UNIVERSITY of MARYLAND MEDICAL CENTER

Chronic fatigue syndrome

Description

An in-depth report on the causes, diagnosis, and treatment of chronic fatigue syndrome.

Highlights

A federal advisory committee has recommended that the name of the condition be changed from chronic fatigue syndrome (CFS) to myalgic encephalomyelitis or myalgic encephalopathy chronic fatigue syndrome (ME-CFS) to more accurately characterize the complex nature of the disease.

Introduction

Chronic fatigue syndrome (CFS) is not a new disorder. In the 19th century the term neurasthenia, or nervous exhaustion, was applied to symptoms resembling CFS. From the 1930s through the 1950s, outbreaks of disease marked by prolonged fatigue were reported in the United States and many other countries. Beginning in the early to mid-1980s, interest in chronic fatigue syndrome was revived by reports in America and other countries of various outbreaks of long-term debilitating fatigue.

A federal advisory committee has recommended that the Department of Health and Human Services change the name of the condition from chronic fatigue syndrome (CFS) to myalgic encephalomyelitis or myalgic encephalopathy chronic fatigue syndrome (ME-CFS). Because fatigue is just one symptom of the condition, the more scientific term ME-CFS would more accurately reflect the complex nature of the condition.

Unexplained chronic fatigue describes fatigue that lasts for more than 6 months, impairs normal activities, and has no identifiable medical or psychological problems to account for it. In addition to fatigue, people may complain of other problems, such as difficulty with memory or concentration, headaches, or sore muscles or joints.

The symptoms of CFS may be categorized as follows:

- *Chronic fatigue syndrome (CFS)*. Patients must have a number of specific symptoms -- not just fatigue -- to be diagnosed with CFS.
- *Idiopathic chronic fatigue*. If the symptoms do not meet the criteria for CFS, the condition is referred to as idiopathic chronic fatigue, meaning the cause is unknown.

Although the exact causes of CFS are not known, researchers think infection, immune system problems, genetics, and the effects of stress on hormone production may play roles in different patients.

Risk Factors

CFS occurs in both sexes, at all ages, and in all racial and ethnic groups. The Centers for Disease Control and Prevention (CDC) estimates that more than 1 million people in the U.S. have the disease, and millions more have similar symptoms but do not meet the full criteria for a CFS diagnosis. Fewer than 20% of CFS patients in this country have been diagnosed, according to the CDC.

Age and Gender

People who are in their 40s and 50s most often experience chronic fatigue. Studies have found that four out of five people with CFS are women, although women do not appear to have more severe symptoms than men with the disorder.

Children and adolescents can also have CFS, although it is less common than in adults. Most studies indicate that girls are more likely than boys to develop CFS.

Depression and Psychological Factors

Depression is very common in the general population. It affects up to one-fifth of all Americans at some point in their lives, and most depressed people feel fatigued.

The link between psychological disorders and chronic fatigue syndrome is problematic because so many of the symptoms overlap. The rates of depression are very high in CFS patients, possibly higher than in patients with other conditions (notably fibromyalgia and multiple chemical sensitivity).

Depression can lead to suicide, which may explain the increased suicide rate in people with CFS. For this reason, depression should be diagnosed and treated promptly in patients with CFS.

Studies report that most children and adolescents with CFS have psychiatric disorders. Psychological factors in childhood may increase the risk of developing CFS later in life.

Stress

There is some evidence that stress may trigger CFS in people who are at risk for the disease because of genetic factors. People who experienced trauma during childhood -- including sexual and emotional abuse -- are significantly more likely to develop CFS than those who did not experience any trauma. Researchers say the stress of abuse may trigger the condition through its effects on the central nervous system, immune system, and neuroendocrine system (which is related to both nerves and hormones). However, most people who experience childhood trauma do not go on to develop CFS.

Conditions That Commonly Occur in CFS Patients

A number of conditions overlap or coexist with chronic fatigue syndrome and have similar symptoms. Patients with CFS may also have a diagnosis of fibromyalgia, multiple chemical sensitivity, or both. It is not clear whether these and other conditions are risk factors for CFS, are direct causes, have common causes, or have no relationship at all with CFS.

Fibromyalgia. Fibromyalgia causes prolonged fatigue and widespread muscle aches. It is the disease most often confused with CFS. The two conditions also commonly appear together. In fact, many experts believe

fibromyalgia and CFS are different forms of the same condition. Up to 30% of children diagnosed with chronic fatigue syndrome may also have fibromyalgia.

CFS patients experience severe fatigue, whereas fibromyalgia patients experience more pain. The connection between the two conditions may have to do with an increased response to stimulation (called central sensitization), which is thought to cause fibromyalgia and may also contribute to CFS.

People with fibromyalgia have at least 11 tender points -- sites that are very sensitive and painful when touched firmly. The sites often include the:

- Side of the neck
- Top of the shoulder blade
- Outside of the upper buttock and hip joint
- Inside of the knee

Some patients with CFS have similar tender pressure points.

