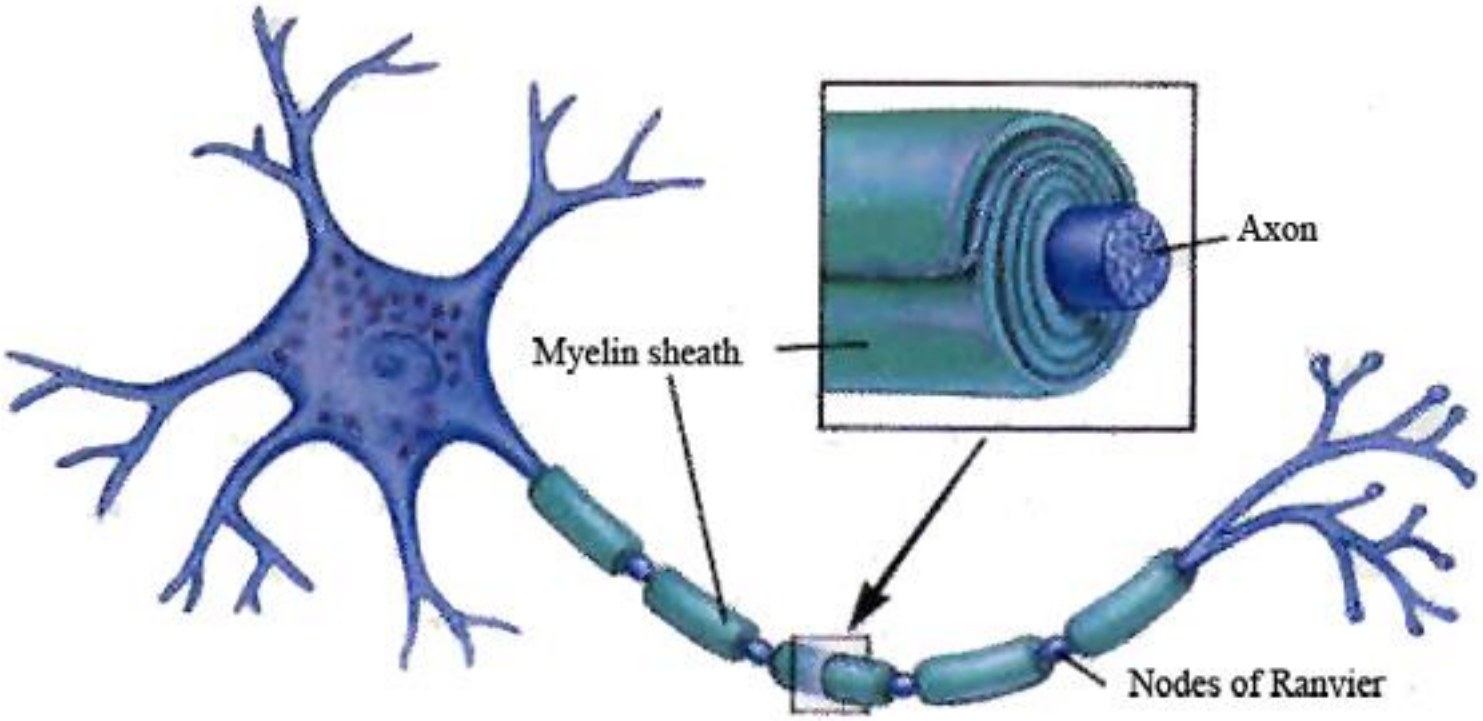
CNS lecture 4

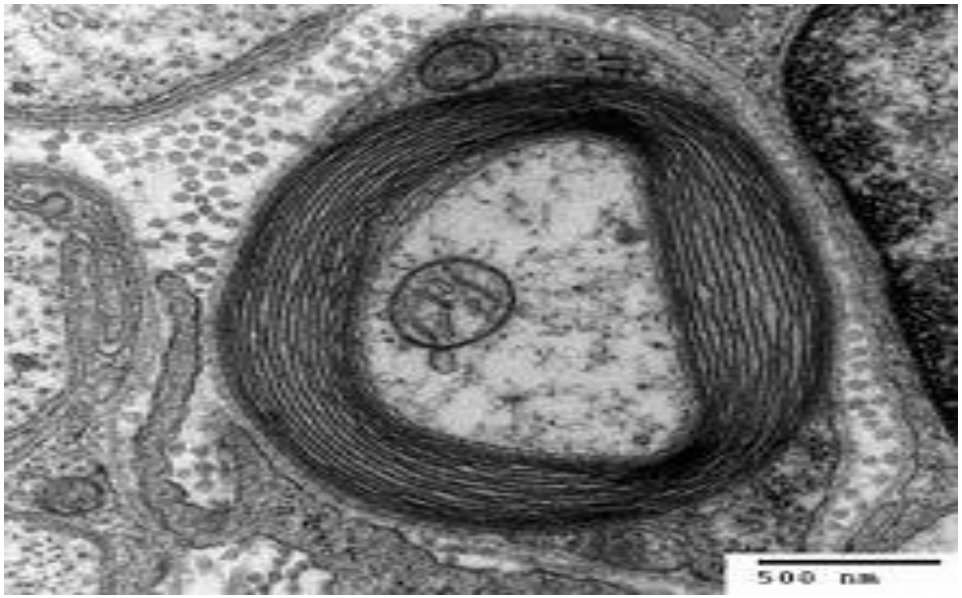
Dr Heyam Awad
FRCPath

Diseases of Myelin

- Myelin: protein-lipid complex that is wrapped around the axons.
- Function: allows rapid propagation of signals.
- Composition: layers of plasma membranes assembled by oligodendrocytes (CNS)
- Myelinated axons are the predominant component of white matter.

