Chronic fatigue syndrome

Alamy

Yaso Shan introduces chronic fatigue syndrome, gives a working definition, outlines treatment options and highlights the problems facing practitioners in making an accurate diagnosis.

Few conditions baffle medical science as much as Chronic Fatigue Syndrome (CFS), but ever since the term 'yuppie flu' was coined, the scientific community has been desperately trying to understand the mechanisms and all the manifestations of this intriguing medical disorder. The media labelling of yuppie flu in the 1980s appeared to trivialise this complex and debilitating condition, which is characterised by significant pain and fatigue. It proved immensely frustrating to sufferers who were not taken seriously. Much of this battle stemmed from trying to define CFS and it continues to this day with many of the health professionals confused about terminology. This is unsurprising since the scientific community were unclear what to call this group of symptoms and how to distinguish it from any other clinical presentations that are distinct and separate to this syndrome. Further confusion resulted when various other terminologies were incorrectly applied to CFS. Other autoimmune conditions such as post-viral fatigue syndrome (PVFS), fibromyalgia, neurasthenia and post-infectious fatigue syndrome (PIFS) are often applied to CFS but Chronic Fatigue Immune Dysfunction Syndrome (CFIDS) would probably fit the description of CFS the best.

Clinical presentation

CFS is technically known as myalgic encephalomyelitis or ME for short. In its literal sense, ME is the swelling of the brain and spinal cord, and although it was first noted in the 1930s as a medical condition, it was only in the 1940s that the symptoms were first recorded. The number of people experiencing it dramatically rose by the 1980s and it was labelled 'yuppie flu' because it appeared to affect a large percentage of the 'young upwardly mobile' professionals in highly stressful jobs.

As there is no clear cause and effect, symptoms are collectively attributed to this syndrome. There is a marked and prolonged fatigue lasting up to six months or more with no identifiable cause and typically with a flu-like illness. There is general muscle weakness and pain with low grade fever, sore throat, painful lymph nodes in the neck and armpits, exacerbation of fatigue after moderate or strenuous exercise for periods of 24 hours or more. Other symptoms include transient pains in a number of joints and various disturbances of neuropsychological function including confusion, irritability, non-refreshing sleep, poor concentration, memory impairment and visual changes. To date, this case definition (revised in 1994 by Fakuda *et al*) constitutes the current criteria for CFS and the most widely used definition internationally.

CFS is frequently viewed in association with psychiatric illnesses such as depression and anxiety even though no causal link has been established. CFS has a significant overlap and co-morbidity with psychiatric disorders despite several

et al 1996, Katon *et al* 1991, Wood *et al* 1991, Wessely and Powell 1989, Manu *et al* 1989). More recent research fails to support this viewpoint on phychiatric causes, with several working groups recommending that pre-existing and co-existing psychiatric disease should not exclude the diagnosis of CFS if the other criteria are also met (Grant 2006).

Finally, there are common misconceptions on the role of stress, either physical or mental, and the impact it has on the development of CFS. Contrary to popular belief that stress is an important factor in conditions characterised by chronic fatigue, there is no firm evidence in the literature to support this view.

Differential diagnosis

To make an accurate diagnosis of CFS is particularly difficult, especially when there are other conditions that have very similar clinical presentations and due to some confusion that still exists in terminology. Diagnosis is ultimately by exclusion, for example, it is made in the absence of any other established cause, determined through standard medical examinations or tests. Other than the sheer physical exhaustion coupled with pain and possibly some of the known symptoms, there is very little to really go on in terms of biological markers. A nutritional analysis to assess status or deficiency states may be useful, as are assays of antibodies for some of the infective agents associated with CFS.

CFS is often confused with fibromyalgia simply because they share a number of symptoms. Many experts think that fibromyalgia and CFS are the same, or at least variations of the same. The difference between one diagnosis and another may simply be a matter of degree to which sufferers have the symptoms. Most patients with CFS have some kind of pain, and of course this is a hallmark of fibromyalgia. Most patients with fibromyalgia report fatigue, a hallmark of CFS. Likewise, both involve a high frequency of sleep and cognitive disturbances and there are few documented differences. Fibromyalgia is often traced to an injury or physical or emotional trauma, whereas CFS tends to have a flu-like onset. Moreover, researchers have found that fibromyalgia patients have abnormal levels of several chemicals, such as serotonin and substance P; these are used in the body to transmit and respond to pain signals. However, only CFS patients are absent of tender points. Overall though, clinicians are still faced with an important diagnostic challenge.

