



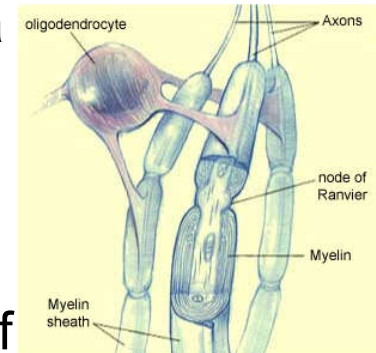
Demyelinating Disorders

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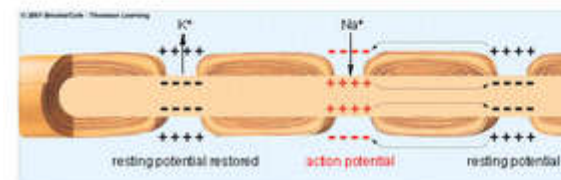
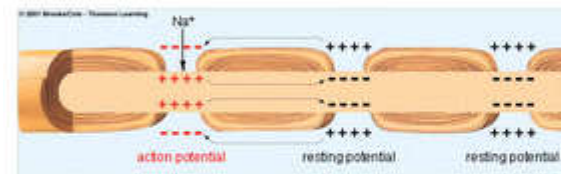
Definition and Classification

- **Myelin** is an electrically insulating material that forms a sheath, the myelin sheath, surrounding the axon of a neuron. It is formed by oligodendrocytes in CNS and Schwann cells in peripheral nerves.
- **Demyelinating disorder:** Any condition that is characterized by the destruction of the myelin sheath of axons.
- Classification demyelinating diseases
 - Acquired demyelinating diseases
 - Multiple sclerosis
 - Other demyelinating syndromes e.g.
 - 1- Optic neuritis
 - 2- Transverse Myelitis
 - 3- Acute disseminated encephalomyelitis
 - Hereditary



Myelin Sheath

A series of Schwann cells
Sheath blocks ion movements
Action potential must "jump" from node to node





Multiple Sclerosis



Multiple Sclerosis (MS)

- Overview
- Epidemiology/Demographics
- Pathophysiology
- Clinical picture
- Clinical course
- Diagnosis
- Treatment options

Multiple Sclerosis – Overview

- MS is an ***inflammatory demyelinating*** disease of the Central Nervous System (CNS)
- Predominantly affects the ***white matter*** tissue, which is responsible for transmitting communication signals both internally within the CNS and the nerves supplying the rest of the body.
- Surrounding and protecting the nerve fibers of the CNS is a fatty tissue called ***myelin***, which helps nerve fibers conduct electrical impulses.
- In MS, myelin is lost in multiple areas, leaving scar tissue known as ***plaques or lesions***.
- Sometimes the nerve fiber itself is damaged or broken.
- Common cause of disability in young adults





