BHARATHIDASAN UNIVERSITY

Program: M.Sc., Biomedical Science

Course Title : Neurobiology

Demyelination

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Demyelination

- Definition: degeneration of previously normal myelin.
- Demyelinating Diseases
  A. CNS
     1. Acute disseminated encephalomyelitis (ADEM)
     2. Multiple Sclerosis (MS)
     3. Neuromyelitis optica (NMO)
  B. PNS
     1. Acute inflammatory demyelinating polyneuropathy (AIDP)
     2. chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
     3. Charcot-Marie-Tooth
     4. Krabbe disease
     5. Metachromatic leukodystrophy

Several Diseases Can Lead to Peripheral Nerve Demyelinating.

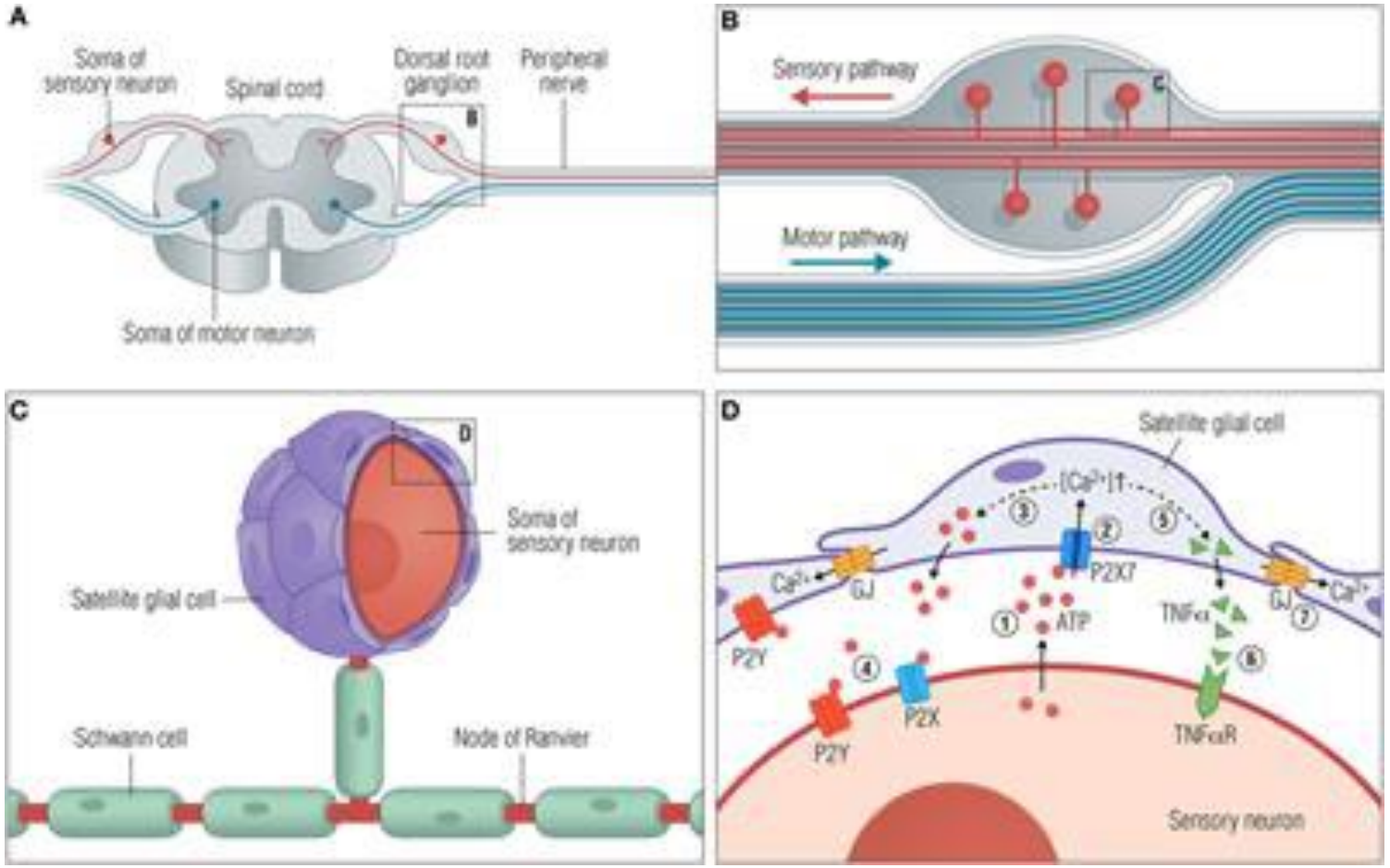
- Schwann cells, derived from neural crest cells
- envelop PNS neurons and their axons in three different ways.

1. Some Schwann cells are flattened out as satellite cells that surround PNS ganglion cells.
2. Others have multiple indentations, each encasing part of a small (unmyelinated) axon.
3. many spiral around individual, larger axons, forming myelin sheaths that allow axons to conduct action potentials more rapidly.

- Each myelinated axon looks like a string of sausages,

length of axon covered by a single Schwann cell form myelin.

