

# Chronic Fatigue Syndrome

Department of Health and Human Services  
Public Health Service  
Centers for Disease Control and Prevention  
National Center for Infectious Diseases

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**  
**Public Health Service**  
**Centers for Disease Control and Prevention**  
**Mailstop A15**  
**Atlanta, Georgia 30333**



## Chronic Fatigue Syndrome

# Chronic Fatigue Syndrome



Use of trade or commercial names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services

.....

Department of Health and Human Services  
Centers for Disease Control and Prevention  
Viral Exanthems and Herpesvirus Diseases Branch  
Division of Viral and Rickettsial Diseases  
National Center for Infectious Diseases  
Atlanta, Georgia

September 2006

### What is CFS?

Chronic fatigue syndrome, or CFS, is a debilitating chronic illness characterized by profound all-encompassing physical and mental fatigue that is not improved by rest. Persons with CFS function at a level of activity substantially lower than that which they were capable of before the onset of illness. In addition to fatigue, the syndrome includes specific accompanying symptoms (unrefreshing sleep, impaired memory and concentration, muscle and joint pain, sore throat, headache, tender lymph nodes, and an increase in symptoms and malaise extending 24 hours after physical or mental activity). The functional impairment associated with CFS is equivalent to that experienced by patients with multiple sclerosis or heart disease and among those undergoing chemotherapy for cancer. Up to a quarter of the people afflicted with CFS are unemployed or on disability, and the average, family in which a member has the illness annually forgoes \$20,000 in earnings and wages. The annual cost, in lost productivity, of CFS to the United States is approximately \$9 billion. CFS is a chronic illness and often persists for years. CFS is a particularly challenging illness for patients and health care providers because the cause or causes have not been identified, there are no characteristic findings on physical examination of patients, and no specific diagnostic laboratory tests are available. Moreover, since many illnesses have incapacitating fatigue as a symptom, care must be taken to exclude other known and often treatable conditions, before making a diagnosis of CFS.

### Definition of CFS

Because there are no characteristic physical signs or laboratory abnormalities, CFS must be diagnosed on the basis of self-reported symptoms and disability. An internationally accepted CFS case definition was published in 1994 and provides the current standard for diagnosis of

# Chronic Fatigue Syndrome

## What is CFS?

Chronic fatigue syndrome, or CFS, is a debilitating chronic illness characterized by profound all-encompassing physical and mental fatigue that is not improved by rest. Persons with CFS function at a level of activity substantially lower than that which they were capable of before the onset of illness. In addition to fatigue, the syndrome includes specific accompanying symptoms (unrefreshing sleep, impaired memory and concentration, muscle and joint pain, sore throat, headache, tender lymph nodes, and an increase in symptoms and malaise extending 24 hours after physical or mental activity). The functional impairment associated with CFS is equivalent to that experienced by patients with multiple sclerosis or heart disease and among those undergoing chemotherapy for cancer. Up to a quarter of the people afflicted with CFS are unemployed or on disability, and the average, family in which a member has the illness annually forgoes \$20,000 in earnings and wages. The annual cost, in lost productivity, of CFS to the United States is approximately \$9 billion. CFS is a chronic illness and often persists for years. CFS is a particularly challenging illness for patients and health care providers because the cause or causes have not been identified, there are no characteristic findings on physical examination of patients, and no specific diagnostic laboratory tests are available. Moreover, since many illnesses have incapacitating fatigue as a symptom, care must be taken to exclude other known and often treatable conditions, before making a diagnosis of CFS.

## Definition of CFS

Because there are no characteristic physical signs or laboratory abnormalities, CFS must be diagnosed on the basis of self-reported symptoms and disability. An internationally accepted CFS case definition was published in 1994 and provides the current standard for diagnosis of

the illness. In 2003 an International CFS Study Group published recommendations concerning application of the case definition in research studies and in clinical practice. To receive a diagnosis of chronic fatigue syndrome, the patient must satisfy three criteria:

1. have severe chronic fatigue of 6 months or longer duration with other known medical or psychiatric conditions excluded by an appropriate clinical evaluation or, if present, adequately treated
2. have four or more of the following eight syndrome-defining symptoms concurrently present with the fatigue:
  - unusual post-exertional malaise lasting more than 24 hours
  - substantial impairment in short-term memory or concentration
  - unrefreshing sleep
  - headaches of a new type, pattern or severity
  - sore throat
  - tender lymph nodes
  - muscle pain
  - multi-joint pain without swelling or redness

These symptoms must have persisted or recurred during six or more consecutive months of illness and cannot have predated the fatigue

3. have chronically fatiguing illness that causes substantial impairment with respect to occupational, educational, social, or recreational activities.

