# Multiple Sclerosis

## Definition of Disease

A chronic inflammatory disease involving degeneration of central nervous system (CNS) myelin, scarring/formation of plaques, and loss of axons is present (Mccance et al., 2014). 0.1% of the population affected, 2.1 million worldwide, higher in whites, and the etiology is unknown (Mccance et al., 2014). MS is the most prevalent CNS demyelinating disorder (Mccance et al., 2014).

## Pathphysiology

MS is described as occurring when a previous infectious insult to the nervous system has occurred in a genetically susceptible individual with an abnormal CNS immune (Mccance et al., 2014). Auto-reactive T and B cells recognize myelin autoantigens and trigger inflammation in the CNS, leading to irreversible tissue damage: ogliodendrocyte injury, demyelination, and axonal degeneration (Mccance et al., 2014). MS degeneration process begins early and continues to progress throughout life.

### Immunopathology

Derived from the experimental autoimmune encephalomyelitis animal model (EAE) (Constantinescu et al., 2011). Following environmental triggers and genetic susceptibility, activation of myelin specific auto-reactive CD 4+ and CD8+ T cells cross blood-brain barrier and enter the CNS and attack myelin (Mccance et al., 2014). Process is driven by the expression of cell surface integrins (VLA-4) on inflammatory cells that mediate their binding to the vascular cell adhesion molecule (VCAM-1) expressed on endothelial cells(Gold et al., 2011). VCAM-1 expression is induced by TNF-α and in IFN-γ during inflammation. Matrix metalloproteases (MMPS) are released by the Tcells to facilitate passage through the extracellular matrix(Gold et al., 2011).

**After entry into the CNS,** T cells are reactivated on encountering CNS-related auto-antigentic peptides within class 2 molecules of the MHC expressed by antigen/dendritic cells(Gold et al., 2011). Production of IL-17 by Th17 cells play an important role within this process (Mccance et al., 2011). Myelin disruption occurs, leading to additional inflammation and activation of complement and specific B lymphocytes to site of tissue injury(Gold et al., 2011). As the inflammatory changes in the CNS increase, loss of brain volume progresses. Demyelination disrupts Na+, Ca++, and K+ ion channels: calcium influx is proinflammatory and neurotoxic(Mccance et al., 2014). The immune cells also produce glutamate, a neurotoxin (Mccance et al., 2014).

## Genetics

Not inherited in a Mendelian fashion, first degree relatives have a 1-5 times increased risk of MS, while the concordance rate in monozygotic twins is 35% (Gold & Wolinsky, 2011).

### HLA

A genetic link exist in the human leukocyte antigen (HLA) complex: a large cluster of genes responsible for many immune functions (Mccance et al., 2014). Patients carrying the class 2 major histocompitability complex (MHC) HLA-DR2 genes are susceptible to MS (Gold et al., 2011). Several risk loci beyond the MHC have been identified, including the interleukin-7 (IL-7) receptor, interleukin-2 receptor alpha chain (IL2RA) and CD58 (Gold et al., 2011).

## Epidemiology

The cause of MS is unknown, however, along with several genetic polymorphisms involved, Vitamin D deficiency, cigarette smoking, and viral infections are know to be associated with MS.

**Viral infections** Strong correlation that suggests influenza A and Epstein Barr Virus (EBV) viral infections are associated with a high occurrence of exacerbation in MS patients (Oikonen et al., 2011). Also, studies have correlated an association of varicella zoster virus with MS (Kang et al., 2011)

**Geographic Factors** MS is relatively common in Europe, U.S., Canada, New Zealand (Wingerchuk, 2011). However, rare in tropical regions: this geographical distribution of MS supports an association between latitude and regional disease prevalence (Wingerchuk, 2011).

**Sunlight/Vit. D** Correlates or contributes to the latitude gradient of MS prevalence (Wingerchuck, 2011). Most people with established MS have relatively low Vitamin D levels and the level appears to decline over time (Wingerchuk, 2011).

