SECTION 4 CHRONIC FATIGUE SYNDROME

464e Chronic Fatigue Syndrome

Gijs Bleijenberg, Jos W. M. van der Meer

DEFINITION

Chronic fatigue syndrome (CFS) is a disorder characterized by persistent and unexplained fatigue resulting in severe impairment in daily functioning. Besides intense fatigue, most patients with CFS report concomitant symptoms such as pain, cognitive dysfunction, and unrefreshing sleep. Additional symptoms can include headache, sore throat, tender lymph nodes, muscle aches, joint aches, feverishness, difficulty sleeping, psychiatric problems, allergies, and abdominal cramps. Criteria for the diagnosis of CFS have been developed by the U.S. Centers for Disease Control and Prevention (Table 464e-1).

EPIDEMIOLOGY

CFS is seen worldwide, with adult prevalence rates varying between 0.2% and 0.4%. In the United States, the prevalence is higher among women (~75% of cases), members of minority groups (African and Native Americans), and individuals with lower levels of education and occupational status. The mean age of onset is between 29 and 35 years. Many patients probably go undiagnosed and/or do not seek help.

ETIOLOGY

There are numerous hypotheses about the etiology of CFS; there is no definitively identified cause. Distinguishing between predisposing, precipitating, and perpetuating factors in CFS helps to provide a framework for understanding this complex condition (Table 464e-2).

Predisposing Factors Physical inactivity and trauma in childhood tend to increase the risk of CFS in adults. Neuroendocrine dysfunction may be associated with childhood trauma, reflecting a biological correlate of vulnerability. Psychiatric illness and physical hyperactivity in adulthood raise the risk of CFS in later life. Twin studies suggest a familial predisposition to CFS, but no causative genes have been identified.

Precipitating Factors Physical or psychological stress may elicit the onset of CFS. Most patients report an infection (usually a flulike illness or infectious mononucleosis) as the trigger of their fatigue. Relatively high percentages of CFS cases follow Q fever and Lyme disease. However, no differences in Epstein-Barr virus load and immunologic reactivity were found between individuals who developed CFS and those who did not. While antecedent infections are associated with CFS, a direct microbial causality is unproven and unlikely. One study identified a murine leukemia virus–related retrovirus (XMRV); however, several subsequent studies have established this virus as a laboratory artifact. Patients also often report other precipitating somatic events such as serious injury, surgery, pregnancy, or childbirth. Serious life events, such as the loss of a loved one or a job, military combat, and other stressful situations, may also precipitate CFS. One-third of all patients cannot recall a trigger.

Perpetuating Factors Once CFS has developed, numerous factors may impede recovery. Physicians may contribute to chronicity by ordering unnecessary diagnostic procedures, by persistently suggesting psychological causes, and by not acknowledging CFS as a diagnosis.

A patient's focus on illness and avoidance of activities may perpetuate symptoms. A firm belief in a physical cause, a strong focus on bodily sensations, and a poor sense of control over symptoms may also prolong or exacerbate the fatigue and functional impairment. In most patients, inactivity is caused by negative illness perceptions rather than by poor physical fitness. Solicitous behavior of others may reinforce a patient's illness-related perceptions and behavior. A lack of social support is another known perpetuating factor.

PATHOPHYSIOLOGY

The pathophysiology of CFS is unclear. Neuroimaging studies have found that CFS is associated with reduced gray matter volume, which in turn is associated with a decline in physical activity; these changes have been partially reversed following cognitive behavioral therapy (CBT). In addition, functional MRI data have suggested that abnormal patterns of activation correlate with self-reported problems with information processing. Neurophysiologic studies have shown altered CNS activation patterns during muscle contraction.

Evidence for immunologic dysfunction is inconsistent. Modest elevations in titers of antinuclear antibodies, reductions in immunoglobulin subclasses, deficiencies in mitogen-driven lymphocyte proliferation, reductions in natural killer cell activity, disturbances

TABLE 464e-1 DIAGNOSTIC CRITERIA FOR CHRONIC FATIGUE SYNDROME

Characteristic Persistent or Relapsing Unexplained Chronic Fatigue
Fatigue lasts for at least 6 months.
Fatigue is of new or definite onset.
Fatigue is not the result of an organic disease or of continuing exertion.
Fatigue is not alleviated by rest.
Fatigue results in a substantial reduction in previous occupational, educational, social, and personal activities.
Four or more of the following symptoms are concurrently present for 6 months: impaired memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, pain in several joints, new headaches, unrefreshing sleep, or malaise after exertion.
Exclusion Criteria
Medical condition explaining fatigue
Major depressive disorder (psychotic features) or bipolar disorder
Schizophrenia, dementia, or delusional disorder
Anorexia nervosa, bulimia nervosa
Alcohol or substance abuse
Severe obesity (body mass index >40)

TABLE 464e-2 PREDISPOSING, PRECIPITATING, AND PERPETUATING FACTORS IN CHRONIC FATIGUE SYNDROME

Predisposing Factors
Childhood trauma (sexual, physical, emotional abuse; emotional and physical neglect)
Physical inactivity during childhood
Premorbid psychiatric illness or psychopathology
Premorbid hyperactivity
↓
Precipitating Factors
Somatic events: infection (e.g., mononucleosis, Q fever, Lyme disease), surgery, pregnancy
Psychosocial stress, life events
↓
Perpetuating Factors
Non-acknowledgment by physician
Negative self-efficacy
Strong physical attributions
Strong focus on bodily symptoms
Fear of fatigue
Lack of social support
Low physical activity pattern