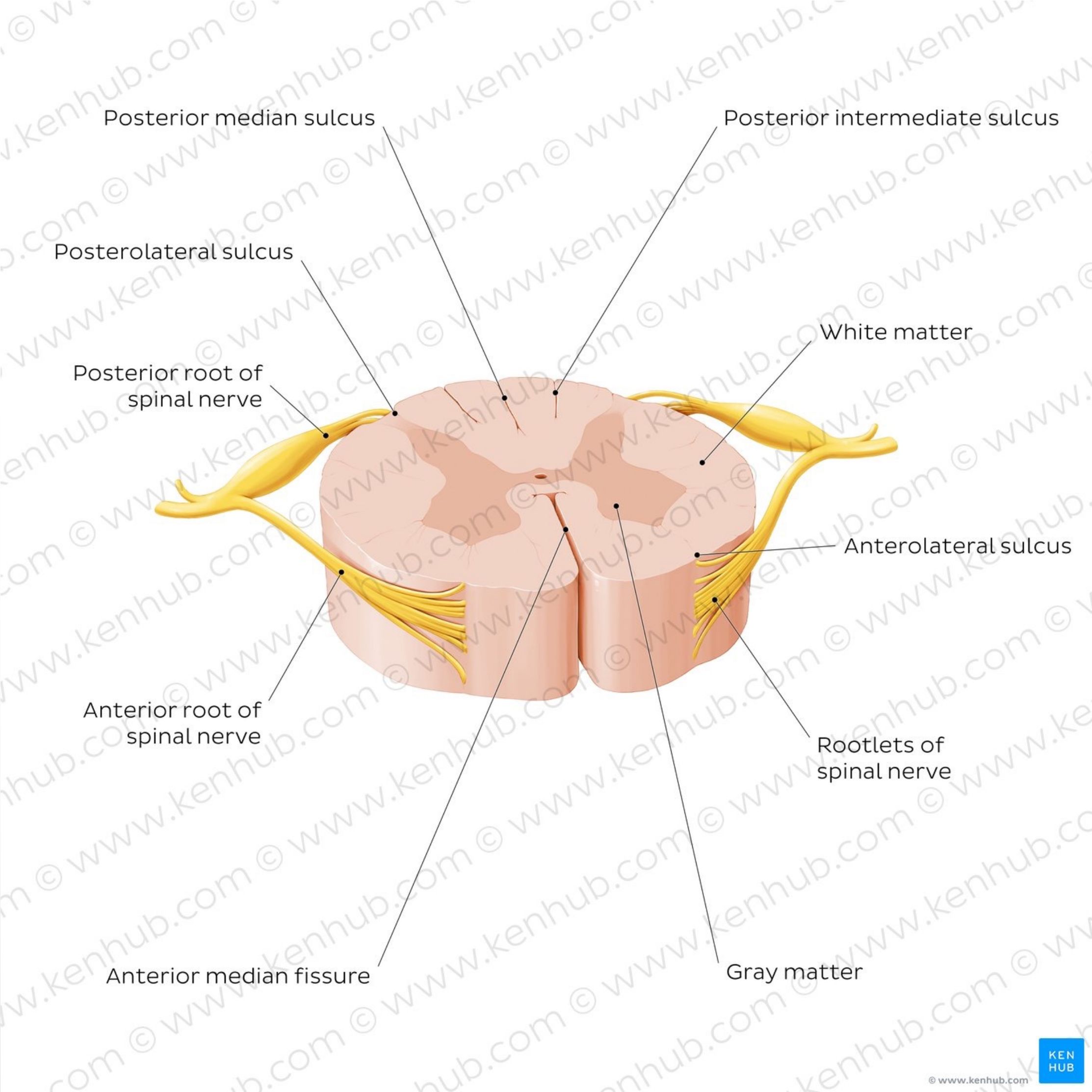
- The major structures: cerebrum, cerebellum, and spinal cord.
- Completely covered by connective tissue layers---meninges.
- Many regions show organized areas of white matter and gray matter.
- White matter: myelinated axons (often as tracts), oligodendrocytes, astrocytes, microglia, and very few neuronal cell bodies.



- Gray Matter: abundant neuronal cell bodies, dendrites, Astrocytes, and microglial cells and is where most synapses Occur.
- Gray matter makes up the thick cortex Of both the cerebrum and the cerebellum; most white matter is in deeper regions.
- cerebral nuclei: Containing large numbers of neuronal cell bodies.

CNS

- Spinal cord: the white matter is peripheral and the gray matter forms a deeper, h-shaped mass
- Two anterior projections; the anterior horns: contain cell bodies of very large motor neurons.
- Two posterior horns contain interneurons which receive sensory fibers from neurons in the spinal (dorsal root) ganglia.
- Central canal: middle of the cord, is continuous with the ventricles of the brain, lined by ependymal cells, and contains CSF.

