Multiple Sclerosis

Objectives:

- Not given.

Team Members: Jawaher Abanumy, Mohammed Habib, Shoag Alahmari, Saud alshenaifi.

Team Leader: Fahad Alzahrani

Revised By: Yara Aldigi and Basel almeflh

Resources: 435 team + Davidson + kumar + Recall questions step up to medicine.

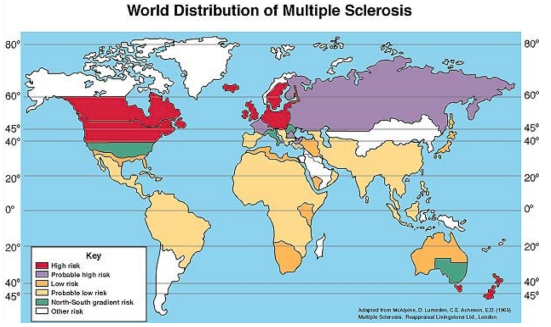
- Editing file
- Feedback

Introduction

- **What is myelin?** it's a lipid dense layer that wraps around the axon of some nerve cells.
- **What is the function of myelin?** Insulates the axon and allows continuous propagation of the electrical impulse.
- **What are schwann (neurilemma) cells?** They are cells in the *peripheral nervous system (PNS)* that produce the myelin sheath around neuronal axons.
- **What are oligodendrocytes[1]?** They are cells in the *central nervous system (CNS)* that produce the myelin sheath around neuronal axons.

★ Definition: Osmosis Video (11:15)

- Multiple sclerosis is an autoimmune inflammatory disease of the CNS (so everything outside the brain & the spinal cord isn't involved) white matter characterized by a relapsing or progressive course (this is an old terminology of multiple sclerosis, because autoimmunity just plays a role in the disease, but it is not the hallmark of etiology) , where we have clinical evidence of dissemination in space, dissemination in time. And provided that there is no other alternative neurologic disease explaining the presentation. This will be explained further on.
- **Multiple sclerosis a clinical diagnosis!** No lab test alone will be able to **confirm** the diagnosis.
- One of the most common central nervous disease (CNS) diseases.



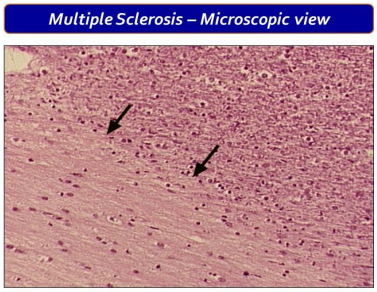
★ Epidemiology:

- It is the second most common cause of neurological disability in young adults.
- Female to male ratio 2.3:1
- Mean Age of onset 28-31 year (range:15-45 year).
  - The peak age is 30 and we can see it before 20 and after 50.
- Ethnicity: white population (northern Europe). Some report incidence of 40 per 100,000 in SA.

Pathophysiology

Check this diagram out after reading what we've wrote (highly recommended).

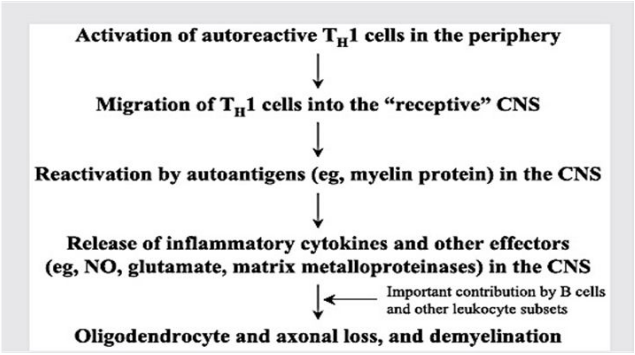
- The pathologic **hallmark** of multiple sclerosis is **multiple focal areas of myelin loss (patches of demyelination) within the CNS (plaques or lesions)**.
- It has to be multiple lesions, if you have a patient with only one lesion then it isn't MS (except in rare cases).
- **Selective demyelination of the white matter of CNS**. (tends to spare grey matter and PNS) (in fact it also affects the grey matter but in a smaller percentage compared to the white matter).



A high power photomicrograph of the MS plaque showing the pallor of the plaque almost devoid of myelin. There is a decrease in oligodendroglial nuclei and an increase of astrocyte nuclei characteristic of an older MS plaque.

[1] Remember; **satellite** oligodendrocytes are **NOT** involved in myelination.