Table 1. Some common drugs used in the treatment and management of CFS

Drug	Comment
Immunoglobulin G (IgG)	Some therapeutic benefits seen
Ribonucleic Acid (RNA) called Ampligen which is a mismatched double-stranded RNA	Some therapeutic benefits seen
Acyclovir	Not very effective
Anticholinergics	
Hormones	
Nicotinamide adenosine dinucleotide (NAD)	
Antidepressants	
Steroids	
Selective Serotonine Reuptake Inhibitors (SSRIs) eg. Fluoxetine	Minimal response
Monoamine Oxidase Inhibitors (MAOIs)	Shows some promise
Non-steroidal anti-inflammatory drugs (NSAIDs)	Mainly prescribed for predominant musculoskeletal complaints
Calcium-blockers to counter exercise-induced fatigue	

Table 2. Nutritional supplementation for CFS patients (Adapted from Werbach, 2000)

Nutrient	Tentative protocol	Possible benefits
Folic acid	1-10 mg/d for a three-month trial	■ Reduced fatigue and depression ■ improved immune function
Vitamin B12	Total of 6,000-70,000µg per week given intramuscularly for a three-week trial	■ Reduced fatigue, depression and pain ■ improved microcirculation
Vitamin C	10-15g daily	■ Improved immune function ■ reduced pain ■ improved microcirculation
Magnesium	■ 100mg is given intramuscularly every week for six weeks in patients with reduced RBC Mg levels. ■ Combination therapy with malic acid (Mg: 600mg/d and malic acid: 2400mg/d) in an eight-week trial	■ Subjective improvement ■ Reduced muscle pain
Sodium	Moderate increases of sodium is diagnosed cases of neurally-mediated hypotension	Subjective improvement
Zinc	135mg/d for 15 days	■ Increased muscle strength and endurance ■ reduced pain and fatigue ■ improved immune function
L-Typtophan	In fibromyalgia, 100mg of 5-hydroxytrptophan was given three times daily in a three-month trial	Reduced pain and fatigue
L-Carnitine	102g given three times daily in a three-month trial	Improvements that can be dramatic
Coenzyme Q10	100mg given daily in a three-month trial	Marked improvement with increased muscle endurance
Essential fatty acids	280mg of GLA and 135mg of EPA given daily in a three-month trial	General improvements noted

Table 3. Benefits of antioxidants in the treatment and management of CFS and their mechanisms of action (Adapted from Logan and Wong 2001)

Antioxidant	Mechanism of Action
Selenium	Supports glutathione peroxidase activity, a Se-dependant antioxidant system
Glutathione	Oral administration of glutathione (GSH) directly increases glutathione levels in plasma and tissues
N-acetylcysteine	Provides cysteine for GSH synthesis
A-Lipoic acid	Increases intracellular GSH by reducing extracellular cystine to cysteine
Coenzyme Q10	A neuroprotective agent and improves mitochondrial function
Oligomeric proanthocyanidins	Protects against radical-induced lipid peroxidation and DNA damage
Ginkgo biloba (ginkgo)	A powerful antioxidant. It increases cerebral perfusion and associated memory and cognitive deficits. It is also a neuroprotective agent
Vaccinium myrtillus (bilberry)	A neuroprotective agent – also protects RBCs from *in vivo* oxidative damage

Treatment and management

There are no firmly established treatment recommendations within conventional medicine and ultimately it is a question of management. Broadly speaking, treatment approaches fall into three areas: conventional, alternative and behavioural (psychological). Most patients will go via the conventional route to begin with, which adopts a symptom-based pharmacological approach. Table 1 summarises the most commonly prescribed drugs for CFS patients.

The alternative route to treatment and management is the nutritional aspect that considers deficiency states and a nutritional analysis such as food intolerances. Logan and Wong (2001) suggest the use of antioxidant therapy in the management of CFS where oxidative stress is implicated. Dietary supplements of glutathione, N-acetylcysteine, alpha-lipoic acid, oligomeric proanthocyanidins and the herbs *Ginkgo biloba* (ginkgo) and *Vaccinium myrtillus* (bilberry) may be beneficial. However, as this is an area of current and future research, it is yet to be established whether it is an effective treatment.

Werbach (2000) suggests a number of nutrients where there is a deficiency. This will not only address any clinical manifestation as a result of the deficiency but also assist the healing process in CFS patients. Magnesium sulphate (MgSO4) is the only substance shown to positively affect the health and functioning of CFS patients in a randomised, double-blind, placebo-controlled study (Cox *et al* 1991). However, three subsequent reports found no evidence of Mg deficiency in CFS patients (Reid *et al* 2000). Table 2 highlights some of the other recommendations by Werbach (2000) and the possible therapeutic benefits in clinical cases.

