6.1.6

Multiple Sclerosis (MS)

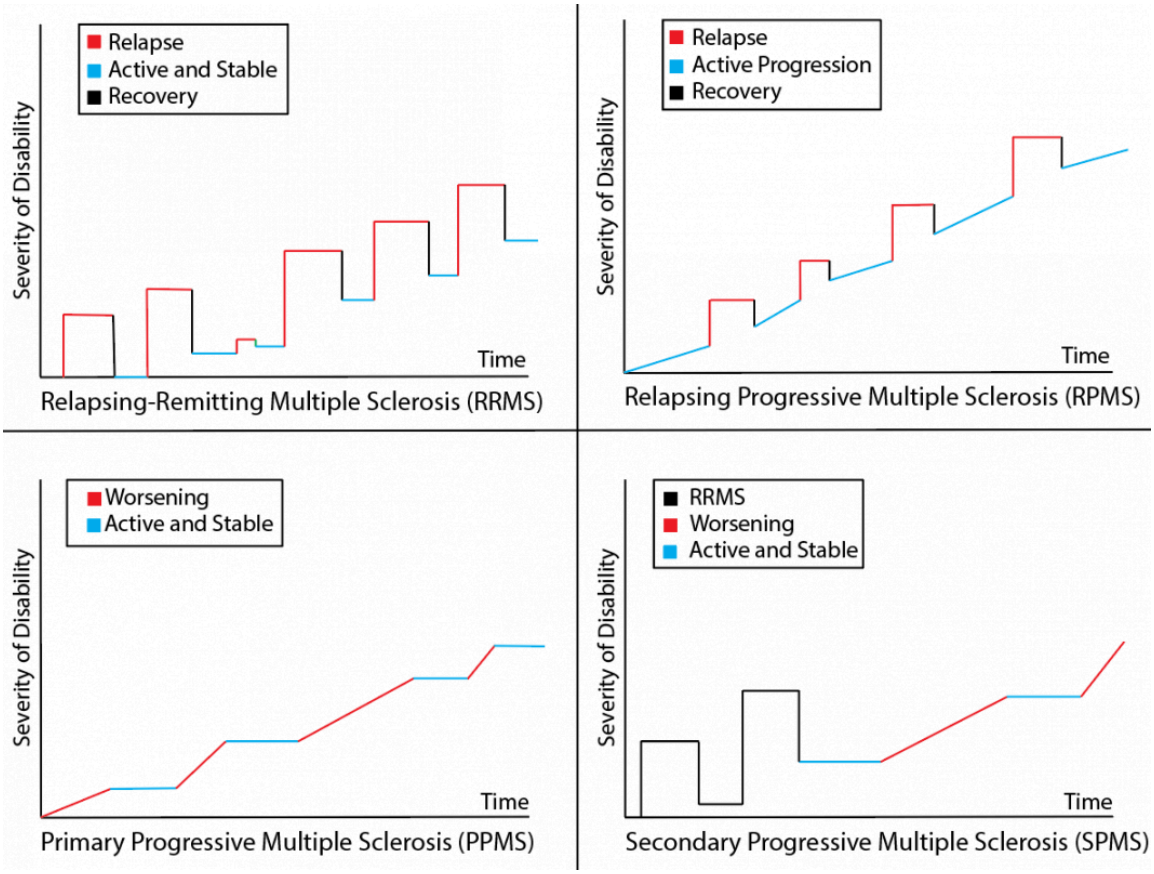
Multiple sclerosis (MS) is an autoimmune disorder where the immune system erroneously damages and degrades myelin within the CNS (white matter). The typical age of onset is 18-45 and women are more often affected. Individuals with HLA-DR2 (a type of MHC-II receptor) are more susceptible. Environmental factors like infections, vitamin D deficiency, and living far away from the equator all increase risk.