### Other Commonly Observed Symptoms in CFS

In addition to the eight CFS-defining symptoms, people with CFS may experience other symptoms. These symptoms

include abdominal pain, alcohol intolerance, bloating, chest pain, chronic cough, diarrhea, dizziness, dry eyes or mouth, earaches, irregular heartbeat, jaw pain, morning stiffness, nausea, night sweats, psychological problems (depression, irritability, anxiety, panic attacks), shortness of breath, skin sensations, tingling sensations, and weight loss. Even though these symptoms do not constitute diagnostic criteria for the syndrome, they, like the eight symptoms mentioned above, need to be evaluated for underlying causes.

### Similar Syndromic Illnesses

A number of syndromic illnesses have clinical features similar to those for CFS. These include fibromyalgia syndrome, myalgic encephalomyelitis, neurasthenia, multiple chemical sensitivities, and post-infectious fatigue (e.g., chronically fatiguing illness following infectious mononucleosis). Although these illnesses may present with a primary symptom other than fatigue, chronic fatigue is commonly associated with all of them.

### Similar Medical and Psychiatric Diseases

A large number of clinically defined medical and psychiatric diseases (many of which can be treated and/or cured) cause fatiguing illness similar to CFS. The presence of any of these diseases precludes a diagnosis of CFS until the condition has been successfully treated and can no longer explain the fatigue and other symptoms. Examples of such diseases include endocrine (diabetes and hypothyroidism), neurologic (multiple sclerosis, stroke, sleep apnea, and narcolepsy), rheumatic and chronic inflammatory (Sjögren's syndrome, rheumatoid arthritis, inflammatory bowel disease), infectious (hepatitis C, AIDS, mononucleosis), organ-specific (heart, emphysema, and hypertension), iatrogenic (reactions to prescribed medications) diseases as well as cancers. Examples of psychiatric disease include bipolar disorders, psychoses, melancholic depression, eating disorders, and alcohol or substance abuse.

## CFS in the Community

### How Common Is CFS?

Many figures have been put forward estimating the occurrence of CFS in the general population. Many of these estimates, especially in the early 1990s, were extrapolations from studies in primary and referral medical clinics. To accurately estimate the occurrence of an illness like CFS, it is necessary to survey entire communities. We are aware of only two such studies, one conducted in Wichita, Kansas, and the other in Chicago, Illinois. Both studies used random digit-dialing to survey large numbers of people (90,000 in Wichita and 18,000 in Chicago) and then performed medical and psychiatric evaluations on all those identified with possible CFS (referred to as CFS-like) illness. The Wichita study found that 235 per 100,000 adults had CFS, and the Chicago study reported 422 per 100,000. In other words, between a quarter and a half percent of the two populations were affected. The most recent study, which surveyed eight regions throughout the United States, was unable to perform medical and psychiatric examinations and estimated that slightly more than 1% of the U.S. population had CFS-like illness. Extrapolation of these percentages indicates that up to 900,000 adults in the United States fulfill all criteria of CFS case definition and as many as 2 million suffer a CFS-like illness.



### Who Gets CFS?

CFS affects both sexes and can develop in people of all ages and races; however, 60% to 70% of patients with CFS are women, and the disease is most common in persons between the ages of 40 and 59 years. As with information estimating the number of CFS cases, information concerning who is at risk for CFS has changed dramatically over time as our knowledge concerning the illness has evolved. In the 1990s, CFS was understood to be an illness of white, middle class, well-educated professional women and an illness that most often began suddenly following an infection. Population-based studies show that CFS is significantly more common among those of lower socioeconomic means and slightly more common among racial/ethnic minorities. Similarly, clinic-based studies reported that the illness typically begins suddenly following an infection. However, community-based studies have found that most patients describe a gradual insidious onset. In addition, community-based studies show that only 16% to 20% of patients with CFS have sought medical care and received a diagnosis. This finding may explain why clinic-based and community-based studies come to different conclusions.

CFS is predominantly an illness of adults, but it also occurs in adolescents, albeit very rarely. Studies by the Centers for

Disease Control and Prevention (CDC) documented CFS in only .05% of teenagers 12 to 18 years of age, which is 10 times less common than among adults. CFS may also affect children younger than 12 years of age, but it is extremely hard to characterize because children of that age have problems perceiving and verbalizing the nature of their symptoms and the degree to which they represent a departure from normal function and sensation. Although CFS is rare in adolescents, the effects of any chronic illness during this important phase of development can have serious and long-lasting consequences. CFS in adolescents has many of the same characteristics as it has in adults. However, it is particularly important that the unique problems of chronically ill adolescents (e.g., family social and health interactions, education, social interactions with peers) be considered as a part of their care. Appropriate dissemination of CFS information to patients, their families, and school authorities is also important.

