

8. CAN EPSTEIN-BARR VIRUS CAUSE MULTIPLE SCLEROSIS?

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Introduction. Multiple sclerosis (MS) is a disabling chronic, autoimmune, inflammatory, neurodegenerative disease of multifactorial pathogenesis, where both, endogenous (i.e. genetic) and exogenous (i.e. environmental) factors play a specific causative role. Among the preventable environmental factors associated with MS, the cumulative evidence strongly points towards previous infection with Epstein-Barr virus (EBV), which recently became extremely important in light of new developments in MS prevention and treatment.

Aim of study. To provide a balanced assessment of evidence on EBV's role on MS etiopathogenesis and critically appraise the existing empirical studies. Key words: Epstein-Barr virus, multiple sclerosis, causality.

Methods and materials. Scoping review of articles published in English in 2000 - 2022 on human studies on EBV and MS had been extracted from OVID Medline and PubMed databases. Boolean search using keywords "Epstein-Barr virus", "infectious mononucleosis", "multiple sclerosis", "causality"/ or "etiology" yielded a pool of 267 abstracts that had been analysed for this review. Information about results, conclusions and gaps was extracted in a master spreadsheet for critical thematic analysis.

Results. Three directions of research on MS causality emerged: 1) strong association between MS and EBV infection; 2) synergistic effects of EBV infection with patients' residence at birth, vitamin D deficiency and smoking on MS progression; 3) genetic susceptibility and immune deregulation that triggers MS in EBV convalescents. As association does not mean causation as yet, to date there is no evidence of a single pathogen being accepted as a causal agent of MS. Hence, both genetic, environmental and the EBV factors are required to trigger the disease. Thus, despite the acknowledgement of being a leading predisposing factor for MS, the EBV infection is not a specific, necessary and sufficient agent capable of causing the disease alone. A notable gap in the literature is the lack of attention on whether a disruption of interaction between the EBV infection, genetic susceptibility and environmental risk factors at the population level would be capable of preventing the MS progression.

Conclusion. Given that emerging experimental developments in MS prevention (via new mRNA and nano-vaccines) and treatment (using new antivirals and immunotherapy) continue to strongly rely on a single dominant etiologic factor, more research is needed (i.e. observational prospective longitudinal trials) to assess the selective and cumulative impact of each and all causative factors on MS progression.