

Review article

Chronic fatigue syndrome – revisited

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Abstract:

Chronic fatigue syndrome (CFS) is a common and disabling problem; although most likely of biopsychosocial origin. The nature of the pathophysiological components remains unclear. It is an illness characterized by persistent and relapsing fatigue, often accompanied by numerous symptoms involving various body systems. The etiology of CFS remains unclear. Celiac disease can present with neurological symptoms in the absence of gastrointestinal symptoms; therefore, celiac disease should be included in the differential diagnosis of CFS.

Key Words: Chronic fatigue syndrome (CFS); Celiac disease.

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Introduction:

Chronic fatigue syndrome is a complicated disorder characterized by extreme fatigue that can't be explained by any underlying medical condition. The fatigue may worsen with physical or mental activity, but doesn't improve with rest. Chronic fatigue syndrome (CFS) myalgic encephalomyelitis (or encephalopathy)(ME) is a relatively common illness. CFS may also be referred to as myalgic encephalomyelitis (ME), post-viral fatigue syndrome (PVFS), chronic fatigue immune dysfunction syndrome (CFIDS). The physical symptoms can be as disabling as multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, congestive heart failure and other chronic conditions. Many different potential aetiologies for CFS/ME – including neurological, endocrine, immunological, genetic, psychiatric and infectious – have been investigated, but the diverse nature of the symptoms can not yet be fully explained. Instead, it lasts a long time and limits ability to do ordinary daily activities. Prevalence of chronic fatigue syndrome range from 0.007% to 2.8% in the general adult population and from 0.006% to 3.0% in primary care. Chronic fatigue syndrome also occurs in children and adolescents but apparently at a lower rate. Most persons of chronic fatigue syndrome are 30–40 years of age, with a female preponderance^{1,2,3,4}

Pathophysiology^{5,6,7,8}

The pathogenesis of chronic fatigue syndrome is currently unknown despite extensive research. Possible etiological characteristics of the disease include oxidative

etic infection by viruses and pathogenic bacteria, hypothalamic pituitary-adrenal axis abnormalities, immune dysfunction as well as psychological and psychosocial factors. Biometrical genetic modeling suggested that additive genetic factors and common environmental effects each accounted for more than 40% of the variance in liability for chronic fatigue syndrome-like illness, familial predisposition for chronic fatigue of varying intensities, with both genetic and environmental contributions. Many theories for the pathophysiology of chronic fatigue syndrome have been suggested, with earlier theories focusing on the prominence of symptoms that suggested an acute viral illness or a psychiatric disorder. Subsequent investigations have suggested abnormalities in rather disparate domains, including brain structure and function, neuro-endocrine responses, sleep architecture, immune function, virological studies, exercise capacity, and divergent psychological profiles. Despite the demonstration of abnormalities across these and other domains, such findings remain largely isolated observations. It is possible that chronic fatigue syndrome is a heterogeneous syndrome with different patho-physiological anomalies manifesting with the same or similar symptoms. Indeed, some elements may predispose an individual to develop chronic fatigue syndrome, others may precipitate the illness, and still others perpetuate the disorder^{9,10}.

Causes & Risk Factors:

Viral infections include Epstein-Barr, human herpes virus 6 and mouse leukemia viruses and abnormal blood levels of hormones produced

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in the hypothalamus, pituitary gland or adrenal gland. Genetic studies suggest that additive genetic factors and common environmental effects each accounted for more than 40% of the variance in liability for chronic fatigue syndrome-like illness. These results should be noted cautiously because of the potential for differential ascertainment bias by zygosity in volunteer twin subjects. However, the findings suggest a familial predisposition for chronic fatigue of varying intensities, with both genetic and environmental contribution^{12,13}. Several symptoms seen in chronic fatigue syndrome patients—including fatigue, impaired concentration, memory and attention and headache—suggest that the central nervous system may be involved in the etiology of the syndrome. In fact, such studies showed a central nervous system (CNS) link to chronic fatigue syndrome by means of structural and functional neuro-imaging, cognitive testing, neuro-peptide assays, and autonomic assessment^{14,15}. Neuropsychiatric impairments include the poorer performance of subjects with chronic fatigue syndrome on complex attention and information related tasks. In general, however, persons with chronic fatigue syndrome appear to possess normal cognitive and global intellectual abilities^{16,17,18}. Neuroendocrine studies reported that abnormalities in the hypothalamic-pituitary-adrenal (HPA) axis and serotonin pathways have been identified in chronic fatigue syndrome patients, suggesting an altered physiological response to stress. About one-third of patients with chronic fatigue syndrome have been shown to exhibit hypocortisolism, which appears to originate from a CNS source rather than a primary adrenal site^{19,20,21}.