### **Clinical Course of CFS**

It is vital to understand the clinical course of CFS so as to design, apply, and monitor treatment results and to address insurance and disability issues. CFS often follows a cyclical course alternating between periods of illness and relative well-being; the nature of the symptom complex often changes over time as well. It is not known what percentage of patients recover, and even the definition of what should be considered recovery is subject to debate. Some patients recover completely with time; others recover to the point that they can resume work and other activities but continue to experience varying degrees of or periodic CFS symptoms, while others seem locked into predictable daily debilitating symptoms. CDC studies have found that 40% to 60% of people with CFS report partial or total recovery, and recovery is most common within the first 5 years of illness. In addition,

studies suggest that family practice physicians may be as capable of caring for CFS patients as physicians working in specialty or referral clinics. While there is little known about the long-term outcomes of CFS, it appears that people who develop CFS precipitously following an acute infectious disease generally improve within 2 years, although they may continue to experience symptoms at a less debilitating level. Individuals with a gradual onset may experience a prolonged course of illness characterized by periods of remission and exacerbation.

### **Is CFS Contagious?**

There is no evidence that CFS is a contagious disease. Contagious diseases must be caused by an infectious agent, and, despite rigorous research efforts, no infectious agent (virus, rickettsia, bacterium, or protozoan) has been consistently associated with CFS. However, post-infectious fatigue is a well-recognized illness, and CFS can and does occur following infectious diseases, such as infectious mononucleosis. Contagious diseases are spread from person to person and typically occur in well-defined clusters, otherwise known as outbreaks or epidemics. While some earlier studies, such as investigations of fatiguing illness in Incline Village, Nevada, and Punta Gorda, Florida, have been cited as evidence for CFS acting as a contagious illness, they did not rigorously document CFS or the occurrence of person-to-person transmission of fatiguing illnesses. CDC has worked with state health departments to investigate a number of reported outbreaks of fatiguing illness and has yet to confirm a cluster of CFS cases. In addition, none of the behavioral characteristics typically associated with contagious disease, such as seasonal or regional occurrence, travel history, occupation, exposure to animals, injection drug use, or sexual behavior, have been associated with CFS in case-control studies.

## Possible Causes of CFS

The cause or causes of CFS remain unknown, despite a vigorous search. While a single cause for CFS may yet be identified, another possibility is that CFS represents a common endpoint of disease resulting from multiple precipitating causes. As such, it should not be assumed that any of the possible causes listed below has been formally excluded or that these largely unrelated possible causes are mutually exclusive. Conditions that have been proposed to trigger the development of CFS include virus infection or other transient traumatic conditions, stress, and toxins.

### Infectious Agents

Due in part to its similarity to mononucleosis, CFS was initially thought to be caused by an active virus infection, most probably Epstein-Barr virus (EBV). We now know that CFS is not an active infection caused exclusively by EBV or by any single recognized infectious disease agent. No firm association between infection with any known human pathogen and CFS has been established. Many studies performed around the world addressing the question of an infectious origin by human pathogens, examined patients for evidence of infection with EBV, human retroviruses, human herpesvirus (HHV) 6 and 7, enteroviruses, rubella, *Candida albicans*, bornaviruses, *Mycoplasma*, Q-fever, Ross River virus, and GB virus-C. No specific agent was identified in any of these studies. Several of these agents (EBV and HHV-6 in particular) are common human pathogens that cause lifelong latent infections; thus, determining whether the virus that is present is responsible for CFS is difficult to prove. However, the possibility remains that an infectious agent in combination with a predisposed host may trigger some cases of CFS.

### Immunology

The earliest studies of CFS focused on the possibility of chronic infection, and therefore examined immune function. These studies found evidence of low-grade chronic immune activation, reduced natural killer cell function, and subtle abnormalities of immune regulation, such as cytokine production. One thing is certain, at this juncture, there are no major immune disorders in CFS patients. Some investigators identified anti-self antibodies and immune complexes in CFS patients, both of which are hallmarks of autoimmune disease. However, no associated tissue damage typical of autoimmune disease has been described in patients with CFS. The opportunistic infections or increased risk for cancer observed in persons with immunodeficiency diseases or in immunosuppressed individuals have also not been observed in patients with CFS.

