

# FM *Monograph*

## Fibromyalgia: Symptoms, Diagnosis, Treatment & Research

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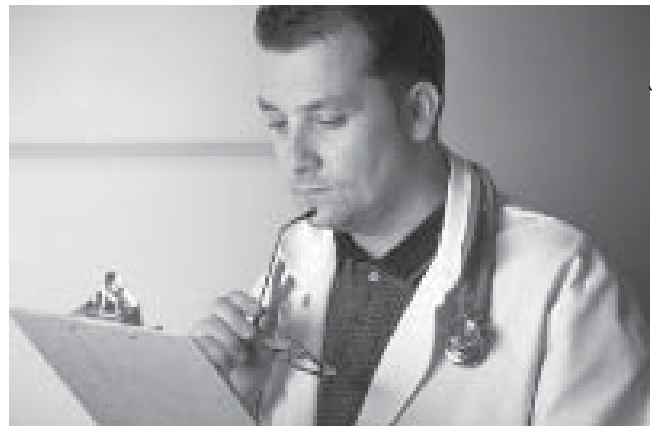
### What Is Fibromyalgia?

Fibromyalgia (FM)) is a complex, chronic condition which causes widespread pain and fatigue and a variety of other symptoms. The name fibromyalgia comes from “fibro” meaning fibrous tissues (such as tendons and ligaments), “my” meaning muscles, and “algia” meaning pain. Unlike arthritis, FM does not cause pain or swelling in the joints. Rather, it produces pain in the soft tissues located around joints and in skin and organs throughout the body. Because FM has few symptoms that are outwardly visible, it has been nicknamed “the invisible disability” or the “irritable everything” syndrome.

The pain of fibromyalgia usually consists of diffuse aching or burning described as “head-to-toe,” and it is often accompanied by muscle spasm. Pain can vary in severity from day to day and change location, becoming more severe in parts of the body that are used the most (i.e., neck, shoulders, and feet). In some people, it can be so intense that it interferes with the performance of even simple tasks, while in others it may cause only moderate discomfort.

Likewise, the fatigue of fibromyalgia also varies from person to person ranging from a mild, tired feeling to the exhaustion of a severe flu-like illness. Although FM does not cause physical deformities or affect a person’s expected life span, until the patient is able to manage it through appropriate treatment(s) and medications(s), fibromyalgia can make life very challenging on many different levels.

The exact prevalence of fibromyalgia in the U.S. population has not been thoroughly studied, but conservative estimates place the total between 4 and 6 million. Other experts believe the true number is closer to 10 million.<sup>1</sup> An estimated 80% of sufferers are women, most of them working age, so FM has obvious consequences in terms of employment and family stress. FM also occurs in all other age groups as well as in men, and it exists in all races worldwide.



Courtesy of Comstock

### Other Conditions Associated With FM

In addition to pain and fatigue, a number of symptoms and syndromes are usually associated with FM. Like pain/fatigue, their severity may wax and wane over time, and individuals may differ in the extent to which they are troubled by them. Typically, patients suffer from one or more of the following:

**Stiffness:** Body stiffness is usually most apparent upon awakening and after prolonged periods of sitting or standing in one position. It may also coincide with changes in relative humidity.

**Increased Headaches Or Facial Pain:** Head/facial pain is frequently a result of extremely stiff or tender neck/shoulder muscles which refer pain upwards. It can also accompany temporomandibular joint (TMJ) dysfunction, a condition which occurs in an estimated one-third to one-half of those with FM and which affects the jaw joints and surrounding muscles.

**Sleep Disturbances:** Despite sufficient amounts of sleep, FM patients may awaken feeling unrefreshed, as if they have barely slept. Alternatively, they often have trouble falling asleep or staying asleep. The reasons for the non-restorative sleep and other sleep difficulties of fibromyalgia are unknown although research in sleep labs has documented alpha brain wave disruptions in the deep (delta wave) sleep of some patients.<sup>2</sup>

**Cognitive Disorders:** Individuals with FM report a number of cognitive symptoms which tend to vary from day to day. These include difficulty concentrating, “spaciness” or “fibro-fog,” memory lapses, difficulty thinking of words/names, and feeling overwhelmed when engaged in multiple tasks. Although the underlying cause of these symptoms has yet to be clearly identified, research has shown that FM patients experience a somewhat decreased cerebral blood flow to the brain (i.e., thalamus and caudate nucleus) compared to

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healthy individuals.<sup>3</sup> In addition, the mental distraction caused by pain and the side effects of some medications commonly prescribed for fibromyalgia may be partly culpable for cognitive difficulties.

**Gastrointestinal Complaints:** Digestive disturbances, abdominal pain, and bloating are quite common with FM as are constipation and/or diarrhea. Together these symptoms are usually known as irritable bowel syndrome or IBS. FM patients may also have difficulty swallowing food. Researchers think this may be a result of abnormalities in smooth muscle functioning in the esophagus.<sup>4</sup>

**Genito-Urinary Problems:** An estimated 40-60% of FM patients may experience increased frequency of urination or increased urgency to urinate, typically in the absence of a bladder infection.<sup>5</sup> These symptoms are usually referred to as irritable bladder syndrome. Some may develop a chronic, painful inflammatory condition of the bladder wall known as interstitial cystitis. Women with FM may have more painful menstrual periods or experience a worsening of their FM symptoms during this time. Conditions such as vulvar vestibulitis or vulvodynia, characterized by a painful vulvar region and painful sexual intercourse, may also develop.

**Paresthesia:** Numbness or tingling, particularly in the hands or feet, sometimes accompanies FM. Also known as “paresthesia,” the sensation can be described as prickling or burning.

**Myofascial Trigger Points:** A significant number of people with FM have a neuromuscular condition known as myofascial pain syndrome (MPS) in which very painful spots (trigger points) form in taut bands in muscles or other connective tissue, often as a result of repetitive motion injury, prolonged poor posture, or illness. Not only are these spots very painful but they also refer pain to other parts of the body in very predictable ways. Unlike FM which affects the entire body, MPS is a localized condition which occurs in very specific areas, typically the neck, shoulders, or lower back. TMJ is considered a form of MPS.

**Chest Symptoms:** Individuals with FM who engage in activities involving continuous, forward body posture (i.e., typing, sitting at a desk, working on an assembly line, etc.) often have special problems with chest and upper body (thoracic) pain and dysfunction.<sup>6</sup> The pain may cause shallow breathing and postural problems. They may also develop a condition known as costochondralgia (also referred to as costochondritis) which causes muscle pain where the ribs meet the chest bone and is frequently mistaken for heart disease. Persons with FM are also prone to a largely asymptomatic heart condition known as mitral valve prolapse (MVP) in which one of the valves of the heart bulges during a heartbeat causing a click or murmur. MVP usually does not cause much concern unless another cardiac condition is

also present. (Note: Anyone experiencing chest pain should immediately consult a physician.)