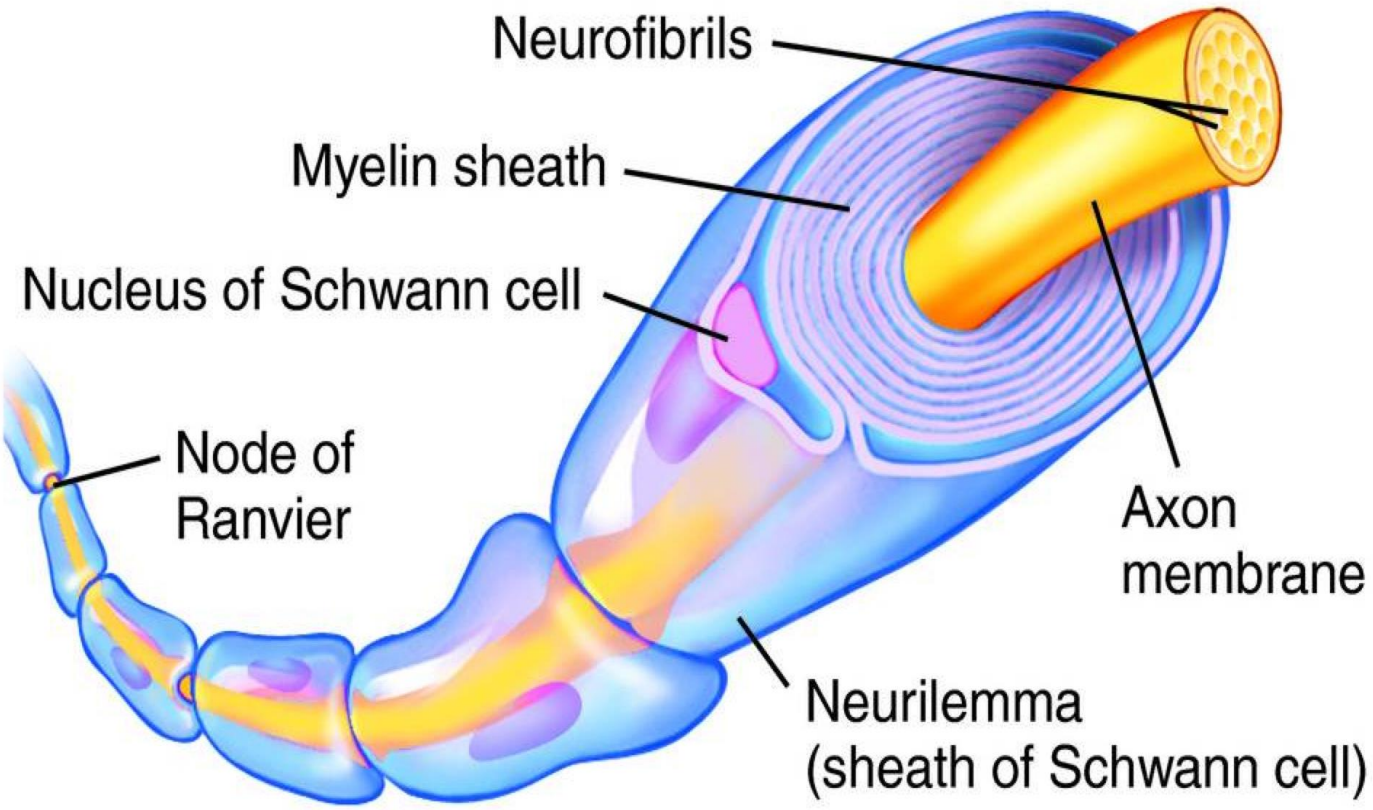

Axon
Myelin sheath
Nodes of Ranvier

EM myelin



- Myelin diseases of CNS do not affect myelin of peripheral nerves.
- WHY???

Myelin in peripheral nerves



Primary diseases of myelin

- 1. **demyelinating** diseases : acquired conditions where there is damage to previously normal myelinated axons due to autoimmune destruction, viral infections, drugs, toxins.

  Most common type: multiple sclerosis
- 2. **demyelinating diseases = leukodystrophy** myelin not formed properly or has abnormal turnover kinetics , result from mutation disrupting function of proteins the form myelin.