- MS is confined to the CNS (it never affects the peripheral nervous system), causing demyelination of ascending and descending tracts:
  - Myelin is relatively rich in lipid (70-80%), it also contains proteins that play a role in it's compaction.
  - Many of the proteins found in CNS differ from those in peripheral nervous system (PNS).
  - It is possible that mutations in the structure of the myelin protein can occur and be responsible for some inherited forms of demyelination. It is also possible that autoantigens develop in MS.
- The disease usually affect:
  - The Brain (cerebral hemisphere).
  - Brainstem.
  - Cerebellum.
  - Spinal Cord.
- Generally starting in the optic nerve, spinal cord or cerebellum.
- **Classical location** of plaques are at the **periventricular** regions of the brain, **optic nerves**, and the **subpial** regions of the spinal cord.
- Several basic processes drive the formation of these plaques: **Inflammation → myelin breakdown → astrogliosis and oligodendrocyte injury → neurodegeneration and axonal loss → remyelination**
- **Blood brain barrier breach results in invasion of brain and spinal cord by some infection allowing leukocytes to enter normally immunologically protected CNS.**
  - ➔ The myelin sheaths degenerate and the myelin is removed by the microglial cells. Astrocytes proliferate leading to formation of the gliotic scar. As demyelination occurs the **conduction** of the nerve impulses in the axons is impeded.
  - ➔ The inflammation and demyelination with loss of myelin sheath results in breakdown of the insulation around the axons and the velocity of AP is reduced and ultimately becomes blocked. (the severity of the symptoms depends on the severity of the inflammation and degeneration).



- Demyelination is accompanied by variable gliosis and inflammation with **relative axonal preservation**. Relative axonal preservation helps us to differentiate MS lesions from necrosis (e.g. trauma). In necrosis; axons and myelin are depleted to the same extent!
- Demyelination with relative axonal sparing is important for the diagnosis of demyelinating lesions, (whereas an infarct is more likely if axons and myelin in lesions are depleted to the same extent)
- Yet despite relative axonal sparing, axonal injury still does occur. This is evident by:
  - the presence of axonal swellings (irregularly swollen axons with a beaded appearance),
  - accumulation of amyloid precursor protein (a marker of focal accumulations of proteins that are typically moved along axons by fast axonal transport), and
  - mild axonal loss.مؤخرًا وجدوا إن حتى الاكسونز تتأثر إلى حد ما
- **Acute** *axonal* injury occurring in early MS lesions contribute to the relapse related disability observed predominantly during the disease's inflammatory phase. While **chronic** *axonal* injury will cause axonal loss or sclerosis resulting in **permanent** deficits.يقولك أن في الحقيقة تأثر الاكسونز هو السبب وراء الأعراض الشديدة اللي تؤدي إلى العجز أثناء الهجمة. أيضًا هو السبب وراء الأعراض التي لا تزول بعد زوال الهجمة
- In the long term; accumulating myelin loss reduces the efficiency of impulse propagation or cause complete conduction block leading to **permanent** impairment of CNS functions.

- T cells comprise approximately 10% of the inflammatory cells populating active demyelinating lesions in MS:
  - Lymphocytic inflammatory infiltrate : mainly CD8-positive cytotoxic T lymphocyte
  - EAE model can be adoptively transferred by injecting an animal with myelin-specific CD4+ T cells.
- The extent of axonal damage in *active* lesions correlates **significantly** with the **number of lymphocytes and activated microglia.**
- Extensive remyelination is apparent by the presence of newly formed myelin sheaths and oligodendrocyte precursor cells. This process is frequently encountered within active plaques of early multiple sclerosis.
- Why don't we classify it as an autoimmune disease? **Direct proof of an autoimmune response is lacking, no specific autoantibody or autoreactive T cells.**

★ Course:

- The course of MS is chronic with exacerbations and remissions. Due to the widespread involvement of the different tracts at different levels of neuroaxis, the signs and symptoms are multiple.
- Remissions in MS is by the remodeling of the demyelinated axonal plasma membrane so that it acquires a higher than normal number of sodium channels which permit AP conduction despite myelin loss.
- In progressive form of disease without remissions patients have substantial damage to the axons as well as myelin suggesting MS has axonal pathology.

Risk Factors

- The cause of disease is **unknown**; may interplay between a viral infection, host immune response and hereditary alone or in combination may play a role.
- Breach in blood brain barrier in genetically predisposing individual would be responsible for MS.
- MS **isn't** a genetic or inherited disease, But it can be **familial (only a small percentage are familial).**

Genetic Factors	
Age	It is a disease of young adults. Most cases occur between the age of 20 and 40 years.
Gender	Females are affected more than males.
Family history	Risk of familial recurrence in MS is 15%, with highest risk in first-degree relatives. Concordance rate in dizygotic twins: 3-5%, and in monozygotic twins: 20%.
Race	The prevalence of MS is low near the equator and increases in the temperate zones of both hemispheres. Rates of MS are higher farther from the equator.
Polymorphism	Polymorphism of HLA proteins is estimated to account for 17%-60% of the genetic susceptibility to MS. Single nucleotide polymorphisms in the chains of **IL2 and IL7 receptors**. MS susceptibility alleles on chromosome 6, a region that contains the HLA gene complex.

