



What is Fibromyalgia?

Fibromyalgia (FM), pronounced: *fy-bro-my-AL-ja*, is a central sensitivity syndrome (CSS) characterized by chronic pain, stiffness, and tenderness of muscles, tendons, and joints without inflammation. For those with severe symptoms, FM can be extremely debilitating and disabling, interfering with even routine daily activities.

Who Gets FM?

FM experts estimate that about 10 million Americans and approximately 3-6% of the population worldwide suffer with FM. It is estimated that the average care cost per patient per year is close to \$2,300.

While FM is most common in women, the illness strikes men, women, and children of all ages and ethnic backgrounds. For those with severe symptoms, FM can be extremely debilitating and disabling, interfering with even routine daily activities.

What Causes FM?

The cause of FM remains elusive, but there are many triggered events thought to precipitate its onset. FM can be triggered in pre-disposed individuals by a traumatic injury to the body or brain (i.e., a vehicular accident or fall), a severe illness or surgery, or acute emotional stress. These triggered events don't cause FM, but they may awaken the underlying physiological abnormalities that are already present in the body of an FM patient.

How Is FM Diagnosed?

FM diagnosis requires hands on evaluation by a skilled medical professional. This evaluation usually consists of:

1. Ruling out medical conditions whose symptoms mimic FM (i.e., thyroid_disease, MS, lupus, etc.)
2. An extensive medical history which includes a discussion of the nature and duration of specific symptoms.
3. A physical examination which includes a tender point exam - The criteria used for diagnosis is widespread pain for a duration of more than 3 months. Another criterion is pain in 11 of the 18 tender point locations when a pressure of 4 kgs is used in the tender point location. ([More about FM Tender Points](#))

What Are The Symptoms of FM?

Fibromyalgia (FM) is characterized by the presence of multiple symptoms. The severity of symptoms can change depending on stress levels, your activity level, the weather, and other illnesses. There's a link between FM flare-ups and the menstrual cycle. Many women who suffer from FM report an increase in headaches, body pain, memory problems and sleep difficulties, in the period leading up to, and during the first half of their menses.

In an article published in PubMed, researchers concluded, "*The menstrual cycle and the onset of menopause affect pain and the severity of other FM-related symptoms in approximately one half of the subjects.*"

Ninety percent of FM sufferers also are afflicted with Chronic Fatigue Syndrome. In addition to pain and fatigue, common symptoms include malaise, headaches, numbness and tingling, dizziness; sleep disturbance, swollen feeling in tissues, stiffness, sensitivity to noise and stress, and cognitive impairment. [More information about symptoms.](#)



How is FM Treated?

Since there is no cure for Fibromyalgia (FM), treatments are geared towards improving the quality of sleep and reducing pain. Treatments take on several different forms.

There are medications, trigger-point injections, physical therapy, occupational therapy, acupuncture, acupressure, relaxation techniques, biofeedback techniques and osteopathic manipulative medicine.

Deep level sleep (stage 4 sleep) is crucial for many body functions such as tissue repair, antibody production, and the regulation of various neurotransmitters, hormones and immune system chemicals.

Therefore, sleep disorders that occur in FM are treated first because they may be a strong contributing factor to the symptoms of FM. There are many different types of treatments for sleep disorders to be considered. [More information about treatments.](#)

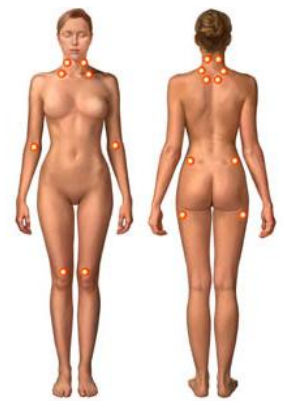
What Are Tender Points?

Tender points are areas that cause pain but do not display the typical signs of discomfort, such as heat, redness, or swelling. There are eighteen tender points that consist of nine bilateral sites adding up to eighteen in total. The red dots in the picture to your left indicate the 18 tender point sites that have been identified by the American College of Rheumatology (ACR).

According to the ACR criteria, FM is present when a patient suffers widespread pain for at least three months and feels pain in 11 or more of the 18 pressure point sites.

