

MULTIPLE SCLEROSIS





Histology of nerve cell and the process of myelination



Raghad Alawi

structure of neuron:



_neuron :is the building unit of the nervous system,and is consists of:

- 1.Dendrite: for receiving signals**
- 2.Cell body (soma):contain the nucleus and organelles**
- 3.Axon:conduct electrical impulse**
- 4.Axon terminals::transmits electrical and chemical signals to other neuronal and effector cells**

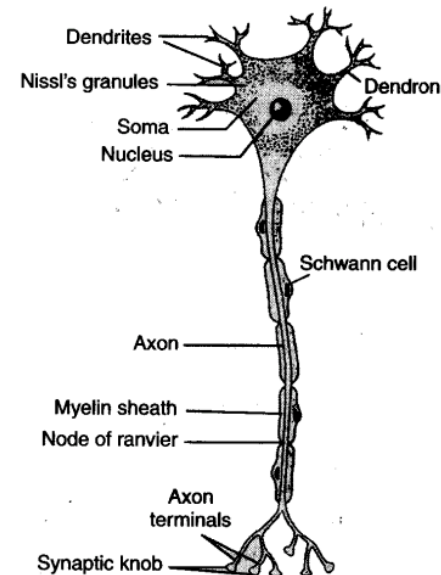


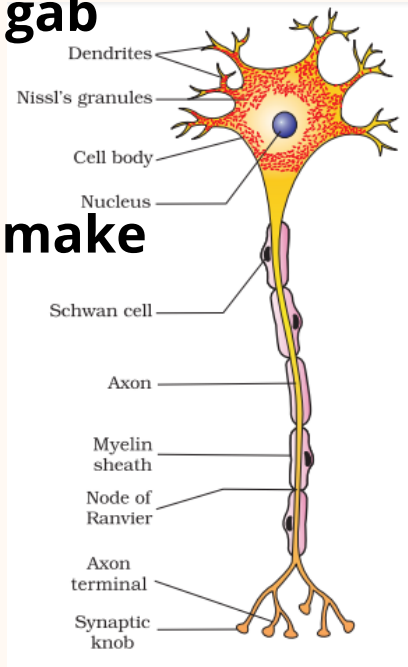
Fig. Structure of Neuron

What is myelination?

.Myelin is thick sheath of lipoprotein that surround the axon of myelinated neuron

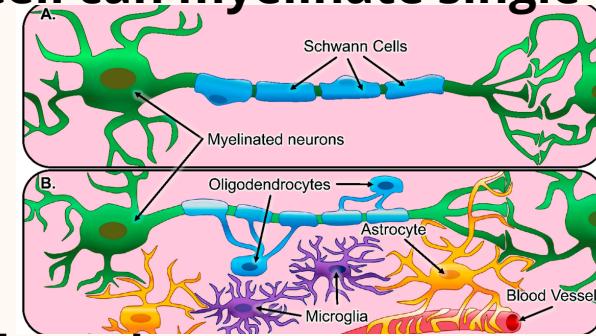
.the myelin sheath is not continuous instead there is intermittent gap where axon is exposed called node of ranvier

.Myelin primarily responsible for white colour of nerve fibre so make what called white mattre in brain.



Cells that produce myelin sheath:

- .in the central nervous system(CNS)myelination is carried out by oligodendrocytes,one cell can myelinated multiple axons by wraps its plasma membrane around axon in spiral fashion.
- .in the peripheral nervous system(PNS) by Schwan cells each cell can myelinate single axon.



The importance of myelin::

- .faster conduction of impulses in which impulse jump from node to the othe by process called saltatory conduction
- .Act as electrical insulator preventing the loss of signal as it travels along the axon

Multiple sclerosis

Definition

Epidemiology

Etiology

Pathophysiology

(MS) lesion

done by maya swaiss

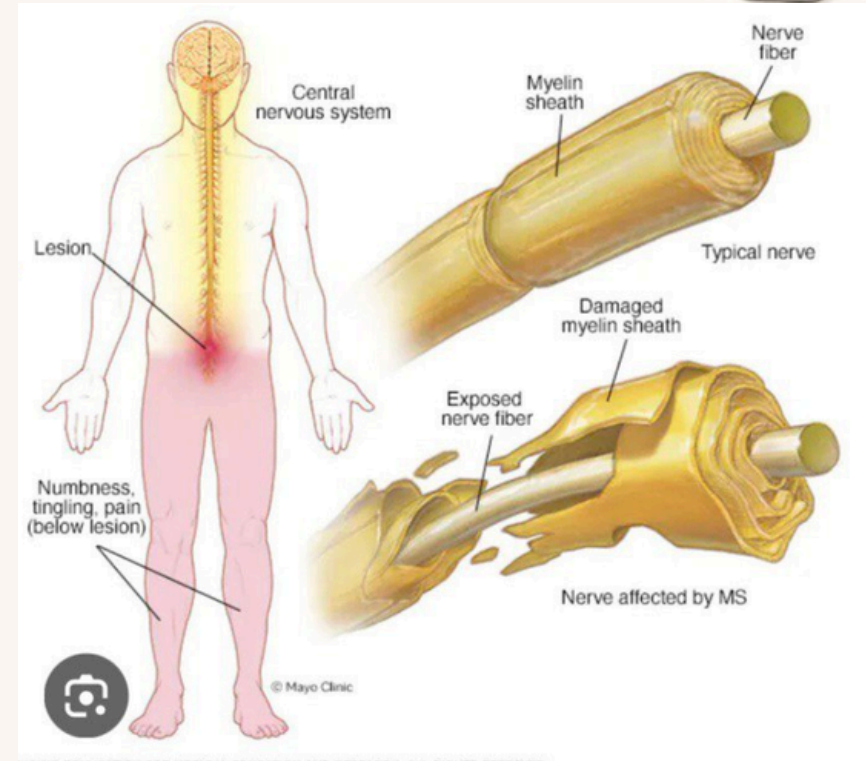
(Definition& epidemiology of MS)

