

CHRONIC FATIGUE SYNDROME

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Chronic fatigue syndrome, or CFS, is a severe, incapacitating fatigue lasting for six months or more, that is not improved by bed rest and that may be exacerbated by physical or mental activity. It is an all-encompassing fatigue that results in a dramatic decline in both activity level and stamina. This syndrome is not new and has a long history. CFS is diagnosed on the basis of symptoms. Although pathophysiological abnormalities exist across many domains, but several lines of research suggest that it may be distinct from psychiatric disorder. The nature of the symptoms, however, can help clinicians differentiate CFS from other illnesses. Center of Diagnosis has developed diagnostic criteria as based upon symptoms & exclusion of other illness. Treatment of CFS is symptom based and includes pharmacological, cognitive and behavioral therapy, with lifestyle exercise and lifestyle management therefore the assessment and treatment of CFS should be multidirectional and tailored to the need of patients.

Key words: Chronic fatigue syndrome, Pain, Stress, Fibromyalgia, Sleep.

INTRODUCTION

CHRONIC fatigue syndrome, or CFS, is a debilitating and complex disorder characterized by profound fatigue lasting for six months, that is not improved by bed rest and that may be worsened by physical or mental activity [1]. Persons with CFS most often function at a substantially lower level of activity than they were capable of before the onset of illness. In addition to these key defining characteristics, patients report various nonspecific symptoms, including weakness, muscle pain, impaired memory and/or mental concentration, insomnia, and post-exertional fatigue lasting more than 24 hours. In some cases, CFS can persist for years. This syndrome is not new, but has a long history. In 19th century it attracted the diagnosis of neurasthenia, but by 20th century it fell to disuse. It is probable that since that time patients have continued to present to doctors with similar symptoms but have been diagnosed with conditions such as vapor, effort syndrome, hyperventilation syndrome, chronic brucellosis, fibromyalgia syndrome, myalgic encephalomyelitis, multiple chemical sensitivities, and chronic mononucleosis and Chronic Epstein Virus Infection [2,3]. Although cause or causes of CFS have not been identified and no specific diagnostic tests are available but the US Center of Diagnosis has developed diagnostic criteria as based upon symptoms and exclusion of

other illness [4].

ETIOLOGY

The diverse name of the syndrome reflects equally numerous and controversial hypotheses about the etiology. However, a number of psychological and biological factors have been identified that play an important role in the onset and perpetuation of the illness. It is likely that different and perhaps multiple factors operate in different cases [4,5].

(a) Infection

Patients frequently give a history suggestive of acute infection at the outset. Fatigue states lasting several months can follow infection such as Epstein Barr virus and Q fever. Infection may therefore trigger chronic fatigue syndrome, but available evidence does not support the hypothesis that infection is the cause of CFS [6,7].

(b) Immune dysfunction

Minor immune abnormalities have been detected in a proportion of patients. Cytokines can cause fatigue. However, no consistent immune abnormality or causal link of these symptoms has been established in the patient with CFS. The role of immune factor remains of interest but is unclear [8].

(c) Stress and emotional disorder

More than half the patient seen in the hospital clinics who meet criteria for CFS also meet the criteria for anxiety and depressive disorders. Therefore, it has been suggested that at least some cases of CFS are due to emotional disorder that is expressed somatically. This is undoubtedly true in some cases, but in many others either absent or in adequate explanation of illness.

(d) Psychological and behavioral factors

There is an evidence that Psychological and behavioral factors play an important role in perpetuating CFS. They include misconception about the nature of illness, excessive avoidance of physical activity so that the person become inactive, repeated seeking of medical care and failure to respond to continuing psychological and social problem [9].

(e) Inactivity

Some patients of CFS are profoundly inactive. This may lead to muscle wasting, changes in cardiovascular response to exertion and postural hypertension. The consequent intolerance of activity may perpetuate the illness.

(f) Dysfunction of central nervous system

Although abnormalities in test of cognitive function and abnormalities in neuroendocrine test and functional neuroimaging have been found but specificity and clinical utility of such test remains unestablished [10].

(g) Sleep disorder

Various sleep abnormalities have been found in patients with CFS. They include both specific disorders like sleep apnoea syndrome and non specific abnormality such as fragmentation of sleep. They may contribute to day time fatigue in at least some cases [11].

EPIDEMIOLOGY

Researchers continue to explore possible causes, risk factors and triggering factors for CFS. Many questions remain, but there are some characteristics that may help health care practitioners identify patients who are most at risk for CFS. The stereotype that CFS is an illness that primarily affects white, middle-class, well-educated, professional women are incorrect.