Doctors measure these tender points in one of two ways: by pressing the site with a finger or by using a slightly higher-tech method called dolorimetry

In the dolorimetry method, the examiner presses a rubber endplate, attached to a spring-loaded force gauge, into the tender point site with increasing force. Patients are then asked to say when they stop feeling pressure and start feeling pain. [More information about FM tender points.](#)



Tender Point Locations in Red

Can FM Be Cured?

Although there is currently no cure for FM, symptoms can be substantially controlled by comprehensive treatment that includes education, medication, and physical conditioning to improve aerobic capacity and flexibility, and psychological intervention aimed at stress management.

How Long Can FM Last?

People with FM may reach a remissive period after a few months, or after many years, or never at all. Often, the symptoms change over time, or cycle irregularly. Relapses are common, especially after stressful life events or additional illness. Exertion can cause not merely a relapse, but a worsening of overall health. Undiagnosed cases of FM often worsen as the sufferer attempts to return to a "normal" level of activity, only to make their condition worse through exertion. Of those FM patients moderately to severely affected, many may expect to remain so for an indeterminate period, even for the duration of their life.



What is Chronic Fatigue Syndrome/Myalgic Encephalopathy? (CFS/ME)

Chronic Fatigue Syndrome Myalgic Encephalopathy (CFS/ME) is a serious, disabling and chronic neuro-immune illness affecting approximately 1 million people in the United States and as many as 17 million people worldwide.

CFS/ME is characterized by debilitating fatigue (exhaustion and extremely poor stamina), neurological problems and a variety of flu-like symptoms.

Myalgic - *meaning muscle* - indicates the pain involved in the muscles. Encephalo - *meaning brain* - indicates that the brain functioning is involved. Pathy - *the word for sickness or illness*.

The illness is also known as chronic fatigue immune dysfunction syndrome (CFIDS).

Who Gets CFS/ME?

CFS/ME occurs four times more frequently in women than in men, although people of either gender can develop the disease. The illness occurs most often in people in their 40s and 50s, but people of all ages can get CFS/ME. Children and adolescents are not immune to its effects. Most studies indicate that girls are more apt to develop CFS/ME than boys, although one study found the incidence of the syndrome to be equal. According to a 1999 study, half of the children and adolescents with CFS/ME also suffer psychiatric disorders, primarily anxiety, and also depression.

CFS/ME occurs in all ethnic and racial groups, and in countries around the world. Research indicates that CFS/ME is at least as common among African Americans and Hispanics as it is among Caucasians. People of all income levels can develop CFS/ME.

CFS/ME is sometimes seen in members of the same family, but there's no evidence that it's contagious. Instead, there may be a familial or genetic link. Further research is needed to explore this.

What Causes CFS/ME?

The cause of the illness is not yet known. Current theories are looking at the possibilities of neuroendocrine dysfunction, viruses, environmental toxins, genetic predisposition, or a combination of these. For a time it was thought that Epstein - Barr virus (EBV), the cause of mononucleosis, might cause CFS/ME but recent research has discounted this idea. The illness seems to prompt a chronic immune reaction

in the body, however it is not clear that this is in response to any actual infection - this may only be a dysfunction of the immune system itself.

Scientists have discovered a potential retroviral link to CFS/ME. Researchers from the Whittemore Peterson Institute, the National Cancer Institute, and the Cleveland Clinic, report this finding online in the Oct. 8, 2009, issue of *Science*.

"We now have evidence that a retrovirus named XMRV is frequently present in the blood of patients with CFS. This discovery could be a major step in the discovery of vital treatment options for millions of patients," said Judy Mikovits, PhD, director of research for WPI and leader of the team that discovered this association.

Researchers cautioned, however, that this finding show there is an association between XMRV and CFS but does not prove that XMRV causes CFS. There is still a long way to go, but at least now it can be proven that CFS/ME is indeed a real illness.

Many medical observers have noted that CFS/ME seems often to be "triggered" by some stressful event, but in all likelihood the condition was latent beforehand. Some people will appear to get CFS/ME following a viral infection, or a head injury, or surgery, excessive use of antibiotics, or some other traumatic event. Yet it's unlikely that these events solely could be a primary cause.



