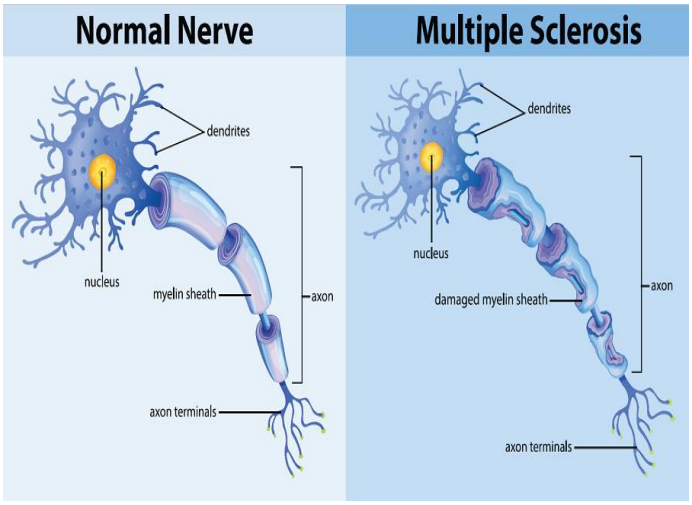
Multiple sclerosis

Introduction:

Definition and overview:

Multiple sclerosis (MS) is a potentially disabling disease of the brain and the spinal cord. In MS, the immune system attacks the protective sheath that covers the nerve fibers and causes communication issues between the brain and the rest of the body. The disease can cause permanent damage or deterioration of the nerve fibers.



Historical context:

Possibly the earliest documentation of Multiple sclerosis is the case of Lidwina. In 1395, age 16 years Lidwina had been diagnosed with Multiple sclerosis as some communicators considered her evidence for a diagnosis of MS. The features of Multiple sclerosis were first well defined by Jean-Martin Charcot, a neurologist at the Hôpital de Salpétrière in 1868.

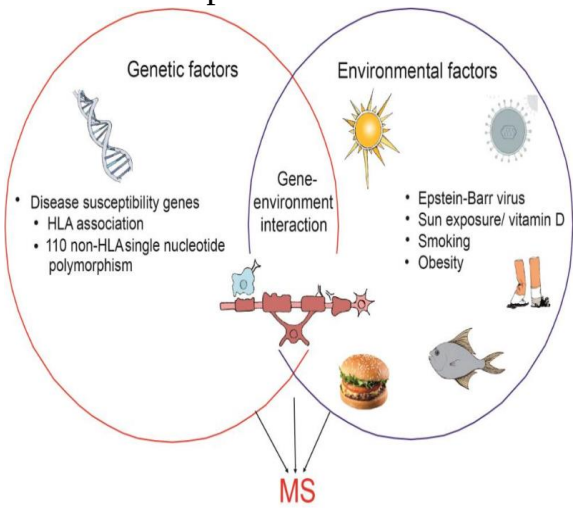
Epidemiology:

The risk of developing MS in the general population is approximately 0.1%. The risk for a child with one parent who has MS is approximately 2%. The risk for a child with two parents who have MS is approximately 12.2%. The risk for a dizygotic twin and other siblings is approximately 5%.

Etiology:

Causes and Risk factors:

The cause of multiple sclerosis is unknown until now. It's considered an immune-mediated disease in which the immune system attacks its tissues. In multiple sclerosis, the immune system destroys the fatty substance that coats and protects the nerve fibers and the spinal cord (myelin). Myelin is like the insulation material on electrical wires. When the protective myelin is damaged the messages that travel along the nerve fibers can be slowed or blocked.



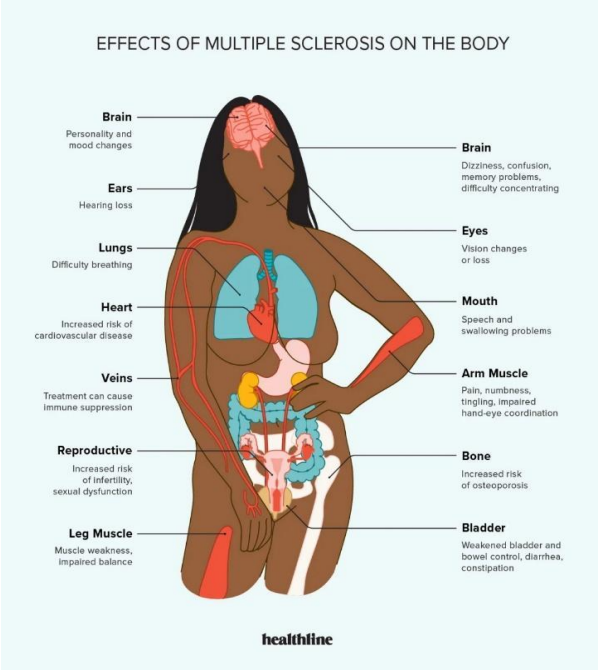
These factors may increase your risk of developing multiple sclerosis:

- Age: MS can occur at any age, but it usually happens between 20 and 40 years.
- Sex: women are more than 2 to 3 times as likely as men to have MS
- Family History: if one of your family has had MS you are at higher risk.
- Smoking and obesity.