- CFS occurs more frequently in women than in men,

although people of both sexes can develop the disease.

- The illness occurs most often in people aged 40-59, but people of all ages can get CFS. CFS is less common in children than in adults. Studies suggest that CFS is more prevalent in adolescents than in children under the age of 12 [12].
- CFS occurs in all ethnic groups and races, and in countries around the world. In the United States, CFS is at least as common among African Americans and Hispanics as it is among Caucasians [13,14].
- People of all income levels can develop CFS, although there is evidence that it is more common in lower-income than in affluent individuals.
- CFS is sometimes seen in members of the same family, but there is no evidence that it is contagious. Instead, there may be a familial predisposition or a genetic link. Further research is needed to explore these possible relationships.

PATHOGENESIS

Despite intensive studies and research, the cause of CFS remains unknown. Different infections and physiologic and psychological causes have been considered, and the search continues. Much of the ongoing research into a cause has centered on the role of the immune, endocrine and nervous system in CFS. More recently, interactions among these factors are under evaluation. Genetic and environmental factors may play a role in developing and/or prolonging the illness, although more research is needed to confirm this. CDC is applying cutting edge genomic and proteomic tools to understand the origins and pathogenesis of CFS. CFS is not caused by depression, although the two illnesses often coexist, and many patients with CFS have no psychiatric disorder [5,15].

CLINICAL FEATURES

Chronic fatigue syndrome shares symptoms with many other disorders. Fatigue, for instance, is found in hundreds of illnesses, and 10% to 25% of all patients who visit general practitioners complain of prolonged fatigue [16,17]. The nature of the symptoms, however, can help clinicians differentiate CFS from other illnesses.

PRIMARY SYMPTOMS

As the name chronic fatigue syndrome suggests, this illness is accompanied by fatigue. However, it is not the kind of fatigue patients experience after a particularly busy day or week, after a sleepless night or after a stressful event. It is a severe, incapacitating fatigue lasting for more than 6 months that has not improved by bed rest and that may be exacerbated by physical or mental activity. It is an all-encompassing fatigue that results in dramatic decline in both activity level and stamina. People with CFS function at a significantly lower level of activity than they were capable of prior to becoming ill. The illness results in a substantial reduction in occupational, personal, social or educational activities. These symptoms include (Table 1 & Fig. 1):

- cognitive dysfunction, including impaired memory or concentration
- postexertional malaise lasting more than 24 hours (exhaustion and increased symptoms) following physical or mental exercise
- unrefreshing sleep

Table 1: Specific Symptoms Reported by Patients with Chronic Fatigue Syndrome [18].

Symptom	Percentage
Fatigue	100
Difficulty concentrating	90
Headache	90
Sore throat	85
Tender lymph nodes	80
Muscle aches	80
Joint aches	75
Feverishness	75
Difficulty sleeping	70
Psychiatric problems	65
Allergies	55
Abdominal cramps	40
Weight loss	20
Rash	10
Rapid pulse	10
Weight gain	5
Chest pain	5
Night sweats	5

Source: From SE Straus: J Infect Diseases 157: 405, 1988.

- joint pain (without redness or swelling)
- persistent muscle pain
- headaches of a new type or severity
- tender cervical or axillary lymph nodes
- sore throat

