بسم الله

Autoimmune Neuropathies

Based on:
- Principles of Neurology, Adams and Victor's, 11th Edition- 2019
- Merritt's Neurology, Elan D. Louis, Stephan A. Mayer, Lewis P. Rowland, 13th Edition – 2022
and
- Iranian Neurology Board Tests

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فهرست

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رنگ مشکی ۱۰۰٪ از کتاب از آدامز است.
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قرمز یعنی مطلب، مهم است.

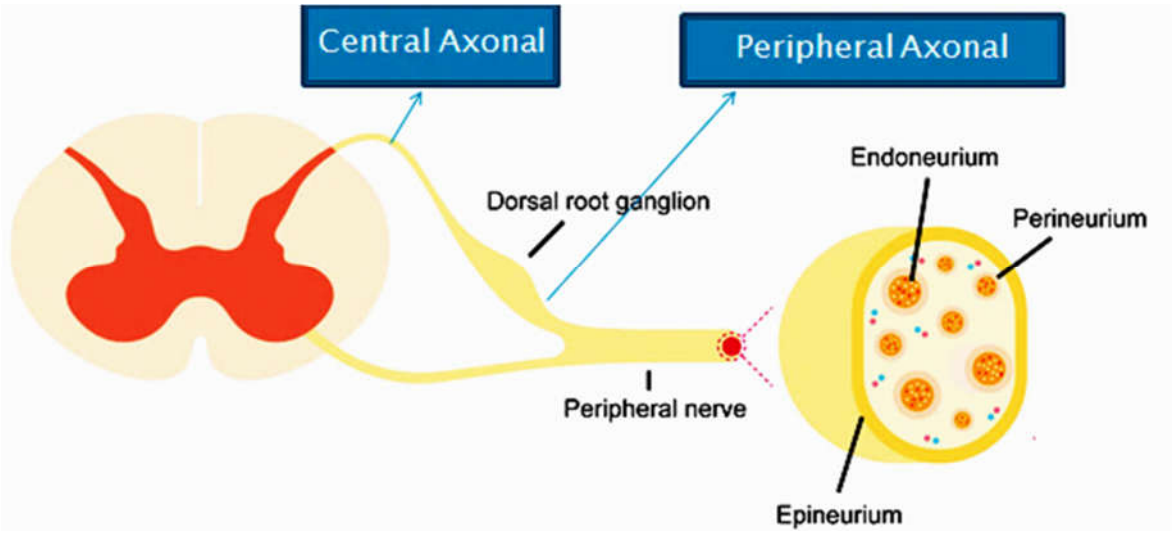
CLASS 1: PART 1; STRUCTURE OF THE PERIPHERAL NERVES

- Because the structure and function of the peripheral nervous system are relatively simple, one might suppose that our knowledge of its diseases would be fairly complete. Such is not the case.
- A group of patients with chronic polyneuropathy were investigated intensively in a highly specialized center for the study of peripheral nerve diseases **several decades ago**, a suitable explanation for their condition could not be found in **24 percent** (Dyck et al, 1981) and **equally discouraging figures** prevail in our clinics today despite genetic testing.
- For these reasons, clinicians now find the peripheral neuropathies among **the most challenging and gratifying** categories of neurologic disease.

GENERAL CONSIDERATION

Where is the Peripheral nervous system (PNS)?

- The PNS includes all neural structures lying **outside the pial membrane of the spinal cord and brainstem** with the exception of the optic nerves and olfactory bulbs, which are special extensions of the brain.
- The nerves within the spinal canal and attached to the ventral and dorsal surfaces of the cord are the *spinal roots*, which continue to form the numbered *spinal nerves*; those attached to the ventrolateral surface of the brainstem are the *cranial nerve roots*, or cranial nerves.
- The **dorsal, or posterior (afferent, or sensory)**, spinal roots consist of "**central axonal" processes of the sensory and cranial ganglia**.
- On reaching the spinal cord and brainstem, the roots extend for variable distances into the dorsal horns and posterior columns of the cord and into the spinal trigeminal and other tracts in the medulla and pons before synapsing with secondary sensory neurons, as described in Chaps. 7 and 8 that are devoted to the neurology of pain and sensation