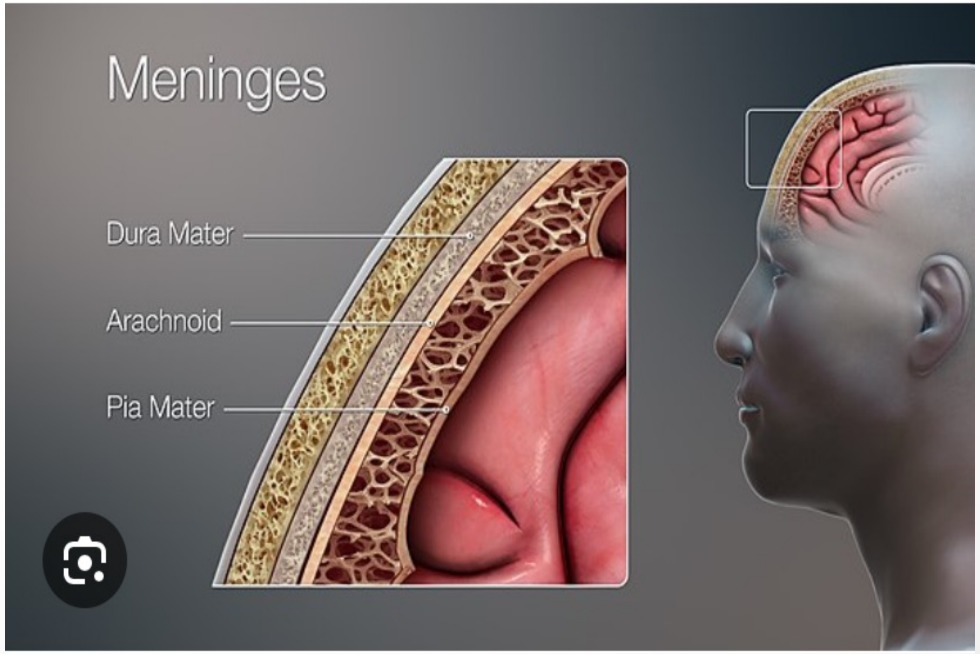


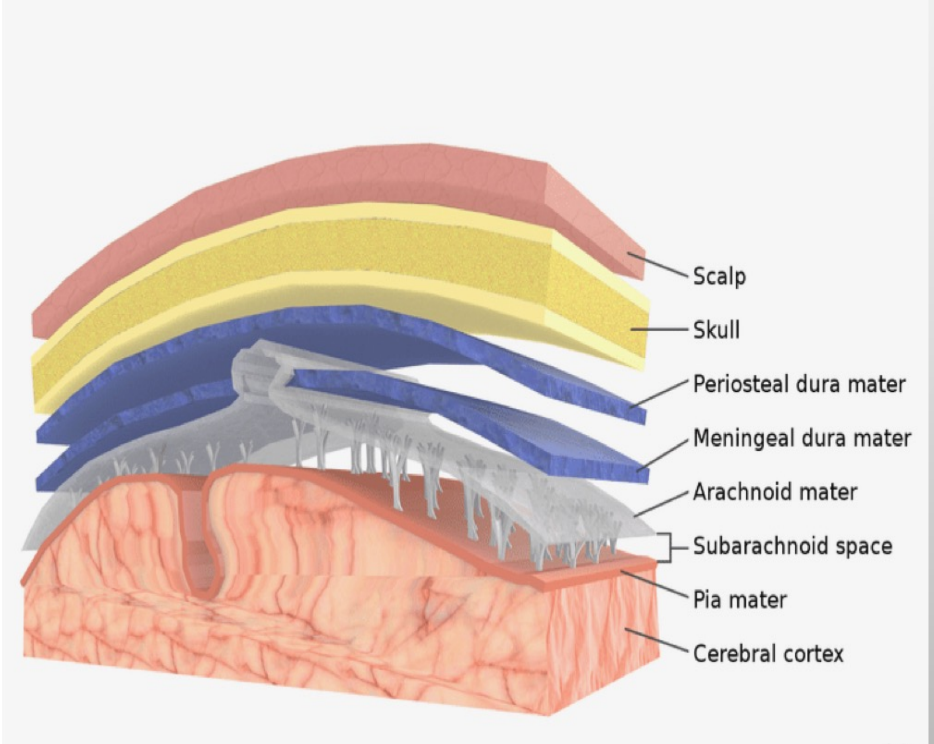
MENINGES

- Membranes of connective tissue between the bone and nervous tissue.
- 3 layesr

1. Dura mater

- The thick external.
- Consists of dense irregular connective tissue organized as an
- Outer periosteal layer continuous with the periosteum of the skull, and an inner meningeal layer.
- Spinal cord: the dura mater is separated from the periosteum by the epidural space.