Schwann cells

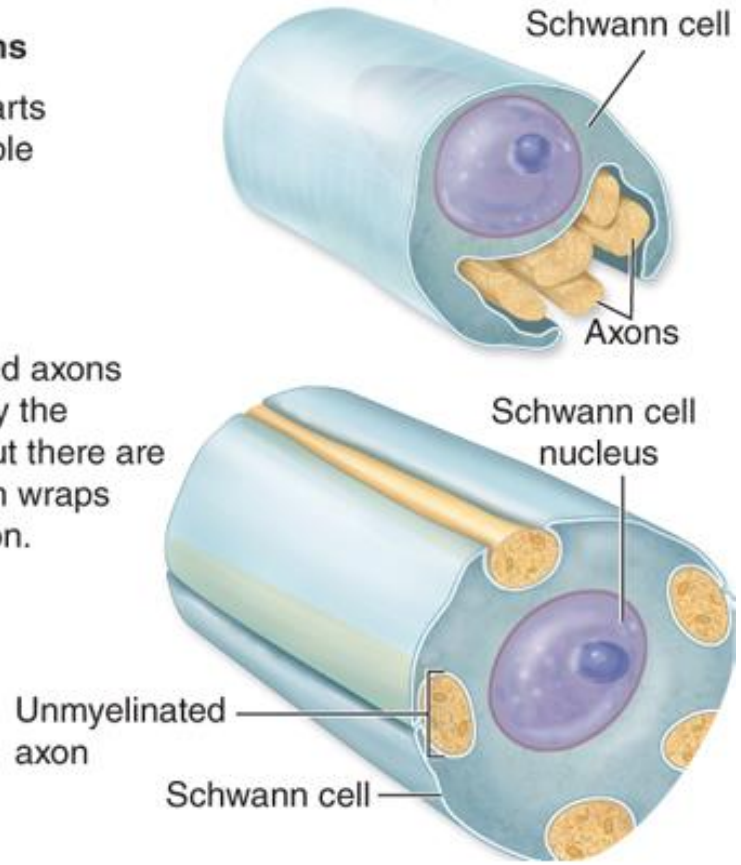


Schwann cells

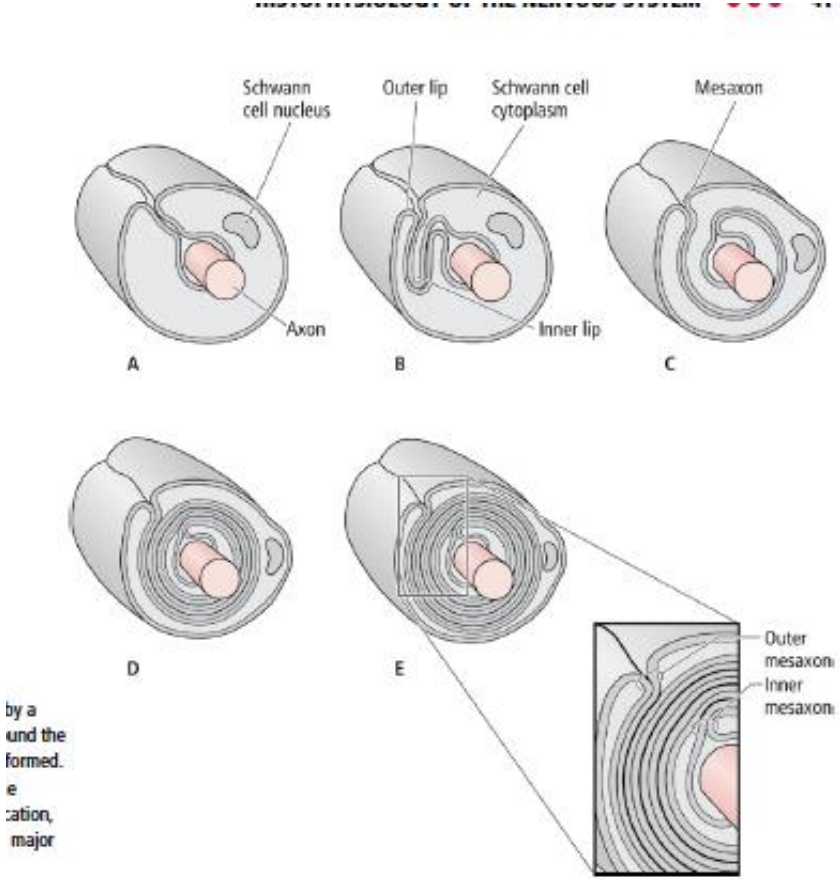
Unmyelinated axons

① Schwann cell starts to envelop multiple axons.

② The unmyelinated axons are enveloped by the Schwann cell, but there are *no* myelin sheath wraps around each axon.