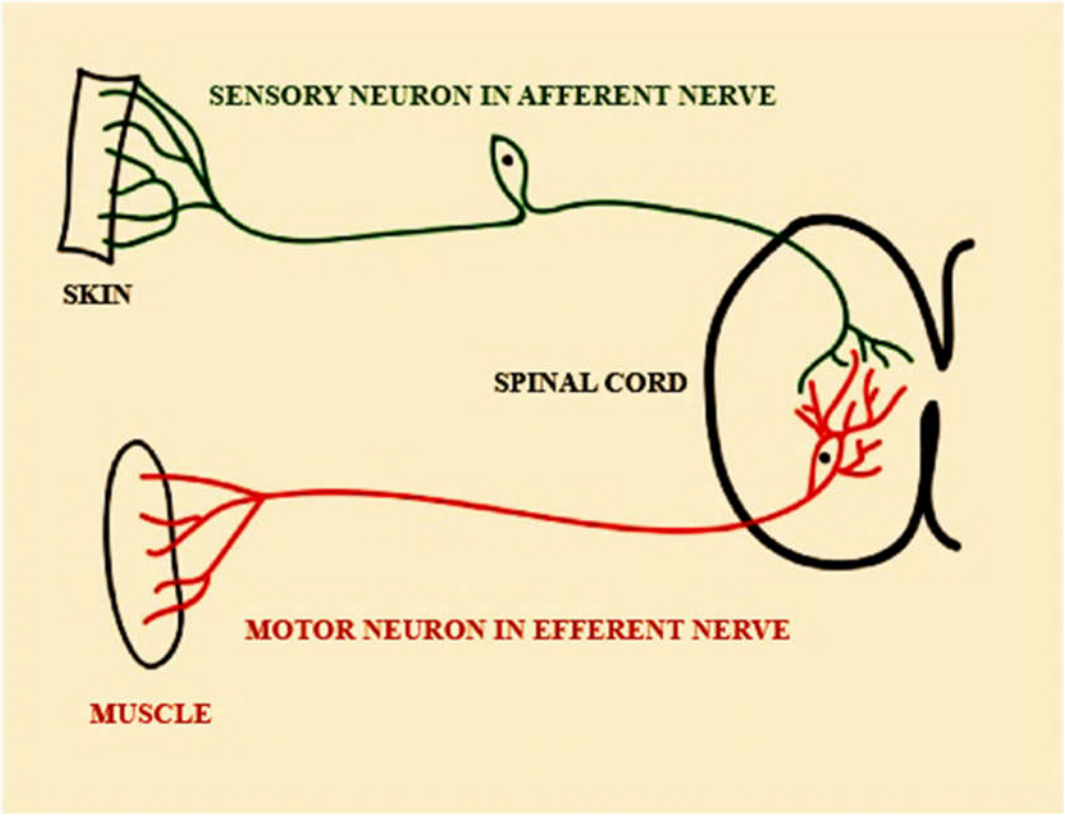


Fig 1: The peripheral nervous system

- The ventral, or anterior (efferent, or motor), roots are composed of the emerging axons of anterior and lateral horn cells and motor nuclei of the brainstem. **Large, heavily myelinated** fibers terminate on **muscle fibers**
- **smaller unmyelinated ones terminate in sympathetic or parasympathetic ganglia.**
- From these autonomic ganglia issue the axons that terminate in smooth muscle, heart muscle and conducting system, and glands.
- Traversing the subarachnoid space, where they **lack well-formed epineurial sheaths**, the cranial and spinal roots (both sensory and motor) are **bathed in and are susceptible to substances in the cerebrospinal fluid (CSF),** the lumbosacral roots having the longest exposure.

