NEUROSCIENCE PATHOLOGY-II

PERIPHERAL NERVOUS SYSTEM PATHOLOGY

DR.EMAN KREISHAN, M.D.

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Feature	Axonal Neuropathies	Segmental Demyelination
Primary Cause	Direct injury to the axon or neuronal body.	Breakdown and loss of myelin sheath.
Mechanism	Distal portion of the affected axon degenerates.	Myelin is lost over a few segments; axon remains intact.
Effect	Decrease in signal strength/amplitude (density loss).	Decrease in conduction velocity and conduction block.
Regeneration	Axonal regrowth and remyelination.	Thinly myelinated internodes of uneven (shorter) length.

2. Anatomic Patterns of Peripheral Neuropathies

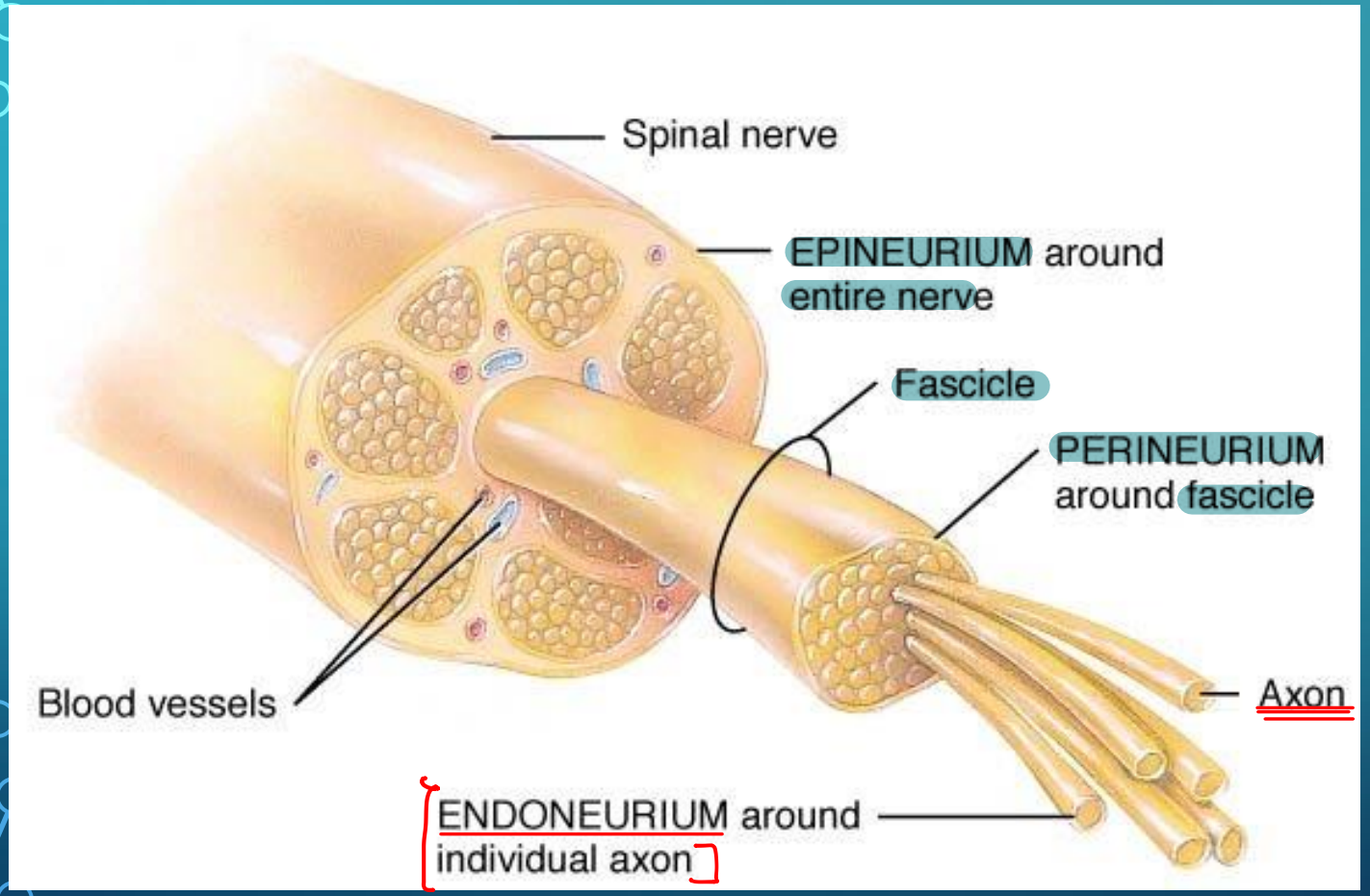
Pattern	Description	Common Causes
Polyneuropathy	Symmetric, length-dependent fashion; starts in toes and spreads up ("stocking-and-glove").	Toxic and metabolic damage (e.g., Diabetes).
Mononeuritis Multiplex	Random damage to individual nerves (e.g., right radial palsy and left foot drop).	Vasculitis (Most common cause).
Simple Mononeuropathy	Involves only a single nerve.	Traumatic injury, entrapment (Carpal tunnel), or infections.