Other common fibromyalgia symptoms include repeated sore throat, headache, low fever, and depression. Like CFS, fibromyalgia is chronic and not curable.

Multiple Chemical Sensitivity. Multiple chemical sensitivity (MCS) is a condition in which certain chemicals appear to cause symptoms similar to those of CFS. MCS has also been observed in people with CFS. The following criteria can help identify MCS:

- The symptoms occur whenever the person is exposed to a chemical. (These are often common chemicals found in popular products, such as perfumes, fabric softeners, and air fresheners.)
- The condition is chronic.
- Symptoms can be produced by exposure to the chemical at levels lower than the person tolerated in the past.
- The symptoms improve when the chemical is removed.
- Symptoms can be triggered by multiple substances that are chemically unrelated.
- Symptoms involve more than one organ system.

As with CFS and fibromyalgia, there is debate as to whether MCS is a specific medical condition or is psychologically based. Everyone is exposed to many chemicals on a daily basis, and it is very difficult to determine whether chemicals are responsible for specific symptoms.

Eating Disorders. Eating disorders, notably bulimia and anorexia, have been observed in patients with CFS. The conditions often have overlapping risk factors, although it is unclear whether one causes the other.

Other Conditions that Commonly Coexist With CFS. The following conditions also may occur along with CFS and are more common in CFS patients than in healthy people:

- Chronic headaches
- Cognitive problems such as difficulty concentrating, impaired memory, and symptoms of attention deficit hyperactivity disorder (ADHD)
- Interstitial cystitis
- Irritable bowel syndrome
- Sleep problems
- Temporomandibular disorder (TMD)

Causes

Theories abound about the causes of chronic fatigue syndrome. No primary cause has been found that explains all cases of CFS, and no blood tests or brain scans can definitively diagnose the condition.

Convergence of Factors. A number of experts believe that CFS develops from a combination of different factors, which may include the following:

- Viruses or other infections
- Genes
- Brain abnormalities
- An overreactive immune system
- Psychiatric or emotional conditions
- Stress-related hormonal abnormalities

Most patients report having a moderate-to-serious physical illness (such as a long-term viral infection) or emotional event (like an episode of depression) before developing CFS. Some experts believe that these factors, alone or in combination, may interact with nervous system and gene abnormalities to trigger CFS.

Still, it is not clear what sequence of events actually leads to the fatigue and other symptoms of this disorder. And experts cannot point to any specific brain or nervous system problem that triggers the condition.

Infections

Because most symptoms of CFS resemble those of a viral illness, many researchers have focused on the possibility that a virus or some other infection causes the syndrome in some cases.

Still, not all CFS patients show signs of infection. Although experts have long been divided on whether infections play any role in this disorder, both viral-related and non-viral CFS may exist.

Viruses. The theory that CFS has a viral cause is based on observations such as:

- In 2009, researchers reported that a retrovirus -- xenotropic murine leukemia virus-related virus (XMRV) -- was present in a large percentage of patients with chronic fatigue syndrome. Initial excitement about this report gave way to disappointment when errors in the research were identified and the researchers retracted their publication.
- Some CFS patients have higher levels of *antibodies* to viruses and other infections that may cause fatigue and other CFS symptoms. These infections include herpesvirus type 6 (HHV-6), human T cell lymphotropic virus (HTLV), Epstein-Barr, measles, coxsackie B, cytomegalovirus, and parvovirus. Many of these viruses are very common, however, and none has emerged as a clear cause of CFS. Well-designed studies of patients with chronic fatigue have not found an increased incidence of any specific infections.
- In up to 80% of cases, chronic fatigue syndrome starts suddenly with a flu-like condition. However, there is no evidence that CFS is spread through casual contact, such as shaking hands or coughing, or by sexual contact.
- In the U.S., there have been reports of cluster outbreaks of CFS occurring within the same household, workplace, and community (but most have not been confirmed by the Centers for Disease Control and Prevention). However, most cases of CFS occur sporadically in individuals, and do not appear to be contagious.
- Adolescents who have had mononucleosis have an increased risk of developing chronic fatigue that

lasts for a year or more after the illness.

Genetic Defects

CFS has been linked with genes that:

- Control the body's response to trauma, injury, and other stressful events
- Are involved with immune system function, communication between cells, and the transfer of energy to cells
- Are related to blood disease and infection

However, no clear pattern has been found, and researchers have been unable to determine how these genes may contribute to CFS symptoms.