Schwann cells



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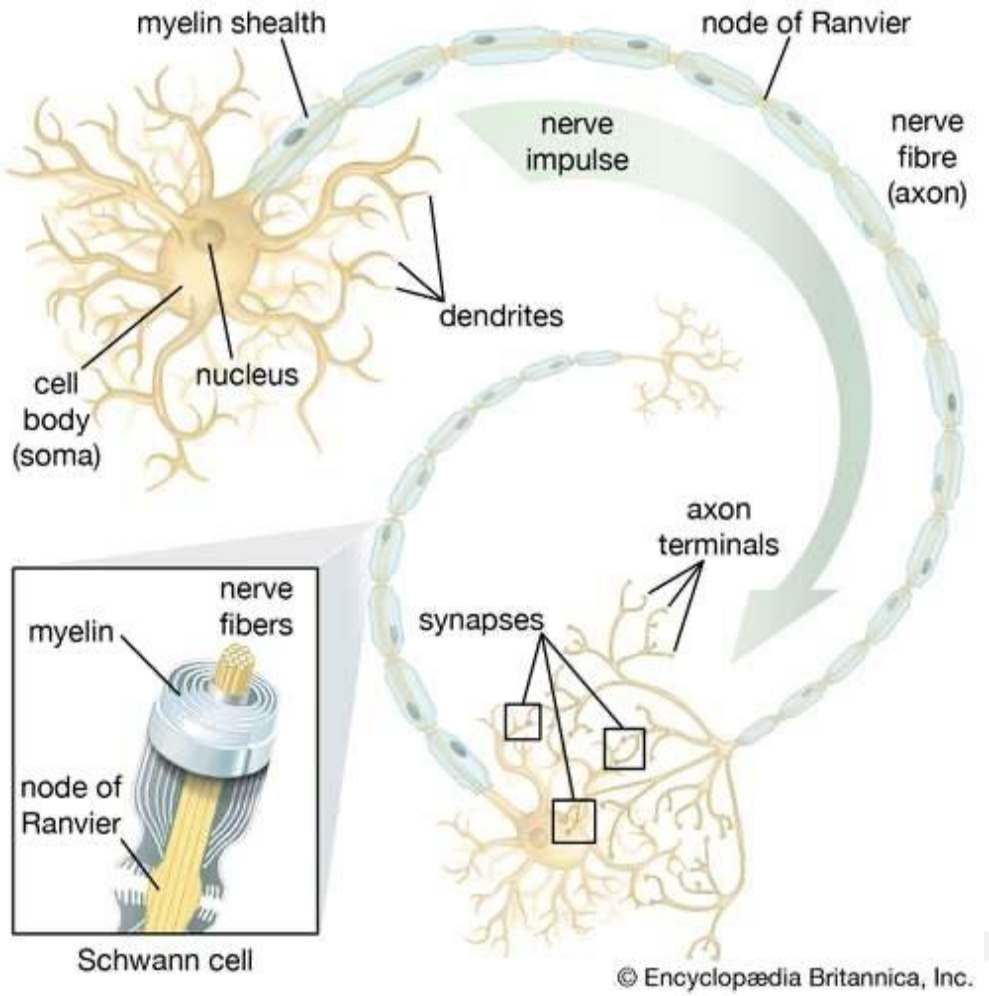


Peripheral Nerve Demyelinating Diseases

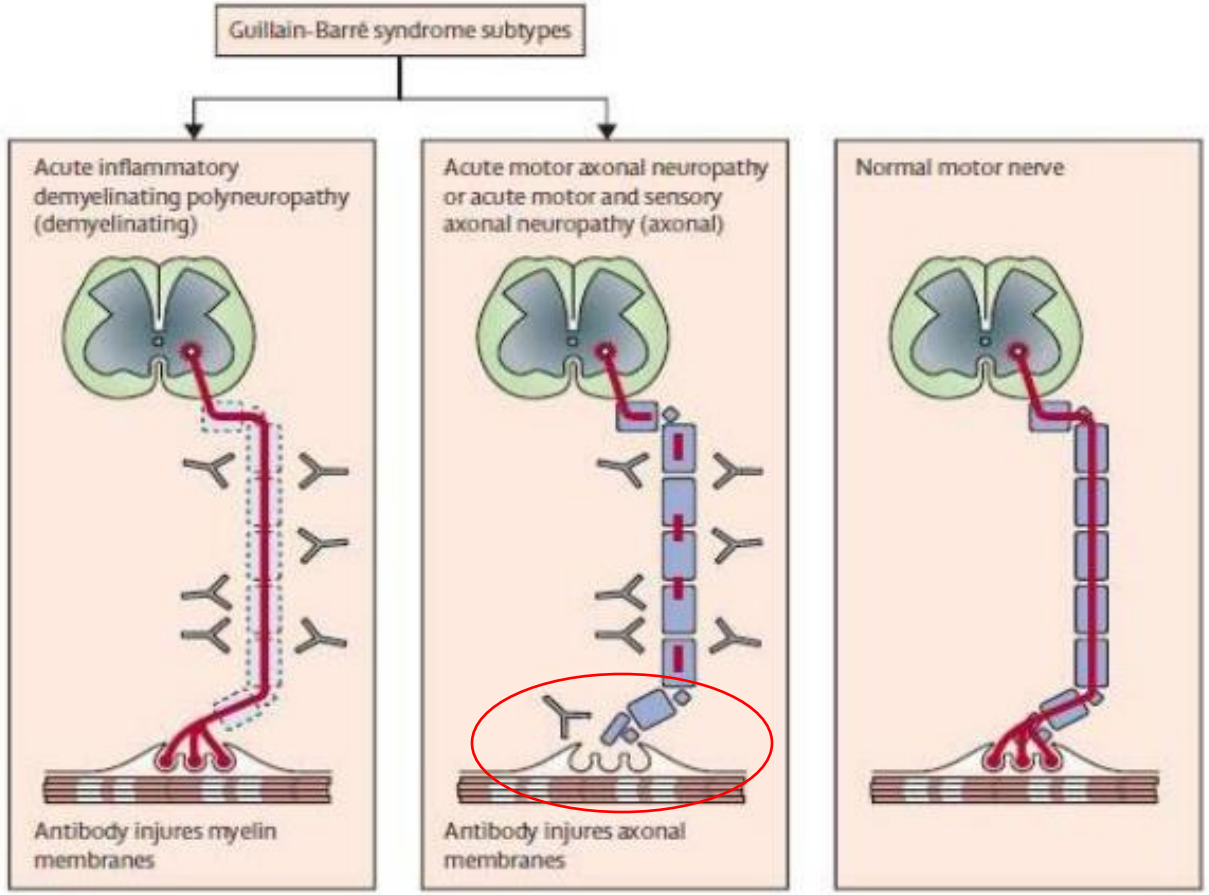
- The injury or a genetic disease of Schwann cells can result in the lack of support of peripheral neurons and/or a loss of efficient neuronal conduction.