Environmental Factors	
Infections	- History of infectious **mononucleosis** (**EBV**[2]) is associated with a higher susceptibility for MS. - Antibodies to EBV were higher in people who developed MS than in control samples. - HHV-6[3]: antibodies were three times higher in women with progressive MS.
Vitamin D	- Sunlight may be protective (ultraviolet radiation or vitamin D). - Sun exposure & serum vitamin D are inversely related to risk/prevalence of MS. - Vitamin D levels are inversely related to MS disease activity. - If you have a patient with MS and a vitamin D deficiency, you need to replace it. - especially more dangerous in childhood
Smoking	- A higher risk of MS in ever-smokers than in never-smokers. - Smoking can also be a risk factor for increased disease progression.
Obesity	- Obesity in adolescence/early adulthood is associated with an increased risk for MS. - Leptin increases the proliferation of auto-aggressive cells responsible for myelin damage.

Signs and Symptoms[4] picture

- Symptoms of MS patients are variant, as they may have symptoms related to the (motor system, cerebellum, spinal cord).

Deficit	Symptom
Transient sensory deficit	- **Most common initial presentation.** - Decreased sensation or paresthesia in upper or lower limbs. - **Lhermitte phenomenon (electric like sensation induced by neck flexion)** - **Uhthoff phenomenon. (heat sensitivity/intolerance)**
Fatigue	- One of the most common complaints.
Motor symptoms	- Muscle weakness, numbness, tingling, or unsteadiness of the limbs is the most common sign. - Spastic paralysis may be present. - Difficulty with walking - Caused by pyramidal tract involvement. (upper motor neuron)
Visual disturbances	- Vision loss 2nd common, double vision, blurry vision.

[2] Epstein-Barr Virus
[3] Human herpesvirus 6
[4] Polysymptomatic onset (correlates with worse outcome), Symptoms may persist for several weeks or may resolve spontaneously over a few days.

	- Optic neuritis most of the cases they recover
	  ○ **Subacute onset (1-10) days.**
	  ○ **Mononuclear / unilateral** visual loss
	  ○ **Pain on movement of eyes.** painful vision loss:MS as most common DDX
	  ○ Central scotoma (black spot in center of vision).
	  ○ Afferent pupillary defect. or Marcus Gunn pupil, it's a sign that indicates optic neuropathy regardless of the cause.
	  ○ Median visual acuity 20/60
	- Internuclear ophthalmoplegia—strongly suggests the diagnosis
	  ○ A lesion in the **medial longitudinal fasciculus** results in **ipsilateral medial rectus palsy** on attempted lateral gaze (adduction defect) and horizontal nystagmus of abducting eye (**contralateral** to side of lesion).
	  ○ Diplopia can occur.

Cerebellar involvement	- Can cause ataxia, intention tremor, dysarthria. - Incoordination and problems with balance and control - Vertigo and dizziness
Autonomic involvement	- May present as impotence, constipation &/or urinary incontinence. - Bowel and bladder dysfunction, usually spinal. - Urinary urgency or retention, - Sexual dysfunction
Cerebral involvement	- Cognitive dysfunction - Cortical demyelination → late onset dementia. - May occur in advanced illness and manifests as memory loss, personality change, and emotional lability; anxiety, mood swings and depression are common.
Neuropathic pain	- A frustrating but common complaint that manifests as hyperesthesias (excessive physical sensitivity) and trigeminal neuralgia.
Dysphagia	- **Speech and swallowing problems** - The prevalence of dysphagia increases with increasing disability putting the patient at risk for **aspiration pneumonia**, **and the congested cough is an indication that aspiration has already occurred.** Very serious complication. - Dysphagia reflects the involvement of cortico-bulbar, cerebellar or brainstem regions.

Types

The disease has several forms which change the course of the management and are therefore important to recognize. Most patients will have a months-long to year-long disease free after their first exacerbation.

