MULTIPLE SCLEROSIS (MS): balancing the immune system

**MS** is a chronic neuroinflammatory disease of the brain and spinal cord.

**RISK FACTORS FOR MS** include:
- Genetic variations
- Low vitamin D status
- Viruses (Epstein-Barr virus, human herpesvirus-6)
- Bacteria (H. pylori, chlamydia, mycoplasmas)
- Heavy metal exposure (methylmercury)

Up to 90% of MS patients are women.

**VITAMIN D DEFICIENT**

3/4 of MS sufferers are women.

**VITAMIN A** and **VITAMIN D** balance immune response.

**BERBERINE**
- Blood-brain barrier permeability and inflammatory infiltration

**LIPOIC ACID**
- Antioxidant
- Neuroinflammation
- Pro-inflammatory cytokines and chemokines produced by astrocytes

**INFLAMMATION**

**DEMYELINATION**

**OLIGODENDROCYTE INJURY**

**NEUROAXONAL INJURY**

**DISEASE PROGRESSION (CNS)**

Coenzyme Q10: Antioxidant, protects neurons from free radical damage and apoptosis.

**REMYELINATION**

**NATURAL INTERVENTIONS FOR MULTIPLE SCLEROSIS**

**DENDRITIC CELL**
- Differentiation
- Activation, proliferation and migration of OPCs

**MUCOSAL SURFACE**
- Bacteria
- Viruses
- Smoke constituents

**THYMUS GLAND**

**MHC class I**

**MHC class II**: major histocompatibility complex II; **CNS**: central nervous system; **Th**: T helper cell; **IFN-γ**: interferon gamma; **TNF-α**: tumour necrosis factor-alpha; **GM-CSF**: granulocyte macrophage-colony stimulating factor; **IL-17**: interleukin-17; **MMPs**: matrix metalloproteinases; **OPCs**: oligodendrocyte progenitor cells; **ROS**: reactive oxygen species; **RNS**: reactive nitrogen species

**IMMUNE SYSTEM DYSREGULATION (PERIPHERAL)**

Although the exact cause of MS remains unknown, it is thought that the disease may be triggered in the periphery during the breakdown of central tolerance due to reduced function of regulatory T (Treg) cells and/or resistance of autoreactive cells to suppression. Once activated, differentiated Th1 and Th17 cells, B cells and innate immune cells cross the blood-brain barrier and infiltrate the CNS leading to inflammation and tissue damage. Genetic and environmental factors, such as infectious agents and smoke constituents, contribute to these events.

**IMMUNE SYSTEM DYSREGULATION (PERIPHERAL)**

Autoreactive T cells escape into periphery

**DIAGRAM**

- Activation, proliferation and migration of OPCs
- Recruitment, differentiation, and remyelination of OPCs
- Neuroprotective and/or neurodegenerative mechanisms
- Chronic neurodegenerative damage
- Neuron damage, loss of neuron connectivity and apoptosis

**IMMUNE SYSTEM DYSREGULATION (CNS)**

Immune cells, activated microglia and astrocytes promote inflammation, demyelination, oligodendrocyte and neuroaxonal injury through the production of pro-inflammatory cytokines, chemokines and antibodies, as well as direct cell contact, e.g. macrophages engulf myelin and myelin fragments.

Following demyelination, microglia and astrocytes become activated and in turn activate resident oligodendrocyte progenitor cells (OPCs). Mitogens and promigratory factors released by activated microglia and macrophages promote the proliferation and migration of OPCs to the sites of demyelination. Recruited OPCs differentiate into remyelinating oligodendrocytes and repair damaged myelin.

Over time, chronic neurodegenerative damage overwhelms the neuroprotective and/or neurodegenerative mechanisms. Oligodendrocytes are damaged and remyelination may fail, which may lead to neuron damage, loss of neuron connectivity and apoptosis.