1. Acute inflammatory demyelinating polyradiculopathy (AIDC)
2. Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)
3. Charcot-Marie-Tooth
4. Krabbe disease
5. Metachromatic leukodystrophy

Acute inflammatory demyelinating polyradiculopathy (AIDC)

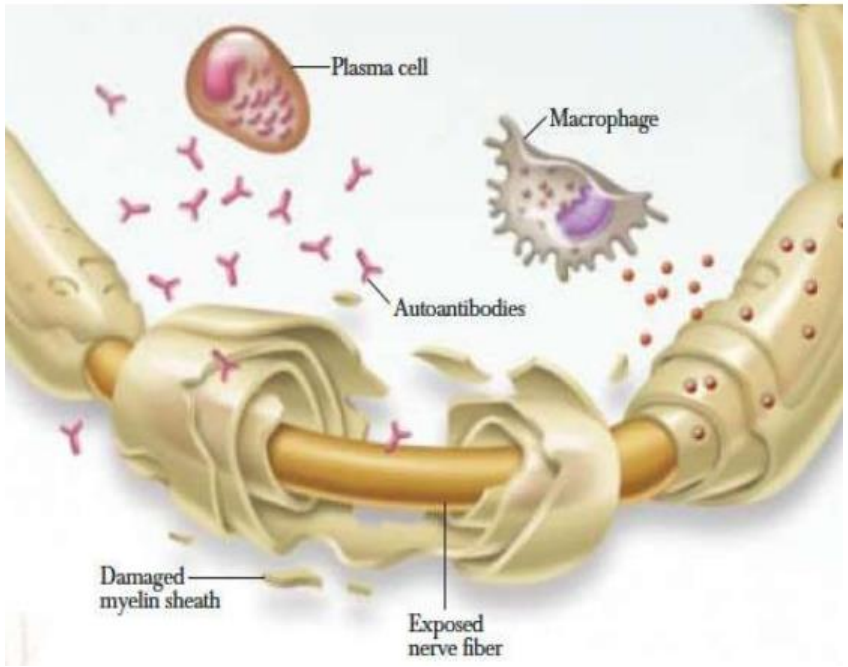
- autoimmune disorder in which the immune system attacks the peripheral nerves, often damaging the Schwann cells
- Autoimmune : immune system recognizes the myelin epitope as “foreign” and targets it for destruction.
- results in weakness, numbness, pain, and autonomic dysfunction, like respiratory failure, HTN, hypotension, Tachycardia, Bradycardia, gastric hypomotility and urinary retention.
- most common AIDC is Guillain-Barre syndrome (GBS).
- Infection of Mycoplasma pneumoniae, Epstein-Barr, cytomegalorvirus, Influenza A, Haemophilus Influenzae, Campylobacter jejuni, & Zika virus

Schwann cells



Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

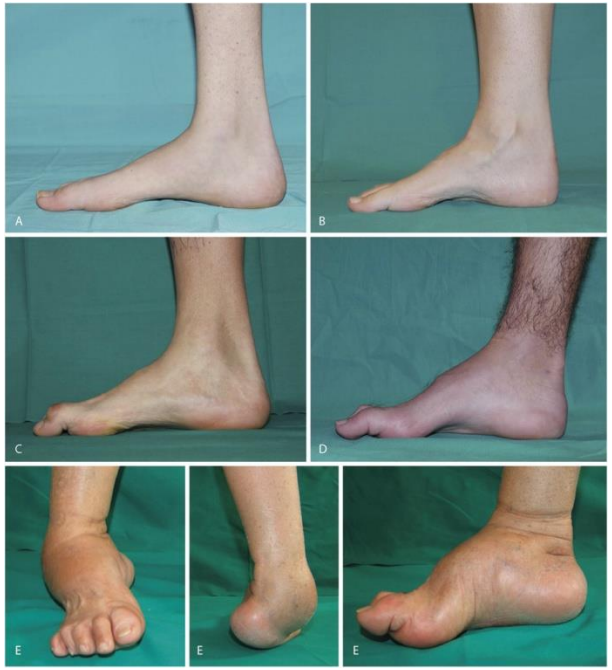
- as the name implies, is a chronic immune attack on the peripheral myelin
- Acquired demyelinating motor and sensory neuron
- All aged ppl get affected, but most ppt get affected at their 50-60 years.
- Both proximal and distal muscles are affected.
- Symptoms: numbing, tingling, pain, progressive muscle weakness, loss of deep tendon reflex, fatigue, & abnormal sensations

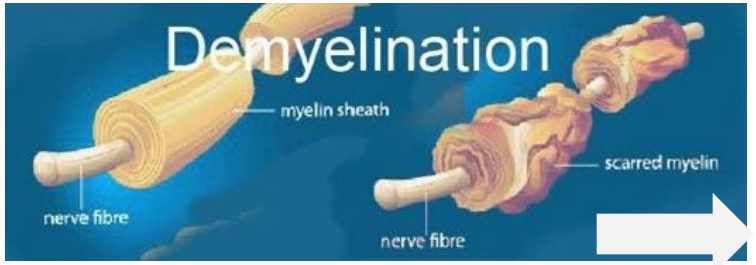


Charcot-Marie-Tooth

- hereditary demyelinating peripheral neuropathy that affects both sensory and motor neurons that control muscles

- due to the mutations in genes that produce number of proteins involved in the structure function of peripheral neuron axon or in myelin sheath.