How Is CFS/ME Diagnosed?

Doctors find it difficult to diagnose CFS/ME because it has the same symptoms as many other diseases. When talking with and examining you, your doctor must first rule out diseases that look similar, such as multiple sclerosis and systemic lupus erythematosus in which symptoms can take years to develop. In follow-up visits, you and your doctor need to be alert to any new cues or symptoms that might show that the problem is something other than CFS/ME. CFS/ME is diagnosed as a process of ruling out everything else!

The criteria for diagnosing CFS were officially defined by the CDC in 1988 and revised in 2001. The Oxford criteria differ slightly. The British criteria insist upon the presence of mental fatigue, although the American criteria include a requirement for several physical symptoms, reflecting the belief that CFS has an underlying immune or infectious pathology.

Centers for Disease Control's Criteria for CFS clinically evaluated, unexplained, persistent, or relapsing fatigue that is:

- ▶ Of new or definite onset
- ▶ Not a result of ongoing exertion
- ▶ Not alleviated by rest
- ▶ Results in a substantial reduction in previous levels of occupational, social, or personal activity

Four or more of the following symptoms that persist or recur during six or more consecutive months of illness and that do not predate the fatigue.

- ▶ Self-reported impairment of short-term memory or concentration
- ▶ Sore throat
- ▶ Tender lymph nodes
- ▶ Muscle pain
- ▶ Multi joint pain without swelling or redness
- ▶ Headaches of a new type, pattern, or severity
- ▶ Unrefreshed and/or interrupted sleep
- ▶ Post exertion malaise (a feeling of general discomfort or uneasiness) lasting more than 24 hours

Exclusion Criteria:

- ▶ Active, unresolved or suspected disease that is likely to cause fatigue
- ▶ Psychotic, melancholic, bipolar depression
- ▶ Psychotic disorders
- ▶ Dementia
- ▶ Anorexia or bulimia nervosa
- ▶ Alcohol or other substance misuse
- ▶ Severe obesity

Oxford (British) Criteria for Chronic Fatigue Syndrome Severe disabling fatigue of at least six month duration that:

- ▶ Affects physical and mental functioning.
- ▶ Is present for more than 50% of the time.
- ▶ Other symptoms, particularly myalgia, sleep and mood disturbances may be present.



What Are The Symptoms of CFS/ME?

According to the 1994 International Case Definition the symptoms include:

- ▶ fatigue lasting for six months or longer that significantly affects lifestyle
- ▶ in addition, four or more of the following symptoms must be present [along with the debilitating fatigue]
- ▶ Postexertional malaise (lasting more than 24 hours)
- ▶ Sleep difficulties / unrefreshed sleep
- ▶ Impaired memory or concentration
- ▶ Muscle pain
- ▶ Multi-joint pain
- ▶ Headaches of new type, pattern, or severity
- ▶ Sore throat
- ▶ Tender lymph nodes in the armpit and neck

Degree of CFS/ME Severity

The degree of severity can differ widely among patients, and will also vary over time for the same patient. Severity can vary between getting unusually fatigued following stressful events, to being totally bedridden and completely disabled. The symptoms will tend to wax and wane over time. This variation, in addition to the fact that the cause of the disease is not yet known, makes this illness difficult to diagnose. In some cases, CFS/ME can persist for years.

Can CFS/ME Be Cured?

Not yet, but there are immune modulating treatments and antiviral/antimicrobials that have been used successfully, if the patient is given a complete examination with tests to identify immune dysfunction and microbial infections treatment strategies can greatly improve if not cure the patient. In addition, there are symptomatic therapies that have shown to be helpful in alleviating symptoms.

What Research Is Currently Going On?

There is a great deal of research going on regarding the possible cause of CFS, many of its symptom mechanisms, possible biological markers, treatments, and epidemiology.