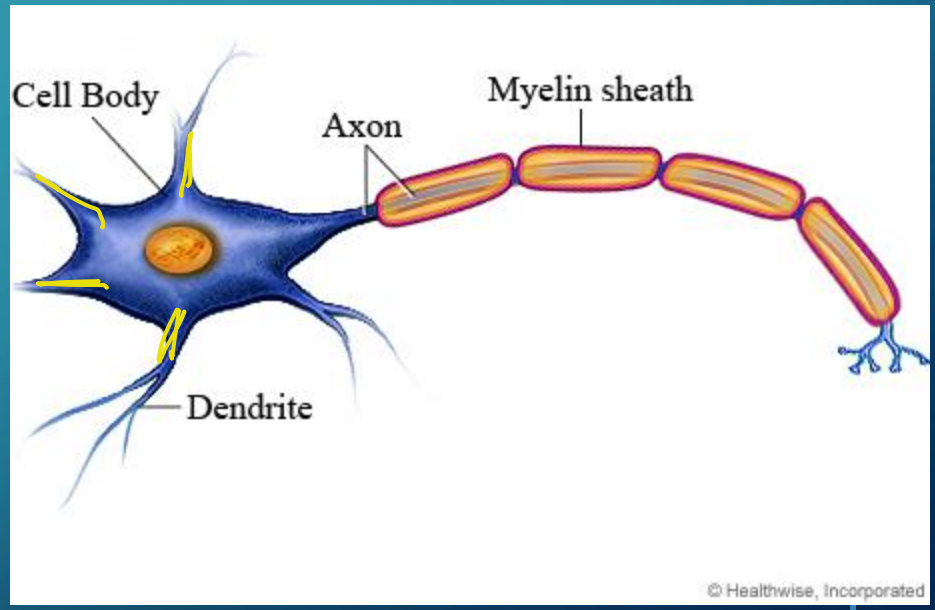
Feature	Guillain-Barré Syndrome (GBS)	Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)
Onset/Course	Acute; life-threatening; can progress in days.	Chronic; persists for at least 2 months.
Clinical Course	Postinfectious (immune-mediated); usually recovers with time.	Chronic relapsing-remitting or progressive course.
Symptoms	Ascending weakness, diminished reflexes, respiratory failure risk.	Symmetrical mixed sensorimotor polyneuropathy, pain, tingling.
Morphology	Acute inflammatory demyelination.	Segmental demyelination and "Onion bulb" structures in long-standing cases.
Treatment	Plasmapheresis, IVIg, supportive care.	Plasma exchange, IVIg, physical therapy.

5. Diabetic Neuropathy Summary

Aspect	Description
Prevalence	Most common cause of peripheral neuropathy.
Most Common Form	Distal symmetric sensorimotor polyneuropathy.
Presentation	Paresthesias, numbness (Sensory), impaired coordination (Motor), or Autonomic issues.
Pathogenesis	Hyperglycemia → Advanced glycosylation end products (AGEs) → ROS increase → Microvascular injury → Axonal/ myelin injury.