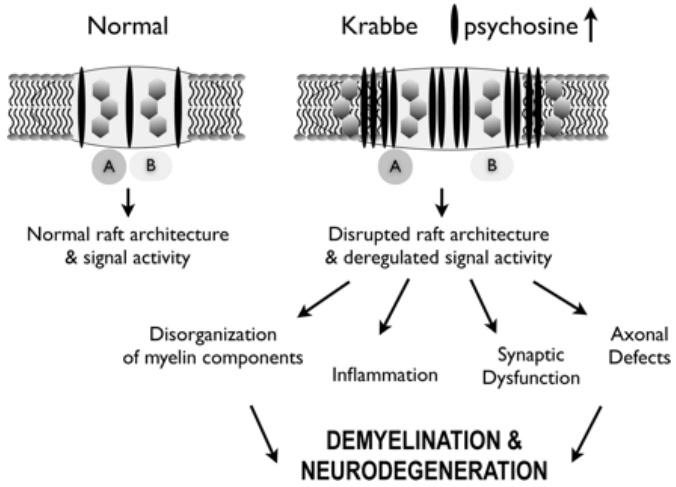


Krabbe disease

- hereditary lysosomal storage disease

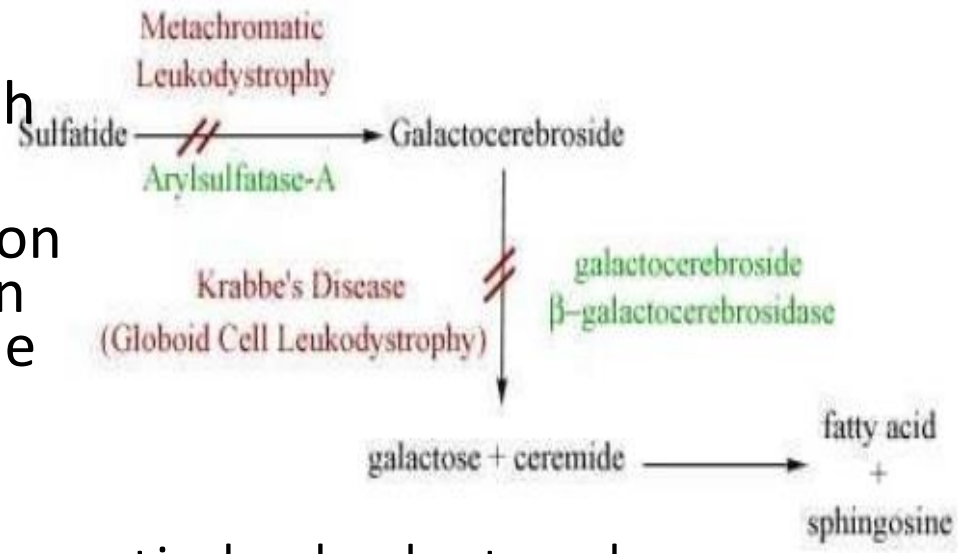
(i.e., deficient in the enzyme galactocerebrosidase or galactosylceramidase)

- Galactosylceramidase is a lysosomal enzyme
- Have no Galactosylceramidase activity
- No GALC leads to increase psychosine which in turn activate secretory Phospholipase A2
- PLA2 breakdowns lysophosphtidycholine and arachidonic acid.
- PLA2 results in death of oligodendrocytes which are responsible for myelin formation.
- in which dysfunctional metabolism of sphingolipids resulting in the destruction of proper myelin that can occur in the PNS and CNS.



Metachromatic leukodystrophy

- Another hereditary lysosomal storage disease that affects both the PNS and CNS
- in which there is an accumulation of sulfatides that destroy myelin (i.e., patients are deficient in the enzyme arylsulfatase A).



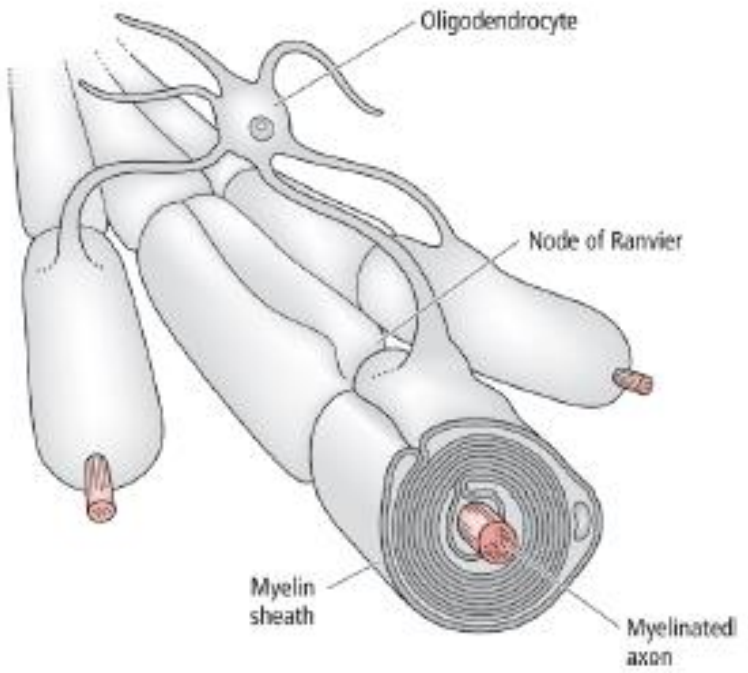
Krabbe disease and Metachromatic leukodystrophy