Table 3 describes possible mechanisms of action of the relevant antioxidants in the treatment and management of CFS.

Behavioural or psychological interventions have had some benefit to patients. Graded aerobic exercise programmes have shown some promise in muscle fatigue and pain, as does cognitive behavioural therapy (CBT). Counselling is a useful adjunct to CBT.

Alternative approaches in the treatment and management of CFS have tended to focus primarily on herbal medicine, either Western, Chinese or Ayurvedic. Some patients have derived benefit from acupuncture, which may alleviate muscle pain, a common symptom in CFS. Western herbal medicine combines the use of key herbs in addition to practical measures such as stress reduction techniques, meditation, biofeedback, counselling and joining a self-help group. Gentle exercises such as yoga, swimming, Tai Chi or slow walking are advocated following a period of initial rest, which in many cases is not by choice but because most sufferers cannot even get out of bed.

Dietary modifications that Western herbalists could suggest include raw foods, organic and animal-free (for general detoxification and to reduce the toxic burden on the system), foods to improve the immune system and those which would rebalance the acid-base equilibrium in the blood. Elimination of refined carbohydrates, caffeine and alcohol is recommended alongside increased consumption of organically grown fruits and vegetables. Food allergies and intolerances such as *Candida albicans* feature heavily, and special diets are devised for those patients. Table 4 highlights the treatment rationale and management approaches in Western herbal medicine in CFS.

Conclusion

CFS is complex and is easy to misdiagnose. This is not aided by the confusion that exists around its definition and the terminology used by health professionals. Despite this, great efforts have been made to understand this condition. Addressing nutritional deficiencies and using conventional and alternative medicine appears to be the most effective way forward in dealing with the multitude of symptoms that are typical features of this disorder. Ultimately, however, it is a question of managing the condition and limiting the severity of these symptoms, particularly the fatigue and pain. Many sufferers seek comfort

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Table 4. Herbal therapeutics in the treatment and management of CFS

Herb Action	Treatment Rationale	Useful Herbs
Immune stimulators and modulators	Herbs to stimulate and regulate immune responses. Some have a general tonic effect while others may have a non-specific action on only certain aspects of the immune system	*Echinacea purpurea* (echinacea) *Baptisia tinctoria* (wild indigo) *Astragalus membranaceus* (astragalus)
Bitter digestive tonics	These will enhance the digestive process, particularly in those who have a poor appetite. It will improve the use of digested food by enabling the body to derive the most essential nutrients from food. They may also stimulate the liver, thereby enhancing the cleansing and detoxification process. This will indirectly boost the immune system by reducing the levels of toxins circulating in the bloodstream.	*Hydrasis canadensis* (goldenseal) *Berberis vulgaris* (barberry) *Taraxacum officinale* (dandelion)
Adaptogens	Herbs that work predominantly on the adrena glands and assist the body in adapting to stress. They are especially indicated where there is long-term debility and weakness.	*Glycyrrhiza glabra* (licorice) *Borago officinalis* (borage) *Eleutherococcus senticosus* (Siberian ginseng)
Stimulants	Mild stimulants are indicated in chronic conditions such as CFS. They replenish on the adrenals and nervous system by acting as nutritive agents. Stronger stimulants are not used as they will deplete energy reserves in the long term and exacerbate the condition.	*Avena sativa* (oats) *Fucus versiculosis* (kelp) Rosmarinus officinalis (rosemary)
Circulatory stimulants	Particularly helpful in combating the 'mental fogginess' that many patients report. Ginkgo is very useful in improving cerebral perfusion and the general microcirculation. Gentian is one of the most useful bitter herbs in uplifting and revitalising.	*Ginkgo biloba* (ginkgo) *Gentiana lutea* (gentian) *Rosmarinus officinalis* (rosemary) *Zingiber officinale* (ginger)
Nervines	Herbs that regulate nervous function by toning and strengthening the system. They are useful in addressing some of the neurological and mental health symptoms in CFS such as depression. Many of them also have other actions which prove useful in treating the variety of symptoms that accompany CFS.	*Verbena officinalis* (verbena) *Scutellaria laterifolia* (skullcap) *Passiflora incarnata* (passion flower)

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and practical support from the various self-helps groups and through counselling to help them cope with this chronic condition that affects all aspects of their lives. Creating a better understanding of this condition and to standardise the use of terminology within medical literature and within the health profession will greatly assist the diagnostic process and enable effective treatment strategies that can only be of significant benefit to CFS patients ■

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