MS is an chronic autoimmune demyelinating disorder that destruct the CNS myelin & oligodendrocytes With a relative preservation of axons in brain and spinal cord characterized by lesion separated both in space and time in the CNS .

MS is the most common demyelinating disorder, may affect any age But mainly between 20 &30 .

it more common among white population

MS is more common in females than males (2:1) .



Etiology(Risk factor)

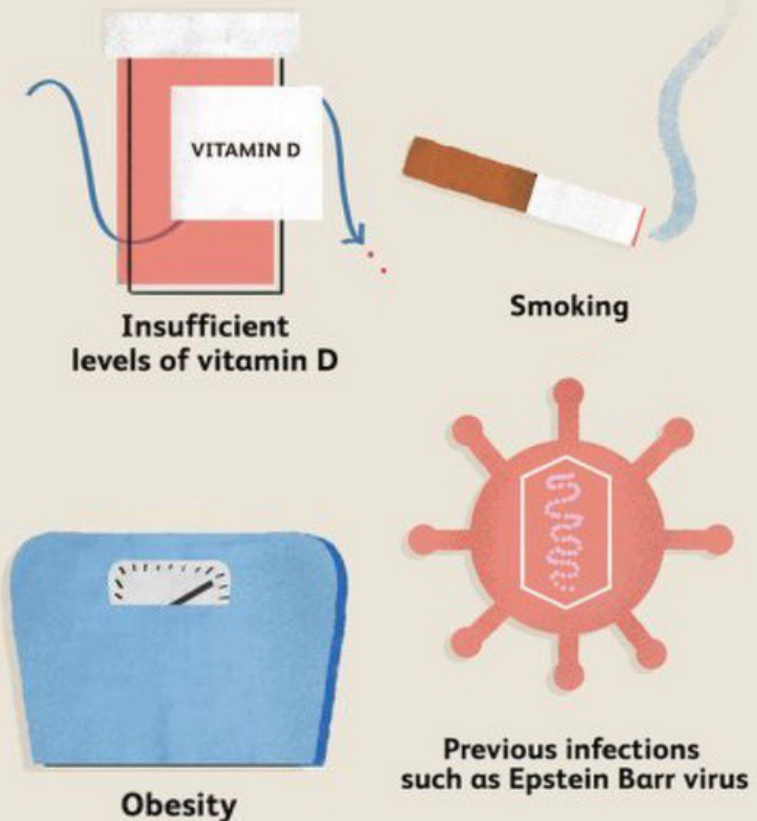
MS like other autoimmune diseases, is believed to be caused by a combination genetic and environmental factors that result in a loss of tolerance to self proteins (the myelin antigens) .

The exact cause is unknown

Risk factors : Viral infection EBV , vitamin D deficiency smoking and Obesity .

genetic factor : increasing incidence in association with a particular human leukocyte antigen alleles such as (HLA-DR) .

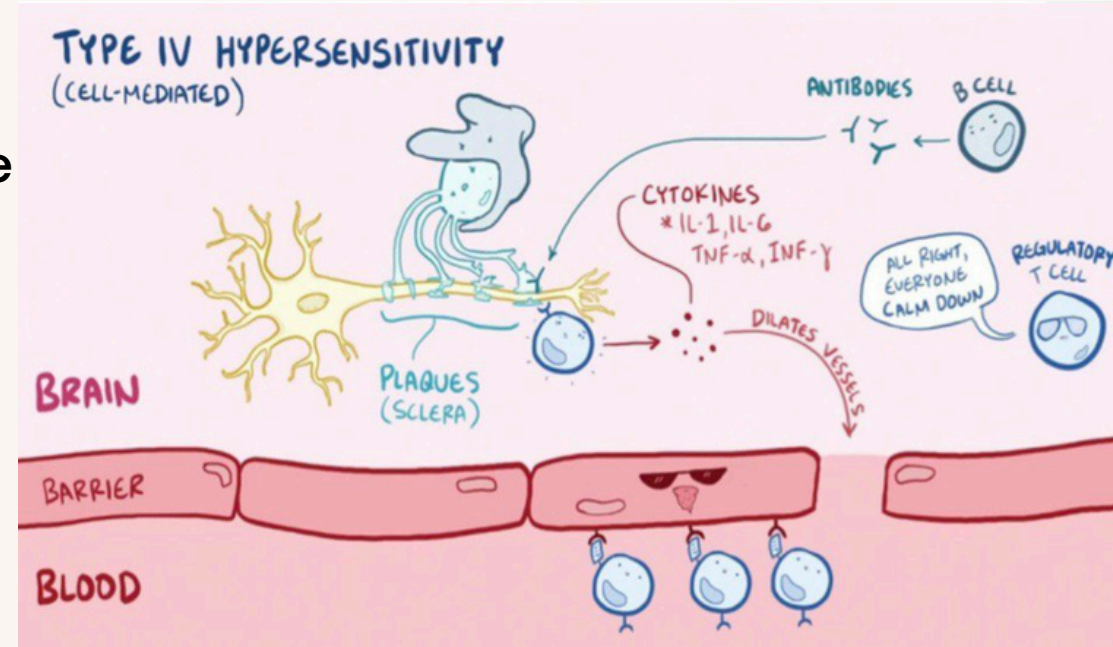
Multiple Sclerosis Risk Factors



(Pathophysiology)