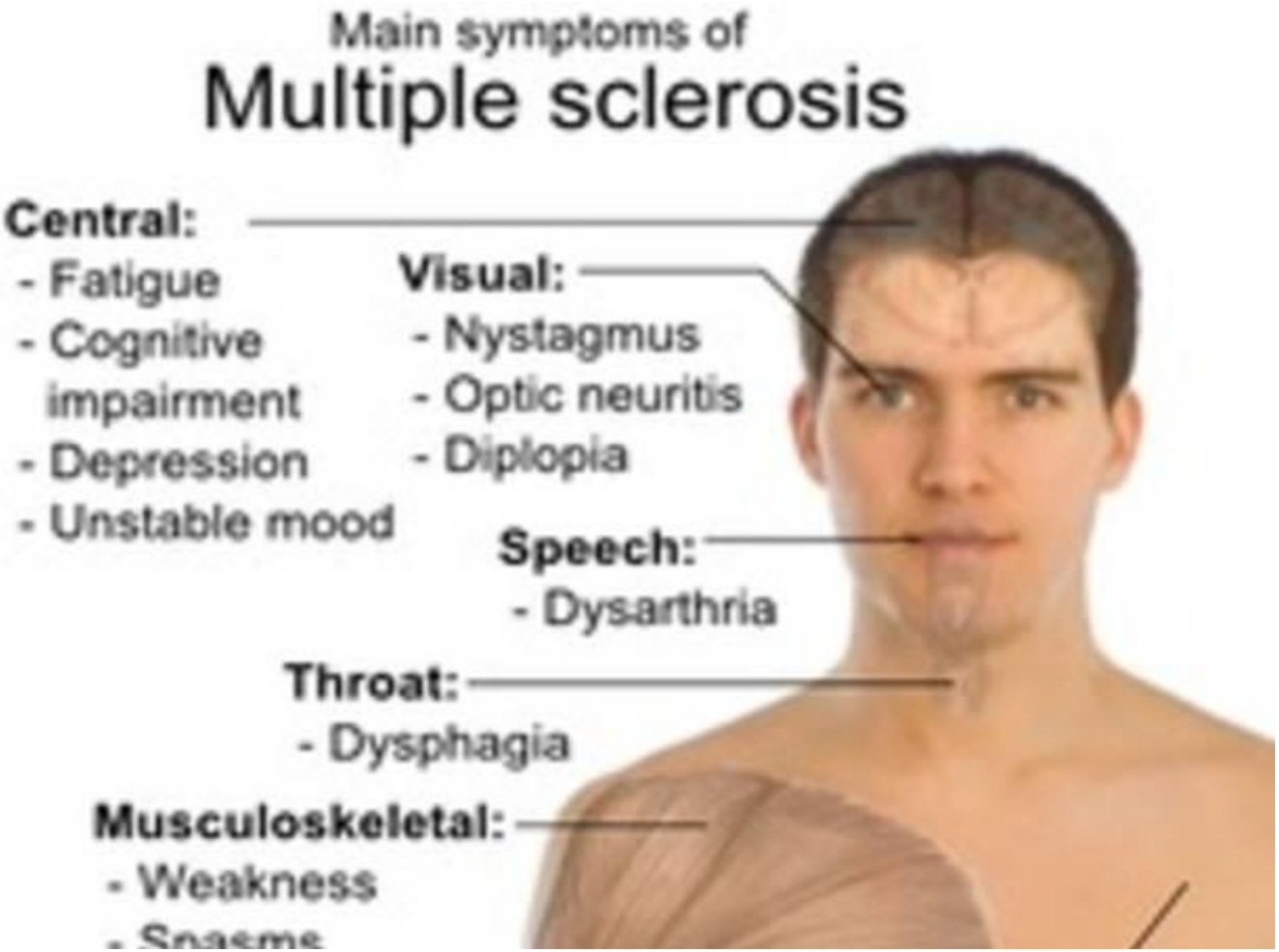
Multiple sclerosis

- Autoimmune
- Demyelinating
- Episodes of neurologic deficits separated in time which are attributed