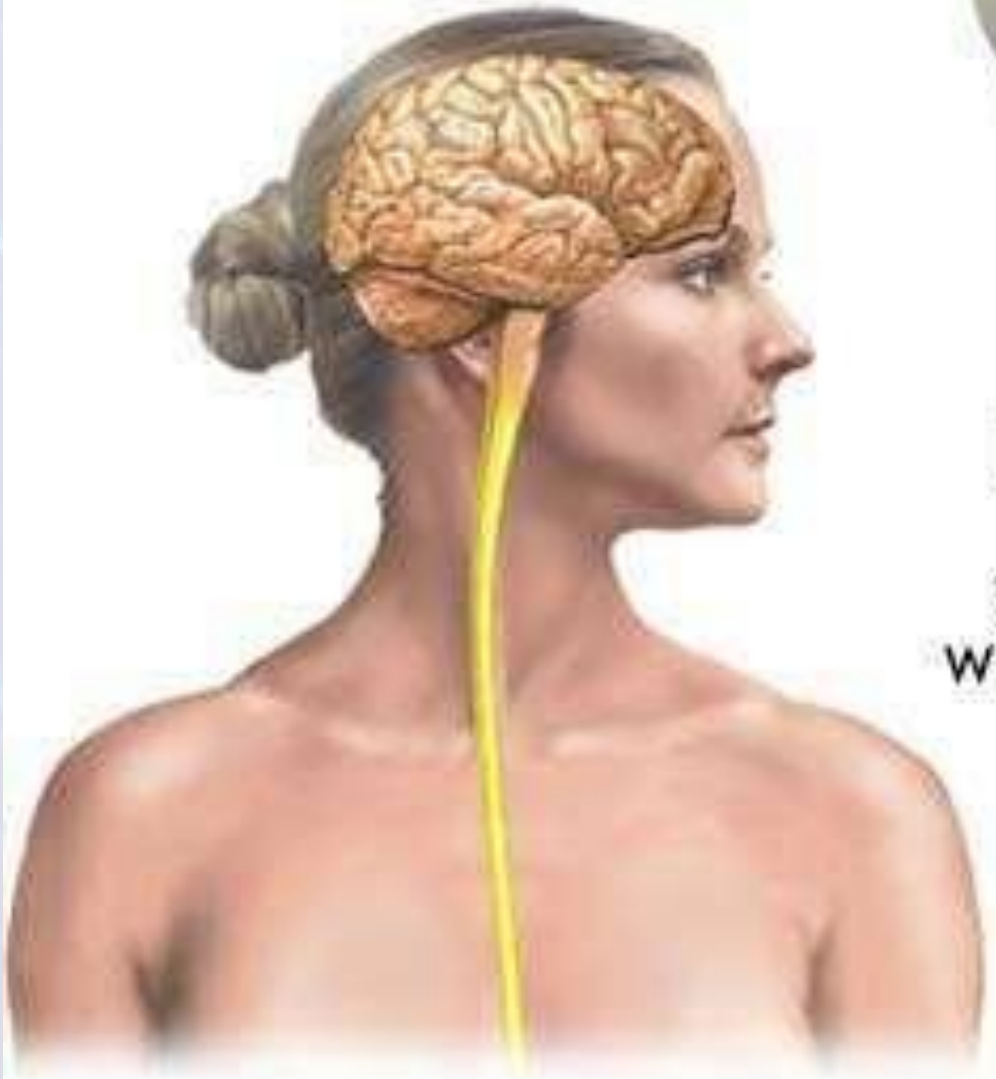
Multiple sclerosis (MS)

Central nervous system
(brain and spinal cord)



In multiple sclerosis the myelin sheath, which is a single cell whose membrane wraps around the axon, is destroyed with inflammation and scarring

Definition

•Multiple sclerosis is an autoimmune inflammatory disease Characterized by appearance of patches of demyelination in the white matter of the CNS, generally starting in the optic nerve, spinal cord or cerebellum by a relapsing or progressive course.

