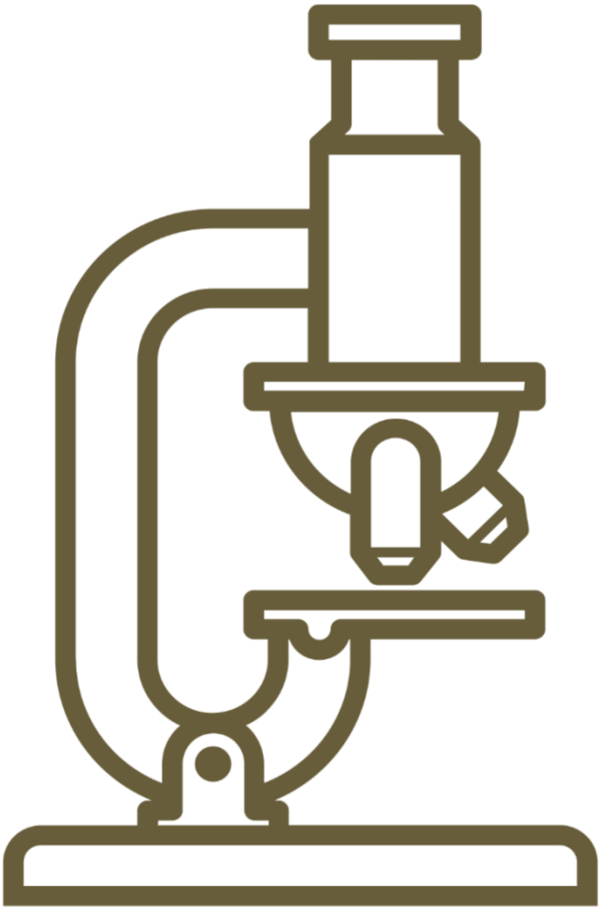
HISTOLOGY



SHEET NO.

19 V2

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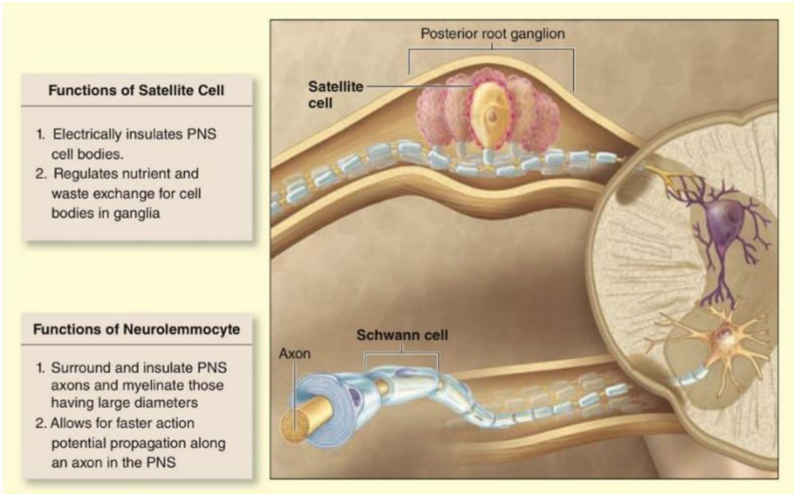
PERIPHERAL NERVOUS SYSTEM

The main components of the peripheral nervous system (PNS) are nerves, ganglia, and nerve endings. Nerves are bundles of nerve fibers (axons) surrounded by Schwann cells and layers of connective tissue.

❖Nerve Fibers:

*الدكتورة ركزت عليها وشرحتها بالتفاصيل

Nerve fibers are analogous to tracts in the CNS, containing axons enclosed within sheaths of glial cells specialized to facilitate axonal function. In peripheral nerve fibers, axons are sheathed by **Schwann cells**, or neurolemmocytes (as shown in the Figure **B**). The sheath may or may not form myelin around the axons, depending on their diameter.