Type	Course
Relapsing remitting (RR-MS) 	**The Most common → 85% of MS patients are diagnosed with RR-MS at onset.** **Clinical exacerbation** of neurological symptoms (**relapse** نكسة) followed by complete or incomplete remission during which the person fully or partially recovers from the acquired neurological deficits.
Primary progressive (PP-MS) 	The **Third** most common type. Symptoms are progressive from the onset of disease with the early onset of disability. Gradual progression of the disease from onset, no overlapping relapse or remission. 10% of cases are diagnosed at onset. **later on will discuss the :حطوا له كرايتيريا لحاله relapses & remissions ولأنه مافيه general criteria of MS diagnosis** **Primary Progressive MS** 1 year of disability progression (retrospectively or prospectively determined) independent of clinical relapse. **Plus two of the following criteria:** • One or more T2-hyperintense lesions characteristic of multiple sclerosis in **one** or more of the following brain regions: periventricular, cortical or juxtacortical, or infratentorial. • Two or more T2-hyperintense lesions in the spinal cord. • Presence of CSF-specific oligoclonal bands.
Relapsing progressive (RP-MS) 	Rarest form of MS: 5% of people with RPMS. The **second** most common type. Initially presents as PP-MS, but, during the course of the disease; individuals develop true neurologic deficit exacerbations. In other words, steady progression of clinical neurological damage with **superimposed relapses and remissions**.
Secondary progressive (SP-MS) 	Progression becomes more aggressive so that a consistent worsening of function occurs. Steady progression of neurological damage with or without superimposed relapses and minor remissions. Patients will have experienced a period of RR-MS before which may have lasted 2-40 years. Relapses and remissions fade over time. **50% of RR-MS will develop eventually SP-MS.**

★ **We have two types of multiple sclerosis according to the criteria of diagnosis:**
- Clinical definite Multiple sclerosis (in which the (patient has typical signs and symptoms).
- Probable multiple sclerosis (when the signs, symptoms and the investigations support the diagnosis but not definitely, so we have to wait and see the course of the disease).

★ Relapse correlates with inflammation and progression correlates with degeneration.

★ **Clinically Isolated Syndrome :** (when the patient comes with an attack of ONE system only, and the MRI shows multiple lesions).

اللفظ الطبي اللي نقوله لمّا يجي شخص لأول مرة مع أعراض تتناسب مع التصلب اللويحي لكن لسى ما بعد تأكدنا

A monophasic clinical episode with patient-reported symptoms and objective findings developing acutely or subacutely, with a duration of **at least 24 h**, with or without recovery, and in the absence of fever or infection; similar to a typical multiple sclerosis relapse (attack and exacerbation) but in a patient not known to have multiple sclerosis.

- Can be monofocal (reflecting pathology in a single location) or multifocal; the specific manifestations of a clinically isolated syndrome depend on the anatomical location (or locations) of the pathology.
- Typical presentations include unilateral optic neuritis, focal supratentorial syndrome, focal brainstem or cerebellar syndrome, or partial myelopathy.

Atypical for CIS (لو المريض جا فيها نفكر بشيء غير التصلب اللويحي)			
Bilateral optic neuritis red flag	Complete ophthalmoplegia	Complete myelopathy	Encephalopathy
Headache	Alteration of consciousness	Meningismus	Isolated fatigue

★ **Clinical Attack (Relapse or Exacerbation):**
- A **clinical attack** is considered if the symptoms are present for **at least 24 hours** and is preceded by more than 30 days of clinical stability, like loss of vision . There has to be no better explanation (other than MS) for the attack and we must rule out **psuedorelapse** (worsening of already existence neurological disability of MS by infection).
- Patient-reported symptoms or objectively observed signs.
- Typical of CNS acute inflammatory demyelinating lesion.
- No fever or infection.

★ **Triggers that exacerbate MS:**
- Since raising the temperature shortens the duration of action potential(AP) one of the early signs is improvement on cooling and worsening by hot bath.
- Infections or trauma may acutely worsen the disease.
- Pregnancy especially the 2 to 3 months following birth.

Diagnosis

★ History & Exam

MS is mainly a clinical diagnosis. Suspect MS if the patient is for example a **young adult** with **relapsing and remitting neurologic signs** and symptoms that are difficult to explain.

Try to exclude other differentials. **MS mimickers:**

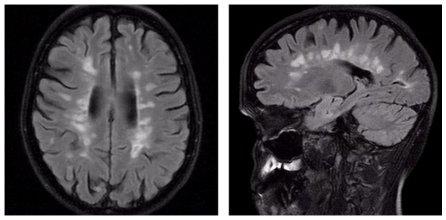
- Sarcoidosis.
- Behcet Disease.
- B12 Deficiency.
- Lyme/brucellosis.

