

INTRODUCTION

Chronic fatigue syndrome (CFS) is a disorder characterized by persistent, incapacitating fatigue of sudden or definite onset unrelieved by rest with associated symptoms which is not explained by any medical or psychiatric illness. The term 'chronic fatigue syndrome' and the criteria for diagnosing the disease were introduced in 1988, however over the past two centuries, illnesses presenting with outbreaks of chronic fatigue, and constellation of other symptoms similar to this disease were identified as neurasthenia, myalgic encephalomyelitis, 'Raggedy Ann syndrome', Royal Free disease and chronic infectious mononucleosis.

EPIDEMIOLOGY

In U. S. the prevalence rates in adults vary between 0.2 – 0.4%. A study from UK reported a 9% prevalence whereas V. Patil et al reported 10% prevalence in women in their study done in Goa. Common age of presentation is between 30 -40 years although it has been reported in children and adolescents too. Cases are reported from all parts of the world. More common in females, in less educated and low socioeconomic strata.

ETIOPATHOGENESIS

The exact etiology and pathogenesis of chronic fatigue syndrome is still an enigma. There is a complex interplay between predisposing, perpetuating and precipitating factors which may vary from individual to individual. Various hypotheses have been given for understanding the pathogenesis. These are based on clinical studies focussing on one or more factors associated with this condition. However these are statistical associations and a consistent causal relationship with any factor has not been established in large proportion of cases. Following factors have been identified -

Genetic

Clustering of CFS cases can occur in a single family but it has not been proven contagious. Twin studies indicate a familial predisposition but no gene /genes responsible have been identified.

Immunologic

- Modest elevation of ANA
- reduced immunoglobulin levels,
- Abnormal natural killer cell cytotoxicity,
- increase immune activation markers,
- greater numbers of CD16⁺/CD3⁻ natural killer cells

None of these are present as a consistent feature in most patients nor does it correlate with severity of disease.

Infections

Multiple infectious agents have been linked to CFS. Borna disease virus, parvovirus B19, glandular fever, Enterovirus, human herpesviruses 4, 6, and 7, Nipah virus encephalitis, Infectious Mononucleosis, Q fever and Lyme disease. The latter three have been associated in a high percentage of cases. While antecedent infections are associated with CFS, a direct causal relationship with any microbial infection has not been established.

Endocrine/Metabolic

- Hypothalamic - pituitary - adrenal (HPA) hypoactivity
- Higher chronic adrenocorticotrophic hormone (ACTH) autoantibody levels
- Low magnesium level,
- Low arachidonic acid level,
- Low L-carnitine level and
- Low cortisol levels. (poorer response to CBT)

Neurological - Neuroimaging studies have revealed

- Glucose hypometabolism in the frontal cortex and brain stem, with
- Decreased number and or affinity for the receptor protein for serotonin in the hippocampus and
- Decreased grey matter volume (in population study)

PSYCHOLOGICAL AND PSYCHOSOCIAL FACTORS

Factors Predisposing to CFS

- Obsessional type of personality,
- High parental mental stress
- Childhood and adult neglect, abuse and maltreatment
- Increased level of stress
- Pre morbid psychiatric illness
- Perfectionist attitude and personality

Factors Perpetuating CFS

- Disordered sleep
- Family illness burden
- Non-acknowledgment by physician

Table 1: Conditions which should be excluded before making a diagnosis of CFS

Medical Illnesses	Psychiatric disorders	Miscellaneous
Anaemia	Major Depressive disorder	Alcohol abuse
Type 2 diabetes	Bipolar Disorder	Substance abuse
Hypothyroidism	Schizophrenia	Morbid obesity BMI (>40)
Connective tissue disorders	Anorexia Nervosa	
Myopathies	Bulimia Nervosa	
Myasthenia gravis and other myasthenia syndromes		
Chronic Heart failure		
Chronic obstructive pulmonary diseases		
Chronic Renal failure		
Chronic liver disease		
Multiple sclerosis		
Neoplastic Disease		

Excessive significance given to symptoms & catastrophic thinking about disease

Fear of fatigue

Avoidance of physical activity

Lack of social support

Self- efficacy to do things despite the problems.

Over-vigorous activity alternating with resting for long periods

DIAGNOSIS

Chronic fatigue syndrome is a diagnosis of exclusion. This is often challenging to the physicians as fatigue is a part of many diseases. Detailed history and thorough clinical examination is a must to rule out disorders causing fatigue (Table 1). Tachycardia is often present. CFS has a considerable overlap with fibromyalgia.

Laboratory tests

No specific test can diagnose CFS. Tests are done to exclude medical illnesses causing fatigue. Extensive testing is not productive. Investigations should be planned judiciously guided by clinical clues.