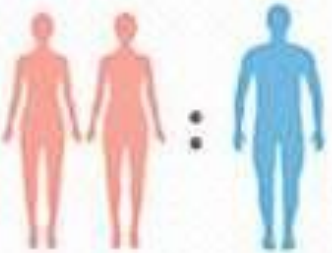
Etiology

- It is a disease of young adults. Most cases occur between the age of 20 and 40 years.
- Females are affected more than males.
- 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.
- Break in blood brain barrier in genetically predisposing individual would be responsible for MS.

YOU CAN GET MS AT **ANY AGE,**

BUT MOST PEOPLE ARE DIAGNOSED BETWEEN THE AGES OF

The ratio of **women** with MS to **men** with MS is 2 : 1.



If you have a **parent or sibling** with MS, you have a **1 - 3% chance** of developing it.

An **identical twin** with MS raises your risk to **30%.**

Pathophysiology

- MS is confined to the CNS, causing demyelination of ascending and descending tracts.
- Blood brain barrier breach results in invasion of brain and spinal cord by some infection allowing leukocytes to enter normally immunologically protected CNS.
- 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.

Clinical manifestations

- Weakness, numbness, tingling or unsteadiness of the limbs is the most common sign.
- Ataxia due to involvement of the tracts of cerebellum may occur, spastic paralysis may also be present.
- Urinary urgency or retention, blurry vision and double vision are all common initial manifestations of the disease.
- Symptoms may persist for several weeks or may resolve spontaneously over a few days.

The most common early symptoms of MS are:

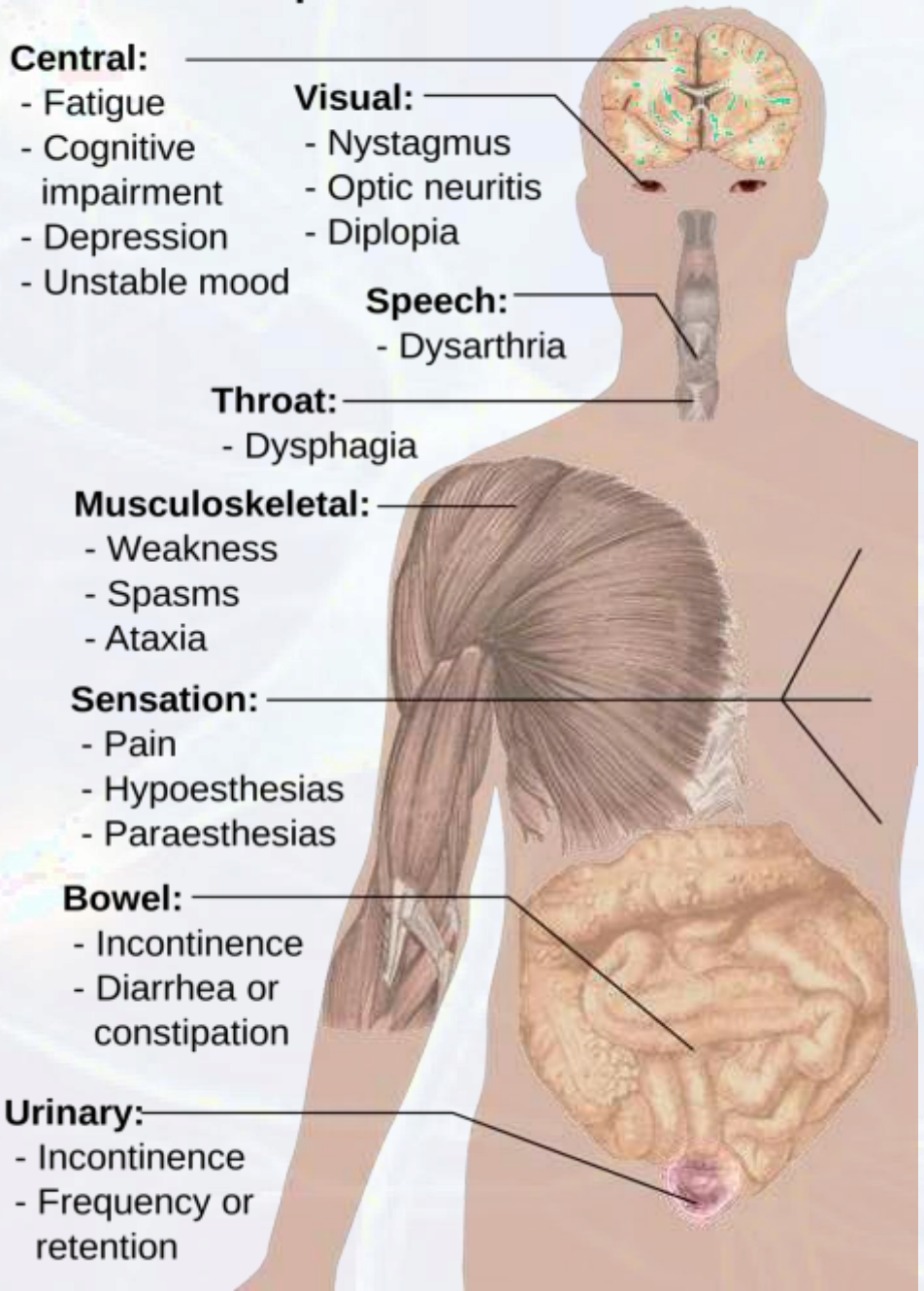
- Fatigue
- Vision problems
- Tingling and numbness
- Vertigo and dizziness
- Muscle weakness and spasms
- Problems with balance and coordination