Normally blood brain barrier prevent immune cells to reach CNS but in certain condition like infection the BBB will become injured and more permeable so the immune cells can reach the CNS neuron

As a result the CD4 (T helper cell) will attack myelin sheath , recruit other cells and develop an inflammatory reaction



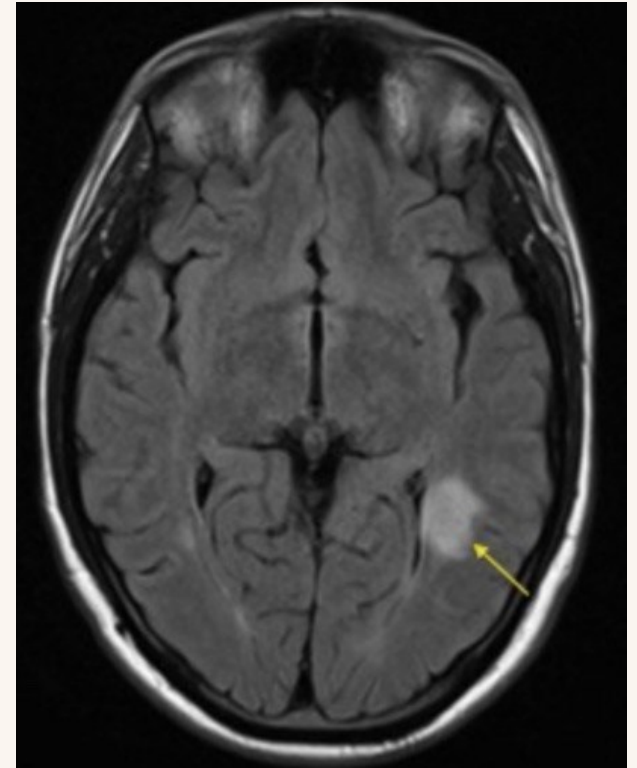
(How The plaque is formed ?)

The demyelination not constant because there is period of partial remyelinating when the process is repeated the plaques will form .

Plaques mainly located in white matter in brain and spinal cord also gray matter can be affected .

They are visible on MRI scans as spots of markedly altered color (usually bright or white spots) .

When the demyelination occurs the symptoms will appear such as (cognitive , motor, sensory and vision) .





Clinical manifestations, course and prognosis of MS

Sara alzaghateet

Clinical manifestations



- MS is diagnosed by finding multiple white matter lesions separated in space and time. The clinical features are defined, as might be expected, by the location of the lesions.
- For example , a right occipital lesion could result in a left homonymous hemianopia, whereas a right cervical spinal cord lesion may lead to an ipsilateral hemiparesis and loss of joint position sense, with contralateral loss of pain and temperature sensation.
- Almost any neurologic symptom, in fact, can be produced by an MS lesion.
- Common clinical features (Table 20-1) include corticospinal tract signs such as weakness and spasticity, cerebellar problems such as intention tremor and ataxia, sensory abnormalities such as paresthesias and loss of vibration and proprioception sensation, and bladder dysfunction. Fatigue is a common complaint. In later stages, cognitive and behavioral abnormalities may occur.

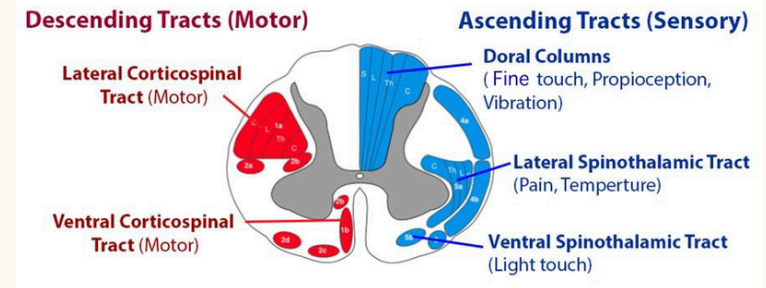
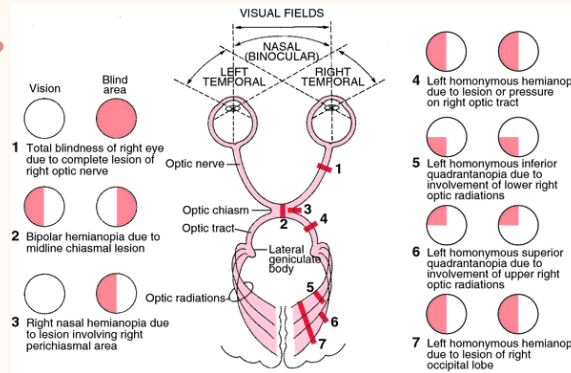
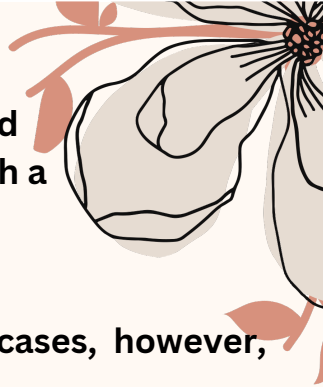
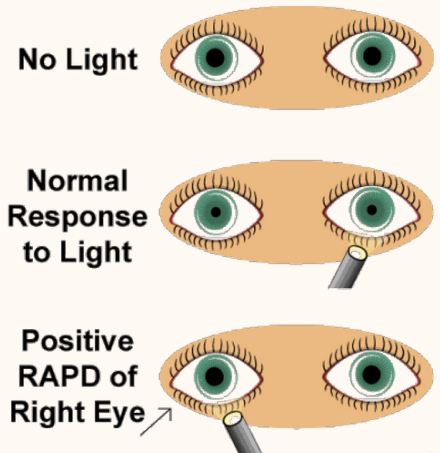