to white matter lesions that are separated in space.

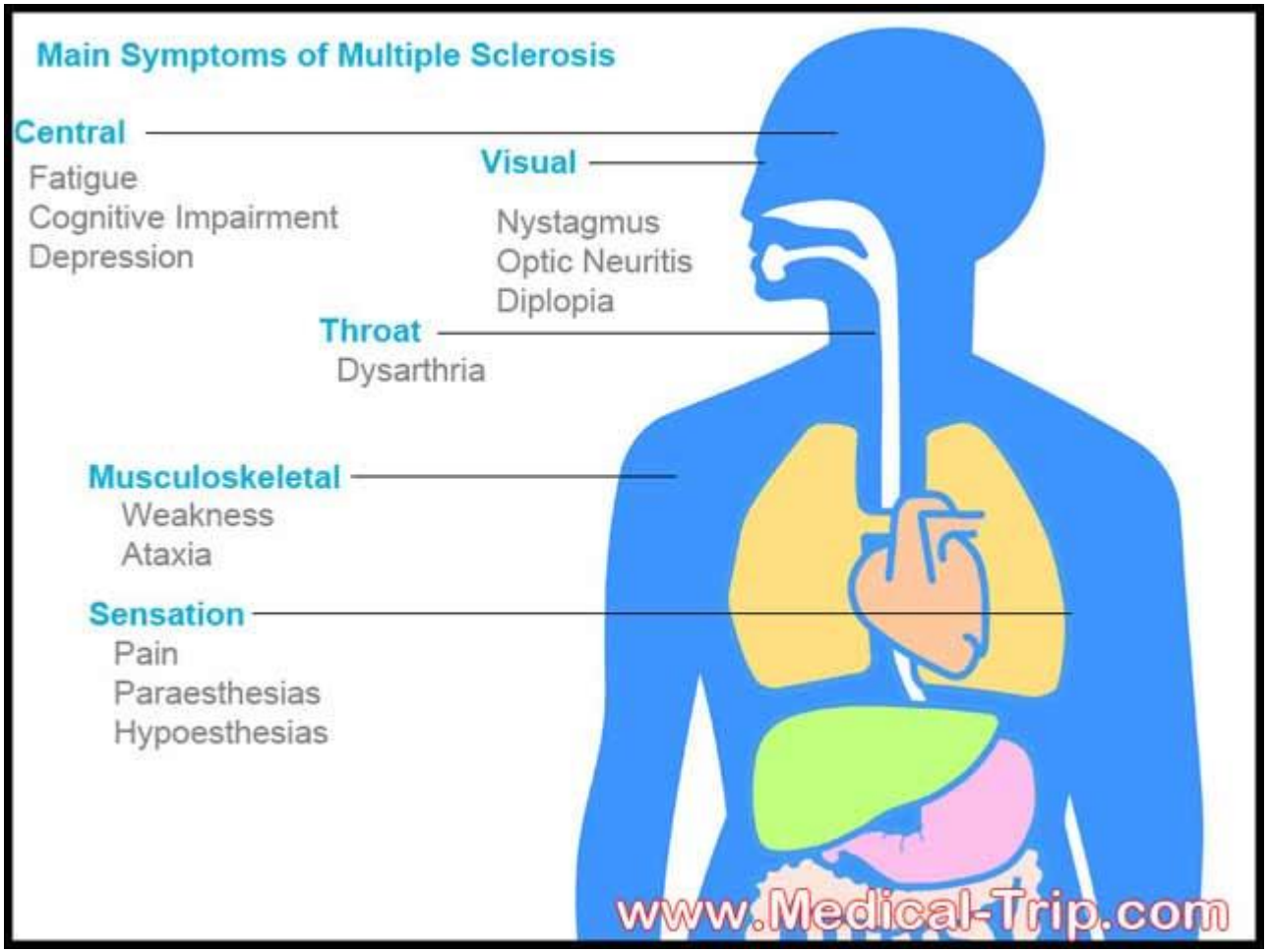
- 1 per 1000 persons in USA and Europe
- Female : male ratio is 2:1