### Hypothalamic-Pituitary-Adrenal Axis

Multiple laboratory studies have suggested that the central nervous system may have an important role in CFS. Significant or unusual physical or emotional stress, which is commonly reported as a pre-onset condition in CFS patients, activates the hypothalamic-pituitary-adrenal axis, or HPA axis, leading to increased release of cortisol and other hormones. Cortisol and corticotrophin-releasing hormone (CRH), which is also produced during the activation of the HPA axis, influence the immune system and many other body systems, particularly the brain. They may also affect several aspects of behavior. Recent studies revealed that CFS patients often have lower levels of cortisol than do healthy controls. However, these levels are not abnormal so cortisol cannot be used as a diagnostic marker for an individual with CFS nor is cortisol an effective treatment for CFS.

## Neurally Mediated Hypotension

Disorders of the autonomic nervous system share many similarities with CFS. Thus, there was considerable excitement in 1995 when investigators at Johns Hopkins University reported that 96% of CFS patients, compared with 29% of controls, manifested abnormalities in the autonomic regulation of blood pressure and pulse (neurally mediated hypotension, or NMH) upon tilt table testing. Confirmatory studies found NMH among 40% to 60% of CFS patients and concluded that autonomic dysfunction resulting in hypotension occurs in a subset of CFS patients as a co-morbid condition. There has only been one placebo-controlled treatment study (using low dose fluudrocortisone) based on this finding, and the results were disappointing: fluudrocortisone, the reference standard treatment for neurally mediated hypotension, failed to prevent NMH in CFS patients. Clearly, NMH is not the cause of CFS, although it may occur as a comorbid condition in some patients and is an important condition to evaluate in patients with classic symptoms of orthostatic intolerance. This finding serves as an important lesson and underscores the need to do placebo-control studies of the co-morbid conditions associated with CFS (e.g., unrefreshing sleep, pain, depression) and not assume that the response to treatment will be that predicted by studies of other illnesses.

## Nutritional Deficiency

There is no published scientific evidence that CFS is caused by a nutritional deficiency. Many patients do report intolerances for certain substances that may be found in foods or over-the-counter medications, such as alcohol or the artificial sweetener aspartame. While evidence is currently lacking for nutritional defects in CFS patients, it should also be added that a balanced diet can be conducive to better health in general and would be expected to have beneficial effects in any chronic illness.

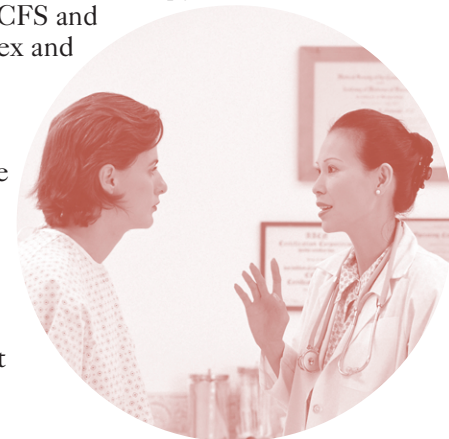
## Diagnosis of CFS

### How Physicians Diagnose CFS

An individual who has experienced incapacitating physical or mental fatigue for 6 or more consecutive months that is made worse by physical or mental exertion and is not relieved by rest and is accompanied by memory or concentration problems, headache, sore throat, tender nodes, or muscle or joint pain has a CFS-like illness and should consult a physician.

The physician needs to evaluate the patient's illness to determine if there is a treatable cause (e.g., hypothyroidism, anemia, cancer). The first step in this evaluation is to obtain a detailed medical history and perform a complete physical examination of the patient. The physician should also order standard laboratory tests of the patient's blood and urine to help identify other possible causes of illness. On the basis of this initial evaluation, the physician may order additional tests as part of the differential diagnostic process. If a cause for the illness is identified, the physician will initiate therapy. If no medical or psychiatric cause can be found, the physician may render a diagnosis of CFS or diagnose another condition (e.g., fibromyalgia, irritable bowel syndrome, unexplained chronic fatigue). The physician will then work with the patient (and perhaps other health professionals) to design and implement an appropriate course of therapy.

Evaluation of patients for CFS and similar illnesses is a complex and occasionally frustrating process. It is important to select a physician in whom you have confidence and to work closely with that physician to follow recommendations for treatment and lifestyle adjustments and to communicate clearly about new symptoms or unusual responses to therapy.





