This is a one-page summary of the MSIF information statement on EBV. This summary only gives a flavour of the topic. To get the full picture of the role of EBV in MS, please read the full statement.

Epstein-Barr virus and multiple sclerosis: one-page summary

The Epstein-Barr virus (EBV) is one of the most common viruses, with up to 95% of the world's population infected. EBV is transmitted through bodily fluids, e.g. saliva, and is often acquired during early childhood or young adulthood. Children who have EBV infections usually do not show symptoms or the symptoms are similar to other short-lived and mild childhood illnesses. EBV infection can be asymptomatic or cause infectious mononucleosis (glandular fever, characterised by extreme fatigue, fever, sore throat, head and body aches, swollen lymph nodes, liver and spleen, and rash).

EBV infects B cells and remains in the cells undetected by the immune system. EBV reactivates periodically inside the infected B cell.

EBV as an MS risk factor

MS is likely caused by a combination of genetic risk factors and environmental exposures such as EBV, smoking, low vitamin D levels, and childhood or adolescent obesity.

At least 99% of people with MS have been infected with EBV. Most people infected with EBV do not develop MS, meaning EBV alone is insufficient to cause MS. However, it is rare for a person to have MS without prior EBV infection. The risk of MS is higher in individuals who have had infectious mononucleosis.

To establish EBV as a key risk factor in MS, we need to understand how EBV affects the immune system and the attack on the central nervous system. Many questions remain, including why some EBV-infected individuals develop MS while others do not, and if, or how EBV may interact with other environmental or genetic risk factors.

How might EBV trigger MS?

This is an ongoing area of work. EBV infection can trigger an abnormal immune response where the immune system mistakenly targets a molecule called GlialCAM in the brain, because it resembles a part of EBV. This is known as molecular mimicry. The immune system has built-in mechanisms that normally destroy immune cells if they mistakenly attack our own bodies, but when EBV reactivates, B cells may multiply, leading to heightened immune activity in the brains of people with MS.

Genes that control the immune system and its interaction with EBV are important, as errors (mutations) in these genes may weaken the immune system's ability to combat EBV. Additionally, the relationship between EBV and other environmental factors like smoking, obesity, and vitamin D is not well understood.

Vaccination against EBV to prevent MS

EBV vaccines have the potential to prevent or reduce the number of people infected by EBV. To understand the impact of EBV vaccines on MS prevention, you would need to vaccinate a large portion of the population and monitor these individuals over decades. Not all researchers agree with EBV vaccination. They argue that if the vaccine does not lead to full EBV immunity, it could delay EBV infections to adolescence or early adulthood, thereby increasing the risk of infectious mononucleosis, which in turn could actually increase MS risk.

Treatment against EBV in people with MS

Targeting EBV activity in individuals with MS may be possible. Antiviral therapies like valomaciclovir have shown promise in trials for EBV-mediated infections. A Phase 2 clinical trial by Atara Biotherapeutics is testing a therapy which seeks and destroys EBV-infected B cells in progressive MS, with results expected in 2027. Some existing anti-CD20 treatments (like rituximab) may be effective by eliminating EBV-infected B cells, indicating a role for EBV in ongoing MS. Studies like these may help us better understand EBV's role in MS progression.

Conclusion

There is good evidence linking EBV infection to MS risk, but it is still an area of ongoing work. Using EBV vaccines to prevent MS is an interesting area of research. It is also important to understand how EBV influences MS disease activity, which may impact future MS treatments and prevention strategies.