★ MRI

- MRI **with contrast** of the brain is the most accurate test to diagnose MS, reaching a sensitivity of 85 to 95% in symptomatic persons.
- Increased T2 and decreased T1 intensity represent the increased water content of demyelinated plaques in the cerebrum and spine.
- Enhancement of lesions with gadolinuim indicates active MS lesions that may enhance for up to 2 to 6 weeks after an exacerbation.
- Small vessel disease vs MS.
- However, the number of lesions on the MRI is not necessarily proportional to disease severity or speed of the progression. MRI is abnormal in 90% of MS patients.

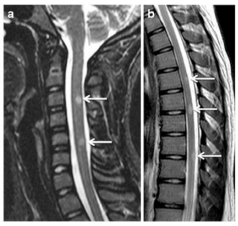
MRI T2

Perivenricular (Dawson finger)

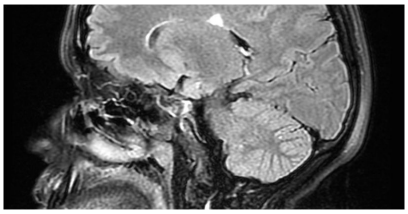


Radiographic feature depicting demyelinating plaques through the **corpus callosum**, arranged at right angles along medullary veins (callososeptal location). They are a relatively specific sign for MS which presents as T2 hyperintensities.
Plaques are usually found in the corpus callosum and it is a very sensitive finding.

Spinal lesion



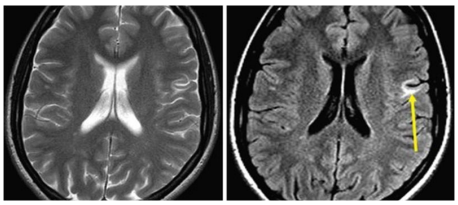
Corpus callosum lesion



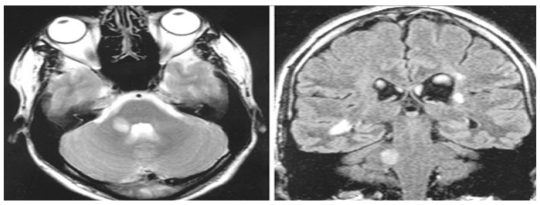
Characteristics of MS lesions on MRI:

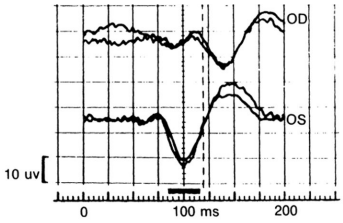
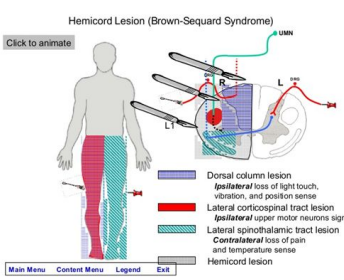
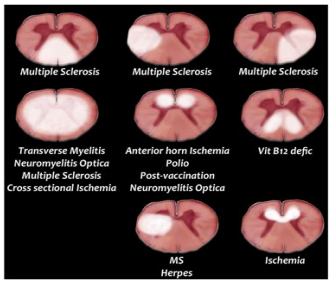
- Large ≥ 3 mm
- Ovoid
- Oriented perpendicular to ventricles
- Enhancing:
- Open ring enhancement
- Multifocal homogenous

Juxtacortical lesion

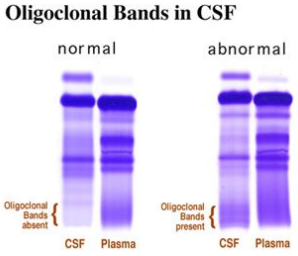


Infratentorial lesion



Delayed Visual Evoked Potentials response	Myelitis in multiple sclerosis partial myelitis
 (VEP) A visual evoked potential is an evoked potential caused by a visual stimulus, such as an alternating checkerboard pattern on a computer screen.These responses usually originate from the occipital cortex, the area of the brain involved in receiving and interpreting visual signals. Evoked response potentials detect slow or abnormal conduction in response to visual, auditory or somatosensory stimuli. The limitations of this test for the diagnosis of MS is that many other neurologic diseases can give an abnormal result.	  **Transverse myelitis** • A general term that indicates inflammation of the spinal cord. • Could be caused by MS, NMO, infections, connective tissue diseases. • Spinal cord related motor, sensory &/or autonomic dysfunction. • Sensory level. • Unilateral or bilateral.

★ Lumbar puncture and CSF analysis (should be done before the MRI).

