

Chronic Fatigue Syndrome (Myalgic Encephalopathy)

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ABSTRACT: Chronic fatigue syndrome is associated with many misconceptions. In this review, we attempt to summarize various pathogenic hypotheses for this disease and discuss new lines of insight into causes and treatments of this baffling and most frustrating condition.

CHRONIC FATIGUE SYNDROME (CFS) has a long history of medical interest. Over the years it has had numerous other names, including chronic Epstein-Barr virus syndrome, chronic mononucleosis syndrome, postviral fatigue syndrome, epidemic myalgic encephalomyelitis, and most recently, "yuppie flu." Even Hippocrates recognized the muscular fatigue associated with deconditioning. In 1869, Beard¹ noted that nervous energy can become exhausted and proposed the term "neurasthenia." Every century brought in new symptoms, names, and diagnostic criteria for this debilitating illness, but its etiology and pathogenesis remain unknown. In 1988 the case definition of CFS was first introduced by the Centers for Disease Control (CDC) in Atlanta, Georgia.² Since then there have been numerous attempts to better define CFS, especially in Australia and Great Britain.^{3,4} Most recently the CDC, the National Institutes of Health (NIH), and the International Chronic Fatigue Syndrome Study Group proposed new diagnostic criteria.⁵ The 1988 CDC criteria for the diagnosis of CFS are presented in Table 1, and the 1994 revised criteria are shown in Table 2. The medical illnesses in the differential diagnosis of CFS are listed in Table 3.⁶

Chronic fatigue syndrome is characterized by the sudden onset of debilitating fatigue together with symptoms such as fever, sore throat, painful lymph nodes, weakness, mus-

cle aches, headache, depression, sleep disturbance, memory difficulties, and confusion. These symptoms can persist from 6 months to many years and can dramatically reduce the quality of life. Since the primary symptoms are muscular fatigue and pain, along with symptoms of encephalopathy (lethargy and cognitive difficulties), it has been recently proposed that CFS be renamed myalgic encephalopathy.

The most common age for onset of CFS is between 20 and 40 years. The female-male ratio is 3:1. The mean time to recovery is about 2 years, but many individuals have CFS for many years. All socioeconomic groups are represented, though the majority of patients are middle class. The incidence of CFS may be as high as 0.3% in the United States,⁷ but recent epidemiologic studies being conducted in the Chicago area (studies in which this Center is actively involved) suggest that the incidence may be significantly higher.⁸ Several pathogenetic hypotheses have been advanced to explain this illness: viral, immunologic, psychiatric, and neurologic.

VIRAL HYPOTHESIS

Much emphasis has been placed on a viral etiology for CFS. The finding that CFS occasionally follows an episode of infectious mononucleosis and evidence of high titers of antibodies to Epstein-Barr virus (EBV) antigen led to suggestions that EBV infection is the cause of CFS. Atypical profiles of antibody responses to EBV were found in many cases.^{9,12} Controlled studies of seroepidemiology¹²⁻¹⁵ and antiviral therapy¹⁶ have shown that EBV infection cannot be the sole explanation for most cases of CFS. No correlation has been found between serologic parameters of EBV activity

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