Connective tissue nerve bundle sheaths

- The vast extent of the peripheral ramifications of cranial and spinal nerves is noteworthy, as are their thick protective and supporting sheaths of perineurium and epineurium that are endowed with a vascular supply through longitudinal arrays of richly anastomosing nutrient arterial branches.
- The **perineurium** comprises the **connective tissue sheaths** that surround and separate each bundle of nerve fibers (fascicles) of varying size, each fascicle containing several hundred axons.
- The sheath that binds and surrounds all the fascicles of the nerve is the **epineurium**.
- As the nerve root approaches the cord, the epineurium blends with the dura (see Fig. 4; TEXTBOOK: 43-1).
- The fine connective tissue covering of individual nerve fibers is the **endoneurium**. Longitudinally oriented and widely anastomotic endoneural vessels also nourish the nerve fibers and are susceptible to disease.

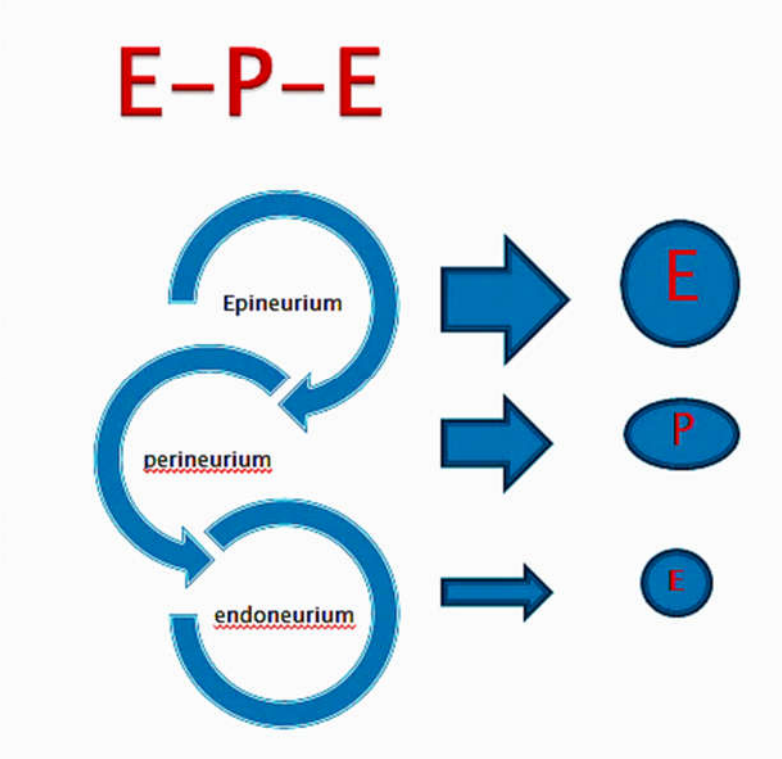


Fig 2: The schematic coverage of peripheral nerves

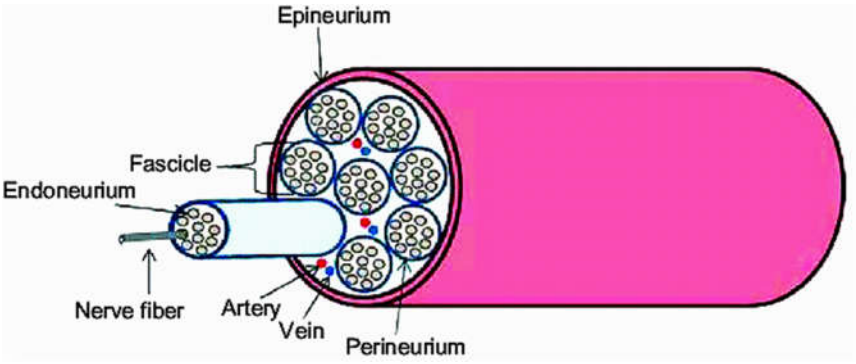


Fig 3: Structure of the peripheral trunk

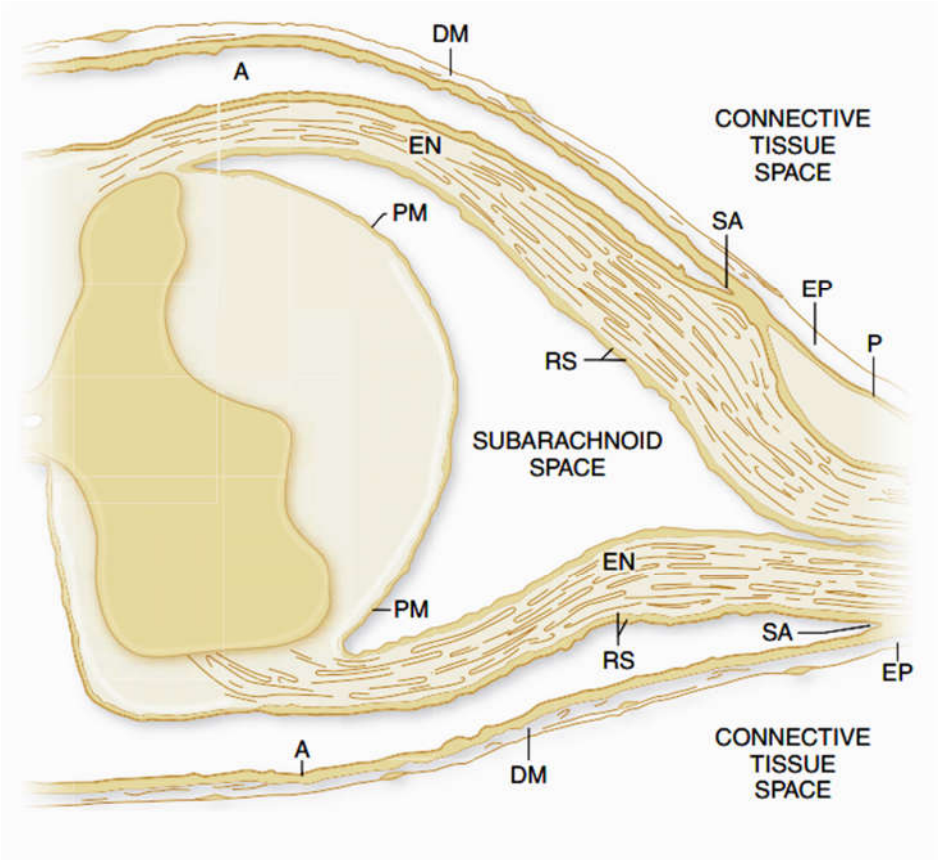


Figure 4; (TEXTBOOK 43-1): Diagram showing the relationships of the peripheral nerve sheaths to the meningeal coverings of the spinal cord. The epineurium (*EP*) is in direct continuity with the dura mater (*DM*). The endometrium (*EN*) remains unchanged root sheath (*RS*). At the