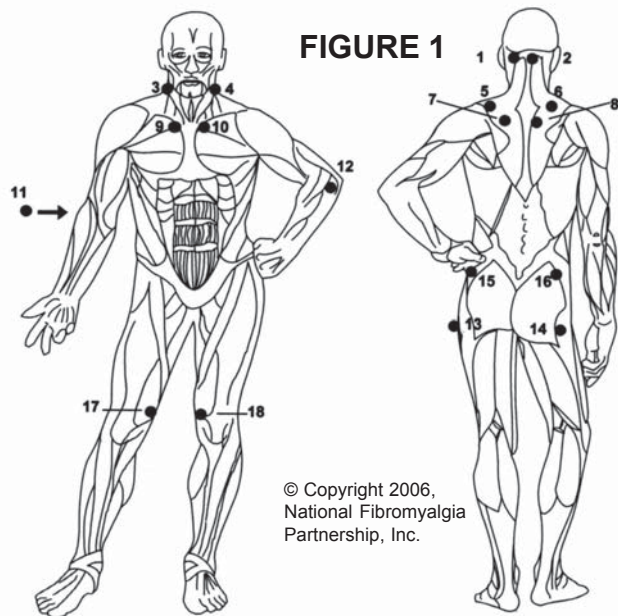
**Dysequilibrium:** FM patients may be troubled by light-headedness and/or balance problems for a variety of reasons. Since fibromyalgia is thought to affect the skeletal tracking muscles of the eyes, “visual confusion” and nausea may be experienced when driving a car, reading a book, or otherwise tracking objects. (Difficulties with smooth muscles in the eye may also cause additional problems with focus.)<sup>7</sup> Alternatively, weak muscles and/or trigger points in the neck or TMJ dysfunction may cause dizziness or dysequilibrium. Researchers at Johns Hopkins Medical Center have also shown that some FM patients have a condition known as neurally mediated hypotension which causes a drop in blood pressure and heart rate upon standing with resulting light-headedness, nausea, and difficulty thinking clearly.<sup>8</sup>

**Leg Sensations:** Some FM patients may develop a neurologic disorder known as restless legs syndrome (RLS) which involves a “creepy crawly” sensation in the legs and an irresistible urge to move the legs particularly when at rest or when lying down. One recent study suggests that as many as 31% of FM patients may have RLS.<sup>9</sup> The syndrome may also involve periodic limb movements during sleep (PLMS) which can be very disruptive to both the patient and to her/his sleeping partner.

**Sensory Sensitivity/Allergic Symptoms:** Hypersensitivity to light, sound, touch, and odors frequently occurs among those with FM and is thought to be a result of a hyperactive nervous system. In addition, persons with FM may feel chilled or cold when others around them are comfortable, or they may feel excessively warm. They may also have allergic-like reactions to a variety of substances accompanied by itching or a rash or a form of non-allergic rhinitis consisting of nasal congestion/discharge and sinus pain. However, when such symptoms occur, there is usually no measurable immune system response like that found in true allergies.<sup>10</sup>

**Skin Complaints:** Nagging symptoms, such as itchy, dry, or blotchy skin, may accompany FM. Dryness of the eyes and mouth (sicca syndrome) is not uncommon. Additionally, fibromyalgia patients may experience a sensation of swelling, particularly in extremities (i.e., fingers). A common complaint is that a ring no longer fits. However, such swelling is not like the joint inflammation of arthritis; rather, it is a localized anomaly of FM of unknown cause.

**Depression And Anxiety:** Although FM patients are frequently misdiagnosed with depression or anxiety disorders (“it’s all in your head”), research has repeatedly shown that fibromyalgia is not a form of depression or hypochondriasis. Where depression or anxiety do co-exist with fibromyalgia, treatment is important as both can exacerbate FM and interfere with successful symptom management.



**FIGURE 1**

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### Fibromyalgia Tender Points Identified By The American College Of Rheumatology In 1990<sup>11</sup>

(at digital palpation with an approximate force of 4 kg)

- 1 & 2, Occiput:** bilateral, at the suboccipital muscle insertions.
- 3 & 4, Low cervical:** bilateral, at the anterior aspects of the intertransverse spaces at C5-C7.
- 5 & 6, Trapezius:** bilateral, at the midpoint of the upper border.
- 7 & 8, Supraspinatus:** bilateral, at origins, above the scapula spine near the medial border.
- 9 & 10, Second Rib:** bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.
- 11 & 12, Lateral epicondyle:** bilateral, 2 cm distal to the epicondyles.
- 13 & 14, Gluteal:** bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.
- 15 & 16, Greater trochanter:** bilateral, posterior to the trochanteric prominence.
- 17 & 18, Knee:** bilateral, at the medial fat pad proximal to the joint line.

## Official Diagnostic Criteria

Fibromyalgia has had a long, if rather obscure, history as an illness. Masquerading behind numerous medical aliases, FM has existed throughout history and throughout the world. It was only in 1990 that official diagnostic criteria for FM were established by the American College of Rheumatology (ACR).<sup>11</sup> They include:

**(1) A History of Widespread Pain:** Chronic, widespread, musculoskeletal pain lasting longer than three months in all four quadrants of the body. (“Widespread pain” is defined as pain above and below the waist and on both sides of the body.) In addition, axial skeletal pain (in the cervical spine, anterior chest, thoracic spine, or low back) must be present.

**(2) Pain in 11 of 18 Tender Point Sites on Digital Palpation:** There are 18 tender points that doctors look for in making a fibromyalgia diagnosis (see Figure 1). According to the ACR requirements, a patient must have 11 of the 18 tender points to be diagnosed with fibromyalgia. Approximately four kilograms of pressure (or about 9 lbs.) must be applied to a tender point, and the patient must indicate that the tender point locations are painful.

As the ACR criteria suggest, a fibromyalgia diagnosis requires the “hands-on” evaluation of a patient by a skilled medical professional, typically a rheumatologist, though other medical specialists are becoming very knowledgeable in this area. As patients are not usually aware of the specific anatomical origins of pain in their bodies, self-diagnosis is not advised.