ANATOMY


Spinal nerve
EPINEURIUM around entire nerve
Fascicle
PERINEURIUM around fascicle
Blood vessels
Axon
ENDONEURIUM around individual axon


Cell Body
Axon
Myelin sheath
Dendrite
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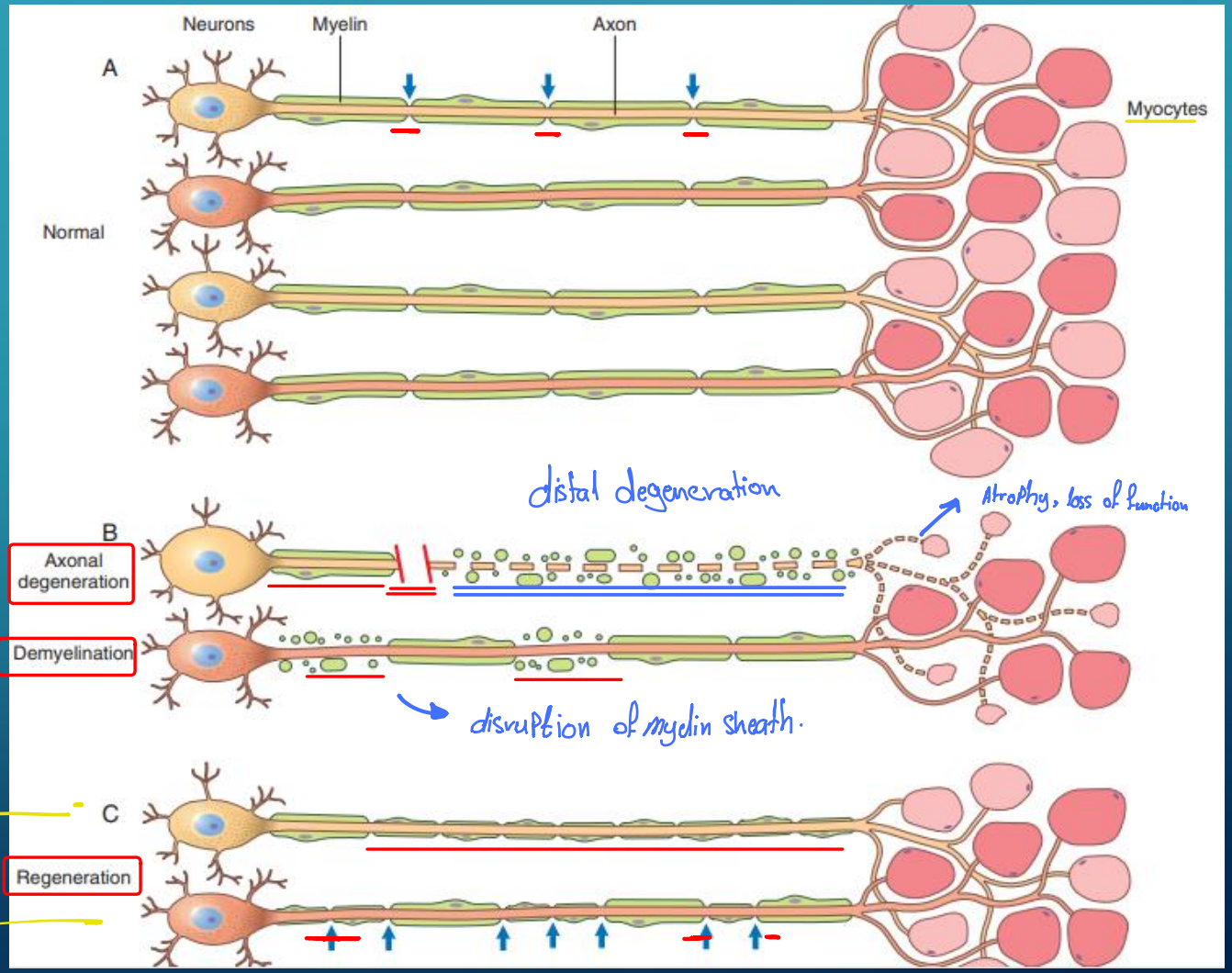
The pathology of peripheral neuropathy follows two basic patterns:

- 1. Axonal neuropathies:
- Caused by direct injury to the axon. The entire distal portion of an affected axon degenerates.
- Caused by pathology of the neuronal body resulting in its inability to keep up with the metabolic demands of the axon.