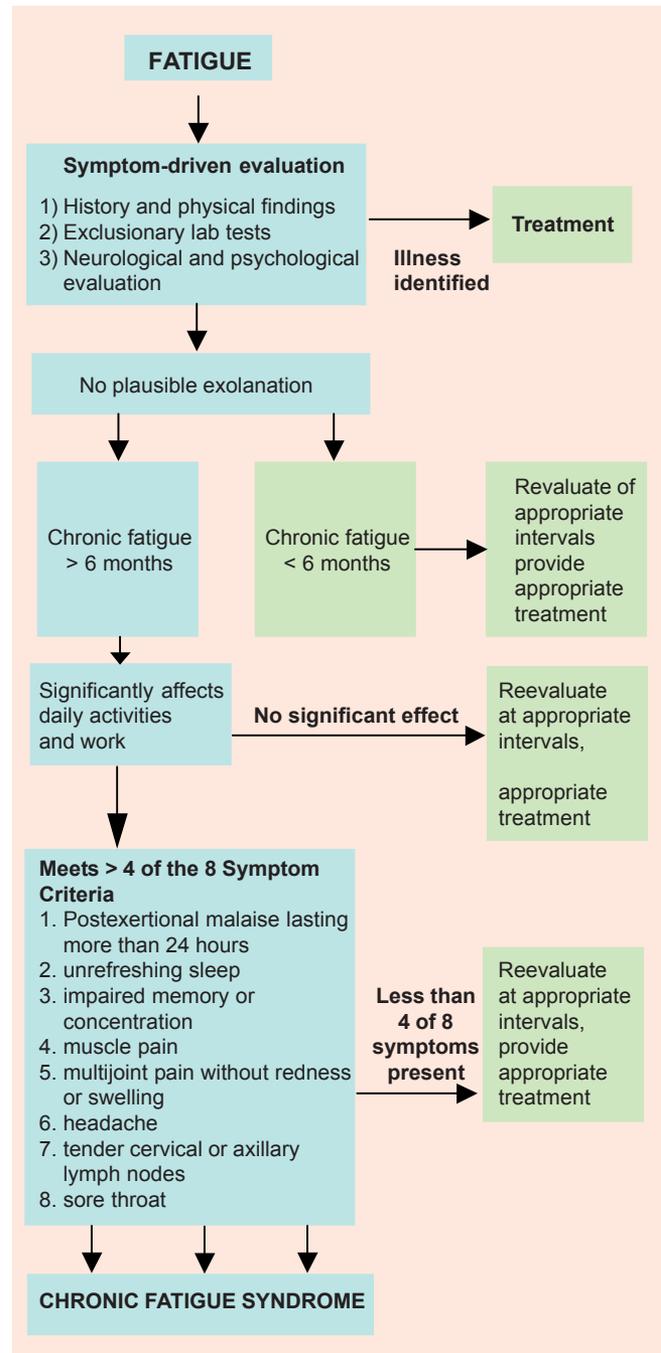


Fig. 1. DIAGNOSTIC MODEL. The 1994 International Case Definition forms the basis for a reliable diagnostic algorithm for CFS, particularly in adults. Clinicians assessing adolescents for pediatric CFS should exercise judgment based on the course of the illness and the patient's medical history.

Other common symptoms

In addition to the eight primary defining symptoms of CFS, a number of other symptoms have been reported by some CFS patients. The frequency of occurrence of these symptoms varies among patients. These symptoms include:

- irritable bowel, abdominal pain, nausea, diarrhea or bloating
- chills and night sweats
- brain fog
- chest pain

Visual disturbances (blurring, sensitivity to light, eye pain or dry eyes) allergies or sensitivities to foods, alcohol, odors, chemicals, medications or noise difficulty maintaining upright position (orthostatic instability, irregular heartbeat, dizziness, balance problems or fainting), psychological problems (depression, irritability, mood swings, anxiety, panic attacks) jaw pain, weight loss or gain.

Diagnosis of CFS (CDC criteria)

To be diagnosed with CFS, patients must experience significant reduction in their previous ability to perform one or more aspects of daily life (work, household, recreation or school). And by definition, all people suffering from CFS experience severe, all-encompassing mental and physical fatigue that is not relieved by rest and that has lasted longer than six months. The fatigue is accompanied by characteristic symptoms that may be more bothersome to patients than the fatigue itself.

Clinicians should consider a diagnosis of CFS if these two criteria are met:

- (i) Unexplained, persistent fatigue that is not due to ongoing exertion, is not substantially relieved by rest, is of new onset (not lifelong) and results in a significant reduction in previous levels of activity.
- (ii) Four or more of the following symptoms are present for six months or more:
 - Impaired memory or concentration
 - Postexertional malaise
 - Extreme, prolonged exhaustion and exacerbation of symptoms following physical or mental exertion
 - Unrefreshing sleep

- Muscle pain
- Multijoint pain without swelling or redness adults
- Headaches of a new type or severity
- Sore throat that is frequent or recurring
- Tender cervical or axillary lymph nodes [1-4,15,19,20]

CLINICAL COURSE

The severity of CFS varies from patient to patient, with some people able to maintain fairly active lives. By definition, however, CFS significantly limits work, school and family activities.

While symptoms vary from person to person in number, type and severity, all CFS patients are functionally impaired to some degree. CDC studies show that CFS can be as disabling as multiple sclerosis, lupus, rheumatoid arthritis, heart disease, end-stage renal disease, chronic obstructive pulmonary disease (COPD) and similar chronic conditions.