Because routine laboratory and x-ray testing is usually normal in fibromyalgia patients, a complete medical history

and physical exam are crucial for a correct diagnosis. Since FM symptoms mimic several other diseases (for example, systemic lupus, polymyalgia rheumatica, myositis/polymyositis, thyroid disease, rheumatoid arthritis, multiple sclerosis, and others), it is necessary to rule out those conditions before a FM diagnosis is made. While a diagnosis of fibromyalgia does not preclude the co-existence of another illness, it is important to ensure that no other condition is mistaken for fibromyalgia so that appropriate treatment may be initiated.

## Limitations of the ACR Diagnostic Criteria

In the absence of diagnostic laboratory tests or x-rays, the ACR diagnostic criteria were a milestone in the recognition and study of fibromyalgia. For the first time, researchers around the world could identify and study FM patients using standardized measures which in turn made the comparison of research studies possible. Patients who had fallen through the cracks of medical science could finally be diagnosed. Nevertheless, the criteria were not without their drawbacks.<sup>13</sup>

First, the tender point paradigm suggested that FM patients only experience pain in anatomically specific sites on the body. However, later studies, such as those reported by Granges and Littlejohn in 1993,<sup>14</sup> began suggesting that individuals with FM are sensitive to painful stimuli throughout the body, not merely at the ACR-identified locations. Today, extensive body pain is commonly associated with FM.

Secondly, it quickly became evident that patient tenderness varied day-by-day and month-by-month. As a result, tender point counts on some days could be below the required 11 while on other days they might surpass it.

Furthermore, patients did not always manifest pain in all four body quadrants. Some had unilateral pain; others had pain solely in the upper or lower halves of the body.

Thirdly, as FM researcher Roland Staud, M.D., has pointed out, while everyone with fibromyalgia has tender points, the number of tender points does not reflect the level of pain which patients are experiencing.<sup>15</sup> In short, tender points do not correlate with pain.

Fourthly, as FM experts Daniel Clauw, M.D., and Leslie Crofford, M.D., remind us, the ACR criteria focus only on pain and do not include many other FM symptoms (i.e., fatigue, cognitive disturbance, IBS, etc.). As a result, the criteria “fail to capture the essence of the FM syndrome” and allow for “greater variability in studies of physiologic mechanisms other than pain processing.”<sup>16</sup>

Finally, the tender point exams conducted by medical professionals require skill to perform and are subject to human error. When performed incorrectly (at the wrong anatomical point or with an incorrect amount of digital palpation), they yield erroneous results. Unfortunately, the tender points of fibromyalgia are also sometimes confused with the trigger points of myofascial pain syndrome. Not uncommonly, FM is mistaken for MPS and vice versa.

The search continues for a foolproof laboratory marker for FM. Meanwhile, the ACR criteria are still the most widely used diagnostic tool for fibromyalgia.

## What Has Been Learned From FM Research?

Researchers once believed that something must be wrong with the muscles of FM patients because they seemed to be the origin of so much pain and dysfunction. In fact, FM’s former name, “fibrositis,” literally meant inflammation of the muscles and soft tissue. However, later studies ultimately found no inflammation or nerve injury. Today, researchers generally concur that FM is a condition which is centrally mediated by the brain and not a disease of the periphery.

What has increasingly become apparent is that there are differences between persons with fibromyalgia, not only in the way they seem to develop FM but also in the way they manifest it symptomatically and respond to treatment. As a result, there has been a lot of speculation as to whether the FM population should be broken down into sub-groups.

In a 2002 editorial in the *Journal of Musculoskeletal Pain*, FM researcher I. Jon Russell, M.D., Ph.D., discussed the implications of such a suggestion. Among the questions he raised were:

- ❖ Is there an established basis in human disease for clinical sub-groups within a single diagnosis?
- ❖ How convincing is the evidence that there may be sub-groups of FM patients?

- ❖ Would sub-grouping help to explain some of the difficulties in defining the pathogenesis of FM?

- ❖ Are sub-groups identifiable by the presumed underlying etiology of FM [proposed etiologies have included: idiopathic, trauma, febrile (feverish) illness, genetically determined, or an associated inflammatory or painful condition] or would clinical sub-grouping more likely be based on a limited variety of human responses to any kind of insult?

- ❖ Could the recognition of a specific, clinical sub-group help to define more specific, and thus more effective, management?<sup>17</sup>

Discussion continues on these and other important, related questions. Meanwhile, what have researchers learned about fibromyalgia in recent years?

Family studies suggest that there is a high prevalence of fibromyalgia among relatives of patients with fibromyalgia, with FM often following the female side of the family. Exciting new genetic studies are now underway to investigate the relative influence of genes and environment in the development of fibromyalgia.<sup>18,19</sup>

Increasingly, researchers have also identified several important abnormalities in the levels of certain key neurochemicals in the brain and central nervous system (CNS). Perhaps best known is the study by I. Jon Russell, M.D., Ph.D., of the University of Texas Health Science Center in San Antonio, which demonstrated that the brain neurochemical Substance P, the agent which signals the brain to register pain, exists in FM patients at a level that is three times higher than in normal controls.<sup>20</sup> Also of interest is the discovery that the neurotransmitter serotonin, which modifies the intensity of pain signals entering the brain, appears to be deficient in patients with FM. Many of the medications currently used to treat fibromyalgia work to counteract this deficit.

As it becomes increasingly clear that there are significant abnormalities in pain processing in fibromyalgia, researchers are trying to determine whether the problem is an exaggerated brain/body reaction to basically normal stimuli (allodynia) or a magnified response to real pain stimuli (hyperalgesia).<sup>21</sup>

A great deal of interest has been directed at the neuroendocrine system and the abnormal status of such neurotransmitters/neurochemicals as calcitonin-gene-related peptide, noradrenaline, endorphins, dopamine, histamine, and GABA. Hormones of the hypothalamus, pituitary, and adrenal glands are thought to be dysfunctional, too.<sup>22</sup> Research by Leslie Crofford, M.D., at the University of Michigan at Ann Arbor suggested that FM is a “stress-associated syndrome” (because it often occurs following physically or emotionally stressful events and is also exacerbated by them) with disturbances in the major stress response systems, the hypothalamic-pituitary-adrenal (HPA) axis, the sympathetic nervous system, and the autonomic nervous system.<sup>23</sup> It also supported earlier ground-breaking research conducted by Robert Bennett, M.D., at the Oregon

Health Sciences University, which found that the growth hormone axis is abnormal in individuals with FM.