- 2. **Segmental demyelination**:
- characterized by breakdown and loss of myelin over a few segments.
- leads to **decrease of conduction velocity** and **conduction block**.

PATTERNS OF PERIPHERAL NERVE DAMAGE



AXONAL DEGENERATION

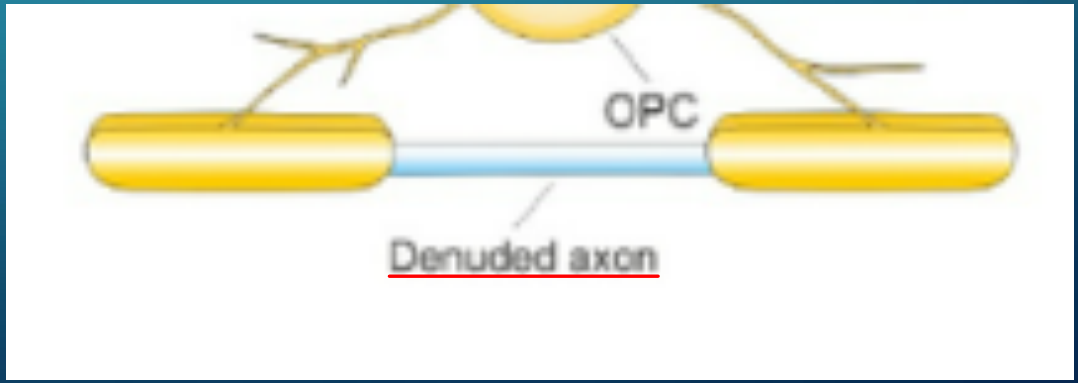
- The morphologic hallmark of axonal neuropathies is a decrease in the density of axons, which in electrophysiologic studies correlates with a decrease in the signal strength or amplitude of nerve impulses.

- Regeneration takes place through axonal regrowth and subsequent remyelination of the distal axon, where the proximal stump of the axon sprouts and elongate.

تحاول ان تنمو وترجع الجزء الي فُقد

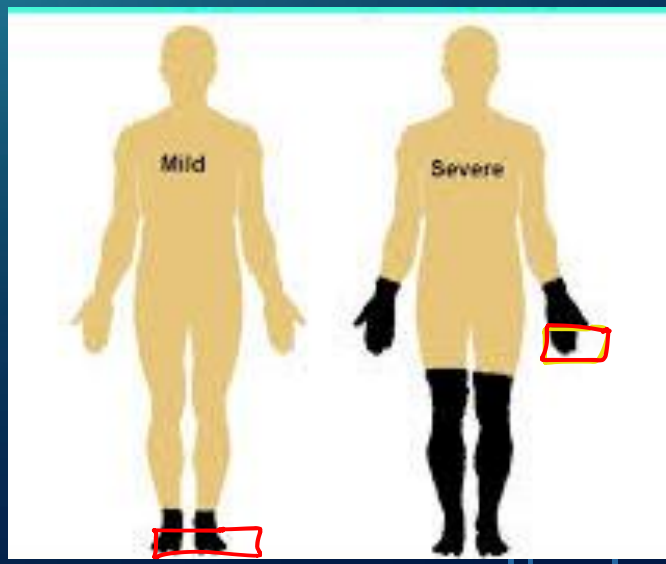
DEMYELINATING NEUROPATHIES

- Denuded axon provides a stimulus for remyelination & cells within the endoneurium differentiating to replace injured Schwann cells.
- Regeneration gives thinly myelinated internodes of uneven length (shorter).



