

Transverse Myelitis and Multiple Sclerosis
The Inter-relationship that Exists between MS and TM and the diagnostic issues relative to these conditions.
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What is Multiple Sclerosis (MS)?

Multiple sclerosis is a disease having multiple sites of sclerosis within the brain or spinal cord. Sclerosis [Gr. *sclerosis* hardness] refers to a firmness of the brain in areas of injury. Areas of sclerosis are also called plaques or lesions. Plaques consist of areas of damage to myelin, which is the "insulation" surrounding the "wires", or axons, of the brain. Myelin consists of a part of a cell called the oligodendrocyte. MS is primarily a disease of myelin, though axons also suffer damage.

In areas damaged by MS, there is an influx of cells from the immune system. It is unknown whether these cells are the cause of the disease (autoimmune) but they appear to be intimately related to the disease process. In chronic lesions, these immune system cells decrease and astrocytes and macrophages increase in number forming a "scar".

What are the symptoms of MS?

MS affects primarily long white matter tracts. The main function of these parts of the nervous system is to transmit information across long distances. Common symptoms include:

Motor pathways: weakness, stiffness (spasticity), leg jumps

Sensory pathways: numbness, pain, tingling, tightness, coldness, Lhermitte's phenomenon

Cerebellar pathways: incoordination

Autonomic pathways: urinary symptoms, bowel symptoms, sexual dysfunction

Visual pathways: blurred vision, double vision

Cognitive pathways: recent memory, speed of processing

Heat intolerance

Fatigue

How is MS diagnosed?

DIAGNOSIS: For a diagnosis of clinically definite MS, at least two lesions spread over space and time must be demonstrated which cannot be explained by another disease

Poser criteria for diagnosis

| Category | Clinical attacks | Clinical Evidence | Paraclinical Evidence | CSF OCB/IgG synthesis |
|--------------------------------------|------------------|-------------------|-----------------------|-----------------------|
| Clinically definite | | | | |
| CDMS A1 | 2 | 2 | | NA |
| CDMS A2 | 2 | 1 and | 1 | NA |
| Laboratory supported Definite | | | | |
| LSDMS B1 | 2 | 1 or | 1 | + |
| LSDMS B2 | 1 | 2 | | + |
| LSDMS B3 | 1 | 1 and | 1 | + |
| Clinically probable | | | | |
| CPMS C1 | 2 | 1 | | NA |
| CPMS C2 | 1 | 2 | | NA |
| CPMS C3 | 1 | 1 and | 1 | NA |
| Laboratory supported probable | | | | |
| LSPMS D1 | 2 | | | + |

MRI: MRI is felt to be the best overall test to demonstrate multiple lesions in space and to eliminate some of the other diseases that might cause similar symptoms. The more advanced the disease, the more likely an abnormal MRI will be found.

Definite MS: 85-100% abnormal MRI

Suspected MS: 62% abnormal MRI

Evoked potentials: EPs are useful in demonstrating additional lesions in areas poorly seen on MRI. Abnormalities on EPs in areas typically found in MS may increase the clinical suspicion for the diagnosis.

Somatosensory EP 72-96% definite MS, 49% suspected MS

Visual EP 75-97% definite MS, 46% suspected MS

Brainstem EP 57% definite MS

Spinal tap: Spinal fluid changes are aimed at eliminating other causes of disease and demonstrating the presence of increased immune system activity.

Oligoclonal bands indicate activation of the immune system within the central nervous system. They are present in about 90% of those with MS (95% of those with clinically definite MS). The IgG index is abnormal in about 90%.

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| Patterns of disease |
|----------------------------|

There are several patterns of MS. Relapsing/remitting, primary progressive, secondary progressive and progressive/relapsing are now recognized.

The relapsing/remitting form has attacks with symptoms develop rapidly over a few days. These symptoms may or may not get better (though they usually improve). The baseline is then stable or improving until the next attack.

The primary progressive form has a slow worsening of the baseline without attacks. The worsening of the baseline may speed up or slow down or hold stable, but attacks are not seen.

The secondary progressive form begins like relapsing/remitting, but with time changes to include a slow deterioration in the baseline which worsens independent of attacks.

The progressive/relapsing form begins with primary progressive disease but then later develops attack superimposed on the sliding baseline.

Because of differing clinical characteristics, research studies are often limited to a particular type of MS so that the entry population is as homogeneous as possible.

Who gets MS?

Sex: 1.9-3.1 female to male ratio

Age: Rare in childhood. Steep rise to a peak at about 30. Most cases occur between 20-40.

Social class: More common in higher social classes

Race: MS is more common in European whites, followed by Blacks and then Orientals. American blacks have a greater incidence than African blacks.

MS is not inherited through a single gene.

About 20% of patients have another affected person in their family.

Risk in siblings is about 4% and in parents about 3%.

Given a parent with MS, the risk to a child is about 2.5%, female, 1% male.

Identical twins have a 26% risk of both having MS, nonidentical twins have 2.3%

The cause of MS

Viral theory:

1. Higher rate of disease in higher latitudes. In both the northern and southern hemispheres, the rate of MS increases with higher latitude. The cause is unknown though a huge number of environmental suspects have been studied and rejected as possible sources of the disease.
2. The risk of developing MS is determined by latitude of residence during childhood (before 10-15 years old). This has been demonstrated in a number of migration studies.
3. Epidemics of MS have also occurred in many locations. The Shetland, Orkney, and Faroe islands have each had unusually high rates of MS. The Faroe Islands had an outbreak shortly after the British occupation during WWII. This outbreak followed many of the epidemiologic characteristics of a viral illness.
4. Numerous examples of viral demyelinating disease are found in animals and humans. The current leading human suspects are Human Herpes Virus 6 (HHV6) and clamidia.

5. On MRI, some lesions worsen at the same time that others are improving. This suggests that local factors in the brain must play a major role in the disease rather than systemic changes in the immune system.
6. HLA/TCR proteins are linked to the disease. These proteins determine how we interact with foreign antigens.
7. An antigen for an autoimmune disease has not been identified.

Autoimmune theory:

1. Pathologic studies have demonstrated immune cells in MS plaques. These have an excess of helper T lymphocytes, which increase immune activity. Macrophages have been seen removing the myelin in MS lesions.
2. Changes in blood immune cells and cytokines have been correlated with disease activity. These show an increase in immune activity just before and during the development of symptoms. They demonstrate a relative increase in helper and decrease in suppressor lymphocytes. There is a shift from TH2 to TH1 type reactions that are more likely to be injurious to tissues.
3. Persons moving from areas of low risk to areas of high risk do not become acutely ill. They might be expected to if they had never been exposed to a virus that causes MS before their move.
4. Experimental allergic encephalomyelitis (EAE). Injection of myelin basic protein into various animal models leads to EAE, an autoimmune disorder resembling to MS. Some of these models have relapsing/remitting courses resembling MS, though most are an acute, fatal illness.
5. HLA/TCR proteins are linked to the disease. These proteins also determine how we interact with our own self-proteins.

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