TABLE 20-1. Common Clinical Features of Multiple Sclerosis

Neurologic System	Clinical Sign or Symptom
Cranial nerves	Optic nerve dysfunction
	Visual acuity loss
	Red desaturation
	Papilledema or optic disc pallor
	RAPD
	Eye movement disorders
	Internuclear ophthalmoplegia
	Nystagmus
Motor system	Weakness
	Spasticity
	Reflex abnormalities
	Increased muscle stretch reflexes
	Babinski signs
	Clonus
Sensory system	Paresthesias
	Vibratory loss
	Joint position sense loss
	Lhermitte's sign
Cerebellar function	Ataxia
	Intention tremor
	Dysarthria
Autonomic system	Bladder dysfunction
Other	Fatigue
	Depression
	Uhthoff's phenomenon
RAPD, relative afferent pupillary defect.	

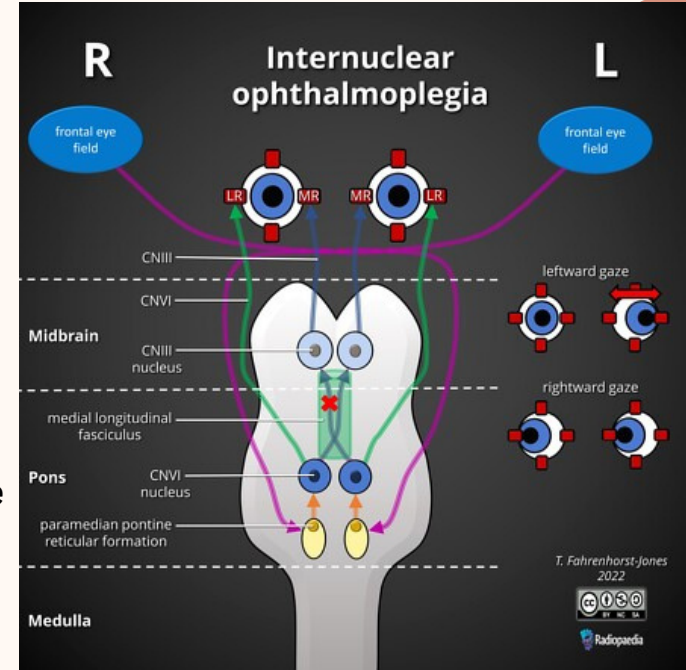


- **Optic neuritis (ON)** is a common initial presenting symptom of MS. (This fact reminds us that the optic nerve is actually an extension of the CNS rather than a peripheral nerve.) ON is characterized by a mildly painful loss of visual acuity in one eye. The visual loss may range from mild blurriness with a loss of color discrimination to a severe episode with complete blindness. Pulling or tugging pain is most prominent when the eye moves.
- Most patients have retrobulbar ON and the optic disc appears normal in the acute stage. In severe cases, however, the optic disc may be swollen, with indistinct margins (papilledema).
- A past history of ON is suggested by the presence of red desaturation (subtle loss of color appreciation), optic disc pallor or atrophy, and a relative afferent pupillary defect (RAPD)
- A relative afferent pupillary defect (RAPD), also known as a Marcus Gunn pupil, is a medical sign observed during the swinging-flashlight test whereupon the patient's pupils excessively dilate when a bright light is swung from the unaffected eye to the affected eye.



- **Internuclear ophthalmoplegia (INO)** is a characteristic finding in MS. INO results from dysfunction of the medial longitudinal fasciculus and leads to an inability to adduct one eye when looking toward the opposite side, with associated nystagmus of the abducting eye. The adduction of both eyes when observing a near target (convergence) is preserved.

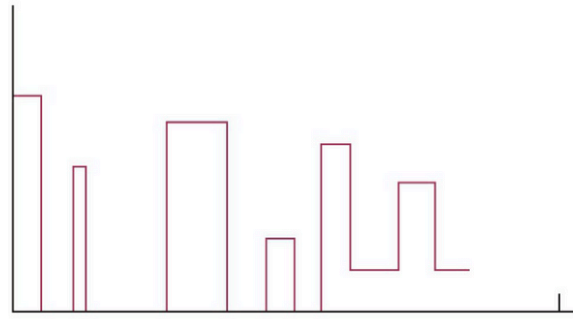
- **Transverse myelitis** is inflammatory demyelination in the spinal cord. Most commonly, this affects particular tracts at the level of the lesion in a patchy way, rather than producing complete involvement of the spinal cord.
- The other clinical features characteristic of MS include **Lhermitte's sign**, a tingling, electric sensation down the spine when the patient flexes the neck, and **Uhthoff's phenomenon**, a worsening of symptoms and signs in the heat.