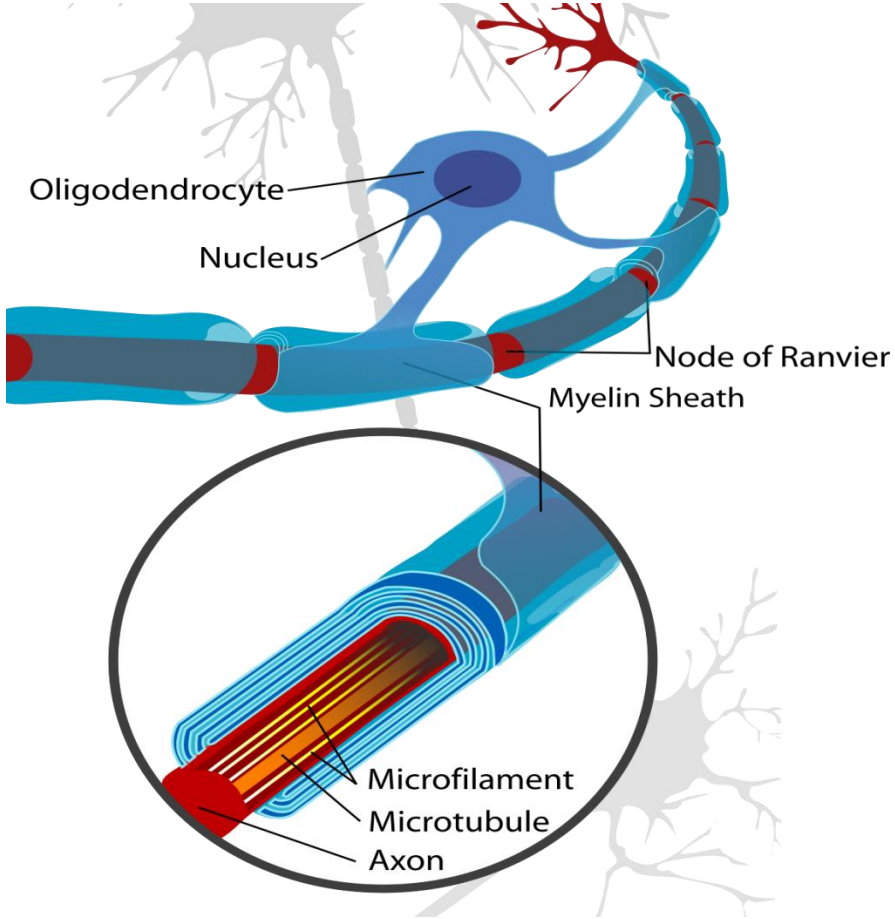
- have no known cure;
- bone marrow transplant can be an optional therapy.

Several Diseases Can Lead to the Demyelination of the Neurons in the CNS.