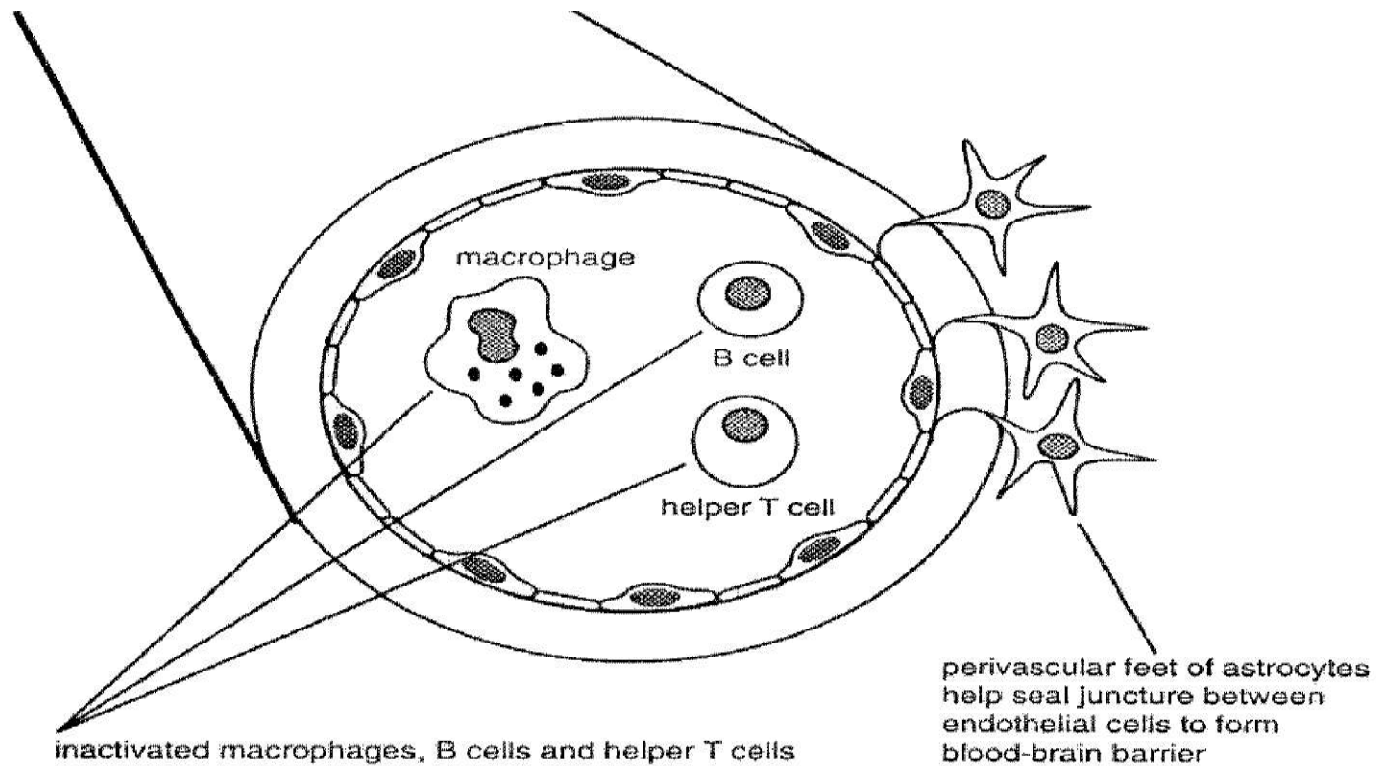
Epidemiology

- Prevalence varies around the world
- Male : Female ratio = 1 : 3
- Our country is basically among low prevalence zones in which the incidence rate is around 5/100.000, However, recently there is remarkable increase in its incidence.
- More in Caucasian people
- Age
 - Onset: 15 to 50 years of age
 - Peak onset: between 20 and 30 years of age
 - Onset rare before age 10 or after age 60

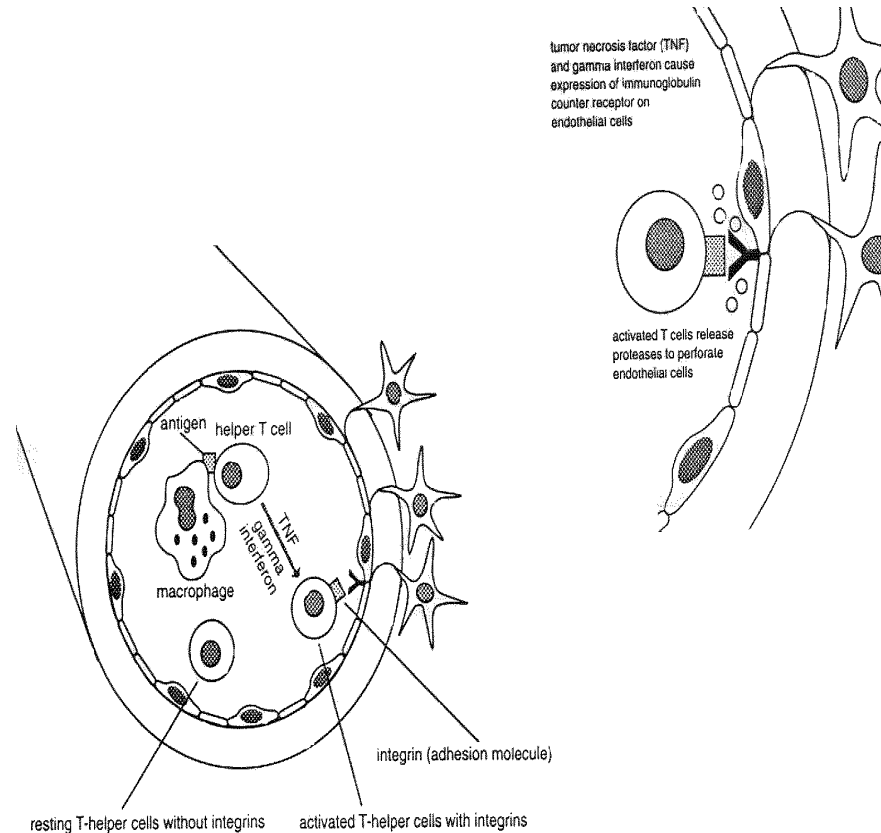
Pathogenesis of MS

- Genetic factors Plays a role in MS pathogenesis as there is increased risk for developing MS in family members of MS patients.
- Environmental Factors including
 - Infections: of all the infectious agents suspected (Varicella, Herpes, Chlamydia, etc.), the Epstein Barr Virus (EBV), has the most evidence to date.
 - Low vitamin D
 - Head trauma
 - Cigarette Smoking
 - Stress