Central Nervous System and Hormone Abnormalities

Abnormal levels of certain chemicals in the brain system known as the hypothalamus-pituitary-adrenal (HPA) axis have been proposed as a cause of CFS. This system controls important functions, including sleep, the stress response, and depression. Of particular interest to researchers are certain chemicals and other factors controlled by the HPA axis:

- *Changes in Important Neurotransmitters*. Some patients with CFS have abnormally high levels of serotonin -- a chemical messenger in the brain (neurotransmitter), deficiencies of dopamine -- an important neurotransmitter associated with feelings of reward, or imbalances between the neurotransmitters norepinephrine and dopamine. However, routine testing for these chemical imbalances is expensive and doesn't have any proven value for diagnosing or treating chronic fatigue syndrome.
- *Stress Hormone Deficiencies*. CFS patients appear to have lower levels of cortisol, a stress hormone produced in the adrenal glands. A lack of enough cortisol may be why CFS patients have an impaired response to psychological or physical stresses, such as infection or exercise. However, taking cortisol only improves symptoms in some patients.
- *Disturbed Circadian Rhythms*. In certain patients, CFS may be a disorder of the sleep-wake cycle. The circadian clock -- a group of nerve cells in the brain -- regulates this cycle. A mentally or physically stressful event, such as a viral infection, may disrupt natural circadian rhythms. An interruption in these rhythms can lead to constantly disrupted sleep. Medications that improve sleep can be very helpful for certain patients with CFS.

It is still not clear whether any of these changes are causes of chronic fatigue syndrome, or are only findings in some patients.

Immune System Abnormalities

CFS has sometimes been referred to as the "chronic fatigue immune dysfunction syndrome." A number of studies have found irregularities of the immune system. Sometimes the immune system overreacts, and sometimes it underreacts, but no consistent picture has emerged to confirm that CFS is a disease of the immune system.

Allergies. Some studies have reported that a majority of CFS patients have allergies to foods, pollen, metals (such as nickel or mercury), or other substances. One theory is that allergens, like viral infections, may trigger a cascade of immune abnormalities that lead to CFS. However, most allergic people do not have CFS.

Autoimmune Abnormalities. The risks for chronic fatigue syndrome are similar to the risks for a number of autoimmune diseases. However, it is not clear whether people with CFS have the autoantibodies (antibodies that attack the body's own tissues) found in people with autoimmune disorders. It is not likely that CFS is caused by autoimmunity.

Low Blood Pressure

Some patients who fit the criteria for chronic fatigue syndrome also have symptoms of a condition known as neurally mediated hypotension (NMH). NMH causes a dramatic drop in blood pressure when a person stands up, even for as little as 10 minutes. Its immediate effects can be light-headedness, nausea, and fainting. However, studies have reported no higher incidence of NMH in chronic fatigue patients.

Psychological Factors

Psychological, personality, and social factors are strongly associated with chronic fatigue in most patients. The complex relationship between physical and emotional factors has yet to be fully understood, however. Studies have not found any consistent association between emotional or personality disorders and CFS. Psychological factors, then, are unlikely to be a primary cause of CFS. However, they may play a role in increasing susceptibility to the disorder. In many cases, CFS leads to psychological and social problems.

Diagnosis

It is very difficult to diagnose chronic fatigue syndrome. Even experts do not have a clear definition of what chronic fatigue actually is, or what mechanisms in the brain or nervous system are responsible for it. The best diagnostic approach is to determine whether the patient matches the criteria for CFS and rule out other possible causes of symptoms.

Criteria for Chronic Fatigue Syndrome

In May 2006, the Centers for Disease Control and Prevention (CDC) released a revised definition for chronic fatigue syndrome. In the revised definition, chronic fatigue syndrome falls under the broader category of chronic fatigue, which is defined as unexplained fatigue that lasts for 6 months or longer. Chronic fatigue is part of an even broader category called prolonged fatigue, which is fatigue that lasts for 1 month or more.

Patients with CFS must meet the following criteria:

1. Unexplained, continuing or returning chronic fatigue that is either new or that started at a definite period of time, the fatigue is not caused by exertion, is not relieved by rest, and significantly reduces activities such as work, education, and social life.
2. Also, four or more of the following symptoms, which must have continued or returned during 6 or more consecutive months of illness and must not have started before the fatigue:
    - Significant impairment in short-term memory or concentration
    - Sore throat
    - Tender lymph nodes
    - Muscle pain
    - Joint pain without swelling or redness
    - Headaches that are new, more severe, or that occur in a different pattern
    - Unrefreshing sleep
    - General discomfort or distress (malaise) that lasts for more than 24 hours after exertion

In 2007, the British National Institute for Health and Clinical Excellence (NICE) released new guidelines for diagnosing and treating CFS in adults and children. According to these guidelines, CFS may be diagnosed if the person has disabling fatigue that starts suddenly, lasts a long time, keeps coming back, and can't be explained by another condition.

People with CFS also can have the following symptoms:

- Difficulty thinking, concentrating, remembering, finding the right words, planning, and organizing
- Difficulty sleeping
- Dizziness or nausea
- General malaise or flu-like symptoms
- Headaches
- Muscle or joint pain in many areas of the body without inflammation
- Painful lymph nodes without disease
- Fast heartbeat (palpitations) without heart problems
- Sore throat
- Worsening of symptoms with physical exertion

After ruling out other possible causes, the doctor should consider a diagnosis of CFS if symptoms have lasted for 4 months in adults or 3 months in children. Children should be diagnosed by a pediatrician.