subarachnoid angle, the arachnoid is reflected over the roots and becomes continuous with the outer layers of the root sheath. At the junction with the spinal cord, the outer layers of the root sheath become continuous with the pia mater (*PM*).

Peripheral VS central myelin

- Nerve fibers (axons) are coated with short segments of **myelin** of variable length (250 to 1,000 µm), each of which is enveloped by a **Schwann cell** and its membrane that constitute the myelin sheath.
- Each myelin segment and Schwann cell has a **symbiotic relationship** to the axon but is morphologically independent.
- The structure of the axonal membrane in the gaps between segments of the myelin sheaths (**nodes of Ranvier**) is specialized, containing a high concentration of **sodium channels** and permitting the **saltatory electrical** conduction of nerve impulses.
- **Unmyelinated fibers**, **more numerous** in peripheral nerves than myelinated ones, also arise from cells in dorsal root and autonomic ganglia. Small bundles of these naked (unmyelinated) axons are enveloped by **a single Schwann cell**; delicate tongues of Schwann cell cytoplasm partition these bundles and separate individual axons.
- The **myelin of these centrally** located fibers is constituted differently from that of the peripheral nerves, being enveloped by **oligodendrocytes rather than Schwann** cells and the nerve fibers are supported by **astrocytes rather than fibroblasts.**

