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Study Finds Evidence of Epstein-Barr Virus in Multiple Sclerosis Brain Tissues; Adds to evidence of link between EBV and MS, but does not prove EBV causes MS

Investigators have reported finding traces of Epstein-Barr virus in postmortem brains examined from people with different forms of MS. They found the traces of EBV infection in immune cells (B cells and plasma cells) that had infiltrated the brain in 21 out of 22 brains from people with MS, but not in brains from people who had other neurological diseases that, like MS, involve inflammation. If these exciting findings are confirmed by other laboratories, they add to growing evidence of a link between EBV and MS. However, it is not possible through this study to determine whether EBV causes MS, or whether its presence is a consequence of MS.

The study, by Dr. Francesca Aloisi (Instituto Superiore di Sanita, Rome) and colleagues from Italy and the United Kingdom, was published early online on November 5, 2007 in the *Journal of Experimental Medicine*. This study was funded by the European Union, the Italian MS Foundation, and the Italian Ministry of Health; most of the brain specimens were supplied by the UK MS Tissue Bank, funded by the MS Society of Great Britain and Northern Ireland.

About EBV and MS: Epstein-Barr virus is a herpesvirus known to cause infectious mononucleosis and other disorders. Most people in the general population have been exposed to the virus. After an initial infection EBV becomes latent or dormant, and can be reactivated. EBV infects B cells, the cells of the immune system that make antibodies. There is currently no vaccine that can protect against an initial infection by EBV, and no anti-viral medication that can fight the active infection or kill latent virus harbored in the body. This virus does not infect other species, so research on EBV can only be carried out in humans.

The cause of MS, an unpredictable immune-mediated disease that attacks the central nervous system, is unknown, but the disease is thought to occur when susceptible individuals encounter...
a triggering factor or factors in their environment. Several previous studies have suggested a possible link between EBV and MS, but other infectious agents have also been linked to MS, leading some researchers to suggest that the way the immune system responds to infections, rather than the infectious agent itself, may lead to the onset of MS. Previous examinations of MS brain tissue for signs of EBV have been for the most part negative. In a report published last year, National MS Society-supported investigators showed evidence that individuals who had signs of significant exposure to EBV were twice as likely to develop multiple sclerosis up to 20 years later.

Study Details: Dr. Aloisi and colleagues conducted a series of studies using several techniques to discern the presence of EBV and EBV gene products in postmortem brains of people who had had MS in their lifetimes. EBV does not normally infect brain cells. In one series of experiments, in 19 out of 20 brains from people with different forms of MS (including relapsing-remitting, primary progressive, progressive relapsing and secondary progressive forms) they found signs of abnormal accumulation of EBV-infected B cells and plasma cells, both in follicles (sack-like structures) in the membrane that surrounds the outer layer of the brain (cerebral meninges), and also in MS lesions (areas of disease activity or damage). They found evidence of both latent EBV and reactivated EBV. They did not find evidence of EBV in nerve cells or myelin-making cells.

Further, the team found evidence of ongoing immune attack directed toward EBV-infected cells at major sites of accumulation, with higher numbers of T cells in brains that showed higher amounts of infiltration of EBV-infected cells.

To test for the presence of EBV early in the course of MS, the investigators examined brain specimens from an additional two people with very severe cases of MS, and found evidence pointing to reactivated EBV in these cases.

All told, they found traces of EBV infection in B cells and plasma cells that had infiltrated the brain in 21 out of 22 people with MS. The team did not find evidence of EBV in brain specimens from seven people with other types of inflammatory neurological diseases. While these specimens had B cells that infiltrated into the brain tissue, those cells did not show evidence of EBV.

Further research by other laboratories is needed to confirm these findings.

Commentary: “These results are very intriguing,” said Dr. John R. Richert, executive vice president of research and clinical programs at the National MS Society. “While they don’t prove that EBV causes MS, they add to a growing body of evidence pointing to EBV as a culprit. If confirmed, then research aimed at understanding how EBV interacts with the immune system in MS will be key. Furthermore, finding ways to treat EBV infection and developing an EBV vaccine would become of paramount importance in our efforts, both because these measures may represent the major means of determining if EBV plays a causative role in MS, and also because of their potential to treat or prevent the disease.”