## International Case Definition for CFS

As discussed above, the current (1994) international case definition of CFS has 3 components that must be fulfilled:

1. Severe persistent or recurring (chronic) fatigue must have existed for at least 6 months or longer, and other known medical or psychiatric conditions must be excluded by an appropriate clinical evaluation and, if present, be adequately treated.
2. The fatigue must be accompanied by four or more of the eight syndrome-defining symptoms: unusual post-exertional malaise lasting more than 24 hours; substantial impairment in short-term memory or concentration; unrefreshing sleep; headaches of a new type, pattern or severity; sore throat; tender lymph nodes; muscle pain; multi-joint pain without swelling or redness. The symptoms must have persisted or recurred during 6 or more consecutive months of illness and cannot have predated the fatigue.
3. The chronically fatiguing illness must cause substantial impairment with respect to occupational, educational, social, or recreational activities.

## Appropriate Tests for Routine Diagnosis of CFS

At present, there are no laboratory tests to confirm a diagnosis of CFS. The search for laboratory markers is an active area of research, but it remains just that—an area of research—and should not be part of routine clinical practice. Laboratory testing is an important part of the work-up of patients with fatiguing illness, but the aim of such testing is to identify known (and treatable) causes of the fatigue, not to diagnose CFS. While the number and type of tests performed may vary from physician to physician, the following tests constitute a typical standard battery to exclude other causes of fatiguing illness: alanine aminotransferase (ALT), albumin, alkaline

phosphatase (ALP), blood urea nitrogen (BUN), calcium, complete blood count, creatinine, electrolytes, erythrocyte sedimentation rate (ESR) or a C-reactive protein, globulin, glucose, phosphorus, thyroid stimulating hormone (TSH) and free T-4, total protein, transferrin saturation, and urinalysis. It is not unreasonable to screen for hepatitis B and C, as well as HIV, in some individuals. Further testing may be required to confirm a diagnosis for illness other than CFS. For example, if a patient has low levels of serum albumin together with an above-normal result for the BUN test, kidney disease would be suspected. The physician may choose to repeat the relevant tests and possibly add new ones aimed specifically at diagnosing kidney disease. If autoimmune disease is suspected on the basis of initial testing and physical examination, the physician may request additional tests, such as for antinuclear antibodies and rheumatoid factor.

## Psychological/Neuropsychological Testing

Virtually all chronic illnesses, including CFS, are accompanied by co-morbid depression in some patients. Pre-existing psychiatric conditions also influence the clinical manifestations of other diseases, and CFS is no exception to such influence. Depression, in particular, is such a common cause of the presenting complaint of fatigue that the physician should assess whether patients complaining of fatigue are suffering from depression and, if so, offer treatment. In some individuals it may be beneficial to assess the impact of fatiguing illness on certain cognitive or reasoning skills (e.g., concentration, memory, and organization). This evaluation may be particularly relevant in children and adolescents, for whom academic attendance, performance, and specific educational needs should be addressed. Testing for current psychiatric disorders other than depression, particularly anxiety disorders, may be necessary in some patients.

## Theoretical and Experimental Tests

A number of tests, some of which are offered commercially, have no demonstrated value for the diagnosis of CFS. These tests should not be performed unless required for diagnosis of a suspected exclusionary or co-morbid condition (e.g., magnetic resonance imaging [MRI] to rule out suspected multiple sclerosis or a tilt test to identify neurally mediated hypotension) or unless they are part of a scientific study. In the latter case, written informed consent of the patient is required. No diagnostic tests for infectious agents, such as EBV, enteroviruses, retroviruses, HHV-6, *Candida albicans*, or *Mycoplasma incognita*, are diagnostic for CFS and, as such, should not be used (except to identify an illness that would exclude a CFS diagnosis, such as mononucleosis). In addition, no immunologic tests, including cell profiling tests (e.g., measurements of natural killer cell number or function), cytokine tests (e.g., interleukin-1 or -6 or interferon), or cell marker tests (e.g., CD25 or CD16), have value for diagnosing CFS. Other tests that must be regarded as experimental for making the diagnosis of CFS include imaging techniques, such as fMRI (functional MRI), PET scan (positron emission tomography), or SPECT-scan (single photon emission computed tomography). These imaging tests are subject to problems with the interpretation of results and have considerable inter-laboratory variability.

## Management of CFS

Since no cause for CFS has been identified, the therapies for this disorder are directed at relief of symptoms and gradual resumption of necessary activities. The physician, together with the patient, will develop an individually tailored program based on some combination of the therapies discussed in this section to provide the greatest perceived benefit.