Box1: Central VS peripheral Myelin extension

Note:

► **Central Myelin Extension,** Oligodendrocyte's, **Astrocytes**

► **Peripheral Myelin Extension,** Schwann cells, **Fibroblast**

- Because of the intimate relation of the nerve roots to the CSF and to specialized arachnoidal cells (the arachnoidal villi), a pathologic process in the CSF or leptomeninges may damage the exposed spinal roots. Diseases of the connective tissues affect the peripheral nerves that lie within their sheaths.

تست ۱: جمله نادرست کدام است؟

الف: PNS از بعد از غشای پیا شروع می‌شود.

ب: غلاف پرینوریوم در زمان اتصال اعصاب محیطی به ریشه‌های نخاعی با غشای پیا ممزوج می‌شود.

ج: بخش مرکزی میلین‌ها توسط سلول‌های الیگودندروسیت‌ها ساخته می‌شود.

د: فیبروبلاست‌ها محافظت‌کننده‌های سلول‌های شوان محسوب می‌شوند.

- Diphtheria, in which the bacterial toxin acts directly on the membranes of the **Schwann cells** near the dorsal root ganglia and adjacent parts of motor and sensory nerves (**the most vascular parts of the peripheral nerve**).
- Polyarteritis nodosa, which causes occlusion of vasa nervorum, resulting in multifocal nerve infarction;
- Tabes dorsalis, in which there is a treponemal meningoradiculitis of the posterior roots (mainly of the lumbosacral segments);
- poisoning by arsenic, which combines with the axoplasm of the largest sensory and motor nerves via sulfhydryl bonds;
- vincristine toxicity, which damages the microtubular transport system.

Pathologic Reactions of Peripheral Nerve

- The three main distinct histopathologic changes are recognized in the **peripheral nerve damages** ones are:
- ***Segmental demyelination,***
- ***Wallerian degeneration***
- ***Axonal degeneration*** (Fig 5; textbook 43-2).