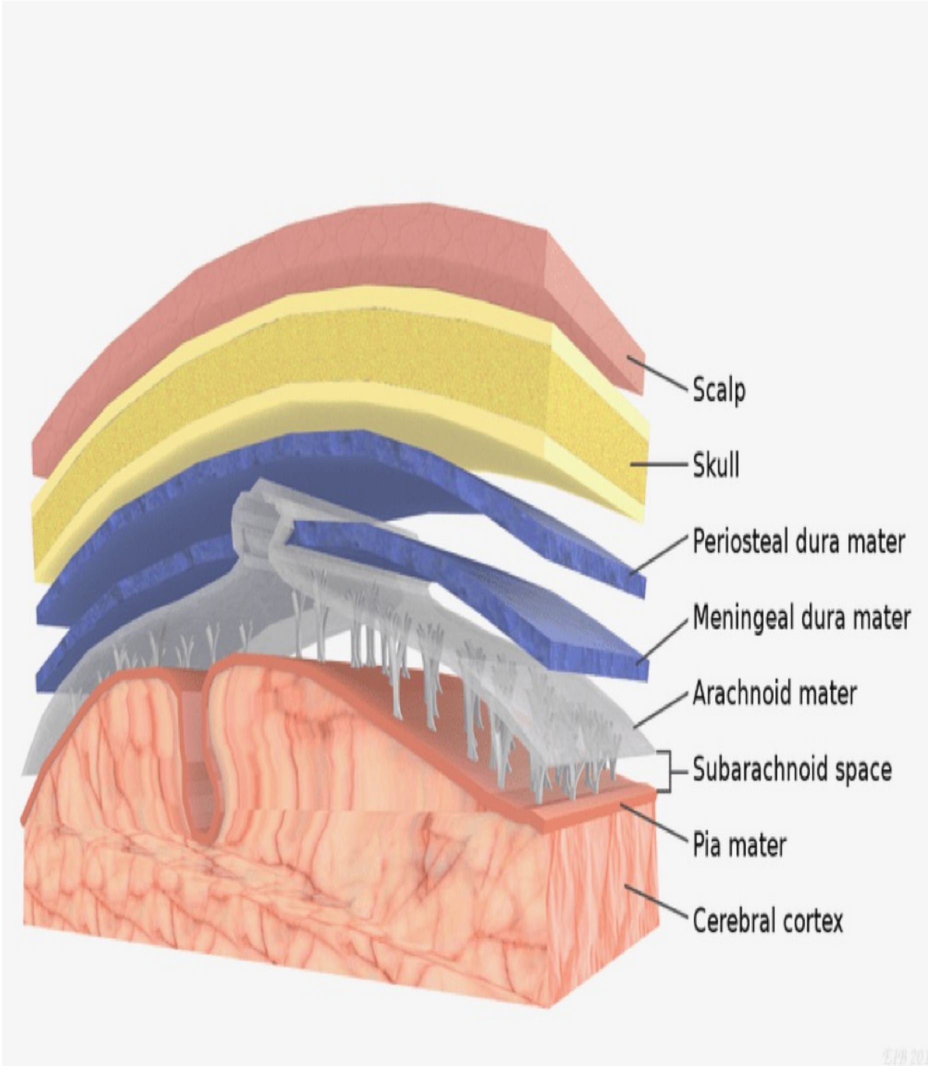
MENINGES

2. Arachnoid

- Has two components: (1) a sheet of connective tissue in contact with the dura mater and (2) a system of loosely arranged trabeculae (collagen and fibroblasts) continuous with the pia mater layer.
- Avascular---lacks nutritive capillaries.
- The arachnoid and the pia mater are intimately associated.

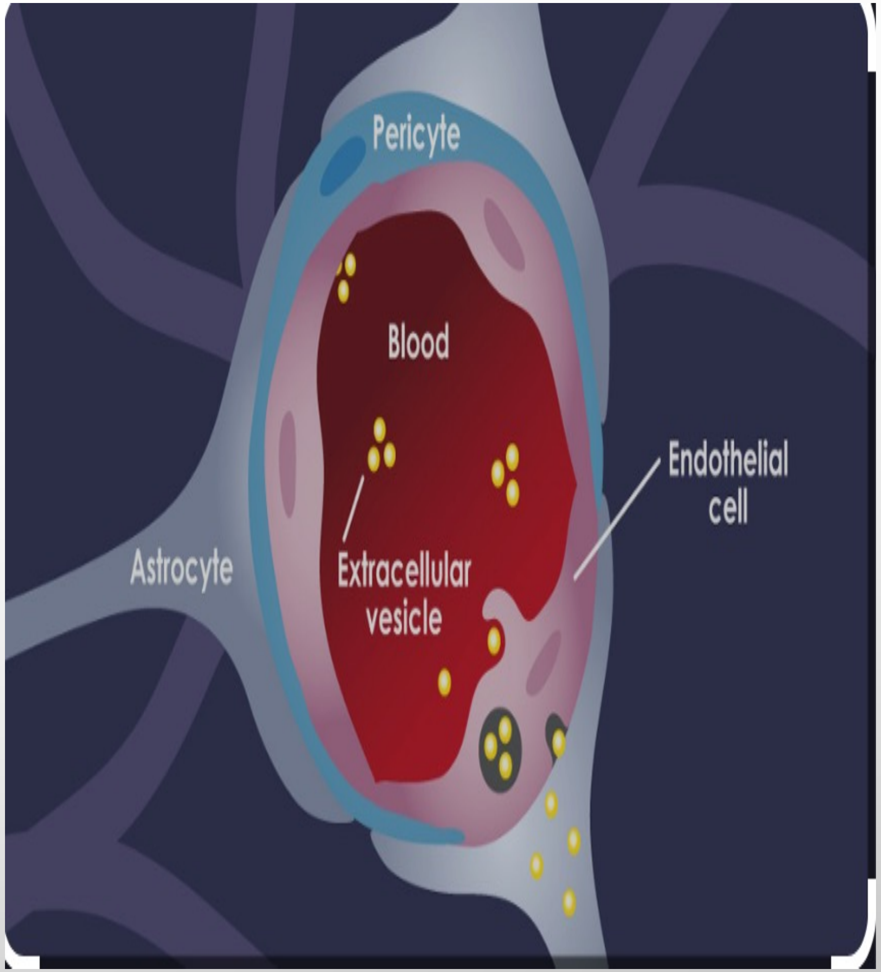
3. Pia mater

- Consists of flattened, mesenchymal-derived cells closely applied to the entire surface of the CNS tissue.
- The pia does not directly contact nerve cells or fibers---thin superficial layer of astrocytic processes (the glial limiting membrane)



BLOOD-BRAIN BARRIER

- A functional barrier that allows tight control over the passage of substances from blood into the CNS tissue.
- The main component is the capillary **endothelium**: cells are tightly sealed together with well-developed occluding junctions, with little or no transcytosis activity, and surrounded by the basement membrane.
- The **astrocytic** feet that envelops the basement membrane of capillaries.
- Protects CNS from bacterial toxins, infectious agents, and other substances, and helps maintain the stable composition and constant balance of ions in the interstitial fluid.
- BBB is not present in regions of the hypothalamus where plasma components are monitored.