B

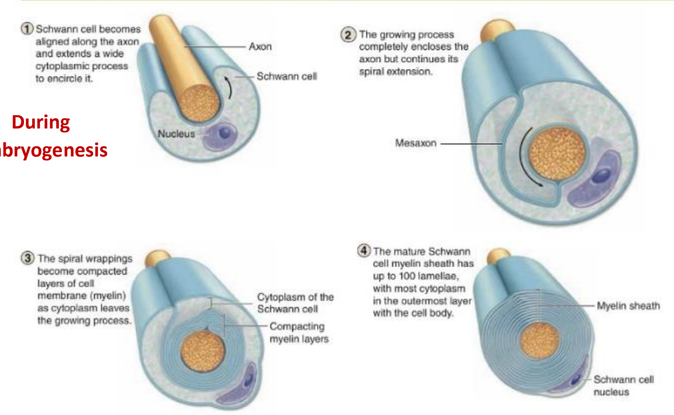
❖Myelinated Fibers:

*الدكتورة ركزت عليها وشرحتها بالتفاصيل

As axons of large diameter grow in the PNS, they are engulfed along their length by a series of differentiating neurolemmocytes and become **myelinated nerve fibers**. The plasma membrane of each covering Schwann cell fuses with itself at an area termed the **mesaxon** and a wide, flattened process of the cell continues to extend itself, moving circumferentially around the axon many times **(Figure 9–21)**. The multiple layers of Schwann cell membrane unite as a thick **myelin sheath** composed mainly of lipid bilayers and membrane proteins.

FIGURE 9–21 Myelination of large-diameter PNS axons.

During embryogenesis



A Schwann cell (neurolemmocyte) engulfs one portion along the length of a large-diameter axon. The Schwann cell membrane fuses around the axon and one thin extension of the Schwann cell elongates greatly and wraps itself repeatedly around the axon to form multiple, compacted layers. The Schwann cell membrane wrappings constitute the myelin sheath, with the Schwann cell body always on its outer surface. The myelin layers are very rich in lipid, and provide insulation and facilitate formation of action potentials along the axolemma.

Mesaxon: plasma membrane of each covering Schwan cell fuses with itself.

Myelin sheath: Membranes of Schwan cells have a higher proportion of lipids than do other cell membranes.

- Myelin is a large lipoprotein complex that, like cell membranes, is partly removed by standard histologic procedure. Unlike oligodendrocytes of the CNS, a Schwann cell forms myelin around only a portion of one axon. With high-magnification TEM, the myelin sheath appears as a thick electron-dense axonal covering in which the concentric membrane layers may be visible **(Figure 9–22)**.

FIGURE **9–22** **Ultrastructure of myelinated and unmyelinated fibers.** *الدكتورة ركزت عليها وشرحتها بالتفاصيل

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.)

UM axons: covered with Schwan cell (not completely) without producing myelin.

*The CNS doesn't have connective tissue>> it has glial cells instead

*The PNS we have connective tissue **(type IV collagen and laminin)** around the schwann cell

- The prominent electron-dense layers visible ultra structurally in the sheath, the major dense lines, represent the fused, protein-rich cytoplasmic surfaces of the Schwann cell membrane. Along the myelin sheath, these surfaces periodically separate slightly to allow transient movement of cytoplasm for membrane maintenance; at these **myelin clefts** the major dense lines temporarily disappear **(Figure 9–23).**

- Remember:

مهم حكت الدكتورة بتحب تجيبه بالامتحان

a- 1 Schwann cell per 1 axon.

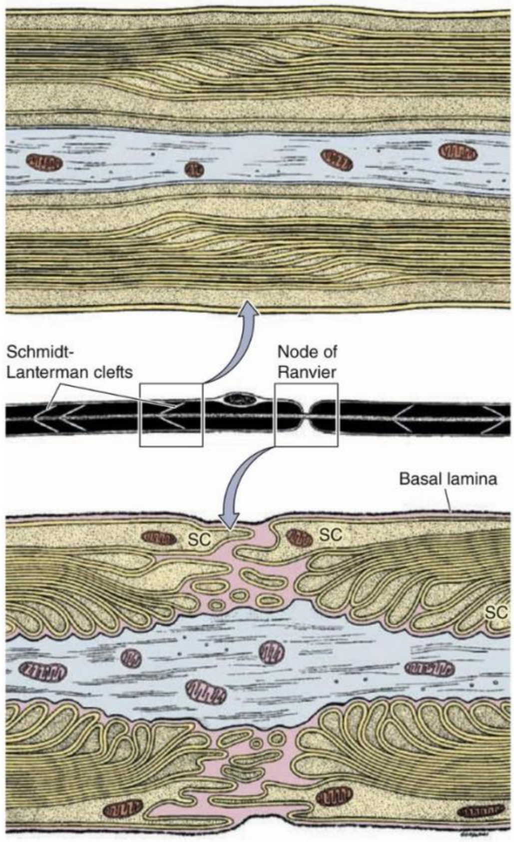
b- 1 oligodendrocytes can wrap more than one axon >>independent nucleus> > its processes go to different segment, different axons.