Mexican researcher Carlos Abud-Mendoza, M.D., studied a subset of fibromyalgia patients who didn't respond well to conventional therapy and found they actually suffered from a form of subclinical hypothyroidism that was not detected by routine lab tests. The hypothyroidism was believed to be rooted in a central nervous system dysfunction.<sup>24</sup>

More recently, Manuel Martínez-Lavín, M.D., of the National Cardiology Institute of Mexico, and others have used a special technology known as heart rate variability analysis to demonstrate that the multi-systemic symptoms of fibromyalgia (i.e., pain, sleep disorders, numbness and tingling, headaches, irritable bowel syndrome, etc.) are in fact a result of a dysfunction of the autonomic nervous system (ANS), which is the system which regulates body temperature, blood pressure, heartbeat rate, and bowel and bladder tone and is capable of acting with great rapidity and intensity.<sup>25</sup>

It is hypothesized that the ANS dysfunction (dysautonomia) which occurs in persons with FM throughout the day and particularly at night features a "relentless" hyperactivity of the sympathetic nervous system, a sub-system of the ANS which is mediated by the neurotransmitter adrenaline (norepinephrine). Furthermore, during times of stress, fibromyalgia patients actually experience a sympathetic hypo-reactivity similar to an overworked engine which cannot respond to commands for more speed when asked to do so.<sup>26</sup> This hypo-reactivity explains the fatigue, morning stiffness, dizziness, brain fog, and low blood pressure often associated with FM.

There have also been some exciting discoveries about the nature of fibromyalgia pain. Researchers from Georgetown University and the University of Michigan used functional MRI (magnetic resonance imaging) testing and discovered that when they applied mild pressure to the thumbnails of a group of FM patients, brain activity was activated in 12 locations compared to only two locations in healthy controls. When the investigators increased thumbnail pressure in the controls, their subjective pain ratings and pain activity also increased, but only eight of the areas of the brain activated were similar to those in the FM patients. One of the lead investigators, Dr. Daniel Clauw, remarked that:

*In all, the fibromyalgia patients' brains had both some areas that were activated in them but not in controls, and some areas that stayed 'quiet' in them but became active in the brains of controls feeling the same level of pain. This response suggests that (FM) patients have enhanced response to pain in some brain regions and a diminished response in others.<sup>27</sup>*

Dr. Roland Staud has also demonstrated abnormalities in fibromyalgia patients' central pain processing by examining their response to repetitive painful stimuli compared to normal controls. Using both thermal and

pressure pain as the stimulus in his studies, he has found that it takes FM patients much longer to recover from repeated applications of painful stimuli compared to control subjects, thus demonstrating that their "pain memory" is increased.<sup>28</sup>

Not only do abnormalities in the brain and central nervous system seem to "spill over" into the body and produce the symptoms we know as fibromyalgia, there is also evidence that injuries, illnesses, or other major stressors in the body can overwhelm the brain and CNS and cause symptoms. For example, post-traumatic fibromyalgia can develop when an individual has been in a vehicular accident or suffered a physical injury.

In 1997, a team of investigators led by Israeli researcher Dan Buskila, M.D., reported on a study of the relationship between cervical spine injuries and the onset of fibromyalgia and found that FM was 13 times more likely to occur following a neck injury than an injury to the lower extremities.<sup>29</sup> Research by Stuart Donaldson, Ph.D.; Mary Lee Esty, Ph.D.; and Len Ochs, Ph.D., has also suggested that FM may actually be a "CNS Myalgia" resulting from a mild traumatic brain injury which in turn causes abnormalities in the functioning of the brain and central nervous system.<sup>30</sup> Severe emotional stress or physical illness is also thought to be a trigger for post-traumatic fibromyalgia in pre-disposed individuals.

Finally, some researchers have searched for an infectious cause of fibromyalgia. For example, using highly sophisticated polymerase chain reaction testing and nucleoprotein gene tracking, Garth Nicolson, Ph.D., of the Institute for Molecular Medicine in California, has been able to confirm the existence of blood infections in patients with fibromyalgia, chronic fatigue syndrome and Gulf War Illness which are caused by a microscopic organism known as a mycoplasma.<sup>31</sup> To what degree these infections explain patients' morbidity is not yet clear.

## Fibromyalgia & Central Sensitivity

Not so long ago, medical researchers viewed fibromyalgia as a discrete medical entity. Increasingly, however, FM is being seen as a condition which overlaps significantly with certain other systemic illnesses and regional conditions that affect particular body organs. One of the earliest proponents of this view was University of Illinois researcher Muhammad Yunus, M.D., who developed the concept of Central Sensitivity Syndromes (CSS). CSS is an umbrella term for a number of associated conditions that share common clinical characteristics and a similar biophysiological mechanism. Dr. Yunus includes nine conditions in addition to fibromyalgia: chronic fatigue syndrome (CFS), irritable bowel syndrome (IBS), tension-type headaches, migraine headaches, primary dysmenorrhea, periodic limb movement disorder, restless legs syndrome (RLS), temporomandibular joint (TMJ) pain and dysfunction syndrome, and myofascial pain syndrome (MPS).

According to Dr. Yunus, members of the CSS family share certain common symptom characteristics (i.e., pain, fatigue, poor sleep, hyperalgesia, absence of structural tissue pathology, etc.); have common demographic features (i.e., female predominant); and exhibit neurohormonal dysfunctions which result in central sensitivity which in turn causes amplified, widespread, and persistent pain.<sup>32</sup>

With this new perspective, the long list of symptoms/syndromes associated with fibromyalgia can be seen in a special context rather than as one long, baffling list of seemingly incongruent complaints. When FM and allied conditions are viewed as part of a spectrum, then new, coordinated, multi-disciplinary approaches to research and treatment can be undertaken.

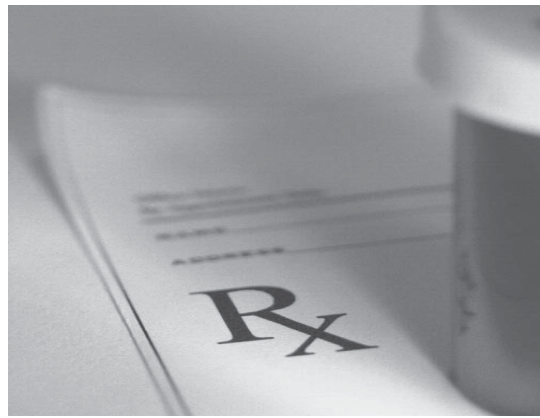
Researchers and patients still disagree on the extent to which systemic conditions like FM, CFS, Gulf War Illness, and multiple chemical sensitivity are similar, or even identical, conditions. Interestingly, Dr. Robert Bennett also points out that while FM patients are unlikely to develop another rheumatic or neurological disease, it is not at all unusual for patients with well established conditions like rheumatoid arthritis, Sjögren's Syndrome, or lupus to develop FM.<sup>33</sup> Other researchers have identified overlaps between FM and conditions such as inflammatory bowel disease and Lyme disease. More research will be necessary to unravel these puzzles.