Peripheral neuropathies exhibit several anatomic patterns

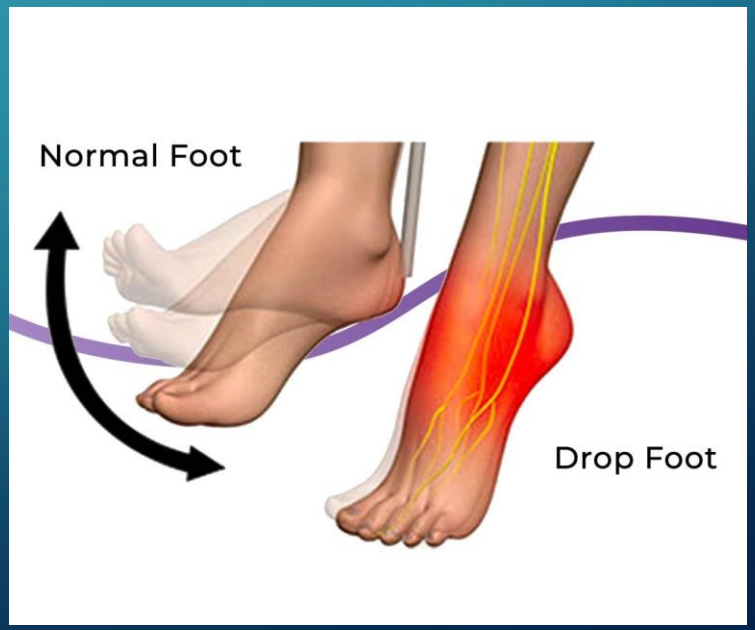
- Polyneuropathies :
  - Affect peripheral nerves in a symmetric, length-dependent fashion.
  - Axonal loss is typically more pronounced in the distal segments of the longest nerves. Patients commonly present with loss of sensation and paresthesias that start in the toes and spread upward. By the time the sensory changes reach the level of the knees, the hands are also affected, resulting in a picture described as "stocking-and-glove" distribution.
  - This pattern is often encountered with toxic and metabolic damage. •



- Mononeuritis multiplex:
  - The damage randomly affects individual nerves, resulting (for example) in a right radial nerve palsy and wrist drop and, at a separate point in time, a left foot drop.
  - Mononeuritis multiplex is often caused by vasculitis. Most common cause

wrist drop

foot drop



- A simple mononeuropathy :

risk & Pregnant.

○only involves a single nerve.

○Commonly caused by traumatic injury, entrapment (e.g., carpal tunnel syndrome), or certain infections such as Lyme disease

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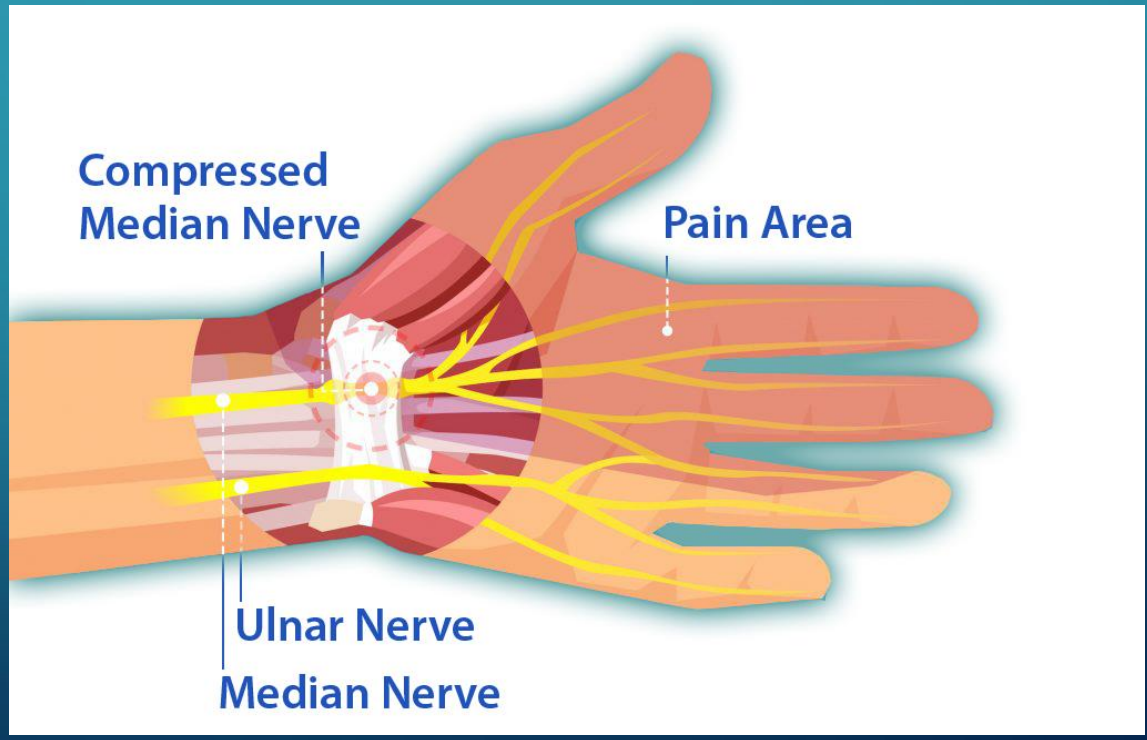