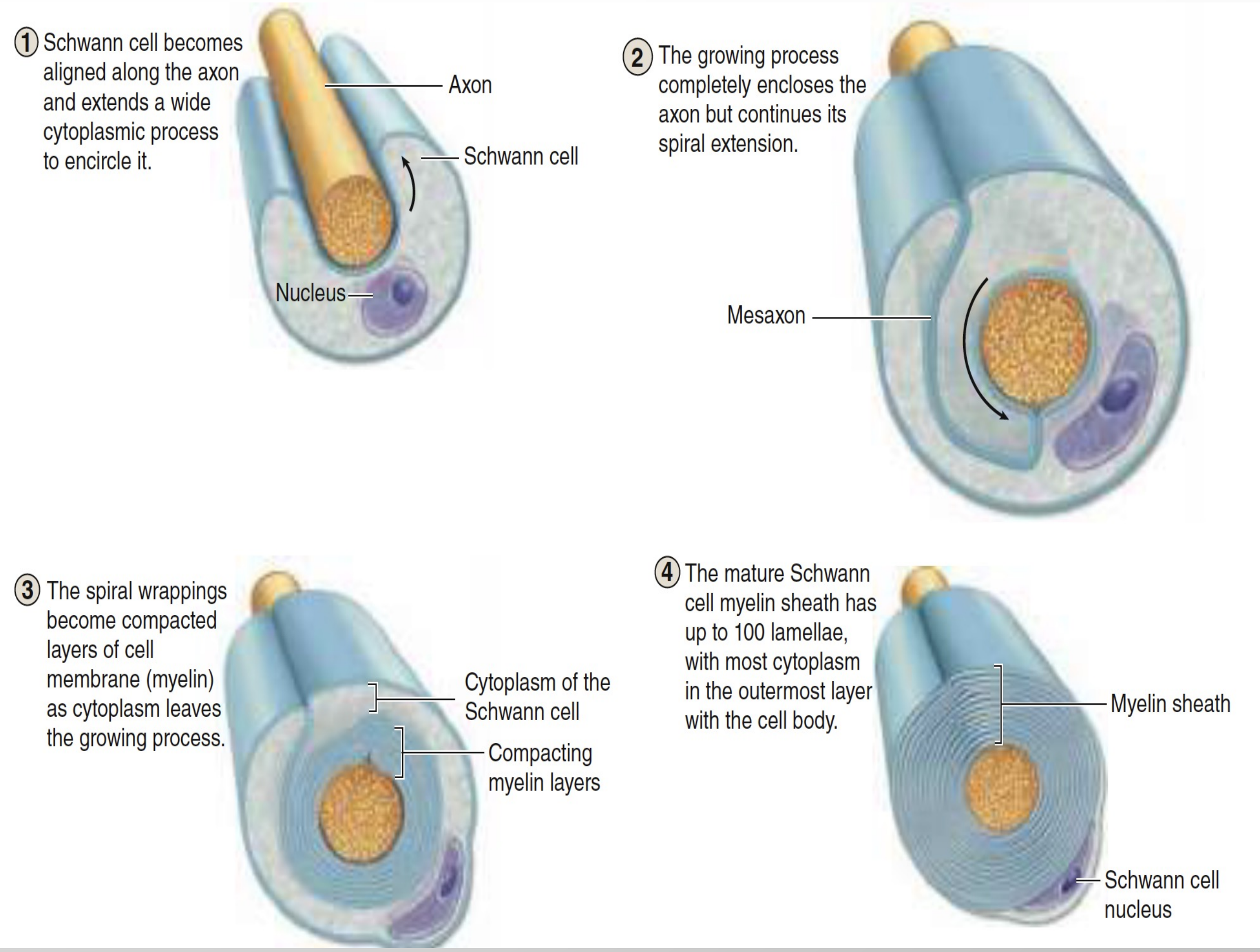
PERIPHERAL NERVOUS SYSTEM

- **The main components:**

➢Nerves, ganglia, and nerve endings.

➢Nerves are bundles of nerve fibers (axons) surrounded by Schwann cells (neurolemmocytes)and layers of connective tissue.

➢Mesaxon: plasma membrane of each covering Schwann cell fuses with itself



MYLEIN SHEATH

- Membranes of Schwann cells have a higher proportion of lipids than do other cell membranes

Cross section of PNS fibers in the TEM reveals differences between myelinated and unmyelinated axons. Large axons (**A**) are wrapped in a thick myelin sheath (**M**) of multiple layers of Schwann cell membrane.

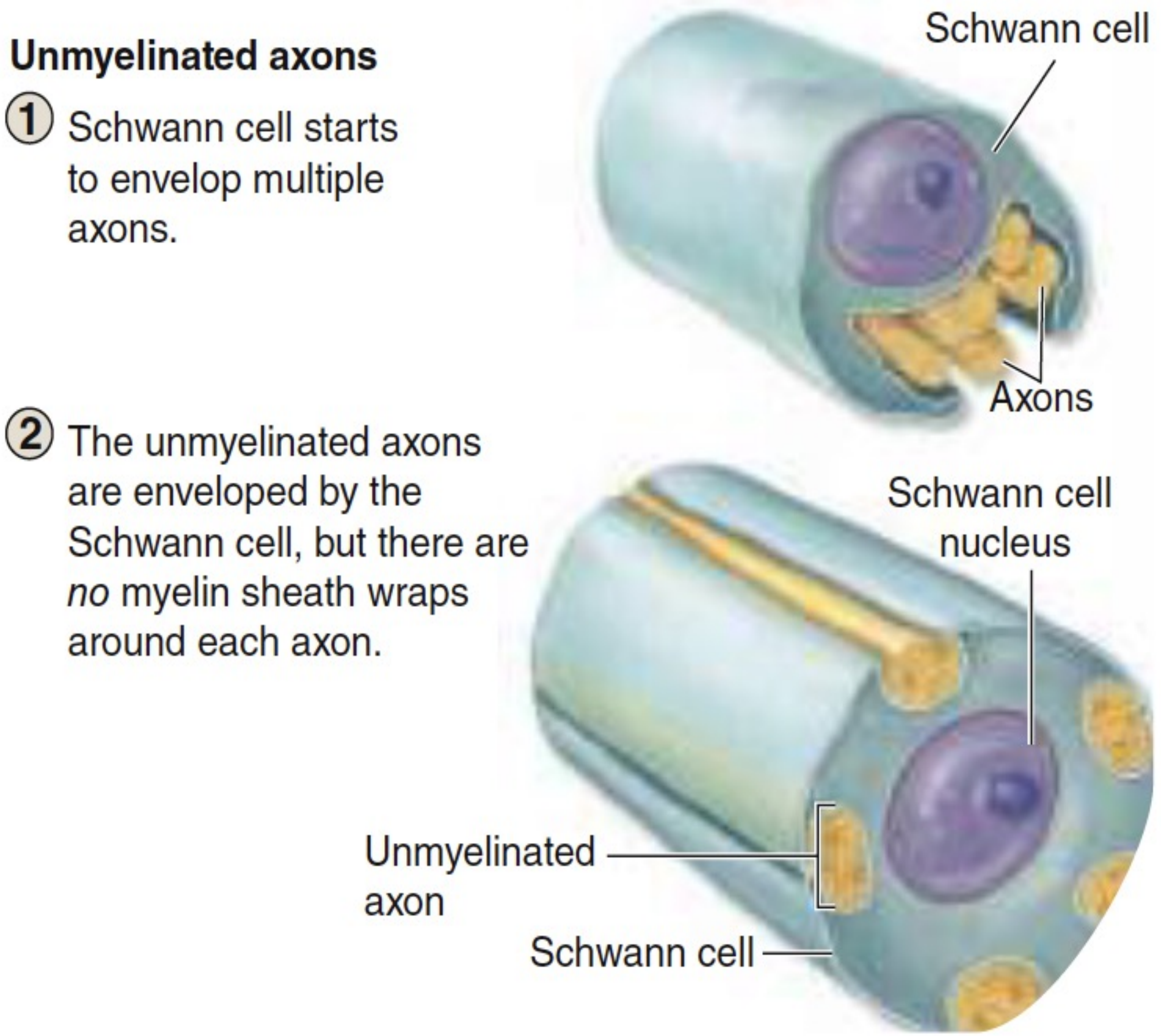
The inset shows a portion of myelin at higher magnification in which the major dense lines of individual membrane layers can be distinguished, as well as the neurofilaments (**NF**) and microtubules (**MT**) in the axoplasm (**A**). At the center of the photo is a Schwann cell showing its active nucleus (**SN**) and Golgi-rich cytoplasm (**SC**). At the right is an axon around which myelin is still forming (**FM**).