## Fibromyalgia Management

Because there is currently no “magic pill” for fibromyalgia, treatment aims at managing FM symptoms to the greatest extent possible. Just as individual manifestations of fibromyalgia vary from patient to patient, so do successful forms of treatment (e.g., what works for one patient may not work for another). In addition, medical practitioners often have different preferences as to treatment. Because successful FM treatment can involve a variety of medical professionals, patients usually benefit from a coordinated, team approach to disease management. The most common treatment strategies, used alone or in combination, are:

### ❖ Prescription Medications ❖

*Note: The overview of prescription drugs included in this section is intended to familiarize you with the medications most commonly prescribed for fibromyalgia. It does not replace advice and treatment from your doctor which you are strongly urged to get before trying any prescription drug. It also does not include supplemental medications that might be recommended to you for the treatment of fibromyalgia-related conditions (i.e., TMJ, restless leg syndrome, irritable bowel syndrome, etc.) Drugs are listed by trade name first, followed by their generic name in parentheses. Special thanks to Russell Rothenberg, M.D., who reviewed this section for accuracy.*



Courtesy of Comstock

**Analgesics** are drugs that have been designed to relieve pain. Those commonly used to treat fibromyalgia include acetaminophen (i.e., Tylenol), anti-inflammatory medications with analgesic properties, and narcotic drugs which are sometimes combined with acetaminophen for added strength. As a group, analgesics are typically used to “take the edge off” of pain or to combat flare-ups.

**Anti-inflammatory medications** used to treat fibromyalgia include traditional NSAIDs (Non-Steroidal Anti-Inflammatory Drugs). As indicated above, because fibromyalgia is not an inflammatory condition, it is the analgesic property of these drugs that can sometimes be useful to FM patients. Among the traditional prescription NSAIDs are:

Indocin (indomethacin)	Voltaren (diclofenac)
Toradol (ketorolac)	Orudis (ketoprofen)
Naprosyn (naproxen)	Feldene (piroxicam)
Relafen (nabumetone)	Daypro (oxaprozin)
Lodine (etodolac)	Mobic (meloxicam)

Because stomach irritation can be a problem with these drugs, many doctors and pharmacists recommend taking them with food as a precaution. In addition, when the drugs are prescribed in large dosages or over a long period of time, they should be closely monitored as they can also cause gastrointestinal bleeding.

**Narcotic medications (opioids)** are controversial in the management of fibromyalgia just as they are in other chronic pain conditions. While these drugs can be very useful in the treatment of patients who are suffering from acute flare-ups of FM, a fear of addiction remains on the part of some doctors and patients. However, many experienced clinicians in the field of FM management have gone on record saying that with careful management, the use of narcotic painkillers need not be problematic. Examples of drugs used in fibromyalgia treatment are:

Vicodin (hydrocodone + acetaminophen)
Darvocet (propoxyphene napsylate)
Percocet (oxycodone + acetaminophen)
Oxycontin (oxycodone hydrochloride)

Despite their reported usefulness in the treatment of episodes of severe FM pain, the effectiveness of narcotics in treating long-term, chronic pain is still uncertain. Rheumatologist Russell Rothenberg, M.D., Chair of the Medical Advisory Board of the National Fibromyalgia Partnership, notes that while opioids can be helpful in the treatment of acute FM flare-ups or in individuals who are highly disabled, they tend to be less effective in the treatment of chronic pain over the long term because they do not (chemically) address the root of the pain. As a result, the musculoskeletal problems associated with fibromyalgia are not dealt with. Because of this, a patient can eventually get worse, and the drugs can cease to be effective. If the patient requires long-term narcotic analgesics as part of a comprehensive treatment program for fibromyalgia, then long-acting drugs are usually preferable to short-acting drugs that can develop rebound pain overnight as the effect of the drug wears off. (Russell Rothenberg, M.D., *Presentation to the National Fibromyalgia Partnership, January 25, 2004*)

Ultracet (tramadol hydrochloride combined with acetaminophen) is a unique new centrally acting, synthetic, opioid analgesic which helps to relieve pain in three ways. Laboratory studies performed by Ortho McNeil suggest that it acts directly on parts of the brain where pain is received and on the spinal cord, and it reduces the size of the pain signal passed from one nerve to another. In a recent study published in the *American Journal of Medicine* (May 2003), rheumatologist/researcher Robert Bennett, M.D., concluded that a combination tablet containing tramadol and acetaminophen is effective for the treatment of FM pain without any adverse side effects.

It should be noted that Ultracet should not be taken by people who are allergic to codeine or other opioids, and it should not be used with alcohol. In addition, because a small percentage of people taking tramadol have reported seizures, particularly after combining Ultracet with other medications that are known to put patients at risk for developing seizures, it is important to first carefully assess an individual's medication profile.

**The Treatment Of Centrally Mediated Pain** and other symptoms has become a more popular concept in recent years as more research points to the brain and central nervous system, and not the periphery of the body, as the source of dysfunction in fibromyalgia.

**Tricyclic anti-depressants** have been adopted for use in the treatment of fibromyalgia because of their ability to boost levels of the brain neurochemical serotonin (usually deficient in FM patients) and to control pain and promote sleep. They are usually prescribed in much lower dosages for FM than for depression, however. Common tricyclics include:

- Elavil (Amitriptyline)
- Pamelor (Nortriptyline)
- Sinequan (Doxepin)
- Desyrel (Trazadone)

One of the early drugs used to treat FM, amitriptyline has undergone extensive testing for effectiveness in fibromyalgia patients. Its primary side effects (similar to the other tricyclics) include: dry mouth, drowsiness, morning hangover, constipation, weight gain, and sometimes anxiety. Because of their sedating qualities, tricyclics are usually taken at bedtime.

**Selective Serotonin Reuptake Inhibitors (SSRIs)** are a form of anti-depressants which not only boost serotonin levels but also help to keep serotonin available longer in the system after it has been secreted by the brain. These medications can help manage the fatigue, cognitive impairment, and depression associated with fibromyalgia and are often taken in the morning. Common SSRIs include:

- Prozac (fluoxetine)
- Serzone (nefazodone hydrochloride)
- Zoloft (sertraline)
- Celexa (citalopram hydrobromide)
- Paxil (paroxetine)

Common side effects include nervousness, insomnia, dry mouth, headache, nausea, diarrhea, and in the case of Zoloft and Paxil, sexual dysfunction.