Clinical course

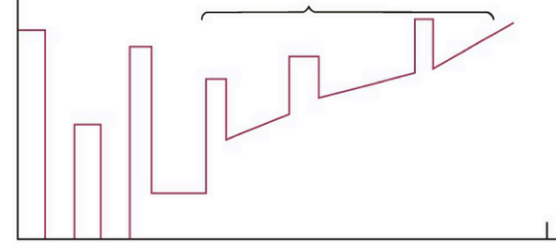
Most MS patients begin with a relapsing-remitting course, in which there are discrete episodes of neurologic dysfunction (relapses or “flares”) that resolve after several weeks or months. Unfortunately, such a course usually evolves into one in which recovery from each relapse is incomplete and baseline function deteriorates (secondary progressive). Rarely, patients may have a relentlessly progressive course from the onset, either with superimposed relapses (progressive-relapsing) or without (primary progressive).

A Relapsing-remitting multiple sclerosis

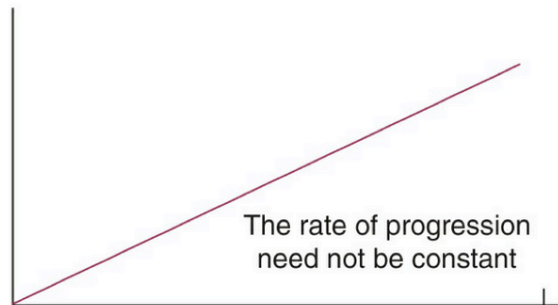


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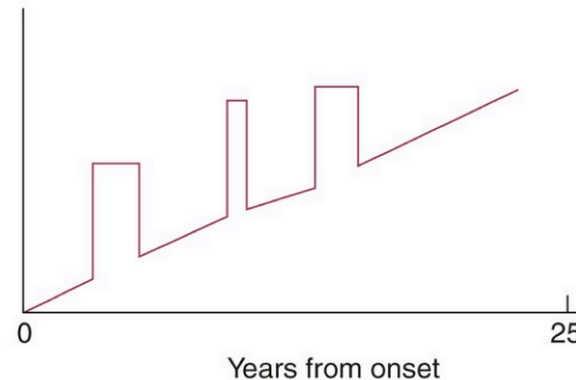
Secondary progressive phase (with or without further superimposed relapses)



C Primary progressive multiple sclerosis

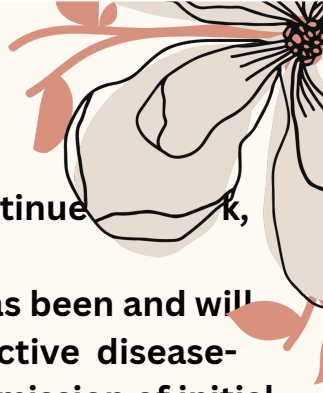


D Progressive relapsing multiple sclerosis



Prognosis

To put the prognosis in broad terms, about 60% of MS patients lead lives of minimal disability and continue to work, about 20% require a walking aid but will remain ambulatory, and about 20% have severe disability, typically becoming wheelchair-bound. There has been and will likely continue to be a trend toward better prognoses in the future because of a greater use of effective disease-modifying agents. Features predicting a good prognosis include young age at onset, female sex, rapid remission of initial symptoms, mild relapses that leave little or no residual deficits, and a presentation with sensory symptoms or ON rather than motor symptoms.



Diagnostic evaluation

Shahd abdalla





- The diagnosis of MS begins with a thorough history and examination
- Patients often present with what appears to be a single episode of neurologic dysfunction, but upon further questioning recall earlier episodes of seemingly unrelated neurologic symptoms that may in fact represent prior lesions.



- History and Physical exam :**
 - **Past neurological history that suggest typical MS features.**
 - **Evidence of old optic nerve or other neurological lesions.**

MRI

- On MRI ,new MS lesions appear as discrete T2 hyperintense areas in white matter of the brain or spinal cord.
- FLAIR also show these lesions particularly well.
- Acute lesions may not be evident on T1-weighted images but may enhance with gadolinium.
- chronic lesions may become T1-hypointense , with black hole appearance.
- MS lesions are ovoid in shape and have predilection for particular areas, including the peri ventricular white matter,juxtacortical regions, corpus callosum and cerebellar peduncles.
- sagittal images may demonstrate foci of demyelination spreading perpendicularly from the corpus callosum,termed **Dawson's fingers**.