- Membranes of Schwann cells have a higher proportion of lipids than do other cell membranes, and the myelin sheath serves to insulate axons and maintain a constant ionic microenvironment most suitable for action potentials.

- Between adjacent Schwann cells on an axon the myelin sheath shows small **nodes of Ranvier** (or nodal gaps), where the axon is only partially covered by interdigitating Schwann cell processes. At these nodes the axolemma is exposed to ions in the interstitial fluid and has a much higher concentration of voltage-gated Na^+ channels, which renew the action potential and produce saltatory conduction (***saltare*** means to jump) of nerve impulses, their rapid movement from node to node. The length of axon ensheathed by one Schwann cell

FIGURE 9–23 **Myelin maintenance and nodes of Ranvier.**

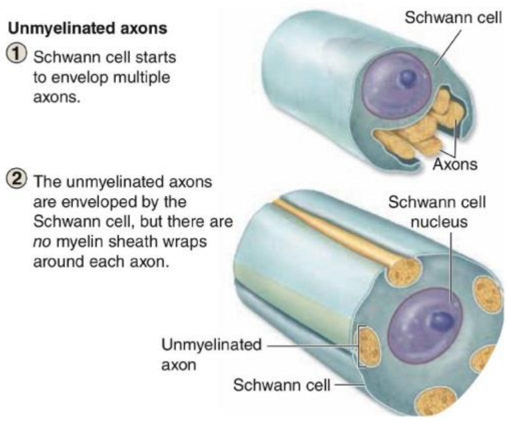
*الصورة للفهم ما كانت بالمحاضرة



❖Unmyelinated Fibers:

Unlike the CNS where many short axons are not myelinated at all but run free among the other neuronal and glial processes, in these unmyelinated fibers the glial cell does not form the multiple wrapping of a myelin sheath **(Figure 9–21).** In unmyelinated fibers, each Schwann cell can enclose portions of many axons with small diameters. Without the thick myelin sheath, nodes of Ranvier are not seen along unmyelinated nerve fibers. Moreover, these small-diameter axons have evenly distributed voltage-gated ion channels; their impulse conduction is not saltatory and is much slower than that of myelinated axons.

UNMYLINATED AXONS: Many axons in one Schwan cell.



The speed of action potential in the myelinated fiber is faster >> Because of nodes of Ranvier >> the part of the axons that has the ion channels, so it jumps from one node to another.

❖Nerve Organization:

- In the PNS nerve fibers are grouped into bundles to form nerves. Except for very thin nerves containing only unmyelinated fibers, nerves have a whitish, glistening appearance because of their myelin and collagen content.

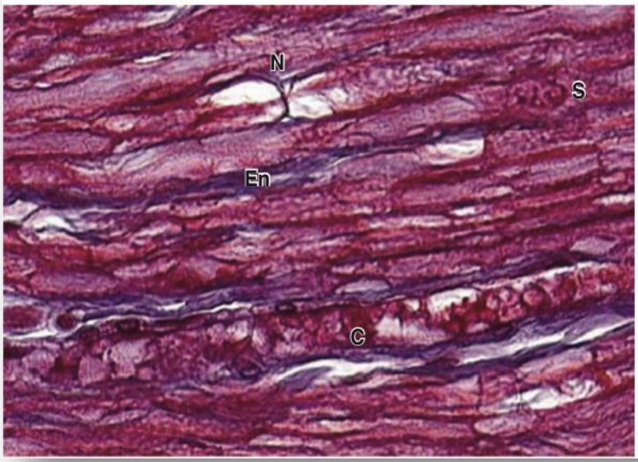
- Axons and Schwann cells are enclosed within layers of connective tissue. **(Figures 9-24,9-26 and 9-27)** Immediately around the external lamina of the Schwann cells is a thin layer called the **endoneurium**, consisting of reticular fibers, scattered fibroblasts, and capillaries.

- Groups of axons with Schwann cells and endoneurium are bundled together as **fascicles** by a sleeve of **perineurium**, containing flat fibrocytes with their edges sealed together by tight junctions. From 2 to 6 layers of these unique connective tissue cells regulate diffusion into the fascicle and make up the **blood-nerve barrier** that helps maintain the fibers' microenvironment. Externally, peripheral nerves have a dense, irregular fibrous coat called the **epineurium**, which extends deeply to fill the space between fascicles.