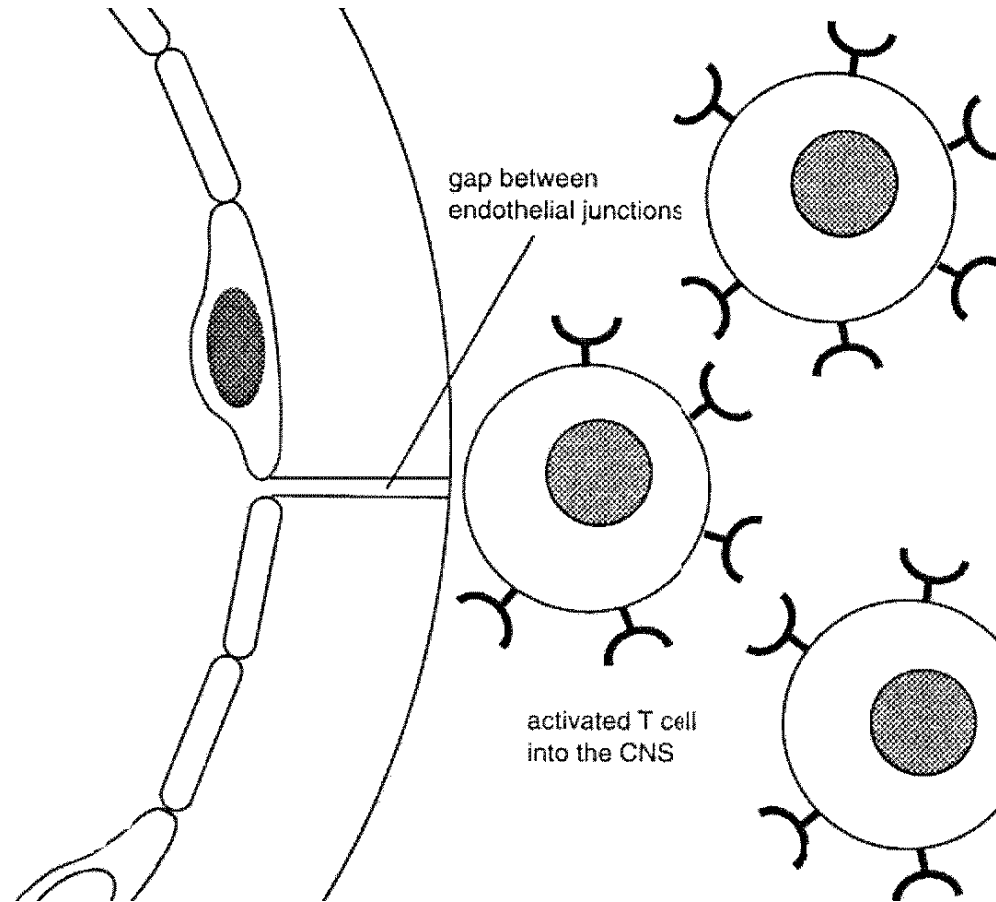
Pathogenesis: Autoimmune Process



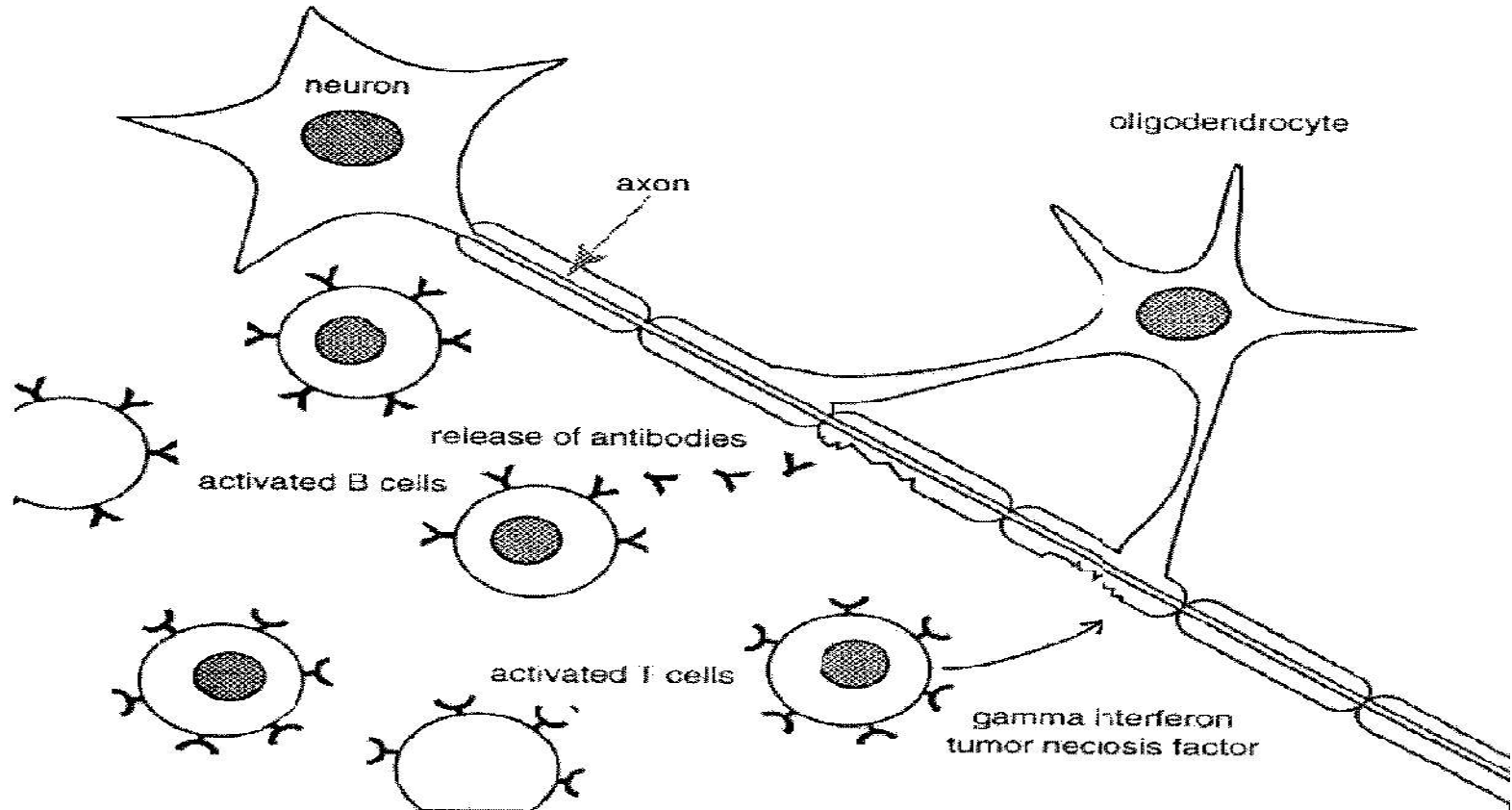
Pathogenesis: Autoimmune Process



Pathogenesis: Autoimmune Process



Pathogenesis: Autoimmune Process



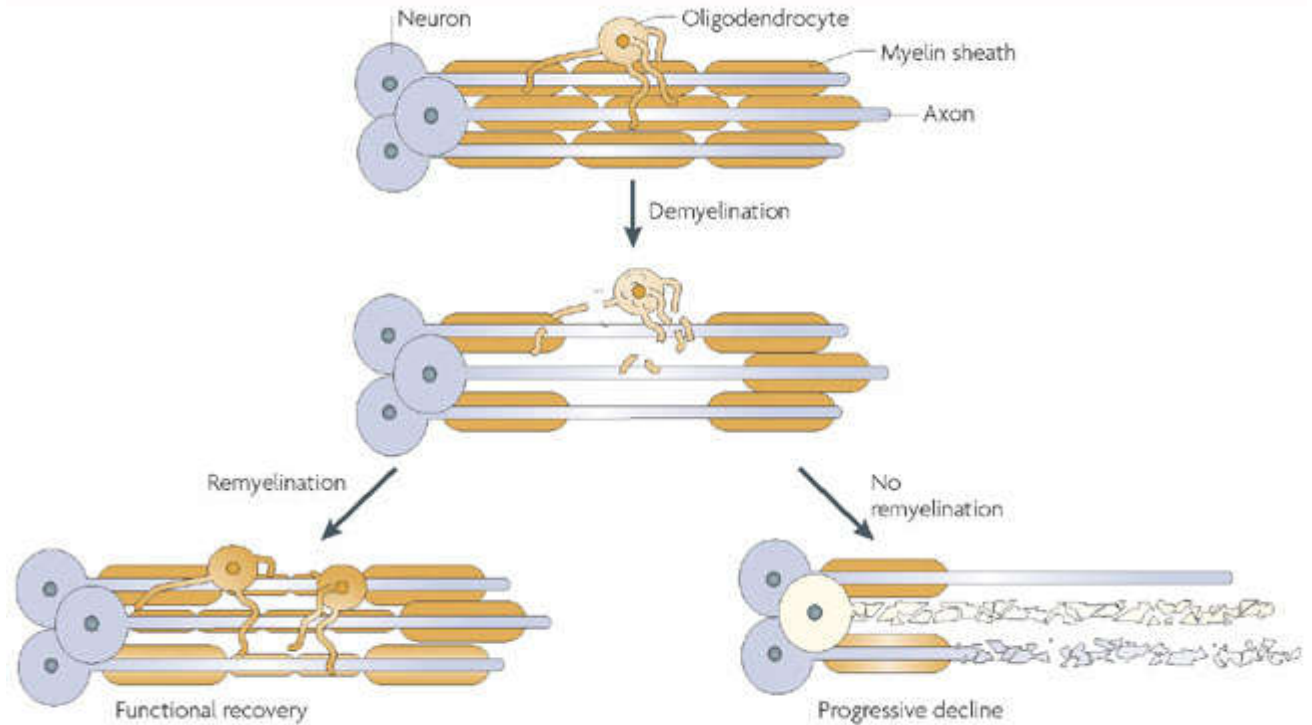


Pathogenesis: Common sites of MS pathology

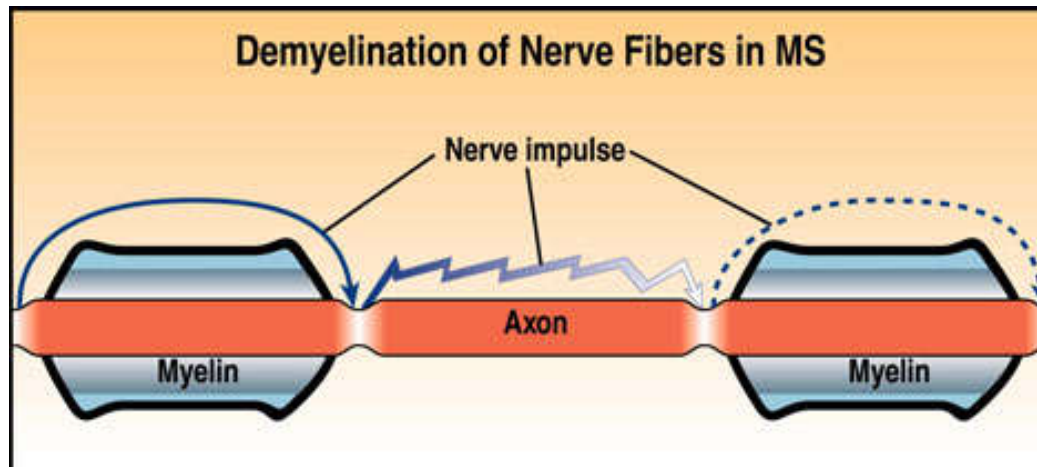