CFS often follows a cyclical course, alternating between periods of illness and relative well-being. Some patients experience partial or complete remission of symptoms during the course of the illness, but symptoms often reoccur. This pattern of remission and relapse makes CFS especially hard for patients and their health care professionals to manage. Patients who are in remission may be tempted to overdo activities when they are feeling better, which can exacerbate symptoms and fatigue and cause a relapse. In fact, postexertional malaise is a hallmark of the illness.

The percentage of CFS patients who recover is unknown, but there is some evidence to indicate that the sooner symptom management begins, the better the chance of a positive therapeutic outcome. This means early detection and treatment are of utmost importance. CDC research indicates that delays in diagnosis and treatment may complicate and prolong the clinical course of the illness.

TREATMENT OPTIONS

Managing chronic fatigue syndrome can be as complex as the illness itself. There is no cure yet, no prescription drugs have been developed specifically for CFS, and symptoms vary considerably over time. It may take some time to find a combination of traditional and alternative therapies that works for the patient, but it is important not to delay symptom management. For

instance, untreated sleep problems can actually make other symptoms-like pain and memory problems-worse.

A multidisciplinary team of health care professionals working together to develop this individualized care plan is the key to manage CFS. This team might include physicians and other primary care professionals, mental health professionals, rehabilitation specialists and physical or exercise therapists. Other professionals, like a sleep therapist or dietician, can be added as needed

PHARMACOLOGICAL TREATMENT

There are many over-the-counter and prescription drug therapies that can be used to treat CFS symptoms. Health care professionals can:

- Use as few drugs as possible. For instance, tricyclic antidepressants help with both sleep and pain.
- Reduce the initial dose because many CFS patients are very sensitive to medications, particularly agents acting on the central nervous system. Try prescribing a fraction of the usual recommended dose to start and gradually increase as necessary and as tolerated.
- Monitor drug side effects like weight gain, secondary fatigue, daytime sedation, cognitive problems and sleep disturbance.
- Recognize that unrefreshing sleep is a case-defining symptom, and the vast majority of CFS patients complain of some form of sleep-related symptoms. Sleep deprivation or disruption may cause or exacerbate other symptoms such as fatigue, impaired cognition, headaches and joint pain, so treating sleep problems should occur early in the treatment program.
- Advise patients to practice standard sleep hygiene techniques. Light exercise and stretching at least four hours before bedtime can also improve sleep.
- Set up a consult with a sleep specialist or schedule a sleep study for a CFS patient if patients identify problems with their sleep.
- Random use of sleep medications may prolong identification of a sleep disorder or induce additional sleep problems. Sleep medication should be based on the patient's responses to a thorough sleep history if a sleep consult is not readily available [21].
- Consider pharmaceuticals if sleep hygiene is not successful. Initial medications to consider are simple antihistamines or over-the-counter sleep products. If this is not beneficial, then start with a prescription sleep medicine in the smallest possible dose. Both sleep-initiating and sleep-sustaining drugs may be indicated for some CFS patients [4].
- Pain therapy should be limited to simple analgesics like acetaminophen, aspirin or NSAIDs. Narcotics should only be considered by a pain specialist after careful identification of patient-specific pain pathways and testing for efficacy of specific agents [19].
- Include nonpharmacological modalities and alternative therapies in your pain management program.
- Treat depression when it is present. Depression is a common comorbid illness in patients with CFS, with as many as half of patients developing secondary depression as a result of the illness. Careful evaluation of the patient is required in order to identify an exacerbation of either illness before therapy can be undertaken. Treating depression can reduce anxiety and stress, and assist in relief of symptoms [10].
- Use caution in prescribing antidepressant drugs. Antidepressants of various classes may act on other CFS symptoms or cause side effects [7].
- There are brief psychiatric screening tools available that can be administered and scored in the primary care setting. Refer patients to a mental health professional if indicated.
- Be alert for symptoms of orthostatic instability, in particular frequent dizziness and light headedness. Patients should be referred for evaluation by a cardiologist or a neurologist to confirm orthostatic problems before initiating treatment.
- Suggest coping and adaptive techniques for cognitive difficulties like memory and concentration problems. Memory aids, such as organizers, schedulers and written resource manuals, are usually recommended. Stimulating the mind with puzzles, word games, card games and other activities can also be helpful.
- Refer CFS patients with disabling cognitive problems to behavioral health professionals for specific techniques to help them function better.

- Prescribe stimulants only for diagnosed conditions. Mild stimulants may be helpful for some CFS patients, but stronger stimulants can precipitate the “push-crash cycle” and cause relapse (see Managing Activity).