- **Do We have blood supply in the axon?**

Yes, Because Schwann cell need nutritious.

FIGURE **9–24** **Node of Ranvier and endoneurium.** الصورة للفهم ما كانت بالمحاضرة*

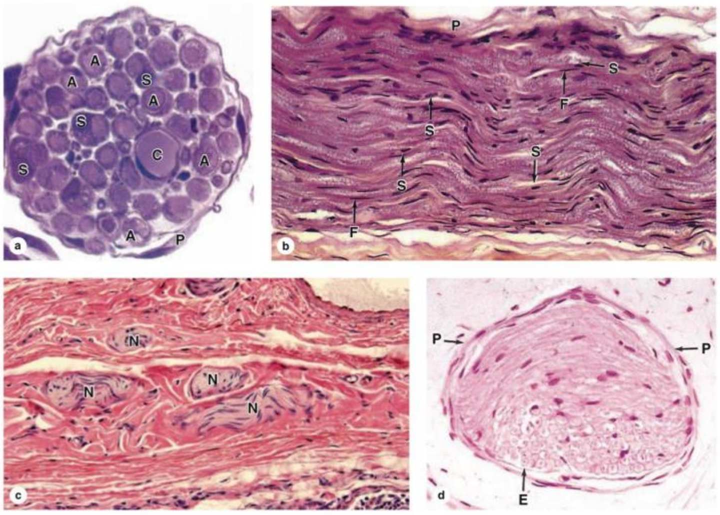


A longitudinally oriented nerve shows one node of Ranvier (**N**) with the axon visible. Collagen of the sparse endoneurium (**En**), blue in this trichrome stain, surrounds the Schwann cells and a capillary (**C**). At least one Schwann cell nucleus (**S**) is also clearly seen. (X400; Mallory trichome)

- Very small nerves consist of one fascicle **(Figure 9–28)**. Small nerves can be found in sections of many organs and often show a winding disposition in connective tissue. PNS establish communication between centers in the CNS and the sense organs and effectors (muscle, glands ..etc)

- Nerves possessing only sensory fibers are called **sensory nerves**; those composed only of fibers carrying impulses to the effectors are called **motor nerves**. Most nerves have both sensory and motor fibers and are called **mixed nerves**, usually also with both myelinated and unmyelinated axons.

FIGURE **9–28** **Small nerves.** *الصورة للفهم ما كانت بالمحاضرة



Small nerves can be seen in sections from most organs.

(a) In cross section an isolated, resin-embedded nerve is seen to have a thin perineurium (**P**), one capillary (**C**), and many large axons (**A**) associated with Schwann cells (**S**). A few nuclei of fibroblasts can be seen in the endoneurium between the myelinated fibers. (X400; PT)

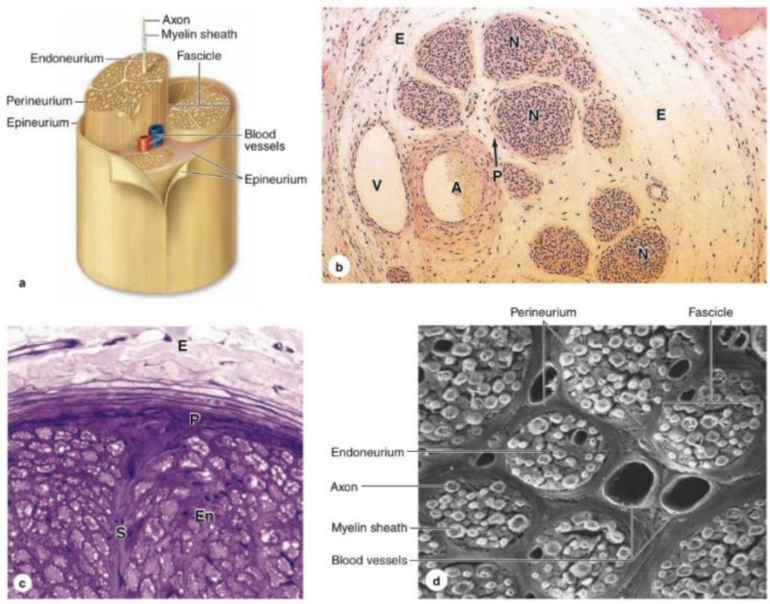
(b) In longitudinal sections the flattened nuclei of endoneurial fibroblasts (**F**) and more oval nuclei of Schwann cells (**S**) can be distinguished. Nerve fibers are held rather loosely in the endoneurium and in low-magnification longitudinal section are seen to be wavy rather than straight. This indicates a slackness of fibers within the nerve, which allows nerves to stretch slightly during body movements with no potentially damaging tension on the fibers. (X200; H&E)