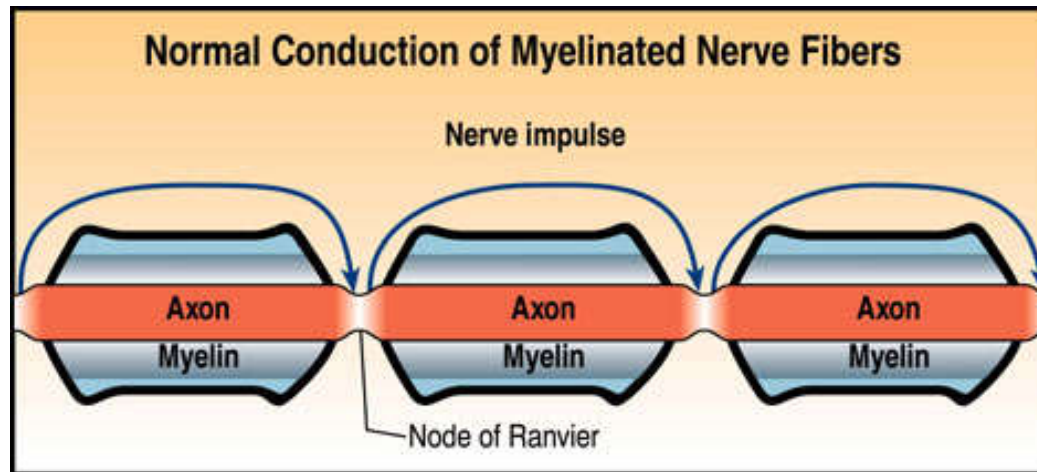
- Optic nerves
- Cerebrum (Corpus callosum - Subcortical White Matter - Periventricular White matter (Lateral ventricles and 4th ventricle))
- Cerebellum
- Brainstem
- Cervical spinal cord

Pathogenesis: Stages of MS pathology

- Demyelination
- Remyelination
- Oligodendrocyte depletion
- Axonal Damage



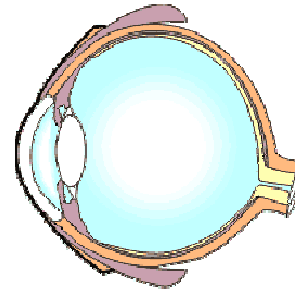