Symptoms^{22,23}

Fatigue is the hallmark of chronic fatigue syndrome. Patients often report excellent pre-illness physical fitness and energy and an abrupt onset of fatigue, typically with a flu-like illness. Many patients also often experience anorexia, nausea, drenching night sweats, dizziness, and intolerance to alcohol, impaired memory or concentration.

Other manifestations include (a) post-exertional malaise, where physical or mental exertions bring on extreme, prolonged exhaustion and sickness. (b) unrefreshing sleep (c) muscle pain (myalgia) (d) pain in multiple joints (arthralgia) (e) headaches of a new kind or greater severity (f) sore throat, frequent or recurring (g) tender lymph nodes (cervical or axillary)

Diagnosis^{24,25,26}

Diagnostic criteria To meet the diagnostic criteria of chronic fatigue syndrome, a person must have unexplained, persistent fatigue for six months or more, along with at least four of the following signs and symptoms:

- (a) Loss of memory or concentration
- (b) Sore throat
- (c) Enlarged lymph nodes in neck or armpits
- (d) Unexplained muscle pain
- (e) Pain that moves from one joint to another without swelling or redness
- (f) Headache of a new type, pattern or severity
- (g) Unrefreshing sleep
- (h) Extreme exhaustion lasting more than 24 hours after physical or mental exercise

Investigations include; A full history (including exacerbating and alleviating factors, sleep disturbance and intercurrent stressors) should be taken, and a physical examination and assessment of psychological well being should be carried out.

Laboratory investigations include: urinalysis for protein, blood and glucose, full blood count, urea and electrolytes, liver function, thyroid function, erythrocyte sedimentation rate or plasma viscosity, C-reactive protein, random blood glucose, serum creatinine, screening blood tests for gluten sensitivity, serum calcium and creatine kinase.

Treatment^{27,28,29}

- (1) Behavioural programme; The development and persistence of chronic fatigue can be understood using a cognitive-behavioural model. This is used to explain the observed progression from the avoidance of most forms of activity during the initial acute illness, which is both necessary and adaptive, to chronic avoidance behaviours, which are maladaptive. This model has been successfully applied to chronic pain. (a) Regular exercise, with which the patient can feel comfortable. (b) A graded increase in exercise, involving walking, swimming etc. (c) Encouragement of exercises such as yoga and callisthenics. (d) Gradual exposure to all avoided activity. (e) Cognitive work to break the association between increase in symptoms and stopping or avoiding the activity. (f) Further cognitive strategies involving alternative explanations for symptoms.
- (2) Healthy diet; bread, rice, potato, fruits, vegetables, milk and milk products, meat and fish.
- (3) Sleep management techniques; good sleeping habits, short-term trial of sedating antihistamines.
- (4) Medications to reduce pain, discomfort, and fever.
- (5) Anti-anxiety drugs. Conventional treatments such as relaxation and anxiety management may all prove successful.
- (6) Antidepressant drugs.; MAO inhibitors, TCA nortriptyline A 60 mg-per day

dose significantly reduced CFS symptoms.

Conclusion:

Chronic fatigue syndrome is unlikely to be caused by a single agent. Findings suggest that physiological and psychological factors work simultaneously to predispose an individual to the

illness and to precipitate the illness. The assessment and treatment of chronic fatigue syndrome should be multidimensional and according to the needs of the individual patient

Conflict of interest: None

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