

# Multiple sclerosis (MS)

Multiple sclerosis (MS) is a chronic [neurological disorder](#) that affects the central nervous system, which includes the brain, spinal cord, and optic nerves. MS is an [autoimmune disease](#) in which the body's own immune system attacks the myelin sheath, a protective covering that surrounds nerve fibers, leading to [inflammation](#), demyelination (loss of myelin), and damage to the [nerve fibers](#) themselves. This damage can result in a wide range of [symptoms](#), including [muscle weakness](#), [spasticity](#), [numbness](#), [tingling](#), [balance](#) problems, and [cognitive impairment](#). MS is a progressive disease, meaning that symptoms typically worsen over time, and there is currently no known cure.

Data support the pathological role of MS [IgG](#) antibodies and corroborate their connection to complement activation and axonal damage, suggesting that [apoptosis](#) may be a mechanism of [neurodegeneration](#) in MS <sup>1)</sup>.

## Key concepts

- an idiopathic demyelinating disease of the CNS producing exacerbating and remitting symptoms disseminated in space and time
- classic clinical findings: [optic neuritis](#), [paresthesias](#), INO and bladder symptoms
- diagnostic criteria (McDonald criteria) use clinical and/or lab results (MRI, CSF...) to stratify patients as: MS, probable MS, or not MS
- MRI: multiple usually enhancing lesions involving optic nerves & white matter of brain (especially periventricular white matter), cerebellum, and spinal cord

## General information

An idiopathic demyelinating disease (thus affecting only white matter) of the cerebrum, optic nerves, and spinal cord (especially the corticospinal tracts and the posterior columns). It does not affect peripheral myelin. Pathologically produces multiple plaques of various ages in diffuse locations in the CNS, especially in the periventricular white matter. Lesions initially evoke an inflammatory response with monocytes and lymphocytic perivascular cuffing, but with age settle down to glial scars.

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Multiple sclerosis (MS) is characterized by widespread immunomodulatory [demyelination](#) of the CNS resulting in nerve cell dysfunction.

The [spinal cord](#) is frequently affected by [atrophy](#) and/or lesions in [multiple sclerosis](#).

[Abdominal reflexes](#) disappear in 70-80 %.

Cell replacement therapy is an effective strategy to repair the myelin in MS.

# Epidemiology

[Multiple sclerosis epidemiology.](#)

## Classification

[Multiple sclerosis classification.](#)

## Pathogenesis

The [pathogenesis](#) of [Multiple sclerosis](#) involves an [autoimmune](#) response against [myelin](#), the fatty substance that covers [nerve fibers](#) in the CNS. [Immune cells](#), including [T cells](#) and [B cells](#), infiltrate the CNS and attack myelin, leading to [inflammation](#) and [demyelination](#). This process disrupts the normal conduction of nerve impulses and can result in a range of neurological symptoms, including motor and sensory deficits, vision problems, and cognitive impairment.

The breakdown of the blood-brain barrier (BBB) is a key step in the pathogenesis of MS. The BBB is a specialized structure that separates the CNS from the rest of the body and regulates the entry of immune cells and other substances into the CNS. In MS, the BBB becomes permeable to immune cells, allowing them to enter the CNS and initiate an inflammatory response.

The exact trigger for the immune response in MS is not clear, but it is believed to involve a combination of genetic susceptibility and environmental factors, such as viral infections, smoking, and vitamin D deficiency. Genetic studies have identified several genes that are associated with an increased risk of developing MS, including genes involved in immune regulation and myelin synthesis.

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Contribution of [MAPK14](#) in the pathogenesis of [multiple sclerosis](#) (MS) has been proposed by several studies. Long non-coding RNA (lncRNA) have been suggested to be functionally linked with Mitogen-activated protein kinase 14 (MAPK14).

Expression levels of MAPK14 and its associated [lncRNAs](#) were measured in the circulation of MS patients compared with control subjects.

Expression levels of [NORAD](#) and [RAD51-AS1](#) were higher in total patients compared with controls (Expression ratio (95% CI) = 1.4 (1.04-1.89), P value = 0.015 and Expression ratio (95% CI) = 1.91 (1.43-2.6), P value = 0.0001, respectively). Conversely, [ZNRD1](#)ASP was under-expressed in cases compared with controls (Expression ratio (95% CI) = 0.61 (0.41-0.8), P value = 0.0005). In spite of the observed abnormal expression levels of these lncRNAs in the circulation of MS patients, their expressions were not correlated with Expanded Disability Status Scale (EDSS) score, disease duration or age at disease onset.