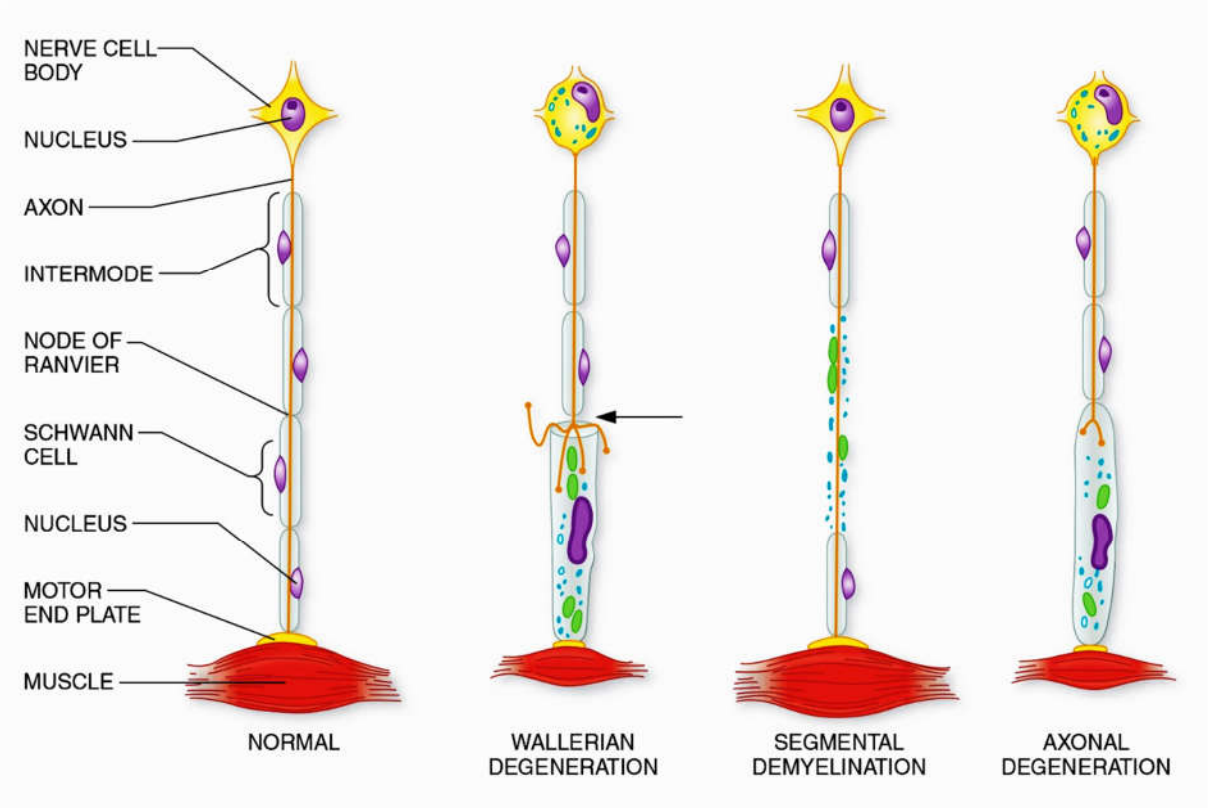


Fig 5; textbook 43-2: Pathologic Reactions of Peripheral Nerve

- The **myelin sheath is the most susceptible** element of the nerve fiber, for it may break down as part of a primary process involving the Schwann cells or of the myelin itself, or it may be damaged secondarily as a consequence of disease affecting its axon.
- **Focal degeneration of the myelin sheath with sparing of the axon is called *segmental demyelination*.**
- The characteristic change of segmental demyelination is the disappearance of the sheath over segments of variable length, bounded on each end by one side of a node of Ranvier and an adjacent preserved segment of myelin.
- This exposes long segments of the axon to the interstitial environment.
- Myelin may also degenerate from axonal disease in a general process that may occur either proximal or distal to the site of axonal interruption.
- Common to many lesions of the peripheral nerve is *wallerian degeneration*, a reaction of both the axon and myelin *distal to* the site of disruption of an axon.

- Wallerian degeneration might be described as "**dying forward**," a process in which the nerve degenerates from the point of axonal damage outward.

Fig 6: Wallerian degeneration, all things in front of a whale dies! (Dying forward) (Just for memorizing!)

- In contrast, when the axon degenerates as part of a "**dying-back**" phenomenon in a more generalized metabolically determined polyneuropathy, it is termed **axonal degeneration**.
- Here, the axon is affected progressively from the distal-most site to the proximal, with dissolution of myelin that occurs roughly in parallel with the axonal change.
- **One possible explanation for this process is that the primary damage is to the neuronal cell body, which fails in its function of synthesizing proteins and delivering them to the distal parts of the axon.**
- Similar **destruction of the dorsal spinal root** produces secondary **Wallerian degeneration** of the posterior columns of the spinal cord, but not of the peripheral sensory nerve because the dorsal root ganglion cell maintains the integrity of the distal axon.
- In other words, destruction of axons results within several days in Wallerian degeneration of the myelin distal to the point of injury but **not transgressing the neuronal cell body.**
- The **myelin breaks down** into blocks or ovoid's in which lie fragments of axons (**digestion chambers of Cajal**). The myelin fragments are then converted, through the action of **macrophages, into neutral fats and cholesterol esters** and carried by these cells to the bloodstream.