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Multiple sclerosis

Multiple Sclerosis is a long-lasting chronic inflammatory disease of the central nervous system (CNS). It is also one of the most common autoimmune disorders, a condition in which the body attacks itself by mistake, and it mostly affects young adults. This disease affects > 2 million people worldwide (~400,000 in the United States), and currently incurable. Some of the neurological disabilities include monocular visual loss due to optic neuritis, limb weakness or sensory loss due to transverse myelitis, double vision due to brainstem dysfunction, or ataxia due to a cerebellar lesion. After 10-20 years people develop disease progresion, eventually manifesting impaired mobility and cognition. There are some medications that help to reduce the frequency of episodes; however, no medication fully prevents or reverses progressive neurological deterioration. The economic cost in the US is ~$10 billion.

MS is a complex disease; many genes modestly increase disease susceptibility in addition to several environmental factors, in particular vitamin D or Ultraviolet B light (UVB) exposure, Epstein-Barr virus (EBV) infection, obesity and smoking. The underlying cause remains uncertain. MS lesions can appear throughout the CNS and are most easily recognized in the white matter as focal areas of demyelination, inflammation, and glial reaction. Demyelination disease is a condition that causes damage to the protective sheath that surrounds nerve fibers.in your brain, the nerves leading to the eyes and spinal cord. When myelin sheath is damaged, nerve impulses slow or even stop, causing neurological problems. Evidence from the MRI and pathology indicates that the earliest stages of white matter demyelination are heterogeneous and evolve over the course of months.

Multiple Sclerosis is most common in females. The main genetic risk associated with MS in HLA-DRB1\*15 and other loci is strong linkage disequilibrium with the allele. The inflammatory infiltrates contain T-lymphocytes, dominated by MHC class I restricted CD8+ T-cells, B-cells and plasma cells are also present. Oligodendrocyte damage and demyelination occur as a result of inflammation. Spinal cord lesions are a major source of clinical disability. Perivascular and circumferential demyelination is often highly inflammatory and can involve gray matter.

In Carcot’s original descriptions of the pathology associated with sclerose en plaques, he described sclerosed plaques affecting the periventricular area, pons and spinal cord. The characteristic pathological hallmarks of MS are perivenular inflammatory lesions to demyelination plaques. Spinal cord lesions are a major source of clinical disability. The difference between low to high chance of progression. Low inflammation, few spinal cord lesions, good endogenous repair, preserved axons and synapses, early treatment, younger age. In high or chronic inflammation, many spinal cord and cortical lesions poor endogenous repair, mitochondrial dysfunction, extensive axon and synapse loss delayed treatment, older age.

Tissue damage in MS results from a complex and dynamic interplay between the immune system, glia (myelin-making oligodendrocytes and their precursors microglia and astrocytes), and neurons. The T-cell side, both helper (CD4+) and cytotoxic (CD8+) T cells have been described in MS lesions: CD$s are more concentrated within the parenchyma.

Drugs that limit T cell access to the CNS can reduce or eliminate new MS lesions. The treatment of MS can be divided into disease-modifying therapies that tend to be MS-specific and symptomatic therapies that are often used in different diseases areas to treat symptoms resulting from neurological dysfunction. Historically treatments have been immunosuppressant (including fingolimod, natalizumab, ocrelizumab) or immunomodulatory (such as interferon beta, glatiramer acetate, teriflunomide), meaning that ongoing treatment is required to maintain suppression of inflammation (and disease activity).

Given that MS is most diagnosed in young women, pregnancy and family planning are real concerns for women with MS. Current evidence suggests that pregnancy does not increase the risk of long-term disability in MS.

As of October 2017, the US Food and Drug administration has approved 15 medications for modifying the course of MS, the monoclonal antibodies natalizumab, alemtuzumab, daclizumab, and ocrelizumab (the first B-cell targeted therapy); the chemotherapy mitoxantrone; and the small-molecule oral agents fingolimod, dimethyl fumarate, and teriflunomide. All these drugs are approved to help relapsing-remitting MS and reduce to various extents the likelihood of developing new white mater lesions. The recent approval for Ocrelizumab if to help reduce progression. The richest conception of MS will allow appreciation of common pathology, which in the setting of variable triggers and clinical courses, makes MS among the most heterogeneous, and remarkable, of all neurological disorders.