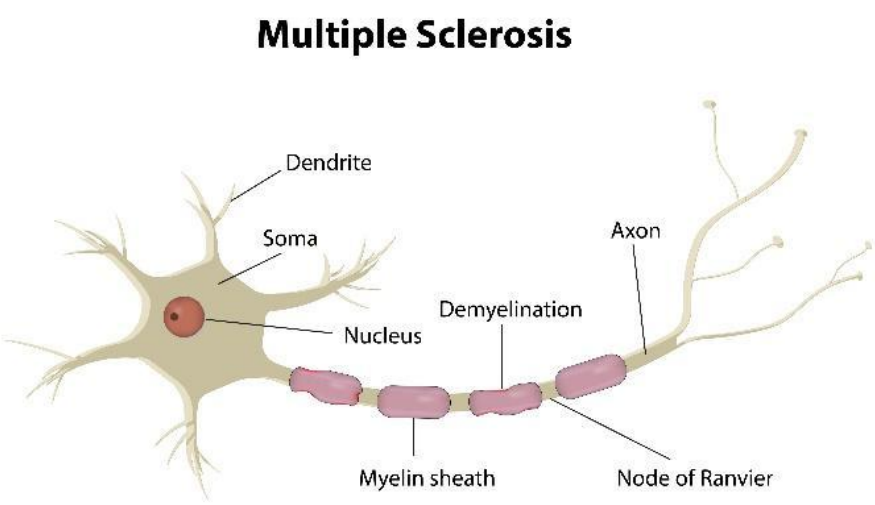
Pathophysiology of Multiple Sclerosis

by Frasat Chaudhry, MD

Multiple sclerosis (MS) is a complex chronic disease that causes inflammation and demyelination of the central nervous system (CNS). It is an immune-mediated disorder associated with inflammation and disruption of the blood-brain barrier. Patients experience axonal and neuronal damage as the disease progresses.



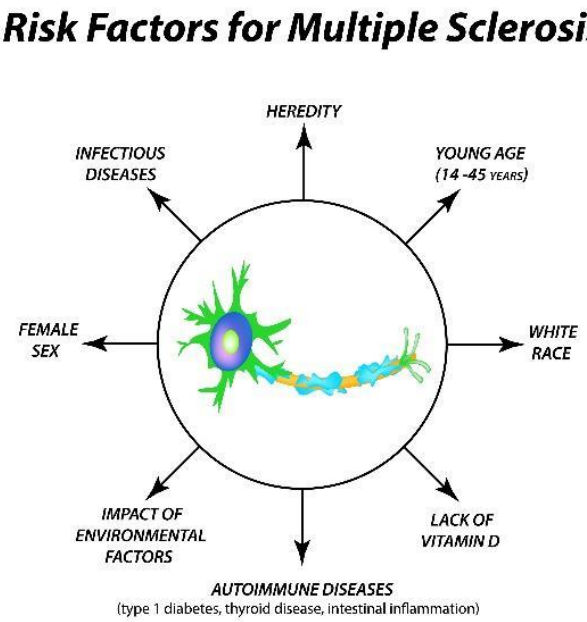
The Roots of MS

Genetic and environmental factors may be related to the etiology and pathogenesis of MS. However, no evidence implicates one particular causative factor.

No autoantigen, antibody, or infectious agent has been directly associated with MS. On the other hand, autoreactive lymphocytes apparently gain access to the CNS and trigger a pathologic series of events leading to demyelination, neuroaxonal degeneration, synaptic loss, oligodendrogliopathy, and, finally, tissue loss and astrogliosis. Demyelination, the hallmark of MS, involves the white matter and the cortical and deep gray matter. Further, T and B

lymphocytes are involved in disease pathogenesis. Axonal injury, noted from the earliest disease stage, has a significant role in physical and cognitive disability related to this progressive condition.

In addition, numerous environmental factors have a suspected relationship with the development and progression of MS. No clear association with any particular entity has been established, although low sunlight exposure, vitamin-D deficiency, obesity, and smoking have shown the strongest evidence for a relationship to the disease.



Types of MS

MS typically is divided into four phenotypes: a clinically isolated syndrome, relapsing-remitting disease, secondary progressive MS, and primary progressive MS.

A clinically isolated syndrome (CIS), the first episode that suggests the disease, occurs in a patient not known to have MS. It typically is a monophasic episode that can develop acutely or subacutely and that must last > 24 hours with or without recovery. Unilateral optic neuritis, painless diplopia, cerebellar syndromes, and myelitis are common presentations.

Approximately 85%-90% of MS cases have a relapsing-remitting phenotype, which is characterized by clear neurologic exacerbations or relapses with full or incomplete recovery. Neurologic symptoms and deficits peak over days to weeks.

Relapsing-remitting MS can evolve to secondary progressive MS. This condition involves gradual worsening with or without occasional relapses, minor remission, and plateaus over 10-20 years after initial presentation.

Primary progressive MS affects 10% of the MS cohort. Affected patients experience progressive disability from time of onset with temporary minor improvement. This diagnosis is made from patient history.

Diagnosing MS

Neurologists rely on five key principles to help confirm the MS diagnosis. First, the syndrome must be consistent with MS-related demyelination. Second, objective evidence of CNS involvement must be distinguished. Third, dissemination in space (magnetic resonance imaging [MRI] criteria) must be present, as should dissemination in time. Finally, there should be "no better explanation" for the presenting symptoms. In other words, no other rheumatologic, immunologic, or neurologic disease that could mimic MS should be present.

Most non-neurologists must be comfortable with identifying the typical syndromes and ordering an appropriate first diagnostic study based on symptoms. Common presentations include optic neuritis, brainstem syndromes, cerebellar syndromes, and transverse myelitis. Brainstem syndromes include internuclear ophthalmoplegia and trigeminal neuralgia.

Detailed history and physical examination are key to evaluation and appropriate testing. The best diagnostic test is MRI of the brain with and without gadolinium contrast. Additional testing includes imaging of spinal cord, cerebrospinal fluid (CSF) analysis, and evoked potentials. MRI lesions typical of MS are noted in the periventricular region, corpus callous, centrum semiovale, and deep white-matter structures. They are ovoid in appearance and are arranged at right angles to the corpus callous (Dawson fingers). Gadolinium enhancement on T1-weighted images indicate an active lesion. Approximately 95% of patients with clinically definite MS have oligoclonal bands in the CSF.

Conclusion

MS diagnosis is based on clinical and objective criteria. Careful history and physical examination findings are a cornerstone to establishing this diagnosis.

ABOUT THE AUTHOR

Frasat Chaudhry, MD

Dr. Chaudhry is a practicing neurologist and assistant professor of Medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell. She is board-certified in Neurology. Dr. Chaudhry received her medical degree from the University of Missouri at Kansas City and completed her internship in Internal Medicine at the University of Illinois College of Medicine in Chicago and her residency in Neurology at Loyola University Medical Center. Her fellowship in Clinical Neurophysiology was completed at Saint Louis University School of Medicine. Dr. Chaudhry's interests and areas of expertise include epilepsy, multiple sclerosis and Alzheimer's disease.