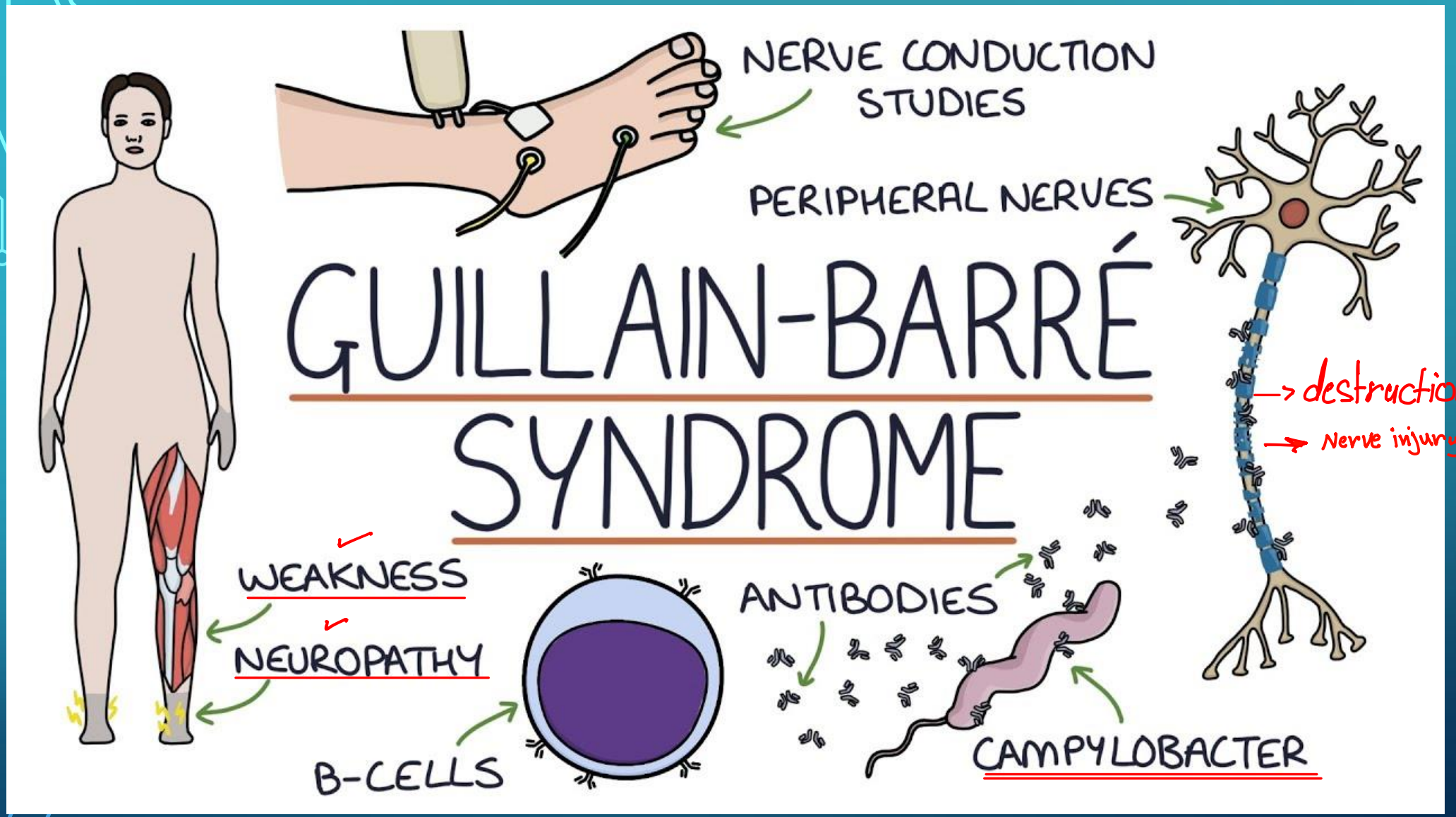
Disorders associated with peripheral nerve injury