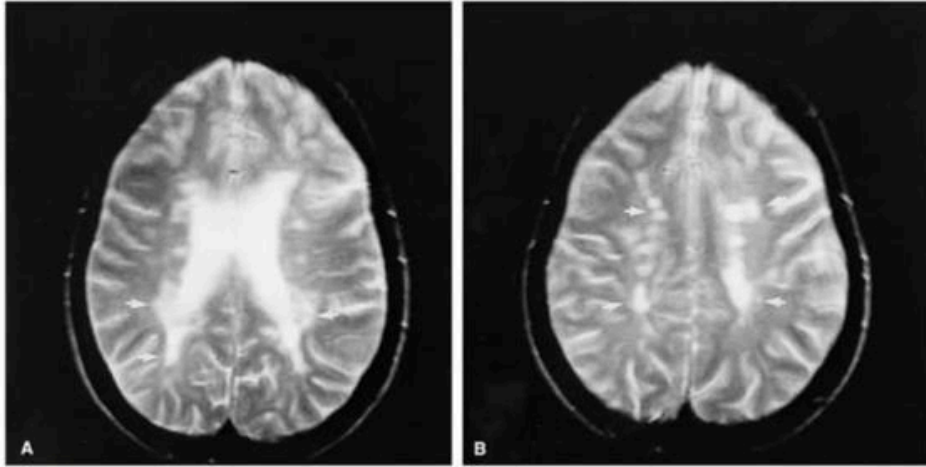
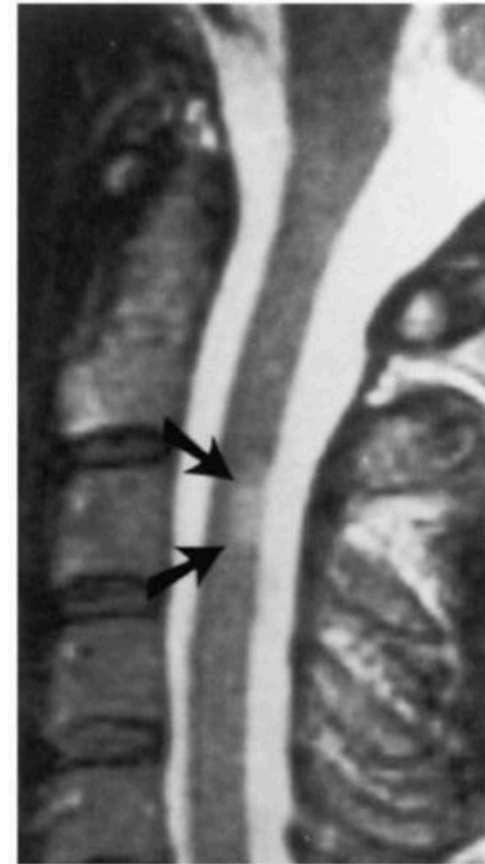
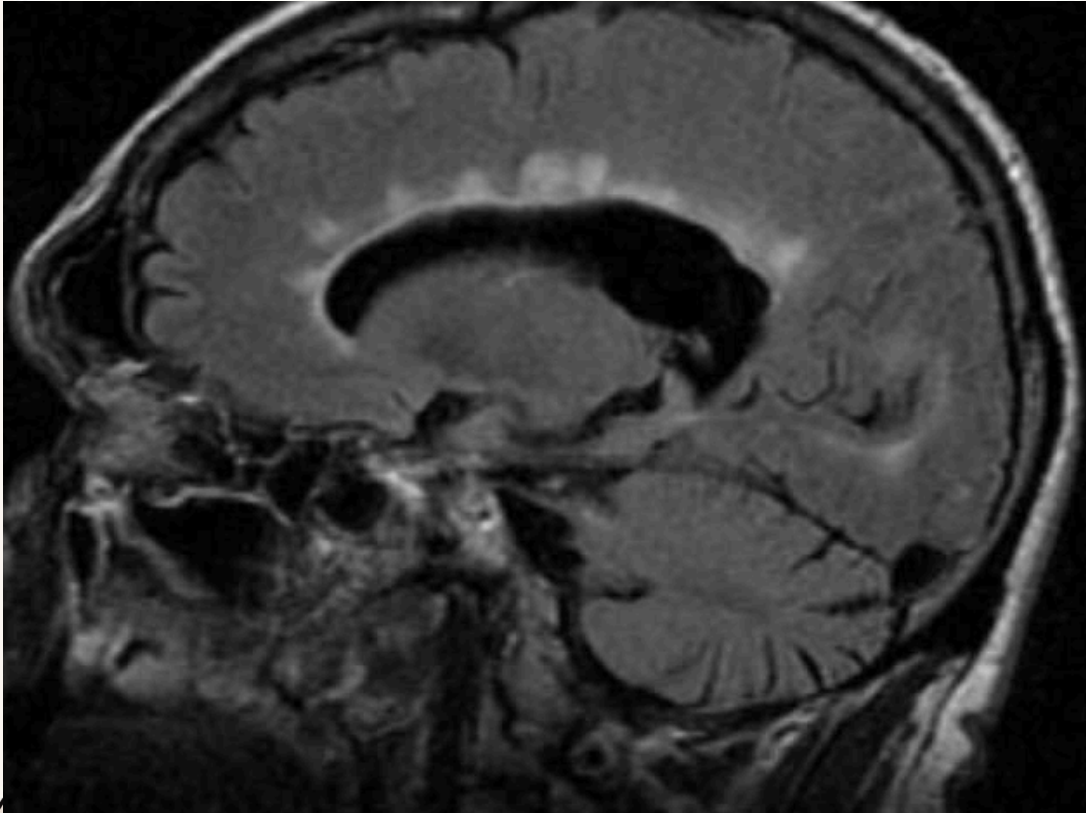
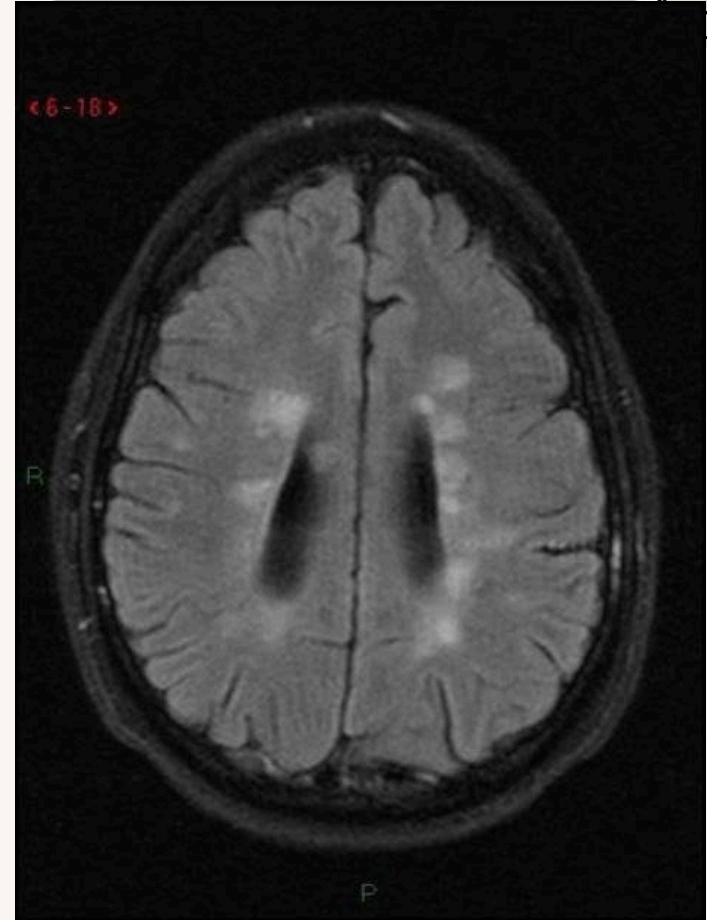