In a 1996 study published in *Arthritis & Rheumatism*, a research team headed by Don Goldenberg, M.D., found that not only were the tricyclic Elavil and the SSRI Prozac each effective in the treatment of fibromyalgia, but when used as a combination treatment, they worked better than either medication alone. Since then, prescribing a SSRI drug during the day and a tricyclic at night has become a new tool in the management of fibromyalgia.

**Selective Serotonin and Norepinephrine Reuptake Inhibitors (SSNRI's)** are a new group of medicines which are thought to work by increasing the activity of chemicals called serotonin and norepinephrine in the brain. Examples of SSNRI's are Effexor XR (venlafaxine hydrochloride) and the drug Cymbalta (duloxetine) which has recently been adopted for the management of fibromyalgia.

Effexor XR (venlafaxine hydrochloride) was evaluated in a small study by Sayar et al. (*Ann Pharmacotherapy*, November 2003). Fibromyalgia patients who took Effexor XR showed significant improvement in pain intensity and disability caused by fibromyalgia as well as in depression and anxiety.

In randomized, double-blind, placebo-controlled trials, the treatment effect of Cymbalta on pain reduction was found to be independent of mood and the presence of major depressive disorder. According to the study authors, Cymbalta was safely administered and well tolerated with only mild side effects reported. However, while female subjects treated with Cymbalta enjoyed improvement on most efficacy measures, male subjects failed to improve significantly on any efficacy measure. (See *Arthritis & Rheumatism*, September 2004 & *Pain*, December 15, 2005.)

**Muscle relaxants** can decrease pain in fibromyalgia patients by minimizing muscle spasms and muscle pain. Because of their sedating qualities, they also help to increase sleep and are usually taken at bedtime. Typically used muscle relaxants are:

Flexeril (cyclobenzaprine hydrochloride)  
Norflex (orphenadrine citrate)  
Soma (carisoprodol)  
Skelaxin (metaxalone)  
Robaxin (methocarbamol)

Common side effects include drowsiness, dry mouth, constipation, headache, and heart palpitations. Soma does have the additional risk of becoming habit-forming.

Like Elavil, Flexeril was one of the earliest drugs used in the treatment of FM and has been well researched. Most recently, FM researcher and sleep expert Harvey Moldofsky, M.D., of the Centre for Sleep and Chronobiology in Toronto, reported on a study of low dose Flexeril on 36 FM patients with alpha EEG sleep disorder. Subjects receiving Flexeril experienced improved pre-and post-sleep pain as well as post-sleep fatigue compared to controls. Their pain scores were also better. The drug is now being researched by VelaPharm Pharmaceuticals for the improvement of sleep quality. (*2003 Annual Meeting of the American College of Rheumatology, Abstract #1654*)

**Anti-Spastic Medications** were developed to treat the muscle spasm associated with multiple sclerosis and certain injuries to the spine but have been adopted for use in fibromyalgia. Two anti-spastic medications of interest in FM are: Zanaflex (tizanidine) and Lioresal (baclofen).

Zanaflex acts on the central nervous system to help relax muscles and decrease muscle spasms, cramping, and tightness. It is of special interest to persons with fibromyalgia because it is an inhibitor of Substance P, a neurotransmitter which signals the brain to register pain. Substance P has been shown to occur in fibromyalgia patients at levels up to three times larger than normal. Side effects associated with this drug may include hypotension, dry mouth, diarrhea or constipation, drowsiness, and nightmares.

Zanaflex was recently studied by FM researcher I. Jon Russell, M.D., Ph.D., in an open-label study. What he found was that Zanaflex significantly lowered cerebrospinal Substance P and improved sleep, pain, and physical function. Although the drug was well tolerated by study subjects, Russell advised that transaminase levels should be monitored during continuous therapy. (*2003 Annual Meeting of the American College of Rheumatology, Abstract #1655*)

Lioresal is another example of an anti-spastic analgesic. It is used to help relax muscles and relieve spasms. Side effects may include confusion, dizziness/light-headedness, drowsiness, nausea, and sometimes muscle weakness.

**Anti-convulsant medications**, originally developed for the treatment of epilepsy, are sometimes prescribed for the relief

of neuropathic pain in fibromyalgia patients (i.e., burning and electric shock-like feelings in the extremities). If tolerated, these medications can help relieve nerve irritation. Examples of anti-convulsants are:

Neurontin (gabapentin)  
Depakote (divalproex)  
Dilantin (phenytoin)  
Tegretol (carbamazepine)

Side effects may include sedation, dry mouth, and dizziness. Patients should be closely supervised by a doctor to monitor blood counts and liver function.

Recently, the NIH's National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) funded a study to measure the effectiveness of Neurontin in reducing the symptoms of fibromyalgia. The study was conducted by Leslie Arnold, M.D., and her colleagues at the University of Cincinnati College of Medicine and at two Boston-area sites.

Lyrica (pregabalin) is a new product recently introduced for fibromyalgia treatment which is structurally related to the amino acid and neurotransmitter GABA. Lyrica has been shown to improve pain, disturbed sleep, and fatigue in a recent FM study (*Arthritis & Rheumatism, April 2005*).

**Sleep medicines** are used to treat insomnia and other sleep disorders. Because persons with fibromyalgia have trouble falling asleep, staying asleep, or getting quality, restorative sleep, sleep medicines have been found useful in FM management. By improving sleep, it is also possible to decrease pain and achieve better daytime functioning. Examples of commonly prescribed drugs include the central nervous system depressants Ambien (zolpidem tartrate) and Sonata (zaleplon). These drugs can be habit-forming and are therefore usually prescribed for short periods of time.

A new product, Lunesta (eszopiclone), is one of the generation of sleep aids like Ambien which helps people to fall asleep without the next day hangover characteristic of older-generation sleep drugs. Lunesta is the first drug to be approved for long-term use (though others may be tested in the future), and it helps people to stay asleep.

Although not yet approved by the FDA specifically for the treatment of fibromyalgia, the central nervous system depressant known as Xyrem is a promising drug currently being assessed for use in individuals with FM. Clinical trials in FM patients have already shown significant pain relief and improved functioning. Sodium oxybate, the active ingredient of Xyrem, is a sodium salt of gamma-hydroxybutyrate (GHB), a substance with a history of abuse. Therefore, Xyrem is highly controlled through a restricted distribution system.

**Benzodiazepines**, also very sedating and usually taken at bedtime, are sometimes used to help patients feel calmer and cope with pain more effectively. They include the following:

Klonopin (clonazepam)  
 Valium (diazepam)  
 Restoril (temazepam)  
 Xanax (alprazolam).

Note: Klonopin and Valium also have muscle relaxant properties that are useful in FM treatment.