Other, less common, symptoms include:

- Speech and swallowing problems
- Cognitive dysfunction
- Difficulty with walking
- Bladder and bowel dysfunction
- Sexual dysfunction
- Mood swings, depression

Main symptoms of

Multiple sclerosis



Types of MS

- 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.
- ***Relapsing remitting disease:*** progression is characterized by relapses of active disease with incomplete recovery during periods of remission.
- ***Secondary progressive disease:*** progression becomes more aggressive so that a consistent worsening of function occurs.
- ***Primary progressive disease:*** symptoms are progressive from the onset of disease with the early onset of disability.

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.

Investigations

- History collection
- Physical & neurological examination
- CT scan
- CSF analysis
- Blood test
- MRI of the brain is the most accurate test to diagnose MS, reaching a sensitivity of 85 to 95% in symptomatic persons.

Characteristic differences between small-vessel disease (SVD) and multiple sclerosis (MS)

Involvement	SVD	MS
Corpus callosum	Rare	Common
U-fibers	Rare	Often
Infratentorial	Late in the course of the disease	Common
	Brainstem: involvement of central transverse fibers	Brainstem: involvement of pial and ventricular surface and intra-axial trigeminal segment
Temporal lobe	Never*	Often
Gadolinium enhancement	Exceptional (subacute infarction)	Common
Black holes	Rare	Typical
Lacunae	Typical	Never
Spinal cord	Never	Common

*With the exception of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL).

Treatment

- The treatment of MS can be divided into disease modifying therapy, treatment of symptomatic relief during an acute exacerbation.

- In 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.

- In 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.

- No approved disease modifying therapy exists at this time of progressive disease.

- Mitoxantrone, cyclophosphamide and natalizumab are not used for a first episode of disease. Natalizumab is associated with progressive multifocal leukoencephalopathy(PML).

- 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.

- In patients with severe disease who are unresponsive to steroid therapy, plasma exchange can be used as an alternative treatment.

- For patients with spasticity, baclofen is the most effective medication. Tizanidine and diazipam are useful for nocturnal spasticity but are limited in their use for daytime symptoms because they cause intense somnolence.

- Pain secondary to trigerminal neuralgia and dysthesias responds well to carbamazepine, gabapentin, phenytoin, pregabalin or tricyclic antidepressants.

- Bladder hyperactivity is treated with oxybutynin, whereas urinary retention is treated with bethanecol. Fatigue may be treated with amantadine or fluoxetine.

- Erectile dysfunction can be treated with sildenafil acetate.

- Disease modifying therapies are contraindicated in pregnancy.

Thank you