The autoimmune theory

The autoimmune theory states that MS is caused by a dysfunction of the immune system. This leads to an attack on the body’s own tissues, in other words an autoimmune disease. The autoimmune attack in MS is directed against myelin.

Some believe that the immune system is genetically prone to reacting to autoimmune targets, or that it is improperly regulated causing an autoimmune disease. Others believe that the immune system learns to attack autoimmune targets. For example, an early life virus may trigger the immune system; this virus might have proteins whose shape resembles the shape of normal brain proteins. When the immune system learns to attack this virus it also learns to attack autoimmune targets. With time, the attack on these autoimmune targets gets honed to produce more damaging attacks on the brain.

There are several observations that support the autoimmune theory

1. **Pathology:** Pathology studies of MS lesions show components of the immune system that are involved in causing damage to myelin. This includes lymphocytes infiltrating acute MS lesions and macrophages engulfing myelin. These immune system cells decrease after the acute attack subsides.

2. **Cerebrospinal fluid changes:** The cerebrospinal fluid bathes the brain and spinal cord. In the cerebrospinal fluid of patients with MS, an increase in IgG is seen along with oligoclonal bands. IgG is one form of antibody made by the immune system to attack a target. Oligoclonal bands are antibodies made by clones of immune cells. Both of these are evidence that the immune system is active within the nervous system.

3. **Changes in blood:** There are measurable changes in immune cells in the blood of patients with MS. These show a shift in the balance of the immune system, with an increase in cells that activate the immune system and a decrease in those that decrease immune activity. These changes are more pronounced at the time of MS attacks.

4. **Experimental Allergic Encephalomyelitis (EAE):** EAE is an animal model for MS. In this model, brain tissue from one species is injected into another species (for example, rabbit brain tissue is injected into a mouse). Now, this is more commonly studied by injecting a single protein from myelin instead of whole brain tissues. This causes an immune attack on the foreign brain tissue or protein. However, the immune attack then spreads to the animal’s own brain causing an acute inflammation and damage to the myelin. The pathology of EAE resembles that seen with MS. It serves as a model to study immune reactions within the brain.

5. **HLA linkage:** HLA proteins are found on the surface of many of the cells of our bodies. These proteins play a key role in the immune system by binding foreign protein targets and presenting them to lymphocytes. Certain HLA types are more common in people with MS compared to people without MS. HLA types have been associated with other autoimmune diseases, perhaps by allowing some self-proteins to be presented to
lymphocytes. The linkage to HLA types in MS suggests that immune reactions are important in the cause of the disease.

6. **Success of immune-based therapies:** The success of therapies directed against the immune system are strong evidence that the immune system plays an important role in MS. All of the current disease-modifying medicines slow the course of MS through an effect on the immune system.

There are several observations that argue against the autoimmune theory.

1. The acute immune attack on the nervous system may not be the first changes to occur. Some MRI studies find changes in the brain occurring weeks to months before the first immune response. Also, some pathology studies find no immune activation in the earliest phases of an acute MS attack.

2. Despite decades of searching, a target for an autoimmune attack in humans has not been identified. Rather, the immune attack appears to be very broad against a wide range of targets.

3. All parts of the immune system are activated in MS. This is not a pattern of a single part of the immune system that is malfunctioning.

4. The Danger Theory: The danger theory states that the immune system cannot be activated unless danger (damage) to tissues occurs first. In other words, something would have to damage the brain first before an immune reaction to myelin could occur. Though there are several components to the danger theory, a key concept is that immune cells come in contact with their targets and are activated in the lymph nodes. This means that the immune system could not become activated against brain targets unless something first damaged the brain to release these targets into the circulation so that they could travel to the lymph nodes.

5. The autoimmune theory does not explain the geography, gender or racial differences of the disease.

6. Treatments directed against the immune system have been successful, but none have completely stopped the disease. Even very aggressive immune therapies have slowed by not stopped the disease. This suggests that the immune system plays an important role, but that other factors must also be present in causing the disease.