- ▶ Scientists have discovered evidence that a retrovirus named XMRV is frequently present in the blood of patients with CFS/ME. This discovery could be a major step in the discovery of vital treatment options for millions of patients," said Judy Mikovits, PhD, director of research for WPI and leader of the team that discovered this association. Researchers cautioned, however, that this finding show there is an association between XMRV and CFS/ME but does not prove that XMRV causes CFS/ME. The scientists provide a new hypothesis for a retrovirus link with CFS/ME. The virus, XMRV, was first identified by Robert H. Silverman, PhD, professor in the Department of Cancer Biology at the Cleveland Clinic Lerner Research Institute. It was found in men who had a specific immune system defect that reduced their ability to fight viral infections.
- ▶ Dr. Mark Demitrack (Univ. of Michigan) and Dr. Stephen Straus (NIH) and others are studying the dysfunction of the hypothalamic-pituitary-adrenal axis as being a possible major explanation for CFS.
- ▶ Prof. Robert Suhadolnik (Temple Univ., Philadelphia) is exploring a possible bio-marker for CFS found in patients' blood.
- ▶ Doctors Hugh Dunstan and Timothy Roberts (Univ. Newcastle, Australia) are researching a possible biological marker found in urine.



What Research Is Currently Going On? (Continued)

- ▶ Dr. Peter Rowe (Johns Hopkins Univ.) is studying the possible link between CFS and neurally mediated hypotension.
- ▶ Dr. Anthony Komaroff (Harvard Univ.) and Dr. Dharam Ablashi (Georgetown Univ.) are researching the possible roles of human herpes virus six and Epstein - Barr virus.
- ▶ Doctors Andrew Lloyd, Ian Hickie, Denis Wakefield and Andrew Wilson (Sydney, Australia) are making broad investigations into many aspects of CFS.
- ▶ Dr. W. John Martin (Univ. Southern California) is researching the "Stealth" virus.
- ▶ Dr. Michael Holmes (Univ. Otago) is researching another mysterious, virus-like particle.
- ▶ Doctors Nancy Klimas, Roberto Patarca (of Univ. Miami) and Jay Levy (UCSF) are investigating immunological abnormalities.
- ▶ Doctors Paul Cheney, Charles Lapp and Jay Goldstein are studying various treatments.
- ▶ Doctors Simon Wessely, Michael Sharpe and other British psychiatrists are exploring the value of cognitive behavior therapy for CFS.
- ▶ The Center for Disease Control (CDC) team led by Doctors Keiji Fukuda and William Reeves are undertaking prevalence studies.

Research studies indicate that the average FM and/or CFS/ME patient takes 4-6 different drugs daily in an attempt to control their symptoms, yet no single therapeutic agent was found to be effective in relieving the symptoms during the seven-year duration of the study (1989 to 1996).

Disability Studies

Reports have shown that FM can be as disabling as rheumatoid arthritis (RA). RA is listed in the Social Security Disability law book, and while FM pain is acknowledged, the condition is not specifically listed.

Due to the difficulties in gaining recognition for FM as a disabling illness, the percentage of patients drawing SSD payments based on FM is only 16.2%. Yet, nearly 30% of FM patients claim that they cannot hold down a steady job due to this condition. The total yearly drain on the U.S. economy is estimated to be over \$20 billion. Preliminary findings indicate that the cancer risk is also doubled in people with FM.

Patients with CFS/ME report critical reductions in levels of physical activity with impairment comparable to other fatiguing medical conditions such as:

- ▶ Multiple Sclerosis (MS)
- ▶ Late-stage AIDS
- ▶ Lupus
- ▶ Rheumatoid Arthritis (RA)
- ▶ Heart disease
- ▶ End-stage renal disease
- ▶ Chronic Obstructive Pulmonary Disease (COPD)
- ▶ Effects of chemotherapy

The severity of symptoms and disability is the same in both genders with strongly disabling chronic pain, but despite a common diagnosis, the functional capacity of individuals with CFS/ME varies greatly. While some lead relatively normal lives, others are totally bed-ridden and unable to care for themselves. Employment rates vary with over half unable to work and nearly two thirds limited in their work because of their illness. More than half were on disability benefits or temporary sick leave, and less than a fifth worked full-time.



Research Findings

Pain is the predominant feature of FM and CFS/ME, but its cause is unknown. Significant abnormalities in the central and peripheral nervous systems have been uncovered in recent years.