Unmyelinated axons (**UM**) are much smaller in diameter, and many such fibers may be engulfed by a single Schwann cell (**SC**). The glial cell does not form myelin wrappings around such small axons but simply encloses them. Whether it forms myelin or not, each Schwann cell is surrounded, as shown, by an external lamina containing type IV collagen and laminin like the basal laminae of epithelial cells. (X28,000, inset X70,000)

(Used with permission from Dr Mary Bartlett Bunge, The Miami Project to Cure Paralysis, University of Miami Miller School of Medicine, Miami, FL.)

UNMYLINATED AXONS

- In CNS, many short axons are not myelinated.
- Each Schwann cell can enclose portion of many axons with small diameters--- no multiple wrapping of a myelin sheath.
- No nodes of Ranvier.
- Evenly distributed voltage-gated ion channels.
- Impulse conduction is much slower than that of myelinated axons.



NERVE ORGANIZATION

- Nerves have a whitish, glistening appearance ---myelin and collagen.
- Endoneurium: immediately around the external lamina of the Schwann cells, consisting of reticular fibers, scattered fibroblasts, and capillaries.
- Perineurium: surrounds groups of axons with Schwann cells and endoneurium---fascicles-- containing flat fibrocytes with their edges sealed together by tight junctions.
- Epineurium: irregular fibrous coat extends deeply to fill the space between fascicles

NERVES

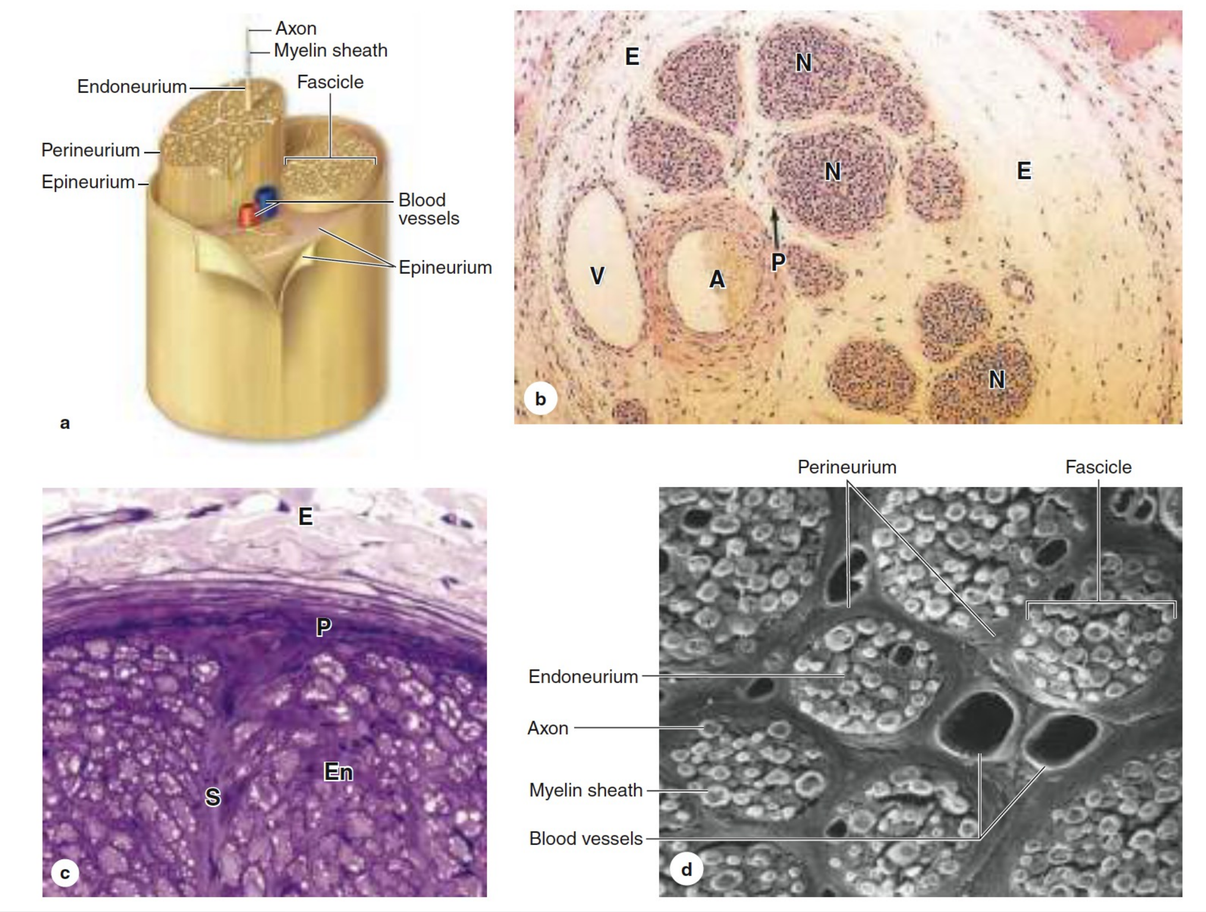
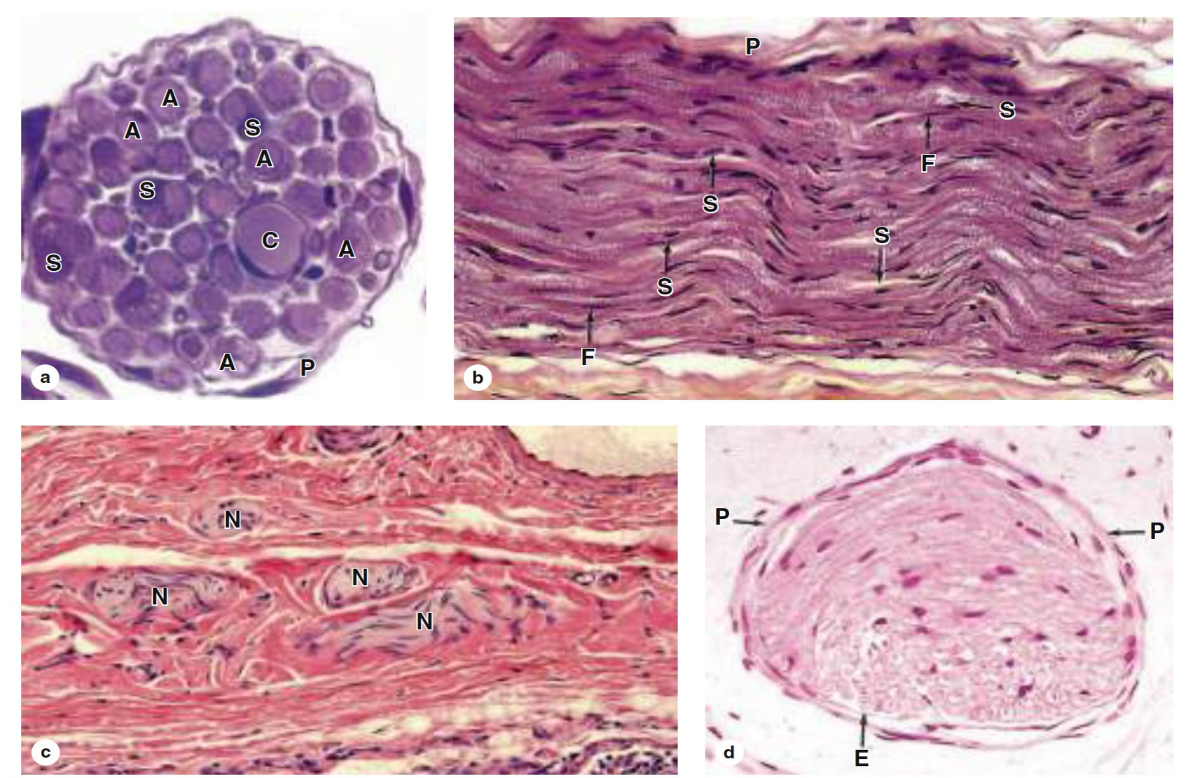