Table 2: Diagnostic criteria for Chronic Fatigue Syndrome

1. Persistent, Severe, debilitating fatigue for 6 months or more
2. Fatigue is not lifelong, it has a new or definite onset
3. Fatigue is unexplained by/unrelated to physical exertion or organic disease
4. Not substantially relieved by rest
5. Fatigue results in a significant reduction in previous social, occupational, educational and personal activity levels
6. Four or more of the following additional symptoms lasting for >6 consecutive months
a. Impaired memory or concentration,
b. Sore throat,
c. Tender cervical or axillary lymphadenopathy,
d. Myalgias,
e. Pain in several joints,
f. Headache of new onset, type or increased severity ,
g. Post exertional (physical or mental) malaise, (which may be delayed in onset with prolonged extreme exhaustion)
h. Un-refreshing sleep.

For the diagnosis of CFS, various diagnostic criteria have been made. The most commonly used diagnostic criteria for clinical and research purpose is the United States CDC (centre for disease control) criteria. This is also called Fukuda criteria and is based on Holman 1988 scoring system.

The Fukuda criteria of CFS are shown in (Table 1).

Exclusion Criteria

Medical, psychiatric and other conditions explaining fatigue (Table 1).

Certain other points need attention -

Cognitive Dysfunction: Significant decrease of cognitive functions is seen in many cases of CFS. The affected domains are attention, memory , information processing and reaction time and this impairment is reflected in day-to-day activities. There is difference in actual and perceived cognition. Motor speech, language, reasoning and intelligence are unaltered.

Severity of disease: CFS can be mild, moderate or severe. Patients with mild CFS are mobile, can care for themselves and can do light domestic tasks with some difficulty. Patients with moderate CFS have reduced mobility and are restricted in their activities of daily living. They may have peaks and troughs in their daily activities. Patients with severe CFS are incapacitated and are able to do minimal tasks only.

Phases of Disease & The triggering event?: The four fennel phases of the disease are described as crisis, stabilization, resolution and integration. Most patients describe an infection, a flu like illness or infectious mononucleosis,

somatic events like pregnancy, injury, child birth & surgery as the triggering event. Serious life events and stressors may also precipitate it.

Other Symptoms: Irritable bowel, nausea, diarrhoea or dyspepsia, chills and night sweats, Brain fog, chest pain, shortness of breath, chronic cough, visual disturbances, Allergies or sensitivities to foods, odours, chemicals, medications or noise, orthostatic instability, irregular heartbeat, dizziness, balance problems or fainting.

Psychological problems are common (irritability, mood swings, anxiety, panic attacks).

MANAGEMENT

Management is often difficult and response is variable. It may take a long time. Functional disability, phase & severity of disease should be assessed. The subjectivity can be eliminated by questionnaire based evaluation. Physician must not negate the presence of symptoms, as this can lead to aggravation of disease.

Three main forms of treatments

Cognitive behavioural therapy (CBT) is a psychotherapeutic approach directed at helping the patient understand the nature of disease, suggestions to change lifestyle to improve symptoms, changing the perception of patient regarding fatigue and exertion-related concerns, reducing a focus on symptoms, and develop coping mechanisms. The patient is encouraged to restore sleep hygiene, to remain as active as possible, and to gradually return to previous levels of exercise and other activity. CBT typically consists of 12–14 sessions spread over 6 months & improves symptoms.

Graded Exercise therapy (GET): GET usually consists of an exercise program based on simple activities like walking or cycling that continues for 3–5 months. Exercise is gradually increased, with set goals for maximal heart rates. The target is to improve upon deconditioning and gradual recovery of exercise intolerance.

CBT and GET appear to improve fatigue primarily by changing the patient's perception of the fatigue and also by reducing the focus on symptoms. Among these two, CBT is more effective.

Pacing: The basic concept is that the energy available to a particular patient is fixed and its expenditure throughout the day may be planned so that the daily activities are accomplished without precipitation of fatigue. Therefore, after each scheduled activity a period of rest or relaxation is introduced.

Other Treatment Interventions

- Healthy diet

- Medications to reduce pain, discomfort, fever **1053** (when present)
- Medications to treat anxiety and depression
- Relaxation and stress-reduction techniques such as:
 - Biofeedback
 - Deep breathing techniques
 - Hypnosis
 - Massage therapy
 - Meditation
 - Muscle relaxation techniques
 - Yoga

Prognosis

About half of the patients of CFS show some improvement, and about 30% continue to remain disabled. Recovery rates of adult CFS have been shown in the range of 5% but are better for children and adolescents. Return to work ranges from 8% to 30% among the patients with CFS. Mortality due to CFS is rare.

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