Most researchers in the field consider FM and CFS/ME to be a central pain state (e.g., central sensitization). Substance P (SP) in the spinal fluid is three times that of normal healthy people. Nerve growth factor (NGF) in the spinal fluid is four times that of healthy people. Increased production of nitric oxide in the spinal fluid and in the peripheral blood of FM and CFS/ME patients has also been found. Proinflammatory cytokines are excessively produced in patients with FM and CFS/ME, pointing to an immune system Th1/Th2 axis disruption.

The 2003 study by Ali Gur et al. demonstrated that the cytokine elevations correlated with abnormalities in brain blood flow based on SPECT scan analysis. Gur's 2002 study showed that elevated IL-8 levels corresponded with pain intensity. It is proposed that pro-inflammatory cytokines produced by activated glial cells within the central nervous system may play an aetiopathogenetic role in FM and CFS/ME.

Indeed, IL-8 has been implicated in a genetic profiling study using micro-arrays in patients meeting the CFS/ME criteria. Although the findings of elevated SP and NGF are substantial, recent research by the author of the NGF finding (Alice Larson, Ph.D.) clearly indicates that elevated SP and NGF are not at the heart of the etiology of FM and CFS/ME. In fact, NK1 receptor antagonists are only likely to help FM and CFS/ME patients when they are co-administered with an upload and noradrenaline (whose metabolite is abnormally low in the spinal fluid of FM and CFS/ME patients - and the same holds true for serotonin and dopamine).

Other significant abnormalities in FM and CFS/ME patients include:

- ▶ Sleep disorder
- ▶ Autonomic nervous system dysfunction
- ▶ Elevated activity of CRH neurons which is believed to cause disruption of many hormonal axes including the HPAaxis.
- ▶ Impaired brain blood flow to the thalamus and other pain-processing centers.
- ▶ Substantially reduced production of growth hormone overall, and additional blunting of growth hormone during exercise.
- ▶ Failure of the diffuse noxious inhibitory control (DNIC or spatial summation) to respond to a painful stimulus.
- ▶ Abnormal windup (or temporal summation) at rest and significantly exacerbated windup during exercise, which may explain the exercise intolerance that FM patients exhibit.

Current Status of Research Spending

Most FM and CFS/ME research at NIH (National Institute of Health) is sponsored by NIAMS (National Institute of Arthritis, Musculoskeletal and Skin diseases). The estimated 2009 FM and CFS/ME research funding level at NIAMS measured out to only \$13 million - not much for the second most common rheumatic disease.

In 1997 the NIH created a Special Emphasis Panel (SEP) specifically for the review of FM and CFS/ME research grant applications, and this continues to lead to increased funding for the condition.

In 1999, the National Institute of Neurological Diseases and Stroke (NINDS) and the Department of Defense (because of overlapping conditions such as Gulf War Illness) became involved in funding research on FM and CFS/ME as well.

While the increase in research funding on FM and CFS/ME is encouraging, the NIH funded research projects are, for the most part, still not focused on the patient-relevant issue of providing improved therapy options.



Current Status of Research Spending (Continued)

A review of the NIH online Computer Retrieval of Information on Scientific Projects (CRISP) system abstracts confirms that less than 10% of government sponsored research on FM and

CFS/ME pertains to therapeutic interventions. However, the combined NIH and DOD expenditures on FM and CFS/ME-related research are estimated to be roughly \$7 million annually.

Recent Therapeutic Success

Medications that have strong Level A evidence (double-blind, placebo-controlled studies) include pregabalin, fluoxetine, and milnacipran. There is some evidence for the effectiveness of cyclobenzaprine. There is also some evidence that tramadol may be effective, which is interesting because it is a weak agonist, an opioid, with serotonin and norepinephrine agonist properties.

There is some evidence for the effectiveness of the NaSRI [noradrenaline serotonin reuptake inhibitors] group of antidepressants, now being used in neuropathic pain, but the evidence is not strong. Then the calcium channel blockers like pregabalin and even gabapentin -- apparently there is some evidence now emerging for their effectiveness in fibromyalgia.

There is no evidence at this point that opioids help fibromyalgia. I have not seen evidence for that nor have I had success using it. There are tricyclics that can be effective or there is some evidence for them, but they are not well tolerated.

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