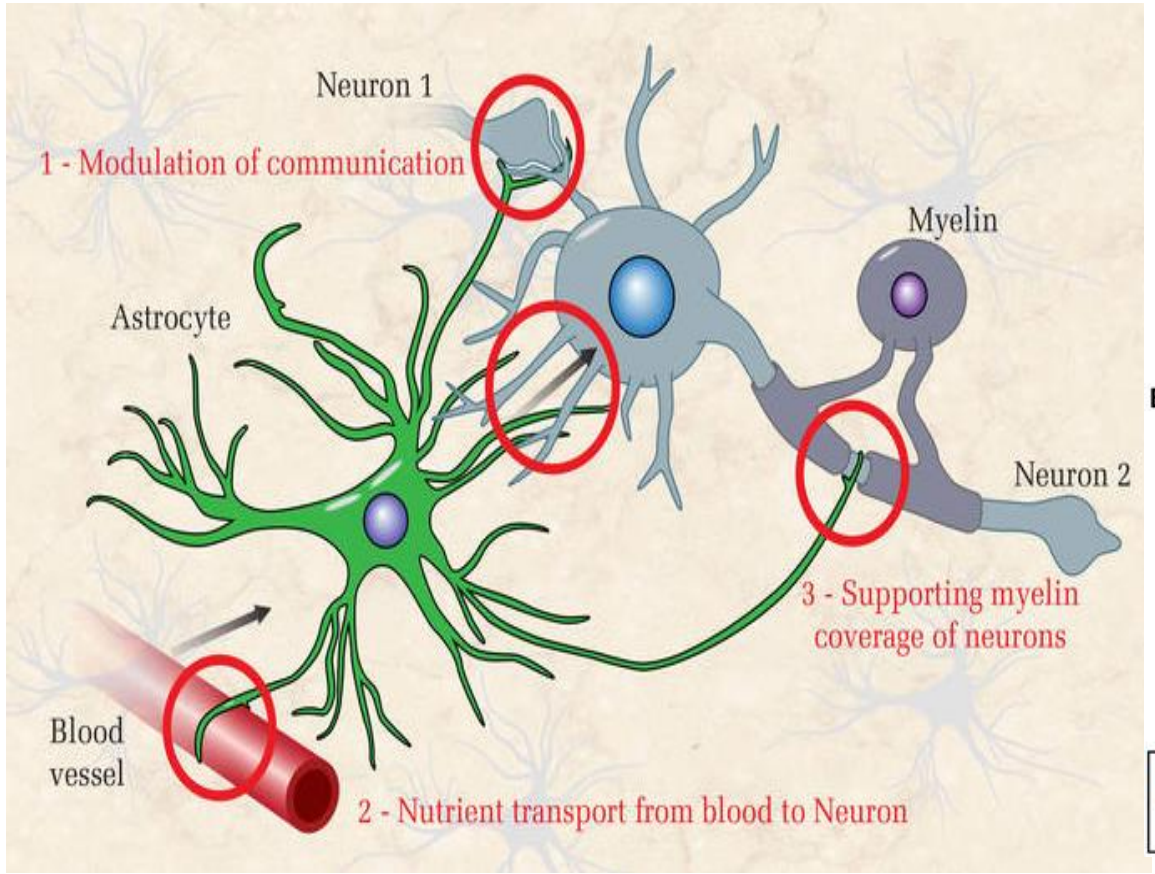
- Oligodendrocytes form myelin sheaths in the CNS.
- Unlike Schwann cells, individual oligodendrocytes have multiple branches, each ending as a segment of myelin around a different axon.
- Astrocytes play multiple roles. Their cytoskeletons provide mechanical support to neighbouring neurons.
- Astrocyte processes cover the parts of neurons not occupied by synaptic contacts and help regulate the ionic composition of extracellular fluids.
- also contact CNS capillaries and help regulate local blood flow and help form the blood-brain barrier.
- assist in the removal of excess neurotransmitter at a synapse.
- Undergo hypertrophy in response to CNS injury and form a kind of scar tissue called gliosis