FIGURE 20-2. T2-weighted MRI demonstrating multiple periventricular hyperdensities in both **A** and **B** (arrows), consistent with a diagnosis of MS. [MRI, magnetic resonance imaging; MS, multiple sclerosis.] (Reproduced with permission from Daffner RH. *Clinical Radiology: The Essentials*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.)





Dawson's Fingers



Lumbar puncture

-Lumbar punctures are very safe, but are often uncomfortable and can cause a headache that occasionally lasts for up to a few days.



CSF findings in MS patient

- The characteristic CSF finding in MS is elevation in the concentration of oligoclonal bands (OCBs).
- OCBs reflect intrathecal production of IgG antibodies by plasma cell clones.
- CSF studies during an acute relapse may show a moderate pleocytosis and elevated protein.



Important note

- The diagnosis of MS begins with a thorough history and examination, particularly directed toward identifying the past episodes of neurologic dysfunction.
- MRI is the best imaging modality to detect both new and old MS lesions.
- The characteristic CSF abnormality is the presence of OCBs.
- Visual evoked potentials may provide evidence of old ON.

Treatment of multiple sclerosis

Areen bani mustafa





Treatment of MS falls into three categories:

Acute therapies for relapses

Chronic therapies that treat the underlying disease

Symptomatic therapies



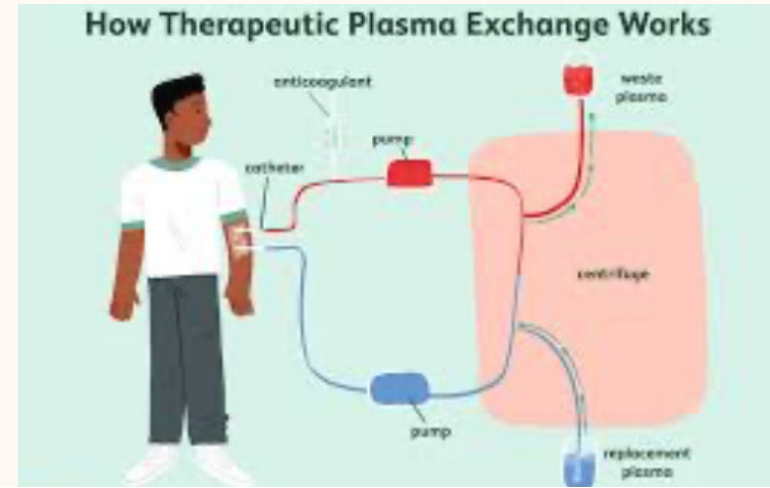
Management of an acute relapse :

In case with acute relapses of MS are most commonly treated with corticosteroids, a course of intravenous methylprednisolone for 3 to 5 days, with or without an oral prednisone. Although the effect of steroids on the long term outcome is unclear, steroids do shorten the duration of acute relapses.



plasmapheresis

,or plasma exchange This is a procedure that involves removing and replacing a person's plasma – the liquid portion of blood. It eliminates antibodies and other proteins that could be contributing to MS-related inflammation. This therapy also is sometimes considered when patients fail to adequately respond to corticosteroid therapy.