Pathogenesis: Pathophysiology



Signs and Symptoms of MS by Lesion Location

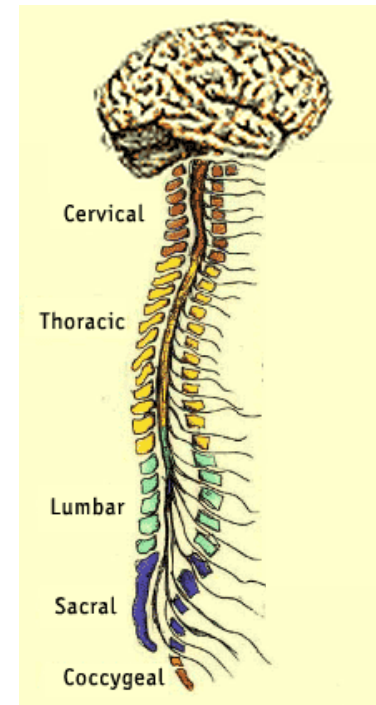
- **Optic nerve**

- Monocular visual loss
- Scotoma



- **Spinal cord**

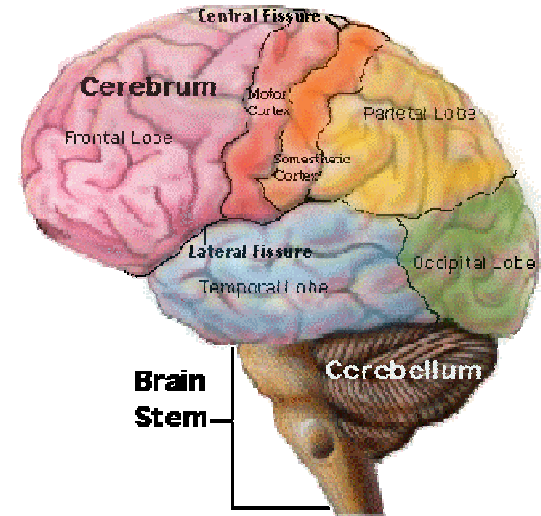
- Limb weakness
- Spasticity and hyper-reflexia
- Sensory Manifestations
- Lhermitte's sign
- Urinary urgency and incontinence