Relapsing and remitting episodes of neurologic deficit variable clinical course.

symptoms


Main symptoms of
Multiple sclerosis
Central:
- Fatigue
- Cognitive impairment
- Depression
- Unstable mood
Visual:
- Nystagmus
- Optic neuritis
- Diplopia
Speech:
- Dysarthria
Throat:
- Dysphagia
Musculoskeletal:
- Weakness
- Spasms

symptoms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Sensation
Pain
Paraesthesias
Hypoesthesias
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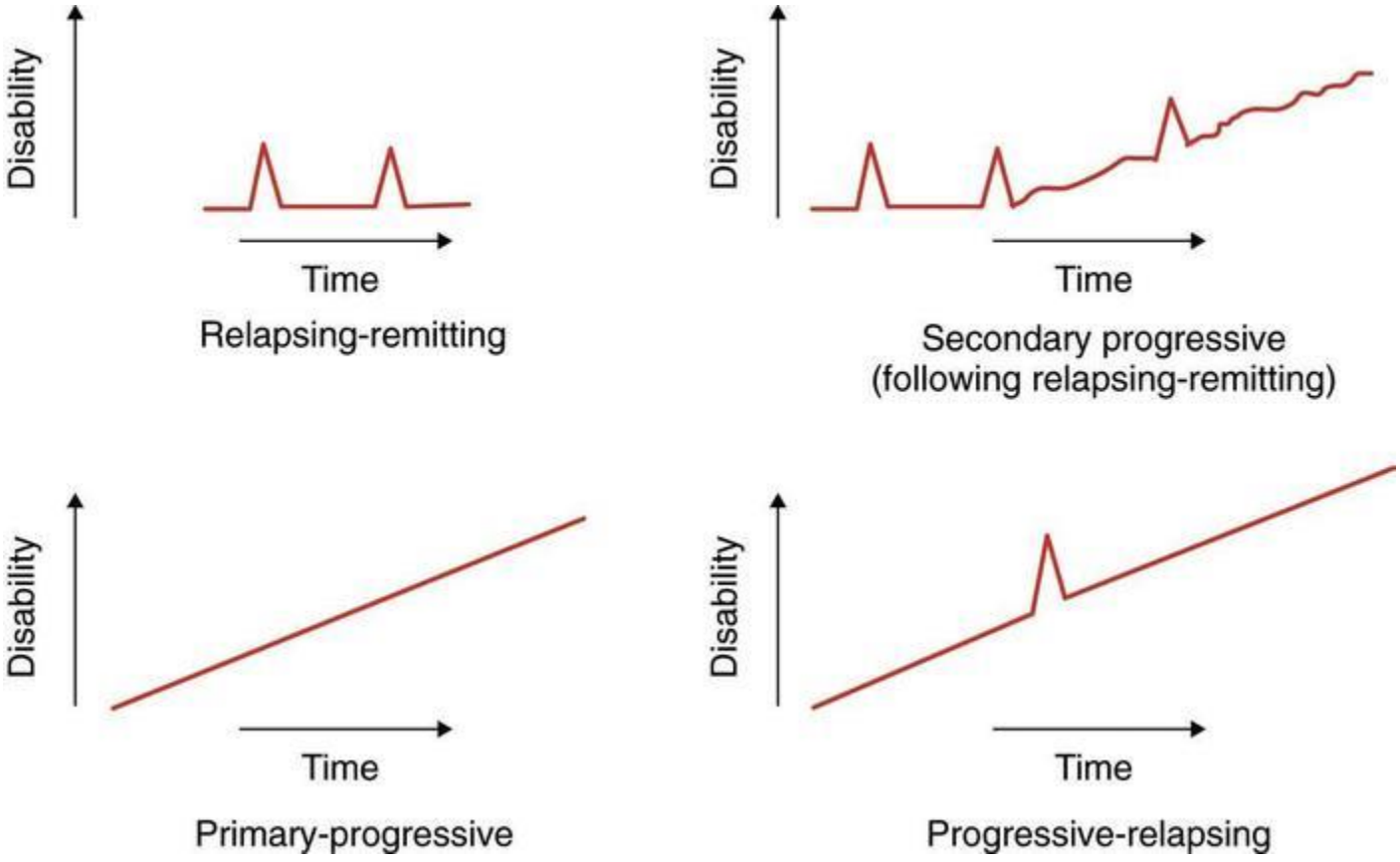
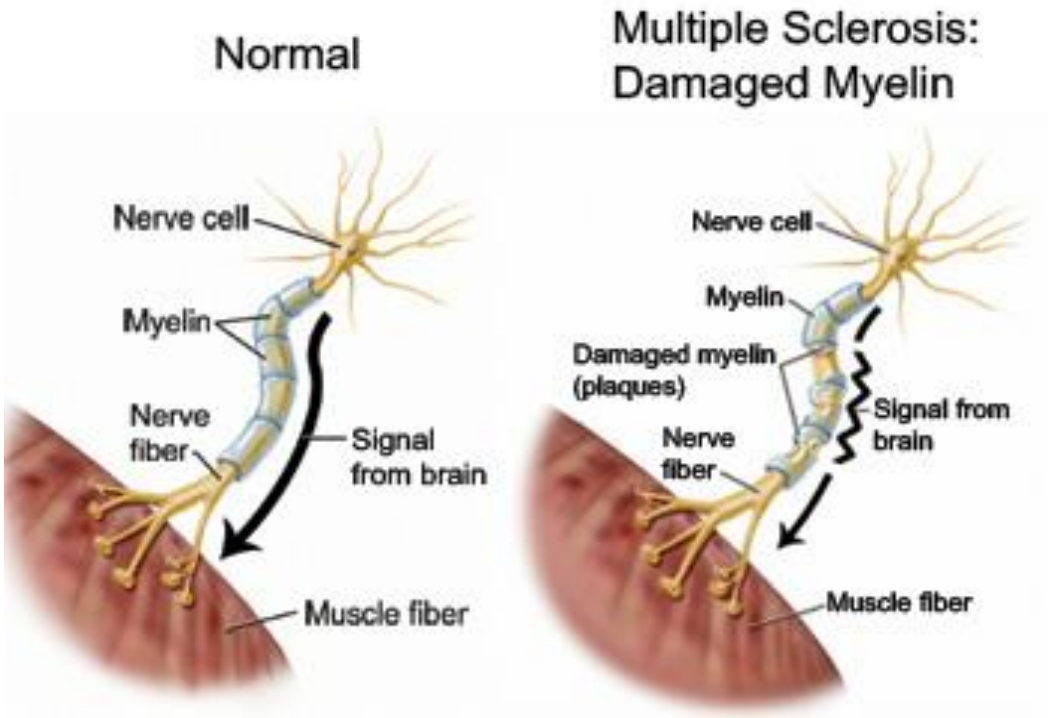
Clinicl course



