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**Association between EBV and CFS:**

There are multiple case definitions for chronic fatigue syndrome (CFS), and these have changed over time. The Institute of Medicine (IOM) states that symptoms must be present for at least 6 months with moderate, substantial, or severe intensity at least half of the time. In addition to fatigue other criteria include: post-exertional malaise, unrefreshing sleep, cognitive impairment, and ortho-static-related symptoms.

The prevalence of CFS is uncertain in part due to difficulty with establishing the diagnosis. Actual CFS represents a very small subset of those who complain of chronic fatigue. Multiple studies (surveys and prospective cohorts) cited on UpToDate estimate the crude point of prevalence of CFS as ranging from 75 to 267 cases per 100,000 and the point prevalence of chronic fatigue not meeting the criteria of CFS as much higher, ranging from 1775 to 6321 cases per 100,000.

Proposed etiologies of CFS are infections from EBV, retroviruses, other viruses, and bacteria; immune system dysfunction; endocrine-metabolic dysfunction; neutrally-mediated hypotension; depression; sleep disruption; and other potentially undetermined genetic causes.

Regarding the relationship between EBV and CFS, UpToDate had this to say:

“EBV received a great deal of attention in the mid-1980s as a possible etiologic agent for CFS. This hypothesis was based upon three observations. First, EBV persists for life and reactivates frequently, thereby affording the virus the biologic potential for chronic illness. Second, patients with CFS were often found to possess higher than expected titers of antibodies to EBV capsid and early antigens, or to lack antibodies to EBV nuclear antigens (EBNA), each suggestive of recent or active infection. Third, some patients clearly attributed the onset of their illness to a mononucleosis-like infection. Several studies have documented that CFS can develop following a well-documented case of mononucleosis or primary EBV infection not producing full-blown mononucleosis [[26,27](https://www-uptodate-com.york.ezproxy.cuny.edu/contents/clinical-features-and-diagnosis-of-myalgic-encephalomyelitis-chronic-fatigue-syndrome/abstract/26,27)]. Thus, primary infection with the virus appears capable of triggering the illness. However, there is no evidence that chronic EBV infection is responsible for ongoing, chronic symptoms.

Most studies have found higher levels of certain antibodies to EBV antigens in patients with CFS compared with matched healthy control subjects. However, that does not prove a causal relationship. Indeed, one possible explanation is that the higher level of antibodies against EBV is an epiphenomenon reflecting subtle immune dysfunction.”

Source: <https://www-uptodate-com.york.ezproxy.cuny.edu/contents/clinical-features-and-diagnosis-of-myalgic-encephalomyelitis-chronic-fatigue-syndrome?search=chronic%20fatigue%20syndrome&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1#H17480707>