Genetic and Environmental influences:

It is not clear why some people have MS and others do not. A combination of genetic and environmental factors appears to be responsible.

- Your genes: A gene on chromosome 6p21 is associated with multiple sclerosis.
- Climate: MS is likely to happen in temperate climate countries like Canada, the northern United States, New Zealand, southeastern Australia, and Europe
- Vitamin D: vitamin D is a protector against multiple sclerosis so lower levels of it and low exposure to sunlight can cause a higher risk of MS.



Clinical features:

Signs and symptoms:

The signs and symptoms of multiple sclerosis can differ from person to person depending on the location of the affected nerve fibers.

Common symptoms:

- Tingling.
- Numbness or weakness in one or more limbs that typically occurs on one side of your body at a time.
- Lack of coordination.
- Blurry vision.
- electric-shock sensations that occur with certain neck movements, especially bending the neck forward (Lhermitte sign).
- Unsteady gait or inability to walk.
- Partial or complete loss of vision, usually in one eye at a time, often with pain during eye movement.
- Problems with sexual, bowel, and bladder function.

Disease Stages and Progression:

Multiple sclerosis has 4 stages. Not all cases will go through the full course

1. Initial (diagnosis)
2. Early (little disability)
3. Later (moderate disability)
4. Advanced (severe disability)

Complications:

People with multiple sclerosis may also develop:

- Muscle stiffness or spasms.
- Severe weakness or paralysis, typically in the legs.
- Problems with bladder, bowel, or sexual function.
- Cognitive problems, like forgetfulness or word-finding difficulties.
- Mood problems, such as depression, anxiety, or mood swings.
- Seizures, though very rare.

Diagnosis:

Diagnostic criteria:

The basis of MS diagnosis is to find damage in at least two separate areas of the central nervous system. Find evidence that the damage happened at different points in time. MS is diagnosed based on clinical findings and supporting evidence from ancillary tests.

Diagnostic Tests and Procedures:

MRI, which can reveal areas of MS (lesions) on your brain, cervical and thoracic spinal cord. You may receive an intravenous injection of a contrast material to highlight lesions that indicate your disease is in an active phase.

Differential Diagnosis:

The main differential diagnoses for MS include, but are not limited to, the following:

Spinal cord neoplasms (eg, astrocytomas, ependymomas), Acute disseminated encephalomyelitis (ADEM), Schilder disease, Baló concentric sclerosis, Sarcoidosis.

Pathophysiology:

Mechanism of Disease Development:

Localized areas of demyelination (plaques) occur, with the destruction of oligodendroglia, perivascular inflammation, and chemical changes in lipid and protein constituents of myelin in and around the plaques. Axonal damage is common, and neuronal cell bodies may die or be damaged.

Fibrous gliosis develops in plaques disseminated throughout the central nervous system (CNS), primarily in white matter, particularly in the lateral and posterior columns (especially in the cervical regions), optic nerves, and periventricular areas. Tracts in the midbrain, pons, and cerebellum are also affected. Gray matter in the cerebrum and spinal cord can be affected but much less.

Cellular and Molecular Changes:

Cytokines are tiny signaling molecules released by immune cells that are essential in immune response regulation. Interferon-gamma (IFN-), tumor necrosis factor-alpha (TNF-α), and interleukin-17 (IL-17) cytokines are increased in MS and contribute to the inflammatory response in the CNS.

Impact on Body Systems:

In MS the protective coat on the nerve fibers is damaged and may be destroyed depending on the place of the damage on the nerve. MS can also affect vision, sensation, coordination, movement, and bladder or bowel control.

Management and Treatment:

Medical and Surgical Treatments:

There is no cure for multiple sclerosis. Treatment focuses on controlling the symptoms, speeding the recovery from attacks, reducing new radiographic and clinical relapses, and slowing the progression of the disease.

Surgery is a viable treatment option for people with MS. Surgical procedures include deep brain stimulation, rhizotomy, and a baclofen pump. Opening blood flow is not recommended

Pharmacological Therapies:

Some drugs used to treat depression, including selective serotonin reuptake inhibitors, may be recommended, Dalfampridine (Ampyra) may help to slightly increase walking speed in some people, but it has side effects, Muscle relaxants such as baclofen (Lioresal, Gablofen), tizanidine (Zanaflex) and cyclobenzaprine may help. Onabotulinumtoxin A treatment is another option for those with spasticity.