* المطلوب فقط المذكور داخل المحاضرة

Etiologic Category	Causative Disorders/Agents
Nutritional and metabolic	Diabetes mellitus Uremia Vitamin deficiencies—thiamine, vitamin B6, vitamin B12
Toxic	Drugs, including vinblastine, vincristine, paclitaxel, colchicine, and isoniazid Toxins—alcohol, lead, aluminum, arsenic, mercury, acrylamide
Vasculopathic	Vasculitis Amyloidosis
Inflammatory	Autoimmune diseases Guillain-Barré syndrome Chronic inflammatory demyelinating polyneuropathy (CIDP)
Infections	Herpes zoster Leprosy HIV infection Lyme disease
Inherited	Charcot-Marie-Tooth neuropathy, type I, type II, and X-linked Hereditary neuropathy with liability to pressure palsy
Others	Paraneoplastic, some leukodystrophies

GUILLAIN-BARRÉ SYNDROME

- Acute Inflammatory Demyelinating polyneuropathy.
- described as a collection of clinical syndromes that manifests as an acute inflammatory polyneuropathy with resultant weakness and diminished reflexes.
- One of the most common life-threatening diseases of PNS, can lead to death from failure of respiratory muscles in days.


NERVE CONDUCTION STUDIES
PERIPHERAL NERVES
GUILLAIN-BARRÉ SYNDROME
—> destruction
Nerve injury
WEAKNESS
NEUROPATHY
ANTIBODIES
B-CELLS
CAMPYLOBACTER

PATHOPHYSIOLOGY

- GBS is a postinfectious, immune-mediated disease.
- Cellular and humoral immune mechanisms probably play a role in its development.
- Many of the identified infectious agents are thought to induce production of antibodies that cross-react with specific gangliosides and glycolipids, such as GM1 and GD1b, that are distributed throughout the myelin in the peripheral nervous system.
- Which organisms???? CAMPYLOBACTER

CLINICAL MANIFESTATION

- usually presents 2-4 weeks following a relatively benign respiratory or gastrointestinal illness .
- complaining of finger dysesthesias and proximal muscle weakness of the lower extremities.
  - unpleasant abnormal sensory perceptions
- The weakness may progress over hours to days to involve the arms, truncal muscles, cranial nerves, and muscles of respiration.