## Disease described/classifications

Along with the signs & symptoms listed below, the major classifications/descriptions of MS are based on the disease pattern: relapsing-remitting, primary progressive, secondary progressive and progressive relapsing (Mccance et al., 2014).

## Sign and Symptoms

MS occurs between 20 and 40 years of age (peak at 30 years). Male to female 1:2 (Mccance et al., 2014). The signs and symptoms of MS can be categorized into established syndromes within location of damage.

**Optico-Spinal (OSMS)** presents with optic nerve and spinal cord axonal loss, evolves rapidly over hours to days. Symptoms include impaired central vision, optic papillitis, and *optic neuritis* (Mccance et al., 2014). Brainstem lesion common symptoms (III through XII) include *Internuclear opthalmoplegia*, nystagmus, diplopia, eye pain, and dysarthria (Mccance et al., 2014). Other brainstem lesion residuals include vomiting, tinnitus, facial weakness/sensory deficit (Mccance et al., 2014).

**Spinal MS** is the second most common type, involving spinal tracts and dorsal column (Mccance et al., 2014). Weakness,numbness, and stiffness in limbs along with lower limbs more affected than upper limbs. *Lhermitte phenomenon* described as an electric shock down the back and to the legs(Richman & Schub, 2013). *Spastic paraparesis* is the most common neurological finding in MS (Mccance et al., 2014). Others include\ spastic bladder, urgency, hesitancy preceding incontinence, constipation and impotence(Mccance et al., 2014).

**Motor deficits/Cerebellar** include deep tendon hyperreflexia, diminished cremasteric reflex, clonus, poor coordination, presence of *Babinski reflex and Hoffman's* sign, spasticity, ataxia, impaired speech/dysphagia (Richman & Schub, 2013). Other cerebellar MS symptoms include the Charcot triad: dysarthria, intention tremor, and nystagmus(Mccance et al., 2014).

**Cognitive deficits** include dementia and depression (Richman & Schub, 2013).

## Diagnosis

Known as the McDonald criteria (Mccance et al., 2014).

**Assessment** onset of symptoms, duration, including pain and fatigue(Richman & Schub, 2013). Signs and symptoms indicating disease with 2 or more episodes lasting at least 24 hours and occurring at least 1 month apart (Richman & Schub, 2013).

**Lab** Analysis of CSF aspirated during lumbar puncture will indicate elevated immunoglobulins, myelin debris, and mildly elevated or normal protein (Richman & Schub, 2013). Immunoglubulin G index is found in 2/3 of individuals with MS and oligoclonal bands of IgG on electrophoresis in more than 90%(Mccance et al., 2014).

**Diagnostic Studies** MRI and CT scan may indicate plaques and/or glial scars in the brain and spinal cord. VEP test may diagnose optic nerve demyelination (Richman & Schub, 2013) (Mccance et al., 2014).

## Treatment

Overall, provide symptomatic relief and reduce risk of complications: permanent neurological damage (Richman & Schub, 2013). Acute relapses treated with corticosteroids: methylprednisolone. Oral and injectable disease modifying drugs are used to decrease relapse, promote remyelination, suppress B&T cell function, prevent demyelination. Options for immunosuppression include interferons (Avonex, Rebif, Betaseron), glatiramer, natalizumab, and and fingolimod (Richman & Schub, 2013).Vitamin D for reduction of risk (Mccance et al., 2014).

**Pain and fatigue** Can be assisted or relieved with analgesics, ice, heat, TENS. Amanadine, modafinil as ordered to combat fatigue (Richman & Schub, 2013).

**Bladder dysfunction & constipation** can be relieved by avoiding bladder irritants, timed voiding, regulating fluid intake, anti-cholinergic medications (Ditropan), and constipation assisted with stool softeners/fiber (Richman & Schub, 2013).

**Spasticity** can be relieved with baclofen or anti-epileptics (Richman & Schub, 2013).

**Referrals** for physical therapy (PT), occupational therapy (OT), and speech therapist based upon disease progression (Richman & Schub, 2013).

## Recommendations & Further Readings

National Multiple Sclerosis Society (http://www.nationalmssociety.org/)

## References

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