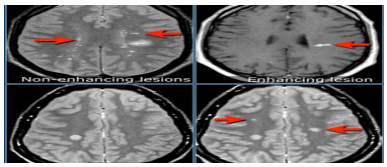


- CSF analysis usually reveals:
  - A mild pleocytosis (lymphocytes).
  - And a total protein that is mildly elevated. A protein level exceeding 100 mg/dl is unusual and should be considered as evidence against the diagnosis of MS.
- The second thing we do is looking for **Oligoclonal bands by electrophoresis** (we look for bands in the IgG):
  - An elevated IgG index is found in 70 to 90% of patients with MS. The finding is non specific.
  - In MS, oligoclonal bands will be positive in the CSF only, and it will be negative in the blood.

★ Mc Donald's MS diagnostic criteria:

- The McDonald criteria, first developed in 2001 and revised in 2005,and in 2010.
- Final revisions of McDonald criteria was in 2017.
- Diagnosis of **"Clinically definite MS"** needs demonstration of **dissemination of space and time.**

Dissemination in **space** (by MRI brain)	Dissemination in **time** (MRI)

• are disseminated throughout the CNS but have a predilection for optic nerves, subpial spinal cord, brainstem, cerebellum, and juxtacortical and periventricular white matter regions
• demyelinated lesions are also commonly found in the cortical gray matter of MS patients
• T2 lesion in ≥ 1 of the following locations:
  ○ Cortical /Juxtacortical (white matter just beneath the cortex)
  ○ Infratentorial
  ○ periventricular(most commonly affected)
  ○ Spinal cord
	• simultaneous presence of gadolinium-enhancing (brand new lesion) and non-enhancing lesions at any time
	• new T2-hyperintense or gadolinium-enhancing lesion on follow-up MRI, with reference to a baseline scan, irrespective of the timing of the baseline MRI
	 

The 2017 McDonald criteria for diagnosis of multiple sclerosis in patients with an attack at onset		
Attacks	**Number of lesions with objective clinical evidence**	**Additional data needed for a diagnosis of multiple sclerosis**
≥2 clinical attacks	≥2	none
≥2 clinical attacks	1 (as well as clear-cut historical evidence of a previous attack involving a lesion in a distinct anatomical location)	none
≥2 clinical attacks	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by **MRI**
1 clinical attack	≥2	Dissemination in time demonstrated by an additional clinical attack or by **MRI** OR demonstration of **CSF-specific oligoclonal bands.**
1 clinical attack	1	Dissemination in space demonstrated by an additional clinical attack implicating a different CNS site or by **MRI.** **AND** Dissemination in time demonstrated by an additional clinical attack or by **MRI** OR demonstration of **CSF-specific oligoclonal bands.**

الزبدة: لازم يكون فيه هستوري لهجمتين + two white matter lesion سواء اكتشفناها بالفيزكل اقزام أو بالـMRIأو هستوري لهجمتين +(one white matter lesion on MRI + abnormal CSF (oligocolonal bands

Management

- The treatment of MS can be divided into disease modifying therapy, treatment of symptomatic relief during an acute exacerbation.
- Disease modifying therapies are contraindicated in pregnancy.

Disease Modifying Therapy	
Relapsing remitting disease	• There are three disease modifying agents(IFN-β1a, IFN-β1b and glatiramer acetate) that have been shown to reduce the number of clinical exacerbations and the number of MRI lesions. • These medications delay disability onset. • Glatiramer is also a known copolymer I.
Primary progressive disease	• There was is no treatment for Primary progressive disease until last year, when they found **ocrelizumab** which can be helpful.
Secondary progressive disease	• IFN-β1b and mitoxantrone have been shown to reduce the number of exacerbations, MRI activity, and delay onset of disability. • In patients who receive mitoxantrone, dose-related cardiotoxicity is a concern; mitoxantrone should only be given to patients with normal EF. • Mitoxantrone is not first line agent due to cardiotoxicity.
In patients with relapsing remitting disease or secondary progressive disease who can not tolerate treatment with IFN-β1b, IFN-β1a or glatiramer acetate treatment can be considered with **methotrexate, mitoxantrone, cyclophosphamide, IV immunoglobulin or azathioprine**. ACTH is no longer used Mitoxantrone, cyclophosphamide and natalizumab are <u>not used for a first episode</u> of disease.	
Symptomatic Management	
Spasticity	baclofen is the most effective medication.
Pain (secondary to trigerminal neuralgia and dysthesias)	Responds well to carbamazepine, gabapentin, phenytoin, pregabalin or tricyclic antidepressants. Tizanidine and diazipam are useful forvnocturnal spasticity but are limited in their use for daytimevsymptoms because they cause intense somnolence.
Fatigue	amantadine or fluoxetine.
Bladder hyperactivity	oxybutynin
Urinary retention	bethanecol.
Erectile dysfunction	sildenafil acetate.

