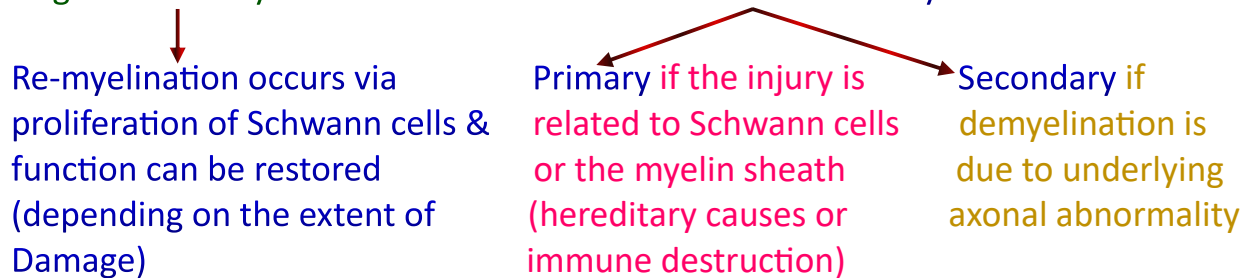


- **Myelin**
  - Protein-lipid complex that is wrapped around the axons.
  - Layers of plasma membranes assembled by oligodendrocytes (CNS) or Schwann cells (PNS).
  - Insulate axons and allows rapid propagation/ quick transmission of neural signals.

### Myelin diseases of the PNS

- In these diseases myelin sheath breaks but the underlying axons remains viable.
- The main pattern of myelin injury in the PNS is known as **segmental demyelination** → occurs due to Schwann cell dysfunction



→ If there are repeated demyelination- re-myelination cycles → increased number of Schwann cells → enlarged nerves (hypertrophic neuropathy) → onion bulb appearance.

-The symptoms are related to impaired function of the damaged nerve:

- Muscle weakness and atrophy
- Sensory loss
- Pain
- Parasthesia = any abnormal sensation including numbness, tingling, pricking, or burning sensation with **NO physical explanation** of the sensation
- Autonomic dysfunction (loss of bowel & bladder control).

### Peripheral neuropathies

- A process that affects the function of one or more of the peripheral nerves due to **axonal degeneration(80-90%)** or **segmental demyelination**.

↓  
**Axonal neuropathies:** caused by any disease process that affects the nerves or their blood supply.

↓  
**Demyelinating neuropathies :**caused by hereditary causes or immune destruction of myelin.

- Any toxins , infections, or infiltrative disease process or vascular disease can affect the nerve and cause neuropathy.
- The most common cause of generalized peripheral neuropathy is **diabetic neuropathy**.

## Diabetic neuropathy

- Neuropathy is the most common complication of diabetes.
- Risk of developing neuropathy depends on: duration of diabetes, and level of control of blood sugar.
- Loss of feeling in the lower limbs is a high risk for limb amputation, which occurs in 1–2% of diabetic patients.
- Can manifest as polyneuropathy or mononeuropathy
- Several forms of neuropathy can occur:
  1. distal symmetric sensorimotor polyneuropathy: the most common form. Symptoms include numbness, tingling, and weakness. It can also cause pain. These symptoms usually start in the longest nerves in the body and so first affect the feet and later the hands → “stocking-glove” pattern.
  2. autonomic neuropathy → changes in bowel, bladder, or cardiac function.
  3. Lumbosacral neuropathy → pain in lower legs.

### -Symptoms of peripheral diabetic neuropathy:

- Numbness or reduced ability to feel pain or temperature changes.
- Tingling or burning sensation. • Sharp pains or cramps. • Muscle weakness
- Increased sensitivity to touch (even the weight of a bedsheet can be painful).
- Loss of reflexes, especially in the ankle. • Loss of balance and coordination.
- Serious foot problems, such as ulcers, infections, and bone and joint pain.

### -Pathogenesis of diabetic peripheral neuropathy:

- Increased glucose in diabetics damages the nerves by two ways:
  1. formation of Advanced Glycated End(AGE) products: formed by nonenzymatic interaction between glucose derived precursors and the amino groups on the proteins → glycosylated proteins are formed → have receptors (RAGE) which are present on macrophages, T lymphocytes, endothelial cells and vascular smooth muscle cells → Interactions between AGE and RAGE → lead to:

- Formation of reactive oxygen species (ROS).
- Cytokines and growth factors formation
- Procoagulant activity
- Proliferation of smooth muscle cells & Increased extracellular matrix.

→ all of these lead to thickening of the vessel wall → Microangiopathy (because it affects small vessels like those innervating nerve endings) → ischemia to the nerves and ischemic damage.

2. changes in polyol pathway: resulting in increased sorbitol, decreased NADPH & reduced glutathione → direct nerve damage. ↓

- Sorbitol cannot cross the plasma membrane so it accumulates in cells causing increased osmotic pressure → water enters cells resulting in edema & damage.

### **Guillain Barre syndrome (GBS)**

- Autoimmune neuropathy.
- Follows bacterial, viral or mycoplasma infection.
- Can follow immunization or surgery.
- After Campylobacter jejuni, CMV, EBV.
- CSF: increased proteins and few WBC.

#### **-Clinical features:**

- Acute symmetric neuromuscular paralysis often begins distally and ascends proximally.
- Sensory and autonomic disturbances may also occur.
- Autonomic involvement → cardiac arrhythmia, hypo or hypertension.
- Muscle paralysis → respiratory difficulty → death.
- **Fisher syndrome:** Guillain Barre syndrome + ophthalmoplegia + ataxia + areflexia.
- Neuropathy resolves 2-4 weeks after onset and most patients recover.
- Patients with COVID 19 can develop GBS.

### **Chronic inflammatory demyelinating polyneuropathy CIDP**

- Characterized by mixed sensorimotor polyneuropathy that persists for 2 months or more.
- It is immune mediated but usually there is no previous history of infection.
- Occurs in patients with other autoimmune diseases and in AIDS patients.