- Diagnosis:
- CSF protein levels are elevated due to inflammation and altered permeability of the microcirculation within the spinal roots.
- Treatments :
- plasmapheresis (to remove offending antibodies), intravenous immunoglobulin, and supportive care, such as ventilatory support.
- Patients who survive the initial acute phase of the disease usually recover with time. → Good Prognosis

chronic inflammatory demyelinating poly(radiculo)neuropathy (CIDP)

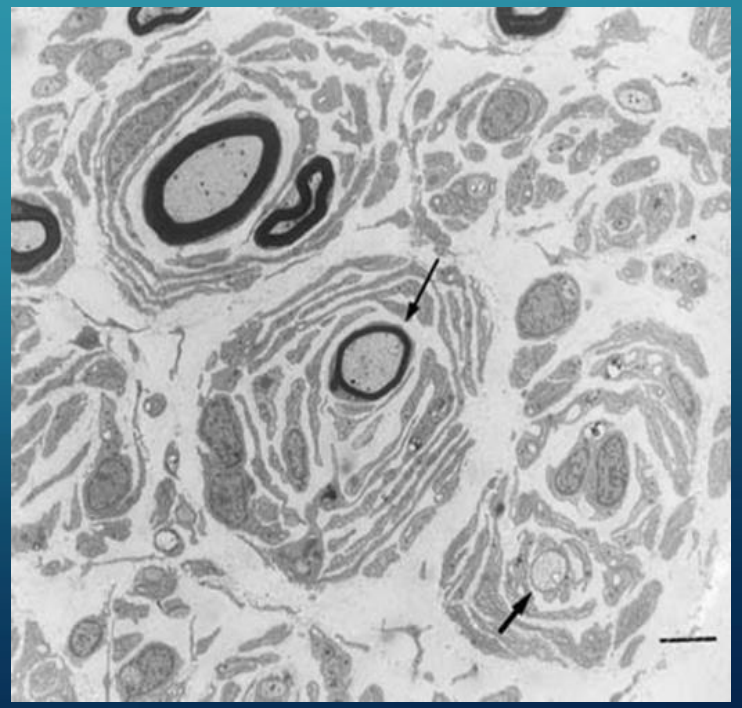
- The most common chronic acquired inflammatory peripheral neuropathy.
- Characterized by symmetrical mixed sensorimotor polyneuropathy that persists for 2 months (at least) or more.
- Abnormalities include weakness, difficulty in walking, numbness, and pain or tingling sensations.
- CIDP is immune mediated also, but in contrast to GBS, CIDP follows a chronic relapsing-remitting, or progressive course.
- Treatment:

✓ plasma exchange or IVIg treatment.

✓ physical and occupational therapy with orthotic devices.

Gross morphology:

- Segmental demyelination and remyelination.
- In long-standing cases, repeated activation and proliferation of Schwann cells result in the concentric arrangement of multiple Schwann cells around individual axons to produce multilayered structures → onion bulbs.



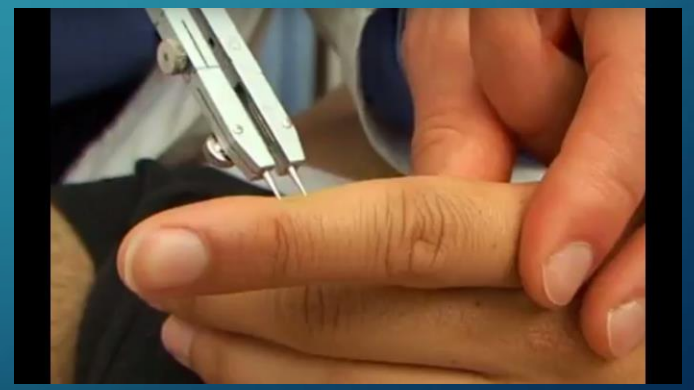
DIABETIC PERIPHERAL NEUROPATHY

- Diabetes is the most common cause of peripheral neuropathy developing with long-standing disease.
- Distal symmetric sensorimotor polyneuropathy is the most common form of diabetic neuropathy.
- Patient usually presented with paresthesias & numbness (due to Sensory axons involvement) .

- Treatment??

DIABETIC NEUROPATHY INCLUDES SEVERAL FORMS

- Autonomic neuropathy:
  - involve the cardiovascular, gastrointestinal, and genitourinary systems .
- Sensory neuropathy:
  - numbness, tingling in stocking-and-glove distribution.
- Sensorimotor neuropathy:
  - impaired fine hand coordination, e.g difficulty with tasks such as opening jars or turning keys



PATHOGENESIS