## Non-pharmacologic Therapy

**Physical Activity.** Physical activity in CFS presents a paradox. On one hand, there is good evidence that a program of graded modest aerobic exercise may improve function in many patients. On the other hand, physical exertion also may prompt brief relapses, typically starting 24-48 hours after the exertion. In general, physicians advise patients with CFS to carefully pace themselves and encourage them to avoid unusual physical or emotional stress. A regular, manageable daily routine helps avoid the “push-crash” phenomenon, which is characterized by overexertion during periods of better health and followed by a relapse of symptoms, perhaps initiated by the excessive activity. Since patients will have to limit their activities, particularly in the early stages of therapy, clinicians may need to explain the disorder to employers and family members, advising them to make allowances as possible. Modest, regular exercise to avoid de-conditioning is important and should be supervised by a physician or physical therapist. When physical activity causes increased fatigue or illness symptoms, the activity level needs to be decreased, at least temporarily. Often it takes repetition of very low levels of activity (e.g., a daily 5-minute walk for several weeks followed by 1-minute incremental increases over a number of weeks to achieve resumption of activity levels approaching normalcy for a sedentary person).

Non-pharmacologic and non-tested therapies sometimes used by CFS patients include acupuncture, aquatic therapy, chiropractic, light exercise, massage, self-hypnosis, stretching, tai chi, therapeutic touch, and yoga.

**Psychotherapy and Supportive Counseling.** Certain psychotherapies, such as cognitive behavioral therapy, have shown promise for facilitating patient coping and for alleviating some of the distress associated with CFS. In addition, any chronic illness can affect the patient’s caregivers and family. In such instances, family therapy may

foster good communication and reduce the adverse impact of CFS on the family.

Cognitive behavioral-therapy (CBT) has been shown to be effective in several, but not all, short-term trials. This therapy is based on a formal, supervised program that emphasizes education of the patient regarding the illness and alteration of patient illness-directed behaviors and may be accompanied by a graded exercise program. The effectiveness of CBT in the treatment of many different types of illness is dependent on the skill and experience of the therapist.

### Pharmacologic Therapy

Pharmacologic therapy should be directed by the patient's primary care provider and is directed toward the relief of specific symptoms experienced by the individual patient. Patients with CFS appear particularly sensitive to drugs, especially those that affect the central nervous system. Thus, the usual treatment strategy is to begin with very low doses and to gradually escalate them only as necessary. The following categories of medications are frequently prescribed for CFS patients. This list does not reflect endorsement of their use; in fact, medications carry side effects and can often aggravate the illness.

**Low-dose Tricyclic Agents.** Tricyclic agents are sometimes prescribed for CFS patients to improve sleep and to relieve mild, generalized pain. Their use in CFS is based on efficacy in a similar illness, fibromyalgia. The tricyclic agents used most often include doxepin (Adapin, Sinequan), amitriptyline (Elavil, Etrafon, Limbitrol, Triavil), desipramine (Norpramin), and nortriptyline (Pamelor). These agents are not used in standard antidepressant doses. Some adverse reactions include dry mouth, drowsiness, weight gain, and elevated heart rate.

**Antidepressant Drugs.** Antidepressants have been used to treat depression in CFS patients. Some studies have not found that antidepressants improve the fatigue, whereas

other studies have found that antidepressants may offer some relief to even those CFS patients who are not currently suffering from depression. Examples of antidepressants used to treat CFS include serotonin reuptake inhibitors (e.g., fluoxetine [Prozac], sertraline [Zoloft], and paroxetine [Paxil]), venlafaxine (Effexor), trazodone (Desyrel), and bupropion (Wellbutrin). A number of mild adverse reactions, which vary according to the specific drug, may be experienced, particularly interruption of restorative sleep.

**Anxiolytic Agents.** These agents are used to treat anxiety and sleeplessness in CFS patients. Examples of these anxiolytic drugs include alprazolam (Xanax), clonazepam (Klonopin), and lorazepam (Ativan). Although useful over short periods for sleeplessness, these agents may aggravate sleep disturbances if used longer than a few weeks or months. Adverse reactions to this group of drugs should be considered prior to their use for symptoms of CFS. Withdrawal symptoms (insomnia, abdominal and muscle cramps, vomiting, sweating, tremors, and convulsions) may occur if the drug is not tapered slowly following prolonged use.

**Nonsteroidal Anti-inflammatory Drugs.** These drugs may be used to relieve pain in CFS patients. Some are available as over-the-counter medications. Examples include naproxen (Aleve, Anaprox, and Naprosen), ibuprofen (Advil, Bayer Select, Motrin, and Nuprin), and piroxicam (Feldene). These medications are generally safe when used as directed but can cause a variety of adverse effects, including kidney damage, gastrointestinal bleeding, abdominal pain, nausea, and vomiting.