(c) In sections of mesentery and other tissues, a highly wavy or tortuous disposition of a single small nerve (**N**) will be seen as multiple oblique or transverse pieces as the nerve enters and leaves the area in the section. (X200; H&E)

(d) Often, a section of small nerve will have some fibers cut transversely and others cut obliquely within the same fascicle, again suggesting the relatively unrestrained nature of the fibers within the endoneurium (**E**) and perineurium (**P**). (X300; H&E)

*الدكتورة ركزت عليها وشرحتها بالتفاصيل

FIGURE **9–26** **Peripheral nerve connective tissue: Epi-, peri-, and endoneurium.**



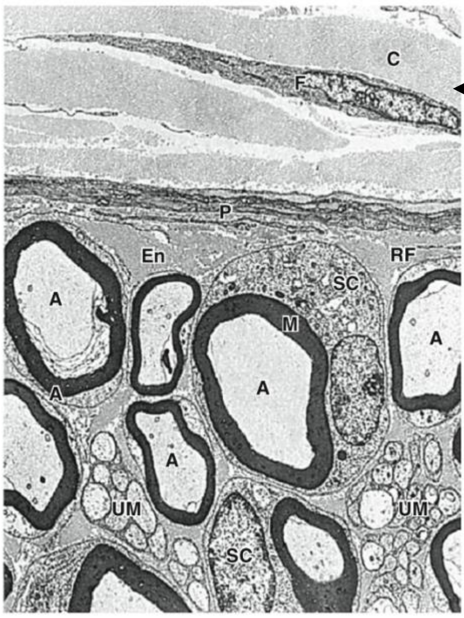
(a) The diagram shows the relationship among these three connective tissue layers in large peripheral nerves. The epineurium (**E**) consists of a dense superficial region and a looser deep region that contains the larger blood vessels.

(b) The micrograph shows a small vein (**V**) and artery (**A**) in the deep epineurium (**E**). Nerve fibers (**N**) are bundled in fascicles. Each fascicle is surrounded by the perineurium (**P**), consisting of a few layers of unusual squamous fibroblastic cells that are all joined at the peripheries by tight junctions. The resulting blood-nerve barrier helps regulate the microenvironment inside the fascicle. Axons and Schwann cells are in turn surrounded by a thin layer of endoneurium. (X140; H&E)

(c) As shown here and in the diagram, septa (**S**) of connective tissue often extend from the perineurium into larger fascicles. The endoneurium (**En**) and lamellar nature of the perineurium (**P**) are also shown at this magnification, along with some adjacent epineurium (**E**). (X200; PT)

(d) SEM of transverse sections of a large peripheral nerve showing several fascicles, each surrounded by perineurium and packed with endoneurium around the individual myelin sheaths. Each fascicle contains at least one capillary. Endothelial cells of these capillaries are tightly joined as part of the blood-nerve barrier and regulate the kinds of plasma substances released to the endoneurium. Larger blood vessels course through the deep epineurium that fills the space around the perineurium and fascicles. (X450)

FIGURE **9–27** **Peripheral nerve ultrastructure.**



*الصورة للفهم ما كانت بالمحاضرة

This low-magnification TEM shows a fibroblast (**F**) surrounded by collagen (**C**) in the epineurium (**E**) and three layers of flattened cells in the perineurium (**P**) which form another part of the blood-nerve barrier. Inside the perineurium the endoneurium (**En**) is rich in reticulin fibers (**RF**) that surround all Schwann cells. Nuclei of two Schwann cells (**SC**) of myelinated axons (**A**) are visible as well as many unmyelinated axons (**UM**) within Schwann cells. (X1200)

- Spinal nerves (mixed nerve) all in the end will separate to:

A) Anterior (motor neuron) >gray matter.

B) Posterior(sensory) >outside the spinal cord in the ganglia.