**Antibiotics** also may have a role in the treatment of fibromyalgia. As previously noted, research by Garth Nicolson, Ph.D., suggests that mycoplasma may be an infectious cause of FM and CFS. Antibiotics used to treat mycoplasma infection include: Doxycycline (tetracycline), Erythromycin, and Zithromax (azithromycin).

### Injections

Trigger point injections are used to treat severe myofascial trigger points which frequently occur in FM patients in muscle or soft tissue. Injected medications usually contain 1% procaine or lidocaine. Many patients experience pain relief from these injections, especially when they are used in conjunction with physical therapy. The effects may last for up to three or four weeks.

Botox injections are a newer and more controversial treatment that some doctors have found to be useful. Botox is a form of the botulinum toxin which is injected into painful muscles, decreasing muscle spasms. At this time, botox injections are costly and are usually not covered by insurance.

### New Drugs Under Investigation

At present, no medication has been approved by the FDA specifically for the treatment of fibromyalgia, so drugs have simply been borrowed from other illnesses. Several promising new pharmaceuticals are currently being investigated for FM. These include:

**Milnacipran:** A selective serotonin and norepinephrine reuptake inhibitor being tested in clinical trials by Cypress Bioscience for possible FDA approval.

**Pramipexole & Ropinorole:** Dopamine agonists being studied by Andrew Holman, M.D., at the University of Washington (Seattle).

### ❖ Physical Rehabilitation ❖

A wide variety of hands-on “body work” therapies are available to individuals with FM. Some can only be provided by trained physical rehabilitation professionals familiar with fibromyalgia while others may be practiced at home under the guidance of a professional. The most widely used therapies are:

**Massage:** Often combined with ultrasound and/or the application of hot/cold packs, massage may be performed in a number of ways and is useful in soothing and increasing

blood circulation to tense, sore muscles. It can also help remove built-up toxins like lactic acid and re-educate muscles and joints which have become mechanically misaligned.

**Myofascial Release:** A technique developed by physical therapist John Barnes, myofascial release is a very gentle form of body work designed to relieve restrictions and tightness in connective tissue (fascia). When properly performed, it often decreases connective tissue’s pull on bones, allowing muscle fibers to relax and lengthen and organs to expand.<sup>34</sup>

**Trigger Point Therapy:** A technique designed to break up the trigger points associated with myofascial pain syndrome, sustained pressure is usually applied by a therapist. When trigger points cannot be broken up by this method, patients may be sent to a physician for trigger point injections.

**Craniosacral Therapy:** “A gentle, non-invasive method of evaluating and enhancing the function of the craniosacral system, the environment in which the brain and spinal cord function...this manual therapy encourages the body’s natural healing mechanisms to improve the operation of the central nervous system, dissipate the negative effects of stress, enhance health, and strengthen resistance to disease.” Patients can perform a form of craniosacral therapy at home using a “stillpoint inducer,” a product which can be purchased commercially or fabricated by knotting two tennis or racquet balls into a sock. The inducer is placed along the back of the head at the line of the ear, for gradually increased lengths of time (usually 2-20 minutes).<sup>35</sup>

**EEG-Based Stimulation:** A promising new FM treatment stemming from the research of Mary Lee Esty, Ph.D.; Stuart Donaldson, Ph.D.; and Len Ochs, Ph.D., uses electroencephalogram (EEG) technology to detect and treat brain dysfunction that has been caused by a mild traumatic brain injury such as in an automobile accident.<sup>36</sup> Patients first have a brain mapping performed to identify areas of the brain which have been injured and are functioning abnormally in terms of brainwave activity. Electrical activity produced by the brain reflects a person’s level of functioning and can be monitored by EEG. A condition known as “EEG slowing” is present in people who have suffered damage to the brain and nervous system as a result of trauma and go on to develop fibromyalgia or other chronic conditions.

In individuals with mild traumatic brain injury, there is typically an inappropriate excess of energy in the slow brainwaves. The goal of treatment is to normalize brainwave patterns using a series of EEG-based stimulation treatments which are administered by a specially trained professional. Later, surface electromyography (sEMG) therapy is conducted to help retrain muscles, and myofascial release therapy is performed to restore proper muscle balance, promote optimum posture, and address other neuromuscular problems.<sup>36</sup>

**Chiropractic:** As explained by chiropractor Eric Terrell, D.C., “Chiropractic philosophy recognizes that the nervous system via the brain, spinal cord, and nerves connects to every part of the body and controls all bodily functions.” Chiropractic care works to remove misalignments in the vertebrae, “unchoke” nerves, and allow the body to heal naturally.<sup>37</sup>

**Osteopathy:** A discipline which proposes that the body is often able to effectively cope with disease on its own as long as it is in a normal structural relationship, has a favorable environment, and suffers no nutritional deficits. Osteopathy uses generally accepted physical, medicinal, and surgical methods of diagnosis and therapy (including the prescription of medications) while placing chief emphasis on the musculoskeletal system. FM patients may also receive manipulation (body work) as part of treatment.

**Stretching:** Gentle stretching can be performed by physical therapists and/or practiced by patients at home. Several videotapes have been specially created for FM patients for this purpose. Stretching is important because it helps to relieve muscle tension and spasm. In difficult-to-treat areas, “spray and stretch” techniques can be used to apply a spray coolant to sore muscles, deadening pain while the muscles are stretched.

**Aerobic Exercise:** Low-impact aerobic exercise is very important for fibromyalgia patients to prevent muscle atrophy (wasting), to promote the circulation of blood containing oxygen and other nutrients to muscles and connective tissue, and to build strength and endurance. Examples of low-impact exercise include walking, warm water walking/exercise, and the use of treadmills or cross-country ski machines. Increasingly, gentle exercise programs designed specifically for fibromyalgia and other chronic pain conditions are being offered through local health/recreation centers throughout the country and via videotape. A cardinal rule for fibromyalgia patients is to start extremely slowly and conservatively and build up exercise tolerance in small increments. Most medical professionals also suggest that patients find a form of exercise they like so that they will stick to it on a regular basis. However, should a FM patient find that exercise repeatedly causes high levels of pain, a consultation with a physical rehabilitation therapist (i.e., physical therapist, chiropractor, etc.) may be indicated. These professionals can help restore normal physiological relationships between muscles and joints, thereby paving the way for successful exercise.

### ❖ Complementary Therapies ❖

A number of other approaches have proven useful in the management of fibromyalgia:

**Postural Training:** While the various forms of body work described above can help patients reduce pain and relax



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muscles, posture or movement training is often required to undo lifelong bad habits which increase pain and to re-educate muscles/joints that have become mechanically misaligned. Physical therapists can help with posture while professionals trained in the “Alexander Technique” can provide movement training. FM patients who have significant problems with foot pain resulting from poor posture or body mechanics may also benefit from special shoe inserts (orthotics) prescribed by a podiatrist.