**Antimicrobials.** An infectious cause for CFS has not been identified, and antimicrobial agents should not be prescribed for CFS unless, of course, the patient has been diagnosed with a concurrent microbial infection. A controlled trial of the antiviral drug acyclovir found no benefit for the treatment of patients with CFS.

**Anti-allergy Therapy.** Some CFS patients have histories of allergy, and related symptoms may flare periodically. Non-sedating antihistamines may be helpful for CFS patients if allergies play a role in symptom production. Sedating antihistamines can also be of benefit to patients at bedtime. Some of the more common adverse reactions associated with antihistamines include drowsiness, fatigue, and headache.

**Other Miscellaneous Experimental Drugs or Therapies.**

The following medications and therapies are mentioned as a point of information since patients may be aware of them or become acquainted with them through their own information-gathering efforts.

Ampligen is a synthetic nucleic acid product originally designed to stimulate the production of interferons, a family of response modifiers with many functions. Although not effective as an interferon inducer, the agent appears to impact several intracellular pathways. Reports of double-blinded, placebo-controlled studies of CFS patients documented modest improvements in cognition and physical activity among Ampligen recipients compared with the placebo group during the several months that the drug was used; it remains unclear if the drug has longer-term benefits. These preliminary results will need to be confirmed by further study. Ampligen is not approved by the Food and Drug Administration for widespread use, and the administration of this drug in CFS patients should be considered experimental.

Dehydroepiandrosterone (DHEA) was reported in preliminary studies to improve symptoms in some patients; however, this finding has not been confirmed and the use of DHEA in patients should be regarded as a research project.

Intravenous gamma globulin preparations are prepared from pooled human plasma. This preparation contains antibody molecules directed against a broad range of common infectious agents and is ordinarily used as a means for passively immunizing persons with compromised immune systems or

persons who have been exposed to an agent that might cause serious disease without immune globulin treatment. Its use with CFS patients is experimental and based on the unsubstantiated hypothesis that CFS is characterized by an underlying immune disorder or chronic infection. Serious adverse reactions are uncommon, although in rare instances, intravenous gamma globulin may initiate anaphylactic shock.

Complementary and alternative therapies (i.e., biologically based therapies, manipulative and body-based interventions, mind-body interventions, energy therapies, and alternative medical systems) have received considerable attention but have not been critically evaluated.

**Dietary Supplements and Herbal Preparations**

**General Comments.** A variety of dietary supplements and herbal preparations are claimed to have potential benefits for CFS patients. With few exceptions, the effectiveness of these remedies for treating CFS patients has not been evaluated in controlled trials. Contrary to common belief, the “natural” origin of a product does not ensure safety. Dietary supplements and herbal preparations can have potential side reactions, and some can interfere or interact with prescription medications. CFS patients should seek the advice of their physician before using any non-prescription remedy and should inform new providers about any remedies currently being used.

**Vitamins, Coenzymes, Minerals.** Preparations that have been claimed to have benefit for CFS patients include adenosine monophosphate, coenzyme Q-10, germanium, glutathione, iron, magnesium sulfate, melatonin, NADH (nicotinamide adenine dinucleotide), selenium, L-tryptophan, vitamins B12/ C, and A, and zinc. The therapeutic value of all these preparations has not been validated. It is important to note that recent studies of vitamin E show potential harmful effects at the previously recommended daily dose of 400 mcg. Vitamin A and iron are also toxic at high doses.

**Herbal Preparations.** Plants are known sources of pharmacologic materials. However, unrefined plant preparations contain variable levels of the active compound as well as many irrelevant, potentially harmful substances.

Preparations that have been claimed to have benefit to CFS patients include astragalus, borage seed oil, bromelain, comfrey, echinacea, garlic, Ginkgo biloba, ginseng, primrose oil, quercetin, St. John's wort, and Shiitake mushroom extract. Only primrose oil has been evaluated in a controlled study, and the beneficial effects noted in CFS patients have not been independently confirmed. Some herbal preparations (notably comfrey and high-dose ginseng) have recognized harmful effects.

## Patient Support

### How to Select a Support Group

CFS patients may find it therapeutic to meet with other people who have this illness, and often this can be accomplished by joining a local CFS support group.

However, support groups are not appropriate for everyone, and some CFS patients may find that a support group

actually adds to their stress rather than relieving it. Most support groups are free, while

others collect voluntary donations or charge modest membership dues to cover basic expenses (e.g., rental of a meeting space, refreshments at meetings, or photocopying costs).

A useful support group have a history indicating that the group is stable and meeting



the needs of its members, and it should include:

- Both newcomers and patients who have had CFS for longer periods of time to provide a balance of perspectives for the group
- People with whom the CFS patient feels comfortable
- Leaders who empathize, gently draw out shy members, keep others from dominating, and who distill discussion into useful information

Some support groups may put their own interests before those of the individual patient. Groups that engage in any of the following activities should be avoided:

- Promise sure cures and quick solutions
- Conduct meetings that are mainly “gripe” sessions
- Urge patients to stop prescribed treatment and recommend a single solution to their problem
- Encourage patients to swap unused medications or supplements
- Insist that patients reveal private or sensitive information
- Demand allegiance to a cult-like, charismatic leader
- Charge high fees
- Require patients to purchase products

### Careful Consideration of Information about CFS

Because the cause of CFS has not been identified and its effect on the body is not well understood, new, non-validated beliefs about cures and causes of CFS are widely circulated periodically. These may be based on one or more recent reports from the peer-reviewed scientific literature, or they may evolve from the anecdotal remarks of clinicians or scientists at medical meetings. In some cases, the origin is obscure. Even work that is of sufficiently high caliber to be published in the scientific literature is not without limitations and design flaws, and all published work needs to be

**Anti-allergy Therapy.** Some CFS patients have histories of allergy, and related symptoms may flare periodically. Non-sedating antihistamines may be helpful for CFS patients if allergies play a role in symptom production. Sedating antihistamines can also be of benefit to patients at bedtime. Some of the more common adverse reactions associated with antihistamines include drowsiness, fatigue, and headache.

**Other Miscellaneous Experimental Drugs or Therapies.**

The following medications and therapies are mentioned as a point of information since patients may be aware of them or become acquainted with them through their own information-gathering efforts.

Ampligen is a synthetic nucleic acid product originally designed to stimulate the production of interferons, a family of response modifiers with many functions. Although not effective as an interferon inducer, the agent appears to impact several intracellular pathways. Reports of double-blinded, placebo-controlled studies of CFS patients documented modest improvements in cognition and physical activity among Ampligen recipients compared with the placebo group during the several months that the drug was used; it remains unclear if the drug has longer-term benefits. These preliminary results will need to be confirmed by further study. Ampligen is not approved by the Food and Drug Administration for widespread use, and the administration of this drug in CFS patients should be considered experimental.

Dehydroepiandrosterone (DHEA) was reported in preliminary studies to improve symptoms in some patients; however, this finding has not been confirmed and the use of DHEA in patients should be regarded as a research project.

Intravenous gamma globulin preparations are prepared from pooled human plasma. This preparation contains antibody molecules directed against a broad range of common infectious agents and is ordinarily used as a means for passively immunizing persons with compromised immune systems or

persons who have been exposed to an agent that might cause serious disease without immune globulin treatment. Its use with CFS patients is experimental and based on the unsubstantiated hypothesis that CFS is characterized by an underlying immune disorder or chronic infection. Serious adverse reactions are uncommon, although in rare instances, intravenous gamma globulin may initiate anaphylactic shock.

Complementary and alternative therapies (i.e., biologically based therapies, manipulative and body-based interventions, mind-body interventions, energy therapies, and alternative medical systems) have received considerable attention but have not been critically evaluated.

**Dietary Supplements and Herbal Preparations**

**General Comments.** A variety of dietary supplements and herbal preparations are claimed to have potential benefits for CFS patients. With few exceptions, the effectiveness of these remedies for treating CFS patients has not been evaluated in controlled trials. Contrary to common belief, the “natural” origin of a product does not ensure safety. Dietary supplements and herbal preparations can have potential side reactions, and some can interfere or interact with prescription medications. CFS patients should seek the advice of their physician before using any non-prescription remedy and should inform new providers about any remedies currently being used.

**Vitamins, Coenzymes, Minerals.** Preparations that have been claimed to have benefit for CFS patients include adenosine monophosphate, coenzyme Q-10, germanium, glutathione, iron, magnesium sulfate, melatonin, NADH (nicotinamide adenine dinucleotide), selenium, L-tryptophan, vitamins B12/ C, and A, and zinc. The therapeutic value of all these preparations has not been validated. It is important to note that recent studies of vitamin E show potential harmful effects at the previously recommended daily dose of 400 mcg. Vitamin A and iron are also toxic at high doses.