NOTE: Dorsal root ganglia absolutely sensory

❖Ganglia:

Are typically ovoid structures containing neuronal cell bodies and their surrounding glial satellite cells supported by delicate connective tissue and surrounded by a denser capsule. Because they serve as relay stations to transmit nerve impulses, at least one nerve enters and another exits from each ganglion. The direction of the nerve impulse determines whether the ganglion will be a **sensory** or an **autonomic** ganglion.

1. Sensory Ganglia

- Sensory ganglia receives 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**).

- The large neuronal cell bodies of ganglia **(Figure 9–29)** are associated with thin, sheet-like extensions of **small glial satellite cells** **(Figures B).**

- Sensory ganglia are supported by a distinct connective tissue capsule and an internal framework continuous with the connective tissue layers of the nerves.

- The neurons of these 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.

2. Autonomic Ganglia

- Autonomic nerves effect the activity of smooth muscle, the secretion of some glands, heart rate, and many other involuntary activities by which the body maintains a constant internal environment (homeostasis).

- 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. Its axon forms a synapse with **postganglionic fibers** of the second multipolar neuron in the chain located in a peripheral ganglion system.

- The chemical mediator present in the synaptic vesicles of all preganglionic axons is acetylcholine.

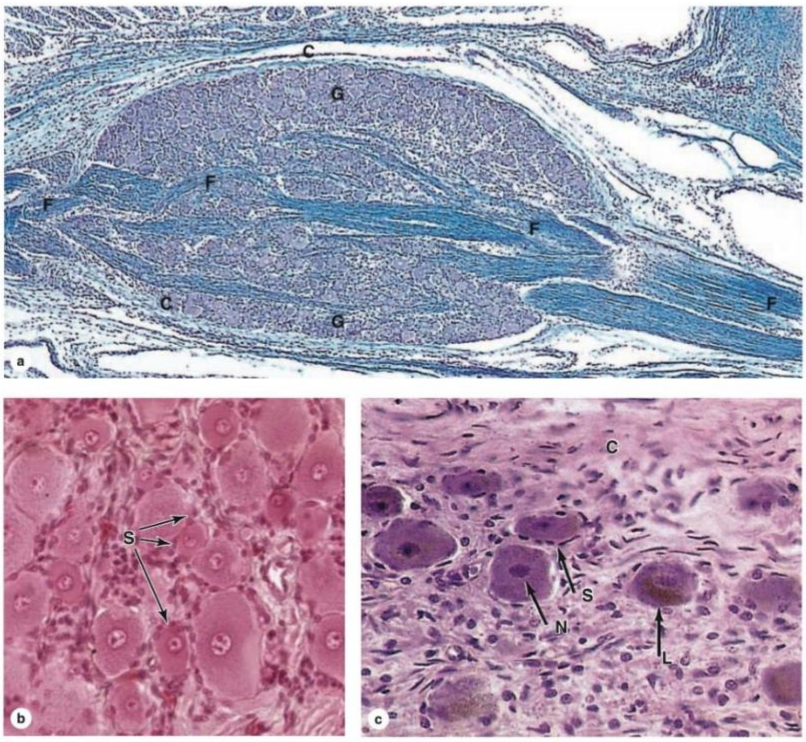
- As indicated earlier autonomic nerves make up the **autonomic nervous system**. This has two parts: the **sympathetic** and the **parasympathetic** divisions.

- Neuronal cell bodies of preganglionic sympathetic nerves are located in the thoracic and lumbar segments of the spinal cord and those of the para-sympathetic division are in the medulla, midbrain and in sacral portion of the spinal cord.

- Sympathetic second neurons are located in small ganglia along the vertebral column, while second neurons of the parasympathetic series are found in very small ganglia always located near or within the effector organs, for example in the walls of the stomach and intestines.

- Parasympathetic ganglia may lack distinct capsules altogether, perikarya and associated satellite cells simply forming a loosely organized plexus within the surrounding connective tissue.

FIGURE 9–29 Ganglia.



