

The Varied Roles of Infectious Agents in the Onset and Progression of MS

By Ashton Embry

Multiple sclerosis is the result of various environmental factors acting upon a genetically susceptible individual. There is not much that can be done about one's genetic makeup. However, a person can either lower their risk of MS or can affect its course by changing their exposure level to the various environmental factors which drive the onset and progression of MS. Thus it is important to understand what environmental factors are involved in MS. In the past I have written mainly about the various nutritional factors which contribute to the MS disease process. These are the easiest factors to address when making changes to one's lifestyle.

Another major environmental factor involved in MS encompasses varied infectious agents that include viruses, bacteria, parasites and fungi. It has become apparent that infectious agents play various roles in MS. MS was first recognized as a specific disease in the mid-part of the 19th century. At this same time it was discovered that infectious agents, mainly bacteria, were the main causes of many diseases. Thus, it was natural for early workers to assume MS was also an infectious disease caused by bacteria. Consequent attempts to identify the specific MS bacterium came up empty and in the early part of the 20th century it was proposed that MS was caused by a viral infection. Again, efforts to identify a specific infectious agent and to treat MS with anti-infection therapies were not successful.

By the late 1930s, the concept of autoimmunity became reasonably well established and the possibility that MS was an autoimmune disease was entertained. From 1940 to 1970, the concept of MS as an infectious disease was gradually supplanted by the view that MS is an autoimmune disease. Currently, the prevailing view strongly favours the autoimmune interpretation although a few researchers still regard MS as an infectious disease caused by a specific virus or bacterium.

Those who advocate that MS is an infectious disease suggest that MS is caused by either a latent virus which is periodically reactivated or a chronic viral infection. It seems every so often a research team announces they have "discovered" the infectious cause of MS and candidate agents have included HHV-6 (roseola), Varicella (chicken pox), Epstein-Barr (mononucleosis) and Chlamydia (a common bacterium), not to mention canine distemper virus, Lyme Disease bacteria and various retroviruses. Further work has disproved the causal role of all the proposed infectious agents but I am sure another one will be trumpeted as the cause of MS in the near future.

Overall, the evidence which supports the infectious hypothesis is rather weak. One strong piece of evidence against this concept is that no specific infectious agent has ever been consistently detected in MS lesions despite the use of extremely sophisticated techniques. An even stronger argument against an infectious cause is that immune suppressant drugs tend to improve the disease rather than make it worse. This latter point is especially convincing because, if infection was driving MS, immune suppression would allow the infectious agent to expand and do more damage. This does not happen. Thus I think we can confidently reject the hypothesis that MS is an infectious disease.

Just because it does not appear that MS is an infectious disease does not mean infectious agents do not play various roles in MS onset and progression. In most cases the MS disease process appears to begin in childhood. The simplest and most widely accepted explanation for the triggering event is

that a common childhood infection such as roseola (HHV-6) or Epstein-Barr (EBV) infection sets MS in motion by resulting in cross reactions between viral antigens (protein pieces) and parts of a protein in myelin. Thus, when the immune system of a genetically susceptible person becomes sensitized to the EBV or HHV-6 antigen, it also becomes sensitized to myelin. At this time a pool of myelin-sensitive, memory, immune cells can potentially form. These cells represent a time bomb which detonates and drives MS in later life when the myelin-sensitive immune cells lead a substantial immune attack on myelin.

As has been discussed in past columns, it appears vitamin D is protective against MS and, that if a child has an adequate blood level of vitamin D, they will be protected from MS. The reason for this is that adequate vitamin D ensures that an infection with an MS-driving virus such as EBV or HHV-6, is well controlled and that a “time bomb” pool of myelin-sensitive, immune cells does not form. Thus MS-causing infections can be rendered toothless by ensuring that children have an adequate blood level of vitamin D (100 nmol/l) at all times. Unfortunately most children do not have an adequate level of vitamin D for at least part of the year and there is no indication that the public realizes the importance of adequate vitamin D supplementation for children.

There is also solid evidence that viral and bacterial infections can initiate exacerbations during the R-R phase of MS. This likely occurs because various infectious agents, including the flu, can activate myelin-sensitive immune cells through cross reactions. Another way infections can drive MS is that infections of the gut can result in increased intestinal permeability (“leaky gut”). This often leads to the passage of food and bacterial proteins across the gut wall. When such proteins meet the immune system, they can also activate myelin-sensitive immune cells. Finally, general infection can cause the release of various inflammatory mediators and these can also contribute to increased autoimmune reactions.

Infectious agents play another, even more surprising role in MS. It is apparent that people who have chronic, parasitic infections are protected against MS. Notably such parasitic infections were standard for everyone during the 4 million year history of human beings. It is only in the last 100 years that such chronic infections have been eradicated in developed countries, where, not by chance, the MS rate has exploded. The main way such parasites protect against MS is that the parasites induce the immune system to produce regulatory immune cells which in turn off the attack side of the immune system. This evolutionary bargain protects the parasite against the host’s immune system and benefits the host by preventing autoimmune disease. Currently, muted parasites are being tested as a therapy for Crohn’s Disease (another autoimmune disease) and are being considered for use in MS. Such a therapy may be quite effective.

In summary, infectious agents play a varied role in MS, from initiating the disease in the first place, to precipitating exacerbations, to potentially being a beneficial therapy. Adequate vitamin D can ensure that infections do not have a noticeable effect on MS progression and do not initiate the MS disease process in the first place.