Personal and Medical History

A doctor should first take a careful personal and family medical history (which may include a psychological profile), and perform a thorough physical examination. Patients should be prepared to answer questions such as:

- When did the fatigue first begin?
- Does anything make it worse or better?
- Is it better at certain times of the day?
- Does physical activity make it worse?
- Are there any other symptoms?
- Has anyone else in the family ever complained of fatigue?
- Is your personal and professional life stressful?

The doctor may also ask about any changes in weight, or request that a patient monitor his or her morning and afternoon body temperatures. Patients should report any drugs they are taking, including vitamins and over-the-counter or herbal medications.

Laboratory Tests

The following tests are typically recommended to rule out other conditions that can cause persistent fatigue:

- Blood count
- Blood tests for gluten sensitivity
- C-reactive protein
- Creatine kinase
- Erythrocyte sedimentation rate or plasma viscosity
- Liver function
- Random blood sugar (glucose)
- Serum calcium

- Serum creatinine
- Serum ferritin levels (only in children)
- Thyroid function
- Urea and electrolytes
- Urine test for protein, blood, and glucose

No one blood, urine, or other laboratory test can diagnose CFS. If any test is abnormal, it is not useful for diagnosing CFS specifically, and the doctor should look for other possible causes.

Research has discovered certain components in urine that are unique in people with CFS, and that may someday be used as markers to diagnose the disease. Potential blood markers, including antibodies to Epstein-Barr virus, increased levels of isoprostanes, and decreased levels of alpha-tocopherol (vitamin E) -- have also been found in some people with CFS.

Identifying Other Causes of Chronic Fatigue

Many other common conditions can lead to temporary exhaustion, including:

- Depression
- Excessive stress
- Extreme exercise
- Infections
- Pregnancy

In most of these cases, getting enough rest can relieve fatigue.

However, long-term fatigue and other CFS symptoms can be signs of more serious medical or psychological problems. It is important to rule out other conditions that can cause these symptoms by performing a careful evaluation and laboratory tests.

Infectious Mononucleosis and Epstein-Barr Virus. Infectious mononucleosis causes fatigue and swollen glands. It primarily affects adolescents and young adults. Research finds that fatigue may last for a year or more in a small percentage of adolescents who have had mononucleosis. Females and people with more severe fatigue are more likely to develop chronic fatigue syndrome after mononucleosis. Blood tests can detect the Epstein-Barr virus (EBV), which causes mononucleosis.

Autoimmune Diseases. Some diseases, including systemic lupus erythematosus, multiple sclerosis, and rheumatoid arthritis are caused by *autoimmunity*, a condition in which the person's immune system attacks the body's own tissues. These diseases, like CFS, occur more often in women than in men. The early symptoms of these conditions, such as muscle and joint pain and fatigue, may mimic CFS symptoms. Most of these conditions can be confirmed with laboratory or x-ray/radiologic tests. However, some autoimmune diseases may develop slowly. Doctors should keep track of any changes in symptoms over time to rule out these serious illnesses.

Post-Lyme Disease Syndrome. Rarely, patients who have been treated with antibiotics for Lyme disease continue to have symptoms that resemble the symptoms of chronic fatigue syndrome. It is not clear whether these symptoms are caused by Lyme disease.

Depression and Severe Mental Disorders. The Centers for Disease Control (CDC), which established the definitions for chronic fatigue syndrome, recognizes depression as one of the symptoms of CFS. More than a third of CFS patients may be depressed. However, according to the CDC, people with major depression or

other severe psychiatric disorders, including bipolar disorder and schizophrenia, does not meet the criteria for chronic fatigue syndrome.

Symptoms of major depression include the following:

- A depressed mood every day
- Significant weight gain or loss (10% or more of a person's usual body weight)
- Insomnia or excessive sleeping
- Restlessness or a sense of being slowed down
- Low energy every day
- Worthless or guilty feelings
- An inability to concentrate or make decisions
- Suicidal thoughts
- Loss of interest and enjoyment

A person who has several of these symptoms and no physical symptoms (such as a sore throat, aches and pains, or fever) is likely to have major depression. The longer fatigue has continued without physical symptoms, the more likely that the diagnosis is depression.

A persistent form of minor depression called dysthymia may be more difficult to differentiate from CFS and may actually account for some CFS cases. Dysthymia has many of the same symptoms as major depression, but these symptoms are less intense and last much longer -- at least 2 years. The symptoms of dysthymia have been described as a "veil of sadness" that covers most activities.