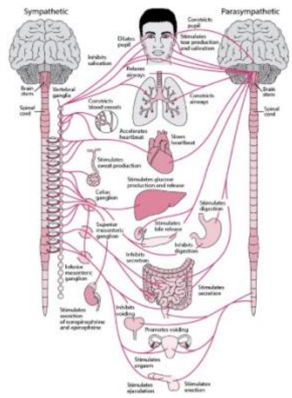
(a) A sensory ganglion (**G**) has a distinct connective tissue capsule (**C**) and internal framework continuous with the epineurium and other components of peripheral nerves, except that no perineurium is present and that there is no blood-nerve barrier function. Fascicles of nerve fibers (**F**) enter and leave these ganglia. (X56; Kluver-Barrera stain)

(b) Higher magnification shows the small, rounded nuclei of glia cells called satellite cells (**S**) that produce thin, sheet-like cytoplasmic extensions that completely envelop each large neuronal perikaryon. (X400; H&E)

(c) Sympathetic ganglia are smaller than most sensory ganglia but similar in having large neuronal cell bodies (**N**), some containing lipofuscin (**L**). Sheets from satellite cells (**S**) enclose each neuronal cell body with morphology slightly different from that of sensory ganglia. Autonomic ganglia generally have less well-developed connective tissue capsules (**C**) than sensory ganglia. (X400; H&E)

*الدكتورة ما ركزت على الصور كثير، بس اللي فوق حكت عنها شوي

Autonomic (2 sets of neurons)



Sympathetic

Preganglionic

In the CNS >> gray matter
in the thoracic and
lumbar of the spinal cord

Q) The axon that brings autonomic motor messages to the GI tract are the axon of?

- Postganglionic neuron

Postganglionic

In the ganglia
outside the CNS

Sent axon to the target organ or smooth muscle, cardiac, glands.

The axon of the pre-gang. Goes to the post-gang.

Pre gang. In the sacral —**Axons**→ Post gang. In the ganglia —**Axons**→ Deliver the message to the target

Parasympathetic

Preganglionic

Spinal cord

(Sacral region)

Within specific nuclei

(Collection of neurons in the CNS)

The set of neurons >> cranial nerve >> the most important one is the vagus nerve (10th cranial nerve)… Because most of the parasympathetic flow come from it.

Postganglionic

❖REGENERATION:

يلا هانت اخر موضوعين :(

- Despite its general stability, the nervous system exhibits neuronal differentiation and formation of new synapses even in adults. Embryonic development of the nervous system produces an excess of differentiating neurons, and the cells that do not establish correct synapses with other neurons are eliminated by apoptosis.

- In adult mammals after an injury, the neuronal circuits may be reorganized by the growth of neuronal processes, forming new synapses to replace ones lost by injury. Thus, new communications are established with some degree of functional recovery.

- This neural plasticity and reformation of processes are controlled by **neurotrophins:** several growth factors produced by both neurons and glial cells.

- Neuronal stem cells are present in the adult CNS, located in part among the cells of the ependyma, which can supply new neurons, astrocytes, and oligodendrocytes.

- Fully differentiated, interconnected CNS neurons cannot temporarily disengage these connections and divide to replace cells lost by injury or disease; the potential of neural stem cells to allow tissue regeneration and functional recovery within the CNS components is a subject of intense investigation.

- Astrocytes do proliferate at injured sites and these growing cells can interfere with successful axonal regeneration in structures such as spinal cord tracts

- In the histologically much simpler peripheral nerves, injured axons have a much greater potential for regeneration and return of function. If the cell bodies are intact, damaged, or severed PNS axons can regenerate as shown in the sequence of diagrams in **(Figure 9–30)**.

- 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 connective tissue.

- Cellular debris including shed myelin is removed by blood-derived macrophages, which also secrete neurotrophins to promote anabolic events of axon regeneration.