FIGURE **9–28** **Small nerves.**



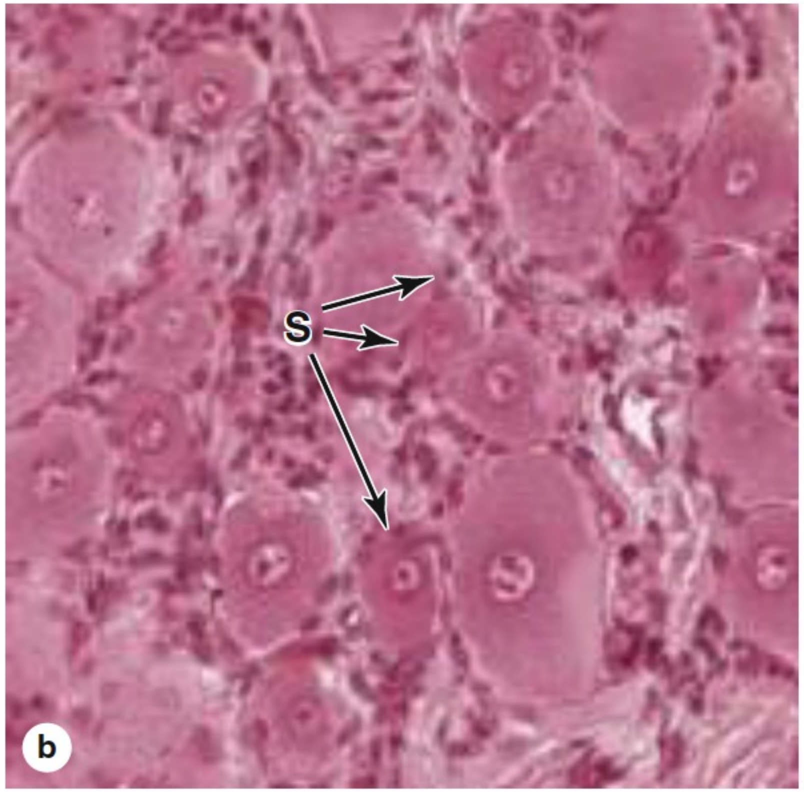
GANGLIA

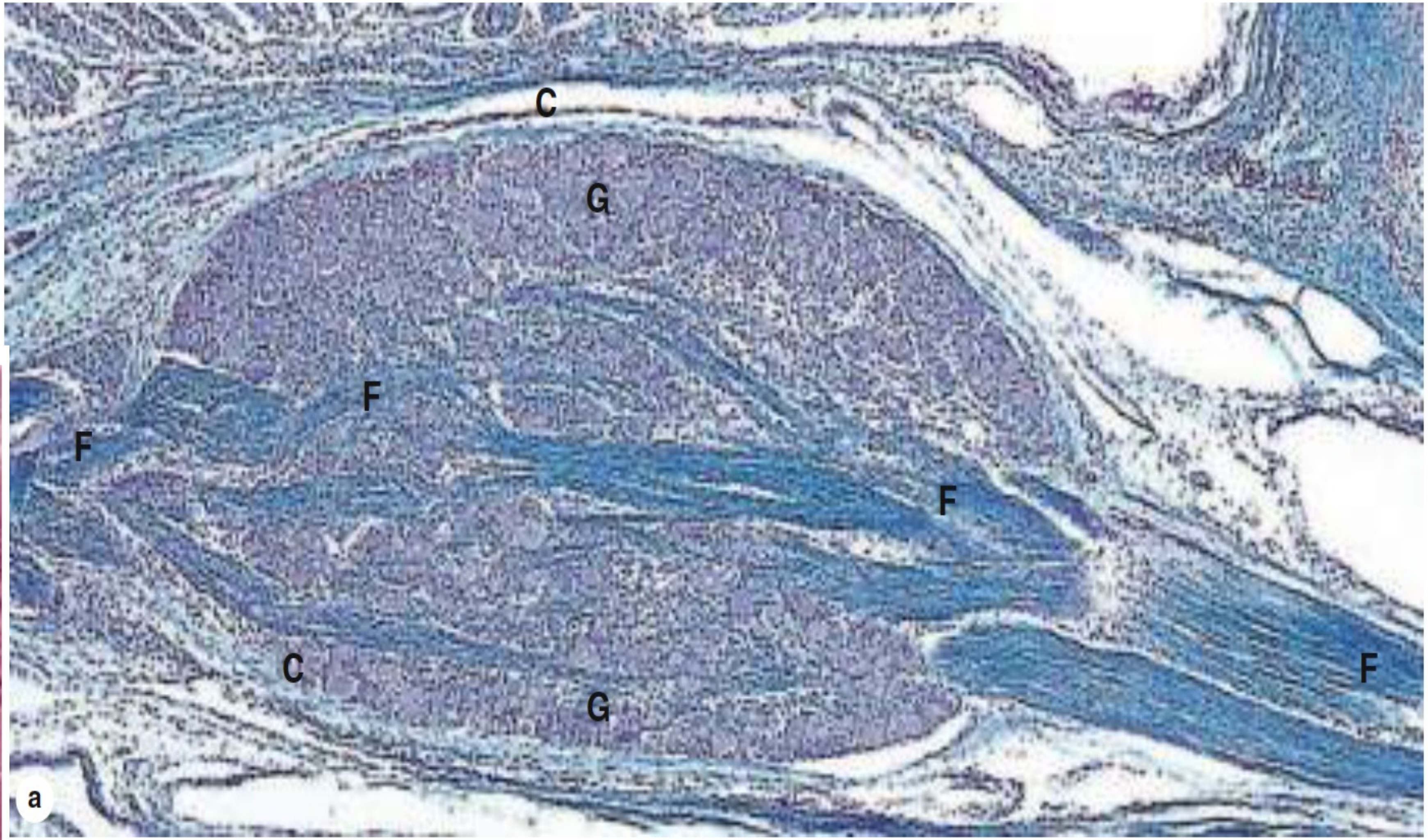
- Ovoid structures containing neuronal cell bodies and their surrounding glial satellite cells supported by delicate connective tissue and surrounded by a denser capsule.

Sensory ganglia

- Sensory ganglia receive afferent impulses that go to the CNS.