Management of Acute Attack
• Acute attacks (relapses) of MS are typically treated with glucocorticoids (IV methylprednisolone for 5 days). steroids don't alter the disease process it just fasten the recovery. If there are two pt. one received steroids and the other didn't after a year they are the same • The length and intensity of an acute exacerbation is shortened by the administration of gluco-corticoids. An exacerbation is treated with 3 days of intense IV steroids followed by a course of oral medication tapered over 4 weeks. • Indications for treatment of a relapse include functionally disabling symptoms with objective evidence of neurologic impairment. • In patients with severe disease who are unresponsive to steroid therapy, plasma exchange can be used as an alternative treatment.

	Route	Mechanism of action	Side effect
Interferon	S/C, IM	Cytokine modulator, decrease expression of matrix metalloproteinases	Injection site reaction
Natalizumab one of the best medication	IV	Alpha-4 integrin monoclonal antibody	Progressive multifocal leukoencephalopathy PML
Fingolimod	Oral	Inhibit egress of lymphocyte from lymph nodes	Cardiac conduction abnormalities
Dimethyl fumarate	Oral	Anti-oxidative, anti-inflammatory	
Teriflunamide	Oral	Inhibit lymphocyte proliferation (anti-metabolite)	
Alemtuzumab	IV	Anti-CD52 (B, T and NK cells)	Autoimmunity
Ocrelizumab	IV	B cell depletion	
Caldribine	Oral	Inhibit lymphocyte proliferation (anti-metabolite)	

Other side effects of MS medications:

- Increase liver enzyme
- Lymphopenia

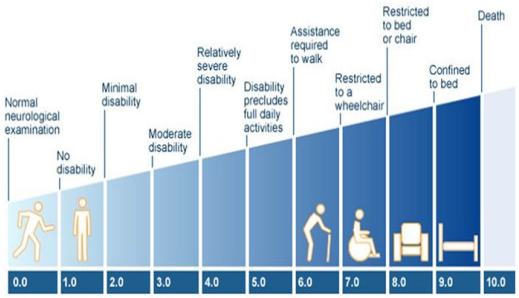
Prognosis

- Fifty percent of patients will require a cane 28 years after disease onset.
- Twenty five percent will require a wheelchair 44 years after disease onset.

Features of a better prognosis in MS include:

1. Onset below 25 years of age
2. Optic neuritis or sensory before cerebellar symptoms on first presentation
3. A long interval (over 1 year) between relapses
4. Fewer lesions on MRI
5. Full recovery from relapses
6. Being a female (MS is more severe in males)

Progressive MS carries a worse prognosis than RR-MS.



Other Demyelinating Diseases

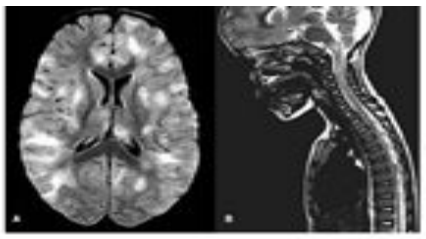
- Damage of the myelin.
- Inherited or acquired.
- PNS & CNS.

Central Nervous System Remember MS belonged here ;-)	**Peripheral Nervous System**
Acute Disseminated Encephalomyelitis **(ADEM)**	Acute Inflammatory Demyelinating Polyneuropathy (Guillain Barre syndrome - **GBS**)
Neuromyelitis Optica **(NMO)**	Chronic Inflammatory Demyelinating Polyneuropathy **(CIDP)**
Progressive multifocal leukoencephalopathy	

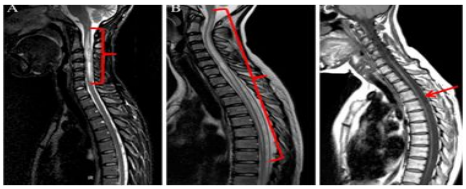
★ Acute Disseminated Encephalomyelitis (ADEM)

Postinfectious encephalomyelitis or ADEM

- Monophasic with preceding event common (70%)
- Most common in children
- Altered LOC and seizures common
- **MRI**: bilateral lesions, grey matter involvement
- Commonly after viral infection in susceptible individual