Oligodendrocytes are cells in the CNS that produce myelin. Myelin acts as an insulating sheath around axons and allows action potentials to conduct faster. With MS, the nerve fibers in the white matter of the brain, spinal cord, and optic nerve become demyelinated. It is believed to occur when TH_1 and TH_{17} cells target myelin antigens and release cytokines. TH_1 cells release INF-γ that activates macrophages. TH_{17} cells act to recruit many leukocytes which then cause the demyelination. Humoral immunity also plays a role as certain immunoglobulins like IgGs can be detected in the CSF of these patients. The lesions where myelin is stripped of the nerves contain CD4+ T-cells and some CD8+ T-cells as well as macrophages and plasma cells. Exactly how immune cells are initially activated is unknown but may involve a viral infection such as EBV.

Symptoms of MS are neurological in nature and include fatigue, paresthesia, optic neuritis (inflamed optic nerve), diplopia (double vision), pain, ataxia (impaired coordination), dysarthria (slurred speech), incontinence, constipation/diarrhea, cognitive dysfunction, and psychological disturbances such as depression and an unstable mood. Some patients with MS have moderate pleocytosis (elevated number of white blood cells) and elevated levels of IgG in the CSF. **Lhermitte's sign** is common in someone with MS. It occurs when neck flexion induces a shock-like tingling (similar to the feeling of banging your "funny bone") that extends down the back and to the legs.

MS patients can be very sensitive to heat. Just a small increase in body or environmental temperature may make their symptoms more profound and increase their pain. Heat affects the ability of nerves to conduct their natural impulses. Patients with MS already have compromised ability to conduct action potentials. When body temperature is increased, these impulses are sometimes incapable of propagating the length of the neuron. This leads to progressively worse symptoms. Before we had the technology to detect this disease, doctors would diagnose MS by placing patients in hot baths and determining their neurological symptoms and reactions to the increased heat. If they appeared worse, they were often diagnosed with MS.

There are 4 categories that the course of multiple sclerosis may follow: relapsing remitting, relapsing progressive, primary progressive, and secondary progressive.



Progression of the Four Categories of MS *Image by Becky Torgerson BYU-Idaho F19*

1. **Relapsing remitting multiple sclerosis (RRMS)** is the most common with 80-85% of MS patients being diagnosed with this type. It is characterized by episodes of acute worsening of symptoms that last a few days to a few months followed by the symptoms improving or disappearing for several months to even years in a period of remission. Over time, most patients slowly progress from relapsing remitting MS to secondary progressive MS. In the past, about 50% of patients moved to secondary progressive within 10 years after diagnosis. However, improvement in medical management has extended this time significantly.
2. **Relapsing progressive multiple sclerosis (RPMS)** is characterized by episodes of acute flare-ups superimposed on a steady progression of worsening symptoms. It is different from relapsing remitting MS because of its progressive nature between flare ups. There are no periods of remission, although flare-ups do diminish. This form is the most rare of all the forms of MS. It is also not commonly used as a diagnosis anymore because it is currently becoming more favorable to consider relapsing progressive MS as a subtype of primary progressive.
3. **Primary progressive multiple sclerosis (PPMS)** involves a nearly continuous neurological deterioration from the onset of the first symptoms. There may be periods of time that the symptoms plateau, but there are no periodic remissions. Primary progressive MS is rare, involving only about 10-15 percent of patients. This type of MS is difficult to treat.
4. **Secondary progressive multiple sclerosis (SPMS)** is not characterized by dramatic changes in symptoms for worse or better, but instead involves a slow, steady progression of the disease. It is similar to primary progressive MS, but secondary progressive MS is different because it begins at some point after a person has been living with RRMS.

Corticosteroids, interferon-beta, and glatiramer acetate are some of the medications used in the treatment of MS. Corticosteroids reduce inflammation and suppress the immune responses involved in autoimmune damage to tissues. Interferon-beta is a cytokine that is thought to help initiate immune suppression and stimulate neuronal growth factors to be released to enhance myelin regrowth. Glatiramer acetate appears to block T-cells from damaging myelin by acting

as a myelin antigen decoy. Because upper motor neurons are involved in this disease, spasticity can develop. Baclofen, dantrolene, and diazepam help with spasticity. Cholinergic drugs are used to help with bladder problems. MRI is useful to detect lesions, monitor progress of lesions, and evaluate the effectiveness of treatment.