pathogenesis

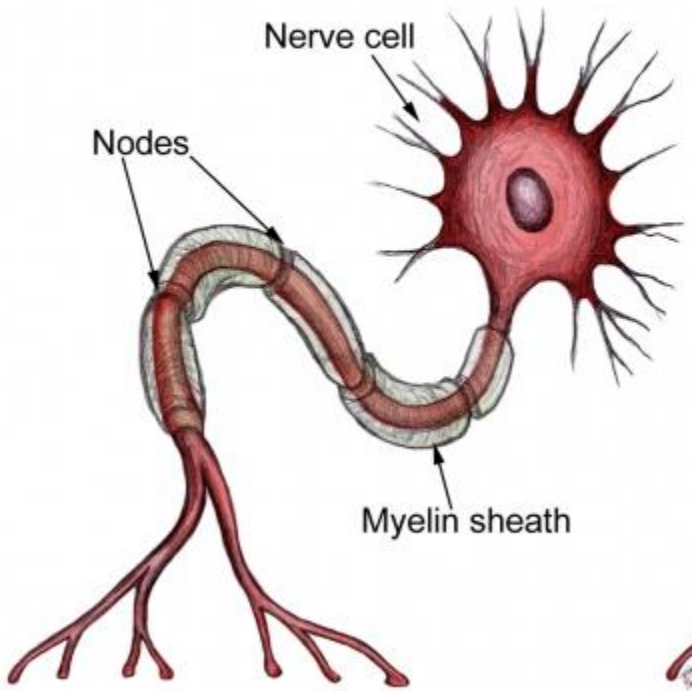


Immune destruction in MS

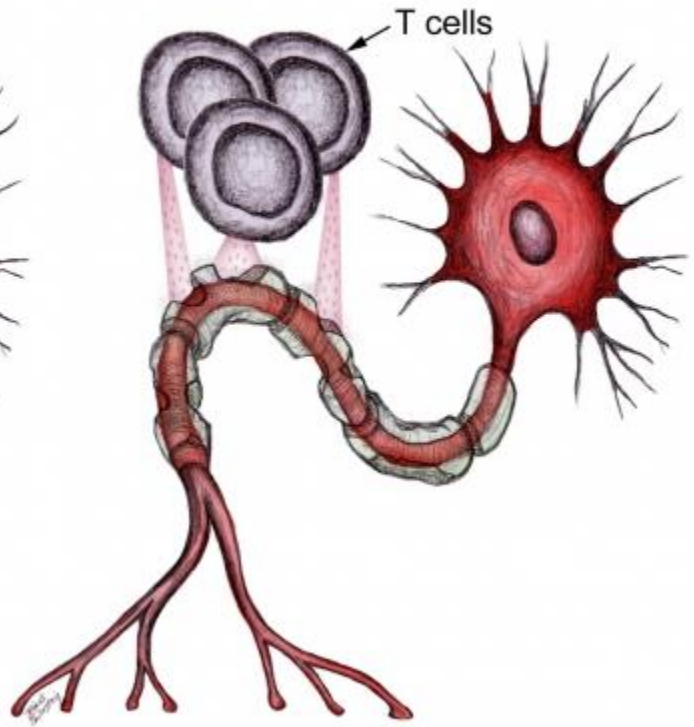
- CD4 T lymphocytes play a major role.
- CD 8 T + B lymphocytes might also play a role.

- In addition to demyelination; axonal damage can occur secondary to toxix effects from lymphocytes, macrophages and the chemicals they secrete.

Normal nerve



Nerve in multiple sclerosis



pathogenesis

- Autoimmune disease
- Environmental and genetic factors
- Loss of tolerance to self protein: myelin antigen
- Initiating agent?? Could be viral infection

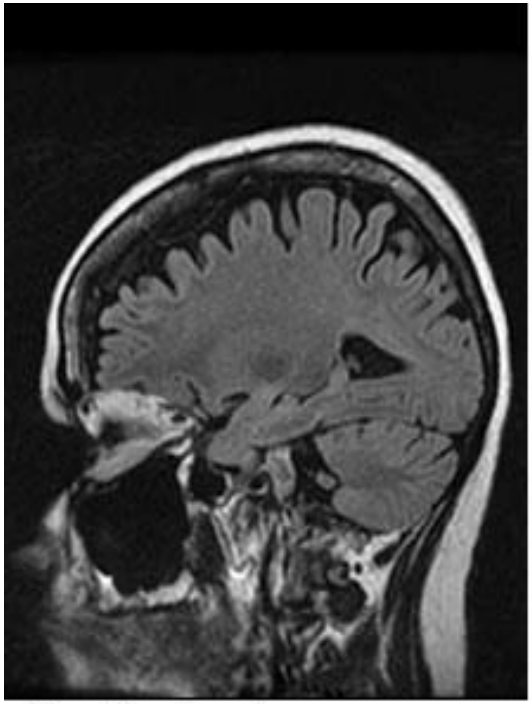
- Genetic predisposition..
- 15 fold higher in first degree relatives
- Concordance rate of monozygotic twins around 25%