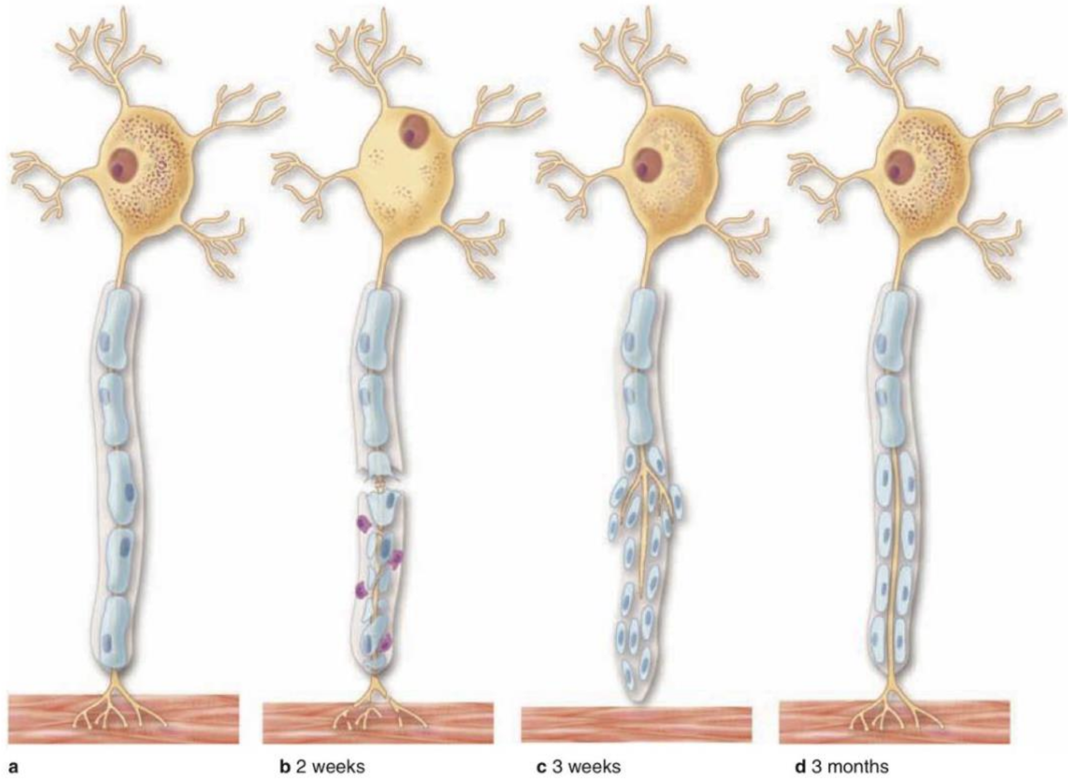
- The onset of regeneration is signaled by changes in the perikaryon that characterize the process of **chromatolysis**: the cell body swells slightly, Nissl substance is initially diminished, and the nucleus migrates to a peripheral position within the perikaryon.

- The proximal segment of the axon close to the wound degenerates for a short distance, but begins to grow again distally as new Nissl substance appears and debris is removed.

- The new Schwann cells align to serve as guides for the regrowing axons and produce polypeptide factors that promote axonal outgrowth.

- Motor axons reestablish synaptic connections with muscles and function is restored.

FIGURE 9–30 Regeneration in peripheral nerves. *الدكتورة ركزت عليها وشرحتها بالتفاصيل



In an injured or cut peripheral nerve, proximal axon segments can regenerate from their cut ends after a delay. The main changes that take place in an injured nerve fiber are shown here.

(a) Normal nerve fiber, with its perikaryon, extensive RER (Nissl substance), and effector cell (muscle).

(b) When the axon is injured, the RER is greatly reduced initially and the nerve fiber distal to the injury degenerates along with its myelin sheath. Debris is phagocytosed by macrophages (shown in purple).

(c) In the following weeks after injury, muscle fiber shows denervation atrophy, but Schwann cells proliferate to form a compact cord penetrated by the regrowing axon. The axon grows at the rate of 0.5-3 mm/d.

(d) After some months, the nerve fiber regeneration is successful and functional connections with the muscle fiber are restored.

Negative aspect about astrocytes >>> limiting the rewiring of the preexisting ones.

❖MEDICAL APPLICATION:

- Regeneration of peripheral nerves is functionally efficient only when the fibers and the columns of Schwann cells are directed properly.

- In a mixed nerve, if regenerating sensory fibers grow into columns formerly occupied by motor fibers connected to motor end plates, the function of the muscle will not be reestablished.

- When there is an extensive gap between the distal and proximal segments of cut or injured peripheral nerves or when the distal segment disappears altogether (**as in the case of amputation of a limb**), the newly growing axons may form a swelling, or **neuroma**, that can be the source of spontaneous pain.

- **neuroma** : حالة مرضية بتخلي المريض يضل حاس بالألم
- في حالات البتر ممكن المريض يضل حاس بالجزء الذي تم بتره (يد،قدم،...) على الرغم من انه فقده فعليًا وبطل موجود.

THE END OF SHEET #19

آخر شيت نظري بالمادة بتمنى بس توصلوا هون تكونوا راضيين عن حالكم وعن كلشي عملتوه وبتمنى تكونوا وصلتوا هون وما عملتوا سكيب عن اخر موضوع :)

GOOD LUCK يا دفعة