To sum up, the current investigation shows dysregulation of MAPK14-related lncRNAs in MS patients <sup>2)</sup>.

# Clinical

[Multiple sclerosis clinical features](#)

## Complications

[Multiple sclerosis related trigeminal neuralgia.](#)

### Brain Tumor

The diagnosis of a [brain tumor](#) in a MS patient is challenging, due to several reasons that include the fact that new neurological symptoms in MS patients are easily attributed to a relapse of the disease and the MRI lesions, even if suspicious, are commonly diagnosed or confused as a tumefactive form of MS. Also the cooccurrence of two neurological diseases in the same patient is uncommon, particularly oligodendroglioma and MS <sup>3) 4) 5) 6)</sup>.

### Cervical stenosis

[Cervical spinal stenosis](#) (CS) and multiple sclerosis (MS) are two common conditions with distinctive pathophysiology but overlapping clinical manifestations. The uncertainty involved in attributing worsening symptoms to CS in patients with MS due to extremely high prevalence of asymptomatic radiological CS makes treatment decisions challenging. A retrospective review was performed analyzing the medical records of all patients with confirmed diagnosis of MS who had coexistent CS and underwent surgery for [cervical radiculopathy/myeloradiculopathy](#). Eighteen patients with coexistent CS and MS who had undergone [cervical spine decompression](#) and [fusion](#) were identified. There were six men and 12 women with an average age of 52.7years (range 40-72years). Pre-operative symptoms included progressive [myelopathy](#) (14 patients), [neck pain](#) (seven patients), [radiculopathy](#) (five patients), and [bladder dysfunction](#) (seven patients). Thirteen of the 14 patients (92.9%) with myelopathy showed either improvement (4/14, 28.6%) or stabilization (9/14, 64.3%) in their symptoms with neck pain and radiculopathy improving in 100% and 80% of patients, respectively. None of the seven patients with urinary dysfunction had improvement in urinary symptoms after surgery.

Cervical spine decompression and fusion can improve or stabilize myelopathy, and significantly relieve neck pain and radiculopathy in the majority of patients with coexistent CS and MS. Urinary dysfunctions appear unlikely to improve after surgery. The low rate of surgical complications in this cohort demonstrates that cervical spine surgery can be safely performed in carefully selected patients with concomitant CS and MS with a good clinical outcome and also eliminate CS as a confounding factor in the long-term management of MS patients <sup>7)</sup>.

## Diagnosis

see [Multiple sclerosis diagnosis](#).

## Differential diagnosis

The plethora of possible signs and symptoms in MS causes the differential diagnosis to extend to almost all conditions causing focal or diffuse dysfunction of the CNS. Conditions

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that may closely mimic MS clinically and on diagnostic testing include:

1. acute disseminated encephalomyelitis (ADEM): generally monophasic. May also have CSF-OCB. Corpus callosum involvement is uncommon
2. [CNS lymphoma](#)
3. other closely related demyelinating diseases: e.g. Devic syndrome
4. vasculitis
5. encephalitis: patients are usually very ill
6. chronic white matter changes: seen in older patients.

Differentiating [neuromyelitis optica](#) spectrum disorder (NMOSD) and [Myelin oligodendrocyte glycoprotein antibody disorder](#) (MOG-AD) from [multiple sclerosis](#) (MS) is important since MS therapies might result in progression and relapse of the former diseases. Evidence of long extending [transverse myelitis](#) (LETM) in magnetic resonance imaging (MRI) is one of the requirements to make an NMOSD diagnosis. However, centrally located lesions on spinal MRI may bring higher sensitivity and specificity to the NMOSD and MOG-AD diagnosis. Diagnostic criteria including the centrality, location, and expansion of the transverse myelitis lesions, in addition to LETM, may be more accurate in the diagnosis of NMOSD and MOG-AD and their distinction from MS <sup>8)</sup>.

## Treatment

see [Multiple sclerosis treatment](#).

## Outcome

Quality of life, in patients with multiple sclerosis is an issue that worries health personnel, it is essential to implement strategies for reducing the impact of the disease on patients' lives, mainly through the application of programs aimed to decrease depression and improve social support <sup>9)</sup>.

## Case series

[Multiple sclerosis case series](#).

1)

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2)

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9)

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