- HLA DR2

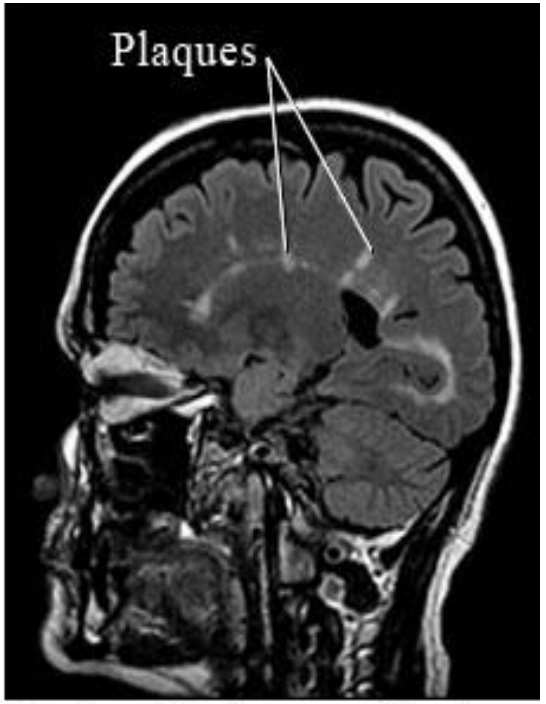
morphology

- White matter disorder
- Multiple well circumscribed slightly depressed grey tan irregularly shaped lesions= plaques
- Commonly seen near ventricles, optic nerves and chiasm, brain stem, cerebellum and spinal cord

plaques



Healthy brain



Brain with damage (lesions or plaques) caused by MS

- Active plaques: ongoing myelin breakdown, macrophages containing myelin debris

Active plaques.. One of four classes

- Type 1: macrophages infiltrating with sharp margins
- 2: like 1 but also complement deposition
- 3: less well defined borders + oligodendrocyte apoptosis
- 4: non- apoptotic oligodendrocyte loss

- Quiescent, inactive plaques: inflammation disappears leaving behind little or no myelin
- Astrocytic proliferation and gliosis prominent

Other demyelinating diseses

- 1. post infectious, most common form
- 2.Neuromeylitis optica
- 3.Central pontine myelinolysis
- 4.Progressive multifocal leukoencephalopathy

Post infectious demyelination

- Not due to direct effect of the virus
- Pathogen associated antigens cross react with myelin antigens…. Provoke autoimmune response against myelin
- Onset: acute, monophasic

Post infecious demyelinating

1. Acute disseminated encephalomyelitis

- Symptoms 1-2 weeks after infection
- Nonlocalizing symptoms: headache, lethargy, coma
- Rapid progression , fatal in 20% of cases
- Survivals: complete recovery

Post infectious demyeinating ..

- 2. acute necrotizing hemorrhagic encephalomyelitis: more dangerous
- Children and young adults mostly affected.

Neuromyelitis optica

- Inflammatory demyelinating disease
- Mainly optic nerve and spinal cord
- Antibodies to aquaporin-4 are diagnostic
- Previously thought a subtype of MS

Central pontine myelinolysis

- Non immune process
- Loss of myelin in centre of pons
- Occurs after rapid correction of hyponatremia
- Edema due to sudden change in osmotic pressure probably is the cause of the damage
- Causes rapid quadriplegia

Progressive multifocal leukoencephalopathy

- Reactivation of JC virus in the immunocompromised
- JC will be discussed in another lecture!

leukodystrophies

- Inherited demyelinating diseases
- Mot are autosomal recessive, some X likned.

- Lysosomal enzyme, perixosomal enzymes, or myelin protein mutations

morphology

- White matter: grey and translucent with decreased volume
- Loss of white matter.. Brain atrophic, ventricles enlarge

- Several types of diseases exist, each with a specific mutation