Signs and Symptoms of MS by Lesion Location

■ Brainstem

- Diplopia (double vision)
- Internuclear ophthalmoplegia
- Pain (acute versus chronic)
 - Trigeminal neuralgia, tic-like extremity pain
 - Aching back pain, burning sensation, leg spasms
- Numbness of face and tongue
- Vertigo (sensation of moving around in space)



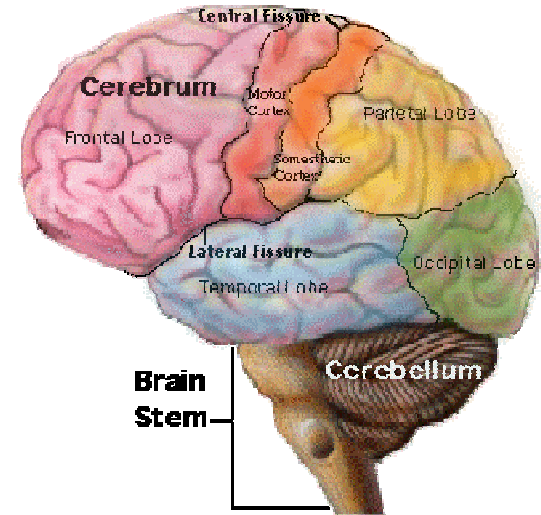
Signs and Symptoms of MS by Lesion Location

■ Cerebrum

- Impairment of concentration or memory
- Hemiparesis (unilateral paralysis)
- Hemisensory loss
- Visual field defect

■ Cerebellum

- Incoordination of limbs
- Ataxic gait



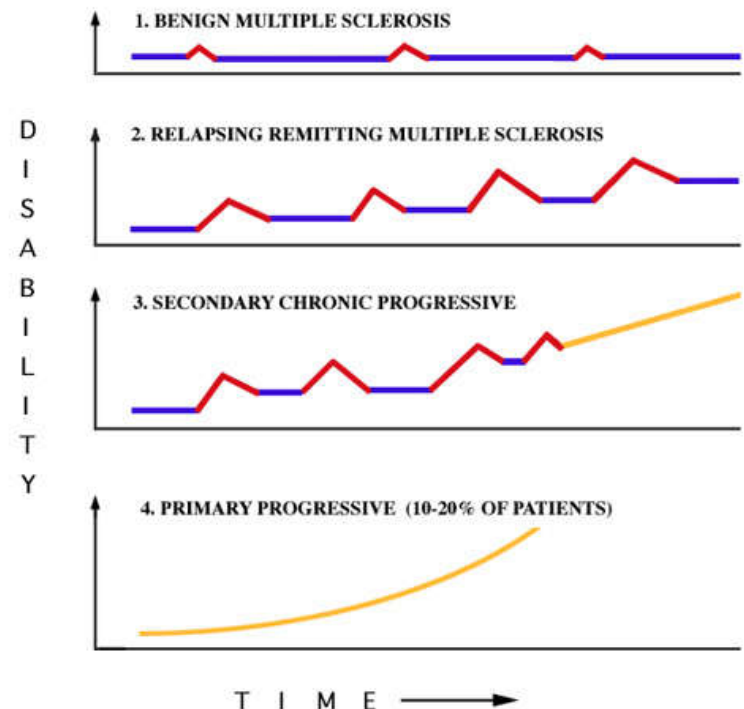
Clinical Courses of MS

- Neurological attacks or aggravation of symptoms
- Indicative of a new immune attack on myelin
- Should last at least 24 hours
- Untreated attacks, can last from weeks to months (resulting in slow recovery/residual effects)
- Precipitating factors can be identified
 - Infections (most common),
 - Heat sensitivity
 - Emotional stress
 - Physical exertion
 - Fatigue

Classification

Click on graphs 1-4 for a description.