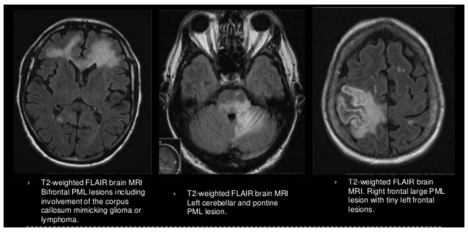


★ Neuromyelitis optica



- Also known as Devic's disease.
- This disease is similar to MS but it doesn't respond to the same treatment.
- They usually have optic neuritis and spinal cord lesions.
- The target here is known which is Aquaporin channel compared to unknown target in MS
- Relapsing (55%), monophasic (35%)
- **MRI**: cord lesions, chiasmal signal changes
- **CSF**: generally >100 wbc, high protein, rare OCB

★ Progressive multifocal leukoencephalopathy



- Rare but serious demyelinating disease of the brain, often resulting in severe disability or death, caused by lytic infection of oligodendrocytes by the JC polyomavirus (JCV).
  Important to know that it comes with **Natalizumab!**

★ Another differential for MS is Behcet's disease:

- This disease affects multiple systems.
- Usually comes with the triad of : uveitis, orogenital ulcers and arthritis.
- The disease also cause neurological manifestations and if you do an MRI you will see similar findings to MS, but the history is the only thing that will help you (orogenital ulcers for example).

Summary

Definition	Multiple sclerosis is an autoimmune inflammatory disease of the CNS white matter characterized by a relapsing or progressive course, where we have clinical evidence of dissemination in space, dissemination in time. And provided that there is no other alternative neurologic disease explaining the presentation.	
Clinical presentation	Symptoms: (3 most common presentation): 1)Transient sensory loss (most common presentation). 2)Motor symptoms: weakness, numbness (2nd most common presentation). 3)Visual disturbance (3rd most common presentation).	Signs: 1) Lhermitte phenomenon 2) Uhthoff phenomenon
Types	There are 4 types of MS, the most common type is the relapse and remission type in which the patient experience the symptoms after that a complete or partial remission and the cycle goes on	
Diagnosis	1- History and physical examination: Look for a young adult with relapsing and remitting neurological signs that are difficult to explain. 2- LP Elevated IgG. 3- MRI Most accurate test.	

Questions

1. What is the pathological landmark for multiple sclerosis?

A. Multiple focal areas of myelin loss within the CNS.
B. Multiple focal areas of myelin loss within the PNS.
C. Single focal area of myelin loss within the PNS.
D. Single focal area of myelin loss within the CNS.

2. Which one of the following is imaging modality of choice for multiple sclerosis?

A. CT scan with contrast
B. CT scan without contrast
C. X-ray
D. MRI with contrast

3. Which one of the following describes the Primary progressive type of multiple sclerosis?

A. Gradual progression of the disease from onset, no overlapping relapse or remission.
B. Steady progression of clinical neurological damage with superimposed relapses and remissions.
C. Steady progression of neurological damage with or without superimposed relapses and minor remissions.
D. Clinical exacerbation of neurological symptoms followed by complete or incomplete remission.

4. Which one of the following describes the mechanism of action of Interferon in the treatment of multiple sclerosis?

A. Alpha-4 integrin monoclonal antibody.
B. Cytokine modulator, decrease expression of matrix metalloproteinases
C. Inhibit lymphocyte proliferation (anti-metabolite)
D. Anti-CD52

5. which one of the following is the CSF analysis finding expected to be in a patient with multiple sclerosis?

A. RBCs with PMNs
B. Lymphocytes with low proteins.
C. Lymphocytes with mildly elevated proteins.
D. Elevated proteins and glucose.

6. Which drug of the following causes PML?

A. Fingolimod
B. Interferon
C. Natalizumab
D. Alemtuzumab

7. How many attacks and lesions are required to diagnose MS clinically ?

A. Tow attacks & one lesion
B. Two attacks & two lesions
C. One attack & two lesion
D. Three attacks & two lesions

8.Which one of the following isn't considered an Atypical Sx of MS?

A. Meningismus
B. Headache
C. Encephalopathy
D. Optic neuritis

9. A 42-year-old woman presents with ataxia. Gadolinium-enhanced MRI reveals multiple subcortical white matter lesions as well as enhancing lesions in the cerebellum and spinal cord. She is diagnosed with MS. Two months later she develops optic neuritis. What feature is associated with a milder disease course?

A. Her age of 42
B. Her initial presentation of ataxia
C. Her female gender
D. Her MRI scan appearance

10. Which one of following is the most common initial Sx to appear in MS ?

A. Fatigue
B. Transient sensory deficit
C. Ataxia
D. Dysphagia

Answers:

1. A 2. D 3. B 4. B 5. C 6. C 7. B 8. D 9. C 10. B