- Sensory ganglia are associated with both cranial nerves (cranial ganglia) and the dorsal roots of the spinal nerves (spinal ganglia).
- Are pseudounipolar and relay information from the ganglion’s nerve endings to the gray matter of the spinal cord via synapses with local neurons.

SENSORY G.





ANS

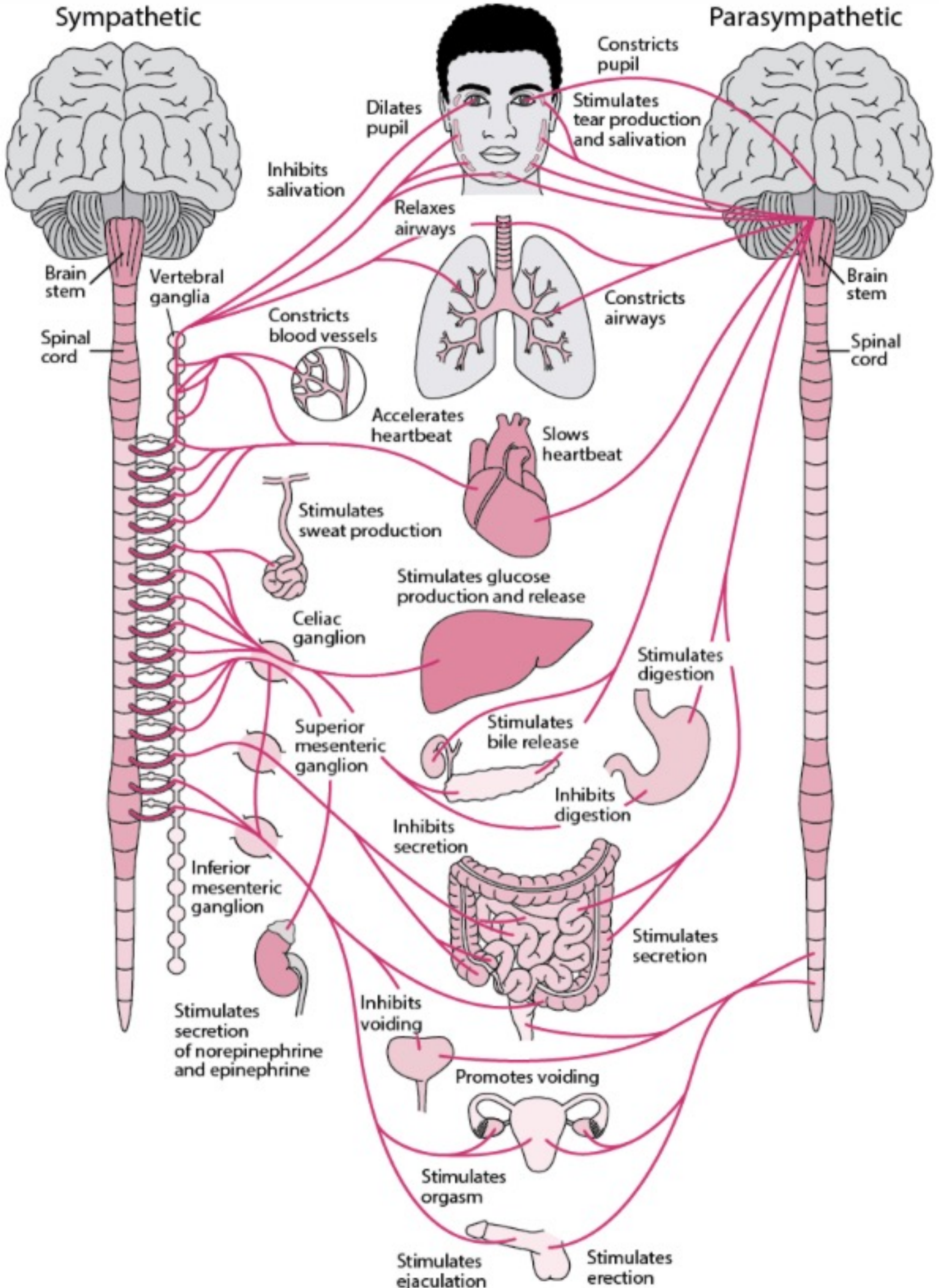
- Two divions: sympathetic and parasympathetic.
- Two-neurons circuits:

1. P**reganglionic** neuron are located in CNS:

➢Sympathetic: thoracic and lumbar segments.

➢Parasympathetic: medulla/midbrain and sacral segment of spinal cord.

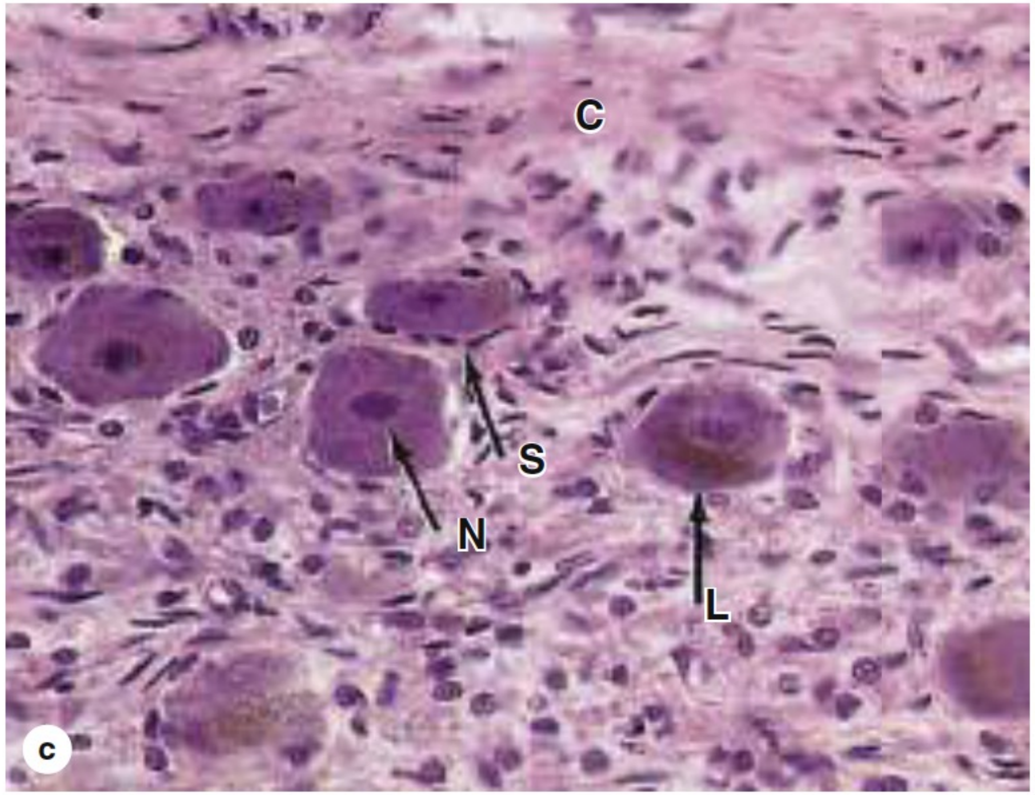
2. P**ostganglionoic** neuron (outside CNS; in a ganglion).



AUTONOMIC NS

Autonomic ganglia

- Small bulbous dilations in autonomic nerves, usually with multipolar neurons.
- Some are located within certain organs, especially in the walls of the digestive tract --- intramural ganglia.
- Autonomic nerves use two-neuron circuits.
- The first neuron of the chain, with the **preganglionic** fiber, is located in the CNS--- synapse with **postganglionic** fibers of the second multipolar neuron in the chain located in a peripheral ganglion system.



NERVE PLASTICITY AND REGENRATION

Major players in nerve regeneration:

- Neurotrophins: growth factors produced by both neurons and glial cells.
- Stem cells.
- Astrocytes.
- Existing neurons.

➢ Neurons regeneration is limited to formation of new synapse by the existing ones.

➢ Present neurons can not divide to replace lost ones.

➢ Division of astrocytes at the site of injury could interfere with axonal regeneration.

➢ Stem cells in CNS are under heavy investigation in regeneration.

NERVE REGNRATION

- Injured axons have a much greater potential for regeneration and return of function if the cell bodies are intact, damaged, or severed ONS axons can regenerate.
- Distal portions of axons, isolated from their source of new proteins and organelles, degenerate; the surrounding Schwann cells dedifferentiate, shed the myelin sheaths, and proliferate within the surrounding layers of CT
- Cellular debris including shed myelin is removed
- By blood-derived macrophages, which also secrete neurotrophins to promote anabolic events of axon regeneration.