— Stable
— Relapse
— Progression

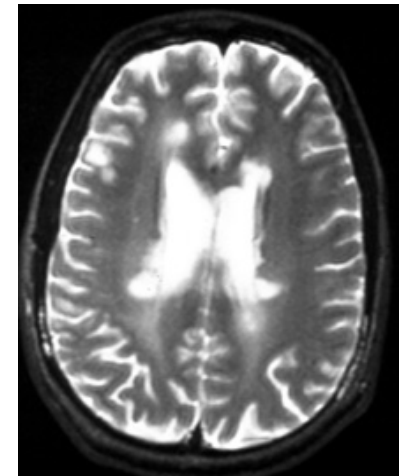


Diagnosis of MS

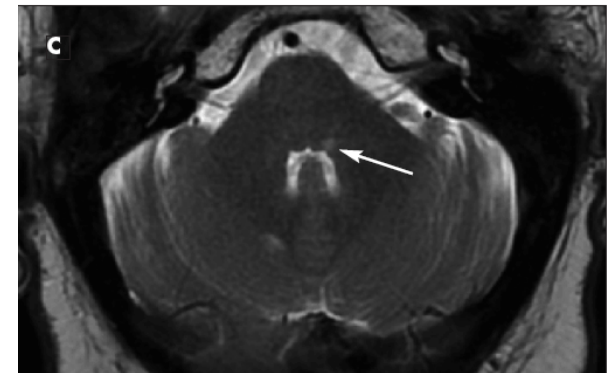
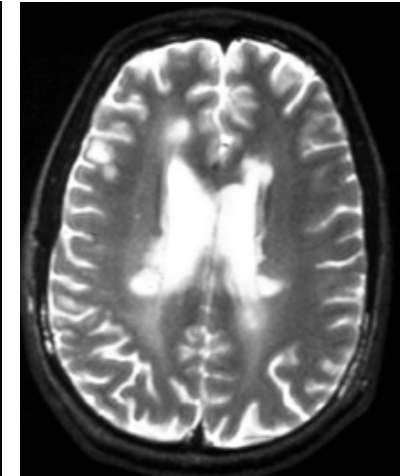
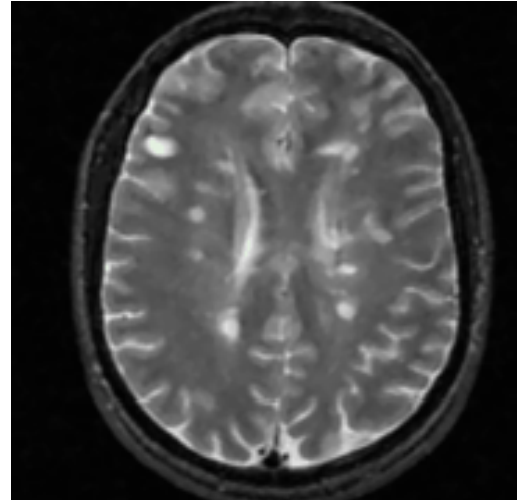
- Lesions disseminated in *time* and *space*
 - Time: More than one attack separated by at least one month
 - Space: CNS involvement of more than one area
- Exclusion of other possible causes
- This can be achieved through
 - ***Clinical findings***
 - History
 - Neurologic exam
 - Clinical picture
 - ***Laboratory evaluations***
 - Magnetic resonance imaging (MRI)
 - Evoked potentials
 - Cerebrospinal fluid (CSF) analysis

Diagnosis: MRI Brain and Spinal cord

- Highly sensitive in detecting MS lesions of the brain and spinal cord
- Evidence of dissemination of lesions in time and space
- Helpful in excluding other causes, such as tumors