Corticosteroids, such as oral prednisone and intravenous methylprednisolone, are prescribed to reduce nerve inflammation. Side effects may include insomnia, increased blood pressure, increased blood glucose levels, mood swings, and fluid retention. Plasma exchange (plasmapheresis)

Lifestyle and Dietary Modifications:

To help relieve the signs and symptoms of MS, try to:

Get some rest, exercise, cool down, eat a balanced diet, and relieve stress

Rehabilitation and Supportive Care:

The MS rehabilitation team includes several specialty areas, including physical therapy, occupational therapy, speech-language pathology, neuropsychology, driver rehabilitation, vocational rehabilitation, and vision rehabilitation

Prevention and Control:

Primary, Secondary, and Tertiary Prevention Strategies:

These lifestyle adjustments are likely to help protect relatives of people with MS who do not show signs of MS:

- Get regular exposure to sunlight.
- Take daily vitamin D supplements (adjusted for the weight of the child)
- Stop smoking.
- Eat a low-saturated fat diet.
- Take omega-3 fatty acid supplements

Public Health Interventions:

Common non-pharmacological interventions were used for fatigue and sleep, mental and emotional health, cognition, physical health, and chronic pain. Several non-pharmacological interventions positively improved the overall quality of life for people with multiple sclerosis. These interventions included exercise, cognitive behavior therapy, and cognitive rehabilitation.

Prognosis:

Disease Outcomes and Survival Rates:

The average longevity for all MS patients is hard to estimate as it varies from one patient to another. The average life span from 25 years to 35 years after the diagnosis of MS is often stated. The frequency of death by suicide was found to be 7.5 times higher among patients with MS compared to the general population. It was found that in suicidal patients, the suicide rate did not correlate with disability.

Factors Influencing Prognosis:

The following factors are associated with a poor prognosis in patients with multiple sclerosis:

male sex, older age at onset, motor or cerebellar signs at onset, short interval between first and second attacks, high relapse rate in the early years of the disease, incomplete remission after first few relapses, early disability, high lesion load on MRI scan

Quality of Life:

It is estimated that for all MS patients, the chance of walking unaided in 15 years following disease onset is 50%. 1/2 of the patients will need assistance in walking or will be wheelchair-bound; another 1/2 of the patients will be able to ambulate unaided. Depressive symptoms significantly affect the QOL of MS patients. About half of the people with MS will experience some problems like cognition, memory, attention span, planning, decision-making, understanding, or concentration. These symptoms can be mild and not noticed by other people or they can be serious and affect employment and social interactions.

Current Research and Future Directions:

Recent Advances and Discoveries:

UCSF's Sergio Baranzini, PhD, leads an international team that discovered some MS patients experience faster MS progression is tied to a particular genetic variant inherited from both parents.

Ublituximab-xiiy (Briumvi) was approved by the FDA in 2022. It is used to treat relapsing-remitting and active secondary-progressive forms of MS. Ublituximab-xiiy is given in a vein and stops certain immune system cells from making antibodies that may damage the brain and spinal cord in MS.

Ongoing Clinical Trials:

Phase 2/3, a multi-arm multi-stage “OCTOPUS” trial in primary and secondary progressive MS is testing several therapies including metformin (a diabetes drug) and alpha lipoic acid (an antioxidant) can slow the rate of brain atrophy and progression. It is expected to be completed in 2028.

Future Research Needs:

Research is ongoing to develop new and better disease-modifying therapies (DMTs) for this disease of the central nervous system. DMTs can reduce the frequency and severity of MS attacks. DMTs also can slow the progression of disability and the loss of brain volume mass

Case Studies:

Example Cases:

A 29-year-old graphic designer, Betty Jackson first noticed her symptoms in the summer of 2019 while she was riding a bike along the lake with her husband. She was having trouble reading signage and clumsiness using her arms while steering her bike. Upon completing her route, she felt excessively fatigued. These symptoms persisted for a few days, eventually affecting her productivity at work, and prompting a visit to her family physician. MRI findings revealed demyelination and plaques in the corpus callosum; the physician classified her event as a “clinically isolated syndrome” of MS. Approximately 10 months later, Betty’s symptoms resurfaced: she experienced the same fatigue, vision disturbances, and arm issues. A secondary MRI revealed more distal demyelination & plaques, prompting a diagnosis of relapsing-remitting MS (RRMS). The physician referred her to a private physiotherapy clinic in the community for motor control training and gait safety education.