The Pathophysiology of MS – The Inflammatory Process

- Axons are surrounded by myelin, a fatty substance that protects them and ensures efficient transmission of nerve impulses.
- The immune system initiates a T-cell-mediated inflammatory response.
- Activated immune cells migrate from the systemic circulation to the central nervous system (CNS).
- T-cells are activated through antigen presentation and produce pro-inflammatory cytokines, which enhance immune response.
- The inflammatory response initiates a cascade of events involving: activation of T-cells, B-cells and immune cells (i.e. macrophages), production of antibodies, cytokines, chemokines and free radicals.

**THE HOSTILE ENVIRONMENT THAT THIS CREATES IN THE CNS RESULTS IN DEMYELINATION AND AXONAL LOSS.**

The Pathophysiology of MS – The Inflammatory Process

- Inflammatory cells demyelinate axons.
- Under normal conditions, myelination and maintenance of the myelin sheath are the responsibility of oligodendrocytes.
- The inflammatory process can lead to damage of oligodendrocytes or stimulate apoptosis. With loss of oligodendrocytes, the support for axonal function and the potential for remyelination is diminished.
The Pathophysiology of MS – Axonal Loss

- Demyelinated axons are less efficient at conducting nerve impulses\(^5,6\)
- Demyelination leads to abnormal distribution and proliferation of sodium ion channels along the axon \(^1,3\)

To reestablish normal conduction of impulses, there is an increase in sodium influx, resulting in slower nerve conduction and perhaps conduction block.

Sodium efflux and calcium influx follow and may trigger injury and lead to neuronal degeneration.

EXPOSED AXONAL SURFACES BECOME SUSCEPTIBLE TO INJURY FROM IMMUNE CELLS (I.E. MACROPHAGES) WHICH MAY RESULT IN PERMANENT NEUROLOGICAL DYSFUNCTION. \(^3,7\)

Clinical Impact of MS

- Ultimately, the loss of axons through demyelination correlates with disability in MS \(^3,7\)
- Axonal loss has been shown to correlate with neurologic disability and cognitive dysfunction, which in turn, correlate with brain atrophy \(^7\)

An increased relapse rate has been associated with disease progression, \(^8\) and axonal loss may contribute to progression of disease.
The MS Disease Continuum

The pathophysiology of MS drives the course of disease over time, which is depicted graphically in the figure below.

- This MS Disease Continuum shows the progression of disease if MS goes untreated
- Inflammatory disease activity leading to demyelination may begin well before disability appears at a clinical level, and it may continue in the background between clinical relapses 10

Relapse activity and brain atrophy progression lead to physical and cognitive disability progression 10.

References