Treatments to modify disease progression:

MS treatments that can alter the course of the disease are referred to as disease-modifying therapies (DMTs). Most of these therapies seek to suppress or modulate the immune system and reduce inflammation, slowing disease progression and helping prevent relapses.



Disease modifying agent:

These include beta-1a interferon and beta-1b interferon, which are injectible medications that have been shown to decrease the rate of relapses, the burden of lesion seen on MRI and the rate of accumulated disability.

Both are currently used in patient with relapsing-remitting MS and in some patient with secondary progressive disease.

side effect of these drugs can include flu-like symptoms, depression and injection-site reactions.

It is important to check a complete blood count and liver function test routinely; interferons may cause leukopenia and reversible transaminitis.

TABLE 20-2. Immune-Modulating Agents Used in the Treatment of Multiple Sclerosis

Drug	Administration	Side Effects
Interferon beta-1a (Avonex)	30 µg IM every week	Flu-like symptoms, anemia, depression, development of neutralizing antibodies
Interferon beta-1b (Betaseron)	250 µg SC every other day	Injection-site reactions, flu-like symptoms, depression, hematologic/liver abnormalities, development of neutralizing antibodies
Interferon beta-1b (Rebif)	44 µg SC three times a week	Flu-like symptoms, anemia, depression, development of neutralizing antibodies
Glatiramer acetate (Copaxone)	20 mg SC daily	Injection-site reactions, injection-related chest pain and shortness of breath
Natalizumab (Tysabri)	300 mg IV every 4 wk	Progressive multifocal leukoencephalopathy, hepatotoxicity, hypersensitivity reaction
Fingolimod (Gilenya)	0.5 mg PO every day	Bradycardia, leukopenia, macular edema
Dimethyl fumarate (Tecfidera)	240 mg PO bid	Flushing, lymphopenia, gastrointestinal intolerance
Teriflunomide (Aubagio)	7–14 mg qD	Hair loss, transaminitis, and gastrointestinal symptoms, teratogenicity
Alemtuzumab (Lemtrada)	First course: 60 mg IV over 5 d. Second course, 12 mo later: 36 mg IV over 3 d	Infusion reactions, autoimmune disease, increased cancer risk
Ocrelizumab (Ocrevus)	600 mg IV every 6 mo	Infusion reactions, upper respiratory tract infection, cannot be administered

1.Natalizumab:

is a monoclonal antibody against alpha-4-integrin that prevents lymphocytes and monocytes from crossing the BBB.it is administered as a series of monthly infusion.it is associated with a small risk of developing progressive multifocal leukoencephalopathy.

patient with low JC virus antibody are at a lower risk for PML,So these antibody should be measure prior starting the treatment.

in addition,natalizumab should not be used in combination with other immunomodulatory agent used to treat MS.



2.Teriflunomide:

It is highly teratogenic and should be used cautiously in women of childbearing age.

3.Alemtuzumab:

Is a CD52 monoclonal antibody indicated for patient with relapsing form of MS who have failed two other MS medications.



Symptomatic drug treatments for complications of MS

Raneem salman



- **Fatigue (a common with of relapses) – amantadine, selegiline or the anti-narcolepsy drug modafinil.**

- **Cerebellar tremor – if mild may respond to clonazepam and gabapentin.**

- **Depression – tricyclic and related drugs in low dosage ; selective serotonin reuptake inhibitors, e.g. sertraline.**

- **Spasticity, flexor spasms – baclofen (oral), dantrolene, , diazepam, though these drugs may increase weakness and cause drowsiness. Other approaches include botulinum toxin injections into affected muscles**



● Bladder disturbances – anticholinergic drugs, e.g. oxybutynin ; patients may also need to be taught intermittent self-catheterization . Urinary infection should be treated immediately.

●Erectile impotence – phosphodiesterase type 5 inhibitors, e.g. sildenafil; intracavernosal papaverine or prostaglandins, the latter may also be given by urethral application.

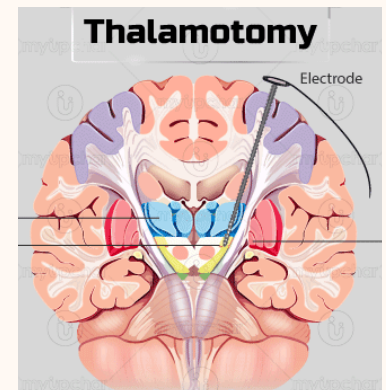
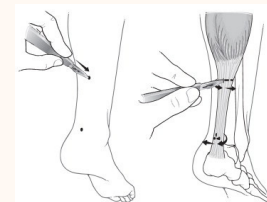
●Pain, paroxysmal symptoms including seizures – carbamazepine, gabapentin. The role of cannabis in the management of pain and spasticity in MS is controversial.



Severely affected patients need general measures appropriate to paraplegic patients, in particular careful nursing attention to pressure areas. Worsening urinary difficulty may need urethral or suprapubic catheterization.

Other surgical measures in extreme case include:

- **tenotomy for spasticity and flexor spasms,**
- **dorsal column stimulation for pain,**
- **stereotactic thalamotomy for severe cerebellar ataxia.**





Thank you

Done by group c1

Raghad alawi

Maya swaiss

Sara alzaghatet

Shahd Al-Shabatat

Areen bani mustafa

Raneem salman



References:

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