**Occupational Therapy:** When job-related tasks contribute to pain (i.e., repetitive movements, uncomfortable work stations, etc.), an occupational therapist can help by suggesting/designing improvements. For example, for FM patients who work at a computer, ergonomic keyboards, chairs, and other products may provide significant relief.

**Relaxation Therapy:** Not surprisingly, the pain and related symptoms of fibromyalgia cause significant stress to the body. Recent research suggests that, physiologically, FM patients simply do not process stress well. Thus, effective stress management programs are recommended. Among those used for fibromyalgia are: biofeedback, watsu, meditation, breathing exercises, yoga, tai chi, progressive relaxation, guided imagery, and autogenic training. Patients need to receive initial training for many of these but can often continue practicing the concepts they have learned on their own. Books, audiotapes, and classes are widely available to help.

**Nutrition:** Nutritional therapy for fibromyalgia can be helpful in counteracting stress, ridding the body of toxins, and restoring nutrients which have been malabsorbed or robbed from the body. Simple approaches may include the use of vitamin/mineral supplements to combat stress, replace deficiencies, and support the immune system. Nutritionists commonly urge fibromyalgia patients to limit the amount of sugar, caffeine, and alcohol they consume since these substances have been shown to irritate muscles and stress the system.

As with other fibromyalgia treatments, a specifically designed nutritional plan that works well for one patient may prove disastrous for another.<sup>38</sup> Unfortunately, a

number of unproven “miracle” diets and supplements are advertised for FM and should be investigated carefully by patients before use. When starting a new nutritional program, it is important to inform your physician as some supplements and foods cause serious, or even dangerous, side effects when mixed with certain medications.

**Acupuncture:** While a number of alternative remedies have been offered for FM management, very few have been rigorously studied in clinical settings. Acupuncture, a treatment which involves the insertion of small needles at specific anatomical points identified as conducive to energy, has received more scrutiny than most. Research has offered evidence that acupuncture enables electromagnetic signals in the body to be relayed at a greater rate than usual, thus allowing the flow of natural pain-killing endorphins to specific pain sites. In addition, it may also encourage the release of the body’s own opioids into the central nervous system during treatment and alter brain chemistry by changing the release of neurotransmitters and neurohormones.<sup>39</sup> In November 1997, the National Institutes of Health convened a Consensus Panel on Acupuncture which issued this statement:

*Acupuncture as a therapeutic intervention is widely practiced in the United States. While there have been many studies of its potential usefulness, many of these studies provide equivocal results because of design, sample size, and other factors. The issue is further complicated by inherent difficulties in the use of appropriate controls, such as placebos and sham acupuncture groups. However, promising results have emerged, for example, showing efficacy of acupuncture in adult postoperative and chemotherapy nausea and vomiting and in postoperative dental pain. There are other situations such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, **fibromyalgia**, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma in which acupuncture may be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program.<sup>40</sup>*

**Cognitive/Behavioral Therapy:** As trite as it may sound, attitude is often one of the strongest predictors of how well

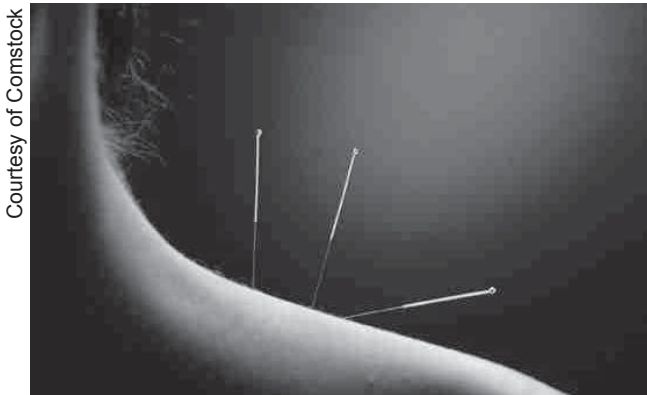
a patient is able to manage FM. Research has shown that patients who are not actively engaged in taking charge of their illness simply aren’t as likely to get better. Those who unknowingly adopt maladaptive illness behaviors (i.e., hopelessness, victim mentality) are less likely to aggressively seek help through exercise, physical therapy, or medications. Getting better with FM can be very tough, but patients should not give up. Constructive help is available even if the patient must find it using his/her own initiative. If negative thinking is a problem, cognitive/behavioral therapy (via classes, audiotapes, and or individual counseling) can be a beneficial resource.

**Common Sense:** Individuals with FM can make a meaningful contribution to their own treatment by learning how their bodies respond to fibromyalgia. For example, do certain activities (especially those involving repeated or prolonged muscle use) tend to exacerbate FM? If so, how can they be modified or replaced and thus better tolerated? Do certain types/levels of activity cause delayed pain reactions a day or two later? Also crucial is learning to pace yourself, take frequent breaks, and say “No” to requests that simply cannot be accommodated on a particularly bad day. If certain commitments cannot be avoided, try to get extra rest before and after to aid in recovery. While these ideas sound simple in theory, they are often difficult to implement.

**Self Tolerance:** It is all too easy for individuals with FM to be excessively hard on themselves. After realizing that they are unable to accomplish all they once did, they can become overly critical or disparaging of themselves in their “self-talk”. Guilt may also become a problem as they must depend on friends and family to a greater extent for help with daily activities while “letting them down” by saying “no” to social outings when symptoms are severe. If surrounded by people who don’t “believe in” fibromyalgia, patients may wonder if their FM really IS just a figment of their imagination or is somehow “their fault.” If a helpful treatment regimen is not discovered right away, they may feel discouraged or worry that others think they just aren’t trying hard enough to feel better.

Newly diagnosed patients need to know that it is not their fault that they have fibromyalgia. FM is a legitimate, medically recognized condition which is being actively researched every day. Public awareness of FM is rapidly increasing, too. It takes enormous energy as well as courage to adjust to FM and find treatments that work well without wasting precious energy on guilt, self deprecation, and doubt.

Rheumatologist and FM specialist Russell Rothenberg, M.D., has words of hope to share. Just because someone starts out with severe symptoms doesn’t mean that (s)he cannot find worthwhile improvement with a skillfully devised and comprehensive treatment program. “Patients need to know that medication, judicious rest, exercise, physical therapy, and good diets can do more than just control the symptoms of fibromyalgia; they can control the disease process as well. There is no cure for FM, but people do get



Courtesy of Comstock

better! Hopefully, as better medications that are more specific for fibromyalgia are developed