Nutritional and herbal supplements

It is not uncommon for people with CFS to take numerous nutritional supplements and vitamins as they desperately seek symptom relief.

- Guide patients in selecting supplements. While there have been few clinical trials to support the use of particular supplements, some may be efficacious. Studies have investigated or reported the use of supplements, including oral NADH, high doses of vitamin B₁₂, essential fatty acids, vitamin C and coenzyme Q10. These studies show inconsistent results, but symptom improvement was reported in some subjects [22].
- Advise your patients to avoid herbal remedies like comfrey, ephedra, kava, germander, chaparral, bitter orange, licorice root, yohimbe and any other supplements that are potentially dangerous.

Cognitive behavioral therapy (CBT)

Cognitive behavioral therapy, or CBT, is often prescribed to help chronically ill patients cope with illness and develop behaviors and strategies that help alleviate symptoms. It has been successful in helping patients with cardiovascular disease, diabetes and cancer, and recent studies indicate that CBT can be useful in treating some CFS patients. CBT is frequently prescribed as part of therapeutic process; it help patients learn to manage activity levels, stress and symptoms. Optimally, CBT can help you better adapt to the impact of CFS and improve your level of function and quality of life [23].

Professional counseling

Consulting a trained professional will help most patients build effective coping skills. A supportive counselor can help patient to cope with the prospects of long-term illness, as well as the anxiety, depression, grief, anger and guilt that often accompany chronic illness. Problem-solving techniques and standard psychotherapy and counseling methods, can help patient work through these issues. In some cases, a therapist may recommend a combination of medication and psychotherapy. Because chronic illnesses like CFS

impact the entire family, not just the patient, you may want to consider family education and counseling. Consulting a behavioral health professional may be helpful to address changes in family dynamics related to living with CFS [24].

MANAGING ACTIVITY AND EXERCISE

Avoiding extremes

For patients with CFS, learning to manage activity levels is key to managing the illness itself. This requires a new way of defining exercise. While vigorous aerobic exercise is beneficial for many chronic illnesses, CFS patients can not tolerate traditional exercise routines. Exercise programs aimed at optimizing aerobic capacity are not recommended.

The majority of people with CFS are affected by postexertional malaise, which is defined as an exacerbation of symptoms following physical or mental exertion, with symptoms typically worsening 12-48 hours after activity and lasting for days or even weeks. It is important, however, not to avoid activity and exercise altogether. Such avoidance leads to serious deconditioning and can actually worsen other symptoms. It is also important not to engage in an endless “push-crash” cycle in which patients do too much, crash, rest, start to feel a little better, do too much again, and so on. Instead, CFS patients must learn to pace activities and work with their health care professionals to create an individualized exercise program that focuses on interval activity or graded exercise [25,26]. The goal is to balance rest and activity to avoid both deconditioning from lack of activity and flare-ups of illness due to overexertion. Effective activity management may help improve mood, sleep, pain and other symptoms so patients can function better and engage in activities of daily living.

Prognosis

The prognosis for functional recovery is relatively good for patients seen in the general practice. It is poor for those sever enough to be referred to hospital clinics

- CFS affects each individual differently. Some people with CFS remain homebound and others improve to the point that they can resume work and other activities, even though they continue to experience symptoms [27].
- Recovery rates for CFS are unclear. Improvement rates varied from 8% to 63% in a 2005 review of

published studies, with a median of 40% of patients improving during follow-up. However, full recovery from CFS may be rare, with an average of only 5% to 10% sustaining total remission [28].

Prevention

As the cause is unknown, there is no specific primary prevention. Secondary prevention is important as it is likely that good early management and avoidance of iatrogenesis will reduce the risk.

CONCLUSION

CFS is an illness characterized by incapacitating fatigue along with cognitive, musculoskeletal, and sleep symptoms. Lack of diagnostic markers and absence of any specific diagnostic tests, makes the diagnosis of patient suffering from CFS a challenging task, but the diagnostic criteria provided by the CDC remains a hallmark for the diagnosis.

Clinical studies and researches suggest that CFS is a heterogeneous and complex condition with multifactor etiology and because of this there is no instant cure of CFS. Hence, further studies are needed to establish the role of genetic and environment factor in development of CFS. Symptom based pharmacological therapy, cognitive behavioral therapy and exercise program can greatly help in improving the patient condition such as major depression, pain, sleep apnea and improve the life of patient. The complexity and heterogeneity of CFS results in a unique manifestation in every patient, hence the treatment should be individualized for each patient built on patient-physician trust and respect.

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