Diagnosis: MRI Brain and Spinal cord



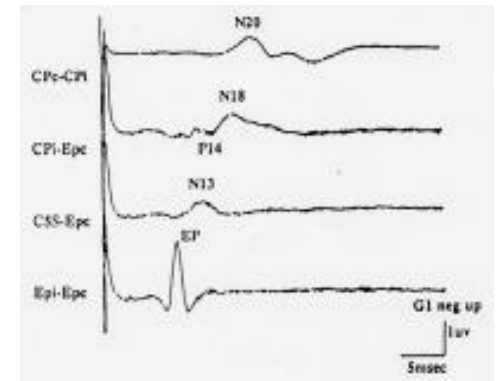
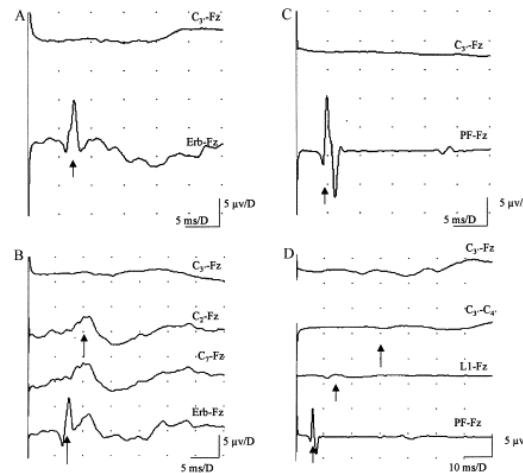
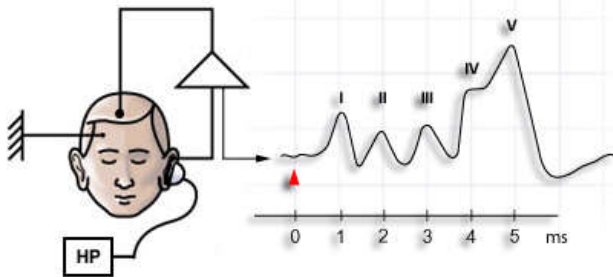
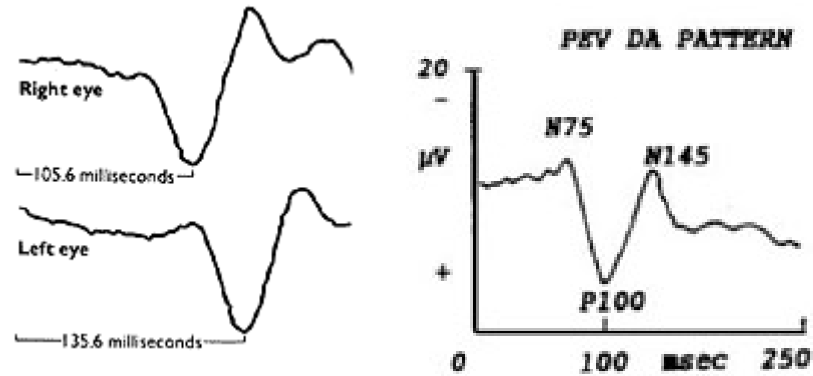
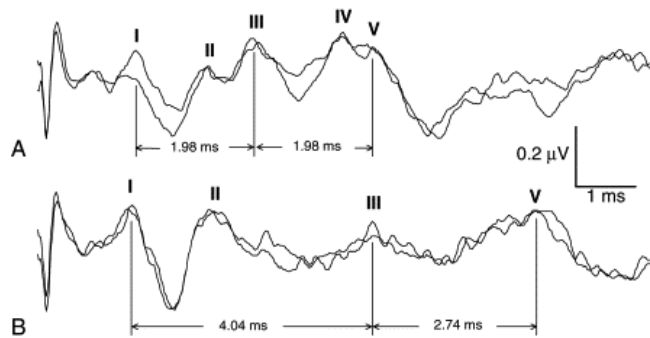


Diagnosis: Evoked Potentials

Evoked Potentials

- Measure nerve conduction velocity
 - Visual
 - Brainstem auditory
 - Somatosensory

Diagnosis: Evoked Potentials



Diagnosis: CSF analysis

Cerebrospinal Fluid Analysis

- Immune abnormalities
 - Increased mononuclear cells
 - Increased total proteins
 - Increased intrathecal Immunoglobulin G (IgG) synthesis with oligoclonal bands present
 - Positive oligoclonal bands
 - Increased IgG index





Treatment of MS

- Treatment of acute attack: Corticosteroids
- Treatment of disease progression:
 - Interferons β :
 - Betaseron[®] (interferon β -1b)
 - Avonex[®] (interferon β -1a)
 - Rebif[®] (interferon β -1a)
 - Immunosuppressive drugs
- Treatment of symptoms



Corticosteroids

- Used in moderate-to-severe exacerbations
- IV methylprednisolone 500 mg/day for five days or 1 gm/day for 3 days followed by oral prednisone (optional)
- Hasten clinical recovery
- Delay recurrence of neurologic events
- Does not alter the course of MS



Interferon Beta

- Indication: relapsing forms of MS
- Reduces rate of clinical relapse
- Reduces the development of new lesions
- Delays the increase in the volume of lesions
- May delay progression of disability
- Has shown efficacy in patients who have experienced a first clinical episode and have MRI features consistent with MS

Interferons β



Dose: 44 mcg SC 3 times per week

Dose: 30 mcg IM once weekly

Dose: 250 mcg SC every other day



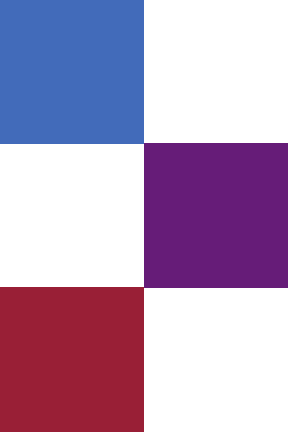


Immunosuppressants

- Show only slight evidence of benefit in MS
- Used only for progressive MS
- Associated with serious side effects
 - Azathiopurine (Imuran)
 - Methotrexate
 - Cyclosporine
 - Mitoxantrone

Symptomatic Treatments

Problem	Symptoms	Management
Spasticity	Painful spasms in the lower and upper limbs	Remove irritating factors Physical therapy, baclofen, diazepam, dantrolene
Paroxysmal phenomena	Trigeminal neuralgia, pain, tonic seizures	carbamazepine, Neurontin, phenytoin
Fatigue	Feeling tired (morning or early afternoon)	Energy conservation, amantidine
Depression	Common, occurs in high percentage of patients	Anti-depressants
Sexual dysfunction	Inability to produce/ sustain an erection	Behavioral therapy Viagra, Cialis
Urinary dysfunction	Urgency, frequency and retention	Detrol, Ditropan, Botox (off label use)



THANK YOU