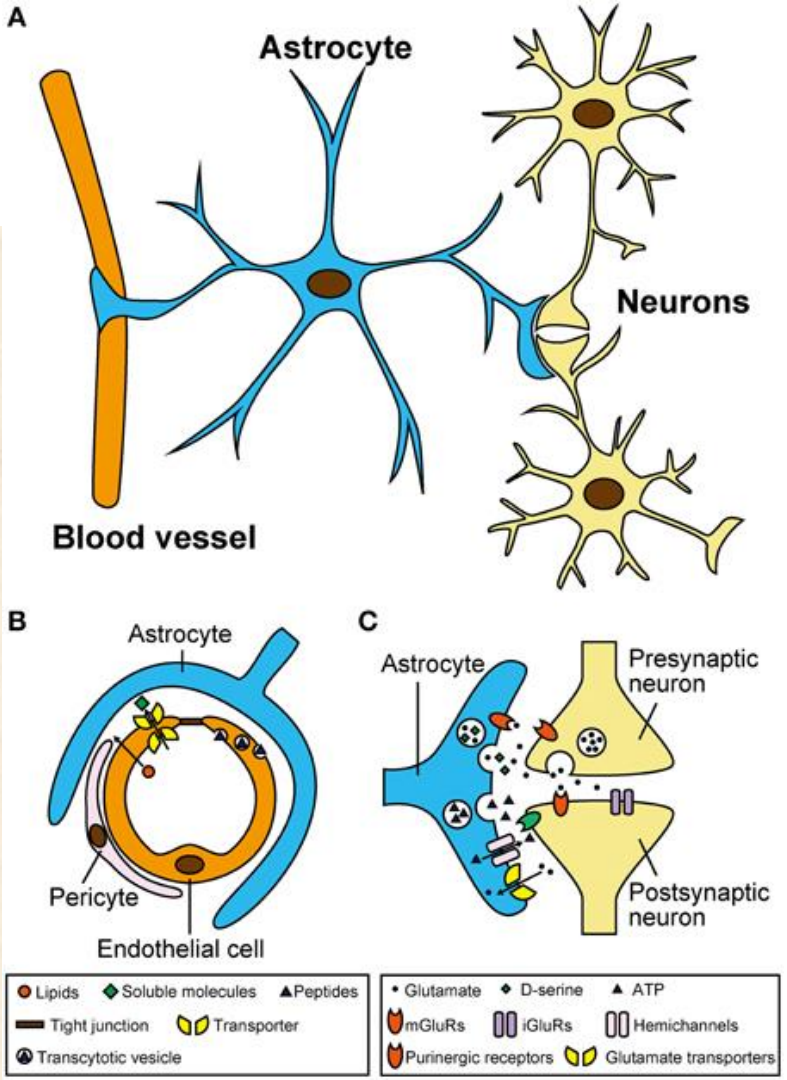
oligodendrocytes



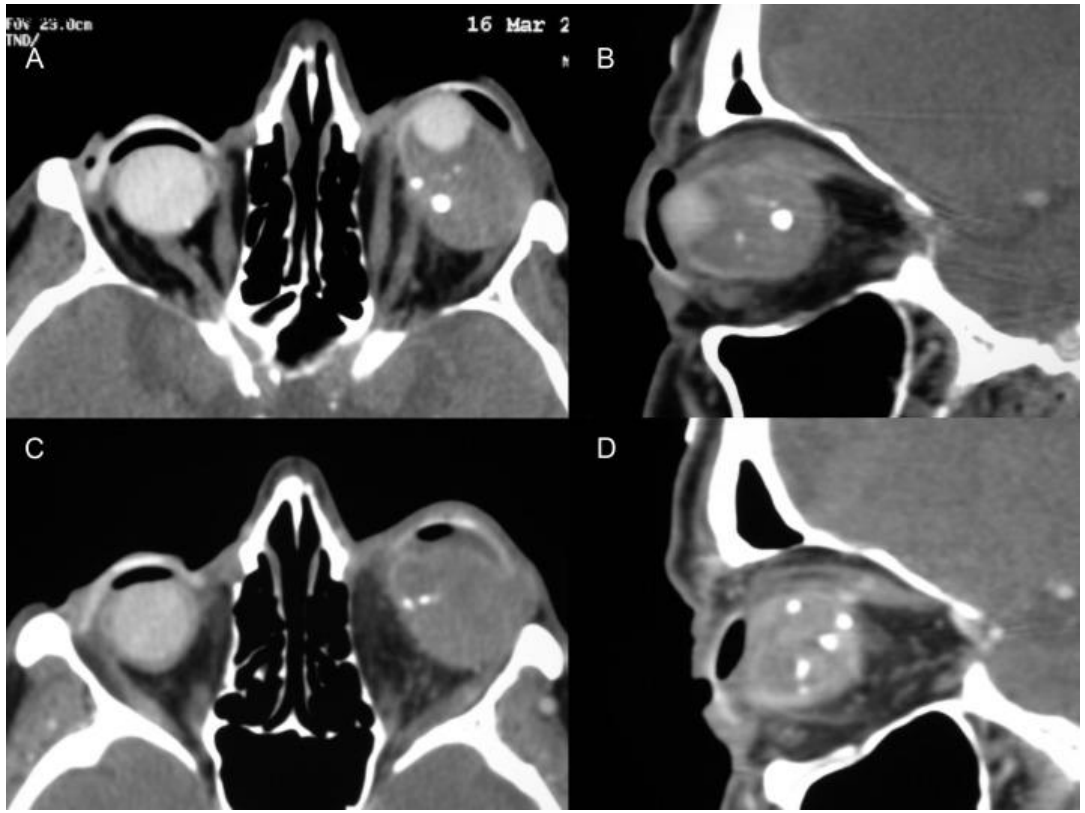


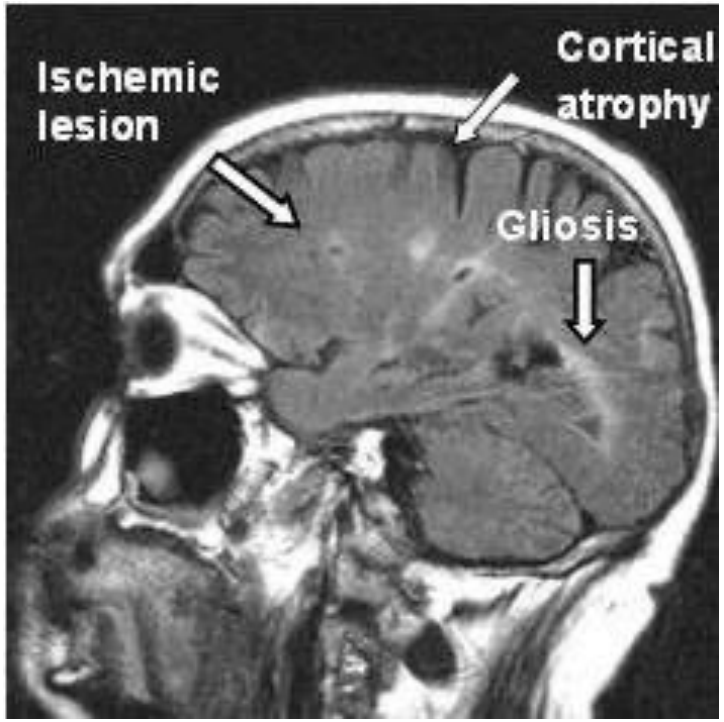
Astrocytes


Neuron 1
1 - Modulation of communication
Myelin
Astrocyte
Neuron 2
3 - Supporting myelin coverage of neurons
Blood vessel
2 - Nutrient transport from blood to Neuron


A
Astrocyte
Neurons
Blood vessel
B
Astrocyte
Pericyte
Endothelial cell
C
Astrocyte
Presynaptic neuron
Postsynaptic neuron
Lipids
Soluble molecules
Peptides
Tight junction
Transporter
Transcytotic vesicle
Glutamate
D-serine
ATP
mGluRs
iGluRs
Hemichannels
Purinergic receptors
Glutamate transporters

Gliosis





Several Diseases Can Lead to the Demyelination of the Neurons in the CNS.

1. Ependymal cells are derived from neuroectoderm
2. Ependymal cells form the single-cell-thick lining of the ventricles.
3. At some locations they are specialized as a secretory epithelium that produces the CSF that fills the ventricles
4. ependymal cells also play a role in neuroregeneration in the CNS
5. Microglia, derived from mesoderm, form a sort of immune system within the CNS.
6. recognize damaged neural tissue and foreign invaders, proliferate, and clean things up.
7. Several microglia can fuse together upon infection, like HIV, resulting in multinucleated giant cells of the CNS.