Patients with depression generally perceive their illnesses differently than people with CFS:

- Patients with depression have significantly lower self-esteem, more thought distortions (for instance, focusing on the negative), and they believe their condition stemmed from psychological factors.
- CFS patients, even those who also have depression or dysthymia, tend to identify medical causes as the source of their problems and to focus on physical symptoms.

Many patients with CFS become depressed and anxious because they feel so exhausted all the time. CFS may also lead to stress due to social isolation and poverty. These problems can contribute to, and even cause emotional disorders, which can worsen CFS.

Sleep Disturbances. Certain sleep disorders may cause persistent fatigue and can be confused with CFS:

- Sleep apnea is a common disorder that causes many temporary pauses in breathing during the night. Many patients are not aware that they have sleep apnea, but they tend to feel tired during the day.
- Other sleep disorders that cause daytime fatigue include insomnia and restless legs syndrome (RLS).

Researchers have found that people with CFS have altered amounts of slow wave sleep, which could indicate a problem with sleep regulation. It is common for people with CFS to be restless sleepers, and to wake up feeling unrefreshed.

Conditions that Cause Joint Pain, Muscle Aches, or Both. A number of illnesses cause CFS symptoms, such as muscle aches and joint pain, fever, and fatigue.

Severe Obesity. People who are severely obese often have symptoms of chronic fatigue because of the stress imposed by their weight. People who are obese are also at higher risk for sleep apnea, which can confuse the diagnosis.

Other Medical Conditions that Usually Rule Out CFS. Many diseases, both minor and serious, can cause long-term fatigue, including:

- Anemia
- Anorexia nervosa or bulimia nervosa
- Chronic kidney disease
- Diabetes
- Hemochromatosis (a hereditary disease caused by iron overload)
- Hepatitis
- Hypothyroidism
- Neuromuscular diseases (such as myasthenia gravis)
- Various forms of cancer

Drugs and Alcohol. Fatigue is a side effect of many prescription and over-the-counter medications, such as antihistamines. In addition, dependence on or abuse of alcohol or illicit drugs may lead to chronic fatigue. Medications should be considered as a possible cause of fatigue in people who have recently started, stopped, or changed medicines. Caffeine withdrawal can also cause fatigue.

Prognosis

The severity of chronic fatigue syndrome varies. Often, patients with CFS report that they have trouble fulfilling both home and work responsibilities. Many people with CFS cannot work more than part-time, and they are unable to do even the simplest tasks, such as light housework.

Patients with CFS are more likely to lose their jobs, possessions, and support from friends and family than are people who have other conditions that cause fatigue.

Mental Incapacity

Most patients say that while fatigue is the most debilitating symptom of CFS, mental impairment (such as an inability to concentrate or remember) is the most distressing symptom. The effects of CFS on mental function are complex. Some experts believe that the impaired mental functioning is due to depression, which is common in CFS patients.

Although general intelligence is not impaired, CFS patients may test lower in certain mental functions, particularly their speed and efficiency in processing complex information. Many also have memory impairments. This impaired mental function may occur, even if the person does not have depression or other psychiatric disorders.

Long-Term Outlook in Adults

Because the illness is hard to define, and there are few objective measures for recovery, experts have found it difficult to determine the long-term course of the disease. Although some studies have reported that more than half of patients who complain of chronic fatigue are still fatigued at 2 years, with long-term treatment many patients can improve and even make a real recovery.

Although CFS itself is not fatal, suicide can be a real risk. Continuing treatment for both CFS and depression can help reduce this risk.

Outlook in Children

Although children with symptoms of chronic fatigue have not been as well studied as adults, limited evidence suggests that CFS can be disabling in young people. Studies report that adolescents who meet the criteria for CFS experience anxiety, depression, and are often absent from school. Children with CFS may have more difficulty paying attention and remembering, which may explain why these kids have more trouble in school than their peers.

Still, some studies indicate that children have a better prognosis than adults and most will recover after 1 - 4 years. Several studies have found that cognitive-behavioral therapy is an effective treatment for adolescents with CFS.

Treatment

There is no proven or reliable cure for CFS, and no drug has been developed specifically for this disorder. Because CFS remains poorly understood, many patients have problems finding good care. Overall, the recommended strategy for treatment includes a combination of the following:

- A healthy diet
- Antidepressant drugs (in some cases), usually low-dose tricyclic antidepressants
- Cognitive-behavioral therapy (CBT) and graded exercise (for certain patients)
- Gradual return to modest-intensity exercise
- Other medications
- Sleep management techniques

Patients who stay as active as possible and try to have some control over their disorder have the best chance for improvement. It is important for patients to choose physicians who think of CFS as a medical condition with psychiatric components. They should be wary of any doctor who recommends excessive and expensive treatments that may have serious side effects and no proven benefits.

Patients with severe CFS that cannot be managed with lifestyle changes and medications should ask their doctor about enrolling in a clinical trial.

Cognitive-Behavioral Therapy

The power of the mind to improve health problems is significant, and treatments that promote a positive outlook are beneficial for any disease, including CFS. Seeing a therapist who is trained in cognitive-behavioral therapy (CBT) can help CFS patients regain a sense of control over their lives.

The Goals of Cognitive-Behavioral Therapy. The primary goals of CBT (or cognitive therapy) are to change any distorted perceptions patients have of the world and of themselves, so they can change their behavior accordingly. This means learning to think differently about fatigue, improving their ability to deal with stressful situations, and better managing their disorder. CBT can also help manage sleep problems and regulate activity levels. Cognitive therapy is particularly helpful for defining and setting limits, behaviors that are extremely important for CFS patients.

The Procedure. CBT is usually performed over 6 - 20 sessions, each lasting about an hour. Patients are also given homework, which usually includes keeping a diary and attempting tasks they avoided in the past because of their negative attitude.

A typical CBT program may involve the following measures:

- Keeping a Diary. An energy diary serves as a general guide for setting limits and planning activities. You use the diary to track any factors, such as a job or relationship, that may be worsening or improving your fatigue. It is also used to track the times of day when your energy levels are at their highest and lowest.
- Pacing activities. This involves adjusting schedules and activities based on energy peaks and valleys recorded in the diary. For instance, you may take a nap during low-energy times and plan important activities during high-energy times. Developing regular daily routines around energy spurts or drops may help you establish a more predictable pattern.
- Confronting Negative or Discouraging Thoughts. Challenge and reverse negative beliefs (such as "I'm not good enough to control this disease, so I'm a total failure."), and use coping statements ("In what ways can I control this disease?") instead.
- Being Flexible. Your energy levels will probably never be entirely predictable. You must be prepared to adapt to energy variations. Instead of taking a long nap, for instance, you may need 5- to 10-minute rest periods, possibly involving relaxation or meditation, every hour or more often.
- Setting Limits. Setting limits helps you manage mental and physical stresses so you do not get into situations in which you are likely to fail. For example, you break tasks down into incremental steps and focus on doing one step at a time.
- Prioritizing. You learn to drop less critical tasks or delegate them to others.
- Managing Impaired Concentration. Seek out activities that are appealing, focus your attention, and increase alertness. Ask for instructions as concise, simple statements. And keep distractions, such as music or talking, to a minimum.
- Accepting Relapses. Over-coping and accomplishing too much too soon can often cause symptoms to return. Respect these relapses and back off. Do not consider them a sign of treatment failure or personal failure.

Using these techniques, you gradually shift from the idea that you are helpless against the fatigue that dominates your life to the perception that fatigue is only one negative experience among many positive ones.

Success Rates. One review of CFS trials reported that, of all therapies available to CFS patients, only cognitive behavioral therapy (CBT) and graded exercise showed conclusive benefits. CBT is effective at reducing the symptoms of fatigue, and it appears to be more effective than other psychological therapies. Although CBT doesn't bring patients completely back to normal, research has found that people who use the therapy have higher mental health scores, and are able to walk faster and with less fatigue than those who do not use CBT. Cognitive therapy may also be an effective treatment for adolescents with CFS. Young patients who receive CBT report improvements in fatigue, function, and school attendance. However, not all studies support the benefits of cognitive therapy for CFS.

It is important to note that different therapists have different assumptions about CBT and may use different techniques. For instance, some therapists believe that CFS is a purely psychological problem. They encourage patients to stop focusing on the physical causes of their condition and stop using assistive devices, and instead take part in challenging exercise programs. Other therapists do not attempt to change patients' beliefs, but instead focus on helping them conserve energy and better cope with the limitations of their illness. When considering CBT, patients and their families must be aware of these important differences in therapists.

Graded Exercise

A number of studies have reported the benefits of a graded exercise program, in which patients gradually perform more intense exercises as their abilities improve. Research has found that most CFS

patients who are able to engage in exercise, particularly aerobic exercise, report less fatigue and better daily functioning and fitness. Exercise works best for CFS when combined with CBT and education.

Graded exercise may not work for all patients with CFS, however. Some CFS patients are so severely affected by their condition that they are unable to exercise. In all CFS patients, over-exercising can intensify symptoms. Some patients experience profound fatigue after even moderate exercise.

The following tips may help CFS patients who are starting on an exercise program:

- Work with your health care provider to determine a good starting level of activity for you. Start slowly, beginning with as few as 3 to 5 minutes of moderate exercise a day. The goal is to increase activity gradually by about 20% every 2 to 3 weeks, until you can handle about 30 minutes a day. Once you reach 30 minutes a day, start to increase the aerobic intensity of your workouts. (Exercise capacity varies greatly among people with CFS. Some people may not be able to increase their aerobic intensity.)
- Establish limits and keep within them to avoid overexerting yourself and relapsing.
- Experiment with different forms of physical activity that suit your energy levels. Some patients report great benefits from yoga or tai chi, which combine exercise with meditation.
- You will have setbacks. Do not get discouraged.

Activity Management

Work with your health care provider to find a level of activity you can handle. Then gradually increase your activity level. Activity management should involve:

- Balancing your time between activity, rest, and sleep
- Spreading out more challenging tasks throughout the week
- Breaking big tasks into smaller, more manageable ones
- Avoiding doing too much on days when you feel tired

Healthy Diet

Although there is no evidence that any specific foods influence CFS, it's always a good idea to eat a healthy diet that includes:

- Plenty of fresh, dark-colored fruits and vegetables, which are rich in antioxidants
- Fiber-rich foods
- Limited saturated fats (found in animal products)
- Omega-3 essential fatty acids, found in certain fish and oils
- Increased salt (*only* for people with low blood pressure)
- Starchy foods, particularly for nausea

Other Approaches for Managing Chronic Fatigue Syndrome

Stress Reduction Techniques. Relaxation and stress-reduction techniques may help you manage chronic pain. These techniques also can help relieve the stress associated with CFS. They are not useful, however, as the main treatment for CFS.

A number of relaxation techniques are available, including:

- Biofeedback
- Deep breathing exercises
- Hypnosis
- Massage therapy
- Meditation
- Muscle relaxation techniques
- Yoga

Supportive Family and Groups. Having strong, supportive relationships with family and friends can help CFS patients get better. However, try not to impose unreasonable expectations on loved ones. Attending support groups in which you share experiences with fellow patients may be very helpful for improving your coping abilities.

Medications

No medications are specifically approved to treat CFS. However, some medications may be useful for pain or other symptoms, or in cases in which CFS has a specific medical cause. Doctors generally use combinations of drugs to accomplish specific goals, such as medication at night to improve sleep and medication in the morning to improve thinking and energy. Treatment is very individualized.

Mild Pain Relievers

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs). Patients with CFS may benefit from using NSAIDs -- common pain relievers that reduce pain and inflammation. Types of NSAIDs include aspirin, ibuprofen (Motrin, Advil, Nuprin), and naproxen (Aleve, Naprosyn, Naprelan, Anaprox).

Patients should use only the lowest effective dose, because NSAIDs can cause heart problems (such as increased blood pressure and risk of heart attack), kidney problems, and stomach bleeding. Patients who are at increased risk for stomach bleeding and ulcers should either switch to another type of pain reliever, or take the NSAID along with a proton-pump inhibitor drug, such as omeprazole (Prilosec) or esomeprazole (Nexium), or with misoprostol (Cytotec). (Misoprostol can cause miscarriage and should not be used by women who may be pregnant.)

People with high blood pressure, severe circulation disorders, or kidney or liver problems, as well as people who take diuretics or oral hypoglycemics must be closely monitored if they need to use NSAIDs on a long-term basis. Because NSAIDs reduce blood clotting, NSAID users should stop taking these drugs a week before surgery.

Other side effects of NSAIDs include:

- Depression (possibly)
- Dizziness
- Headaches
- Ringing in the ears
- Skin rashes

COX-2 Inhibitors (Coxibs). Coxibs inhibit an inflammation-promoting enzyme called COX-2. This drug class provides pain relieving and anti-inflammatory benefits equal to those of NSAIDs while causing less gastrointestinal distress and bleeding. However, following numerous reports of heart problems and strokes, as well as skin rashes and other harmful side effects, two COX-2 inhibitors were withdrawn from the market.

Celecoxib (Celebrex) is still available, but it must be used with great care. Patients should discuss with their doctors whether this drug is appropriate and safe for them.

Antidepressants

Because of the association between depression and CFS, patients often try taking antidepressants, with varying degrees of success. Common side effects of many antidepressants include:

- Constipation
- Dry mouth
- Reduced sexual drive
- Restlessness
- Slightly increased heart rate

Almost all antidepressants interact with other drugs, and some of these interactions are very serious.

Tricyclic Antidepressants. Antidepressants known as tricyclics affect brain chemicals that are involved in managing pain. These medications may be particularly helpful for CFS patients. For example, the tricyclic amitriptyline (Elavil) is known to relieve many CFS symptoms, including sleeplessness and low energy levels. Other tricyclics include doxepin (Sinequan), desipramine (Norpramin), nortriptyline (Pamelor), clomipramine (Anafranil), and imipramine (Tofranil, Janimine). Tricyclics improve sleep and relieve pain. However, it can take 3 to 4 weeks for symptoms to improve.

Patients with CFS normally respond to much lower doses of tricyclics than those used to treat people with depression. In fact, many CFS patients cannot tolerate the higher doses commonly used to treat depression. As with all medications, tricyclics must be taken as directed. An overdose can be life-threatening.

Other Antidepressants. Other antidepressants, including bupropion (Wellbutrin), nefazodone (Serzone), or mirtazapine (Remeron) affect combinations of different neurotransmitters, and some may have moderate benefits for CFS patients. For example, nefazodone may improve mood, fatigue, and sleep disturbances.

SSRIs. The popular antidepressants known as selective serotonin-reuptake inhibitors (SSRIs) may be helpful for CFS patients who experience significant depression. These drugs include fluoxetine (Prozac), sertraline (Zoloft), and paroxetine (Paxil). Cymbalta (duloxetine) is a new antidepressant that is classified as a selective serotonin and norepinephrine reuptake inhibitor (SSNRI) because it affects both neurotransmitters. SSRIs should not be taken with tricyclics, because the combination may cause dangerous side effects.

Other Drugs Being Investigated for CFS

S*timulants*. Stimulant drugs, which are often used to treat attention deficit hyperactivity disorder (ADHD), may be helpful for patients with CFS who also have cognitive problems, such as difficulty concentrating and memory problems. Stimulants include Dexamphetamine, Adderall, methylphenidate (Ritalin) and Ritalin-like drugs such as Focalin, Concerta, Ritalin LA, and Metadate.

Strattera and Provigil are two other drugs that have been evaluated for the treatment of fatigue, but they have not been well studied.

Alternative Remedies

Because of the difficulties in treating chronic fatigue syndrome, many patients seek alternative therapies.

Some of these therapies, such as acupuncture, yoga, and relaxation techniques, may be helpful and are not dangerous.

Some people find that vitamin and mineral supplements relieve their CFS, but there is no scientific evidence that these supplements work. Herbal and dietary supplements that are sometimes used for CFS include coenzyme Q10, vitamin B12, vitamin C, magnesium, multivitamins, DHEA, ginseng, and acetylcarnitine. More research is needed to determine whether any herbs can actually benefit patients with CFS.

The FDA does not regulate herbal remedies and dietary supplements, which means manufacturers and distributors do not need FDA approval to sell their products. The amounts of the active ingredients in these remedies may not always match what is claimed on the label. Any substance that can affect the body's chemistry can, like any drug, produce side effects that may be harmful. There have been a number of reported cases of serious and even lethal side effects from herbal products. Some herbs, such as St. John's wort, ginkgo, and comfrey may cause serious side effects and drug interactions.

Many problems occur with herbal remedies imported from Asia. One study reported that a significant percentage of these remedies contain toxic metals. Studies have suggested that up to 30% of herbal remedies imported from China have been laced with potent prescription drugs, such as phenacetin and steroids.

CFS patients should be wary of the following remedies:

- St. John's wort. This herbal remedy is being investigated for mild depression. In one study, St. John's wort lessened fatigue in CFS patients, even in those who did not consider themselves to be depressed. However, St. John's wort may have some serious side effects; for example, it can interact with blood thinning medications.
- Melatonin. Some CFS patients use melatonin to improve sleep. However, the small amount of research available has not shown melatonin to be helpful for CFS.
- Gingko. Although gingko is generally safe, there is an increased risk of bleeding when it is taken at high doses. In addition, gingko can interact with high doses of vitamin E and anti-clotting medications. Commercial gingko preparations have also been reported to contain colchicine, a substance that can be harmful in pregnant women and in people with kidney or liver problems.
- Comfrey. Comfrey is an herbal remedy used for a number of inflammatory problems. However, comfrey can be toxic to the liver, and animal studies have reported a possible cancer risk. Comfrey is banned in Canada and other countries. It is still widely available in the U.S., although the FDA has asked supplement manufacturers to remove it from their products.
- Ma Huang. This ingredient contains the stimulants ephedrine and kola nut. Serious adverse reactions, including seizures, psychosis, and death, have been reported in people taking this supplement.

Other alternative remedies with no proven benefit and possible dangerous side effects include:

- Bee pollen (can cause an allergic reaction)
- High colonic enemas
- Hydrogen peroxide injection (can cause blood clots or strokes)
- Injections of liver extract
- Megadoses of vitamins (can be toxic and have shown no benefits)
- Superoxide dismutase (SOD)

Resources

- www3.niaid.nih.gov -- National Institute of Allergy and Infectious Diseases

- www.cdc.gov/cfs - Centers for Disease Control and Prevention, Chronic Fatigue Syndrome information
- www.cfids.org -- The Chronic Fatigue and Immune Dysfunction Syndrome Association of America
- www.ncfsfa.org -- National Chronic Fatigue Syndrome and Fibromyalgia Association
- www.theacpa.org -- American Chronic Pain Association
- www.ampainsoc.org -- American Pain Society
- www.iasp-pain.org -- International Association for the Study of Pain
- www.medicalacupuncture.org -- American Association of Medical Acupuncture

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- Harvey Simon, MD, Editor-in-Chief, Associate Professor of Medicine, Harvard Medical School; Physician, Massachusetts General Hospital. Also reviewed by David Zieve, MD, MHA, Medical Director, A.D.A.M., Inc.

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