Effects of Oxidative stress on Multiple Sclerosis: A Narrative Review

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INTRODUCTION

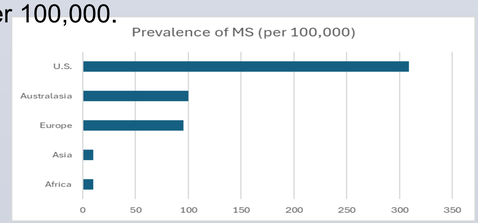
Multiple sclerosis (MS) is a chronic neurological condition characterized by the immune system attacking the protective sheath (myelin) that covers nerve fibers, leading to communication issues between the brain and the rest of the body. This debilitating disease can result in a wide range of symptoms, including physical, cognitive, and emotional challenges. Among the myriad of factors that influence the progression and severity of MS, stress has emerged as a significant contributor. Stress is an inevitable part of human life and its impact on individuals with MS is of particular interest. Stress may exacerbate symptoms, influence disease progression, and affect the quality of life. The relationship between stress and MS is complex, involving biological, psychological, and environmental dimensions.

Types of Multiple Sclerosis

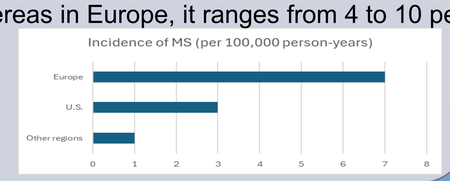
- **Relapsing-Remitting MS** (RRMS)
  - Most common form of multiple sclerosis
  - Characterized by distinct relapses, followed by remissions, where symptoms partially or fully subside
- **Secondary progressive MS (**SPMS)
  - Often follows RRMS, involving a gradual worsening of neurological function between increasingly infrequent relapses
  - The progression rate varies, making the transition unpredictable.
- **Primary-progressive MS** (PPMS)
  - Least common type of MS
  - Steady decline in neurological function without the distinct relapses and remissions, diagnosed later in life and progresses more aggressively

Epidemiology

- **Global Distribution**: MS prevalence varies geographically, with higher rates observed in North America, Europe, and Australasia compared to Africa and Asia. The prevalence in the U.S. is estimated at around 309 per 100,000 people, while in Europe, it ranges from 83 to 108 per 100,000.



- **Incidence Rates**: Incidence rates also show geographical variation. For example, in the U.S., the incidence is approximately 2.5 per 100,000 person-years, whereas in Europe, it ranges from 4 to 10 per 100,000 person-years.



DISCUSSION
Benefits & Consequences

Managing Multiple Sclerosis effectively requires a comprehensive approach that includes diet, exercise, stress management, and social support. A balanced, anti-inflammatory diet rich in antioxidants, omega-3 fatty acids, and vitamins helps reduce inflammation and support immune health. Regular physical activity is essential for maintaining strength, mobility, and well-being. Stress management techniques like mindfulness meditation, yoga, and deep breathing can reduce stress levels, which is crucial since chronic stress can worsen MS symptoms. Avoiding smoking and limiting alcohol intake are important, as smoking can accelerate MS progression and excessive alcohol can impair coordination. Good sleep hygiene, including a regular sleep schedule, helps manage fatigue. Adequate vitamin D levels have protective benefits against MS progression. Social support provides emotional support improving the quality of life. Together, these lifestyle factors significantly enhance MS management and overall well-being.

Stress induced Pathophysiology

Elevated sympathetic activation associated with the feeling of being “stressed out” leads to oxidative stress at the cellular level, which has major implications for the progression of autoimmune diseases such as multiple sclerosis. Central and peripheral nervous system components are damaged excess production of reactive oxygen species (ROS) and impairment of microglia and lymphocyte function.

MS pathogenesis and progression can be linked in part to malfunctioning microglia and lymphocytes. Specifically T helper cells, regulatory T cells, B-cells, and myeloid-derived suppressor cells have all been shown to contribute to lesion formation in MS. Primarily, autoreactive CD4+ Th1 and Th17 cells are the mediators of macrophage activation and leukocyte recruitment that drives lesion progression. However, now there is expanding evidence that structural and functional stability in T-regulatory cell lineages through Foxp3 gene mutations is also a significant contributing factor.

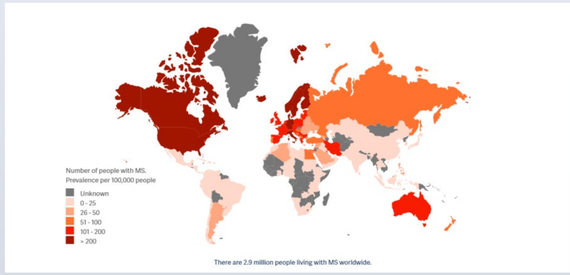
With dysfunctional T-reg cells failing to suppress autoreactive T-cell action, chronic inflammatory responses produce massive amounts of ROS which damage myelin sheath cells and cause their phagocytosis by macrophages. In addition, a majority of MS patients show a mutation in the Nrf2 transcription factor, which functions as an upregulator of detoxifying enzyme and antioxidant protein genes in cells throughout the body. With uncontrolled autoreactivity and the failure of cells to produce effective amounts of antioxidant agents, MS lesions are able to progress beyond control.

Conclusion & Future Research of Systematic Review

MS is a complex autoimmune disease with multifactorial etiology, highlighted by neurodegeneration and loss of nerve conduction due to myelin and oligodendrocyte destruction. Ongoing research aims to unravel these interactions further and improve prevention, diagnosis, and treatment strategies. CD4+ Th1 and Th17 cells are the primary mediators of lesion progression, but recent research indicates malfunctioning T-regulatory cells with Foxp3 gene mutations play a significant role as well.

Lack of suppression of autoreactive T-cells combined with a reduced antioxidant capacity produces overwhelming ROS production, and oxidative damage to neuronal components and disease progression. Treatment aimed at increasing antioxidative protein production (Nrf2 pathway activation) has shown to improve antioxidant capacity as well as slow disease progression.

Moving forward, continuing to upregulate antioxidant producing components as well as producing treatments aiding in autoreactive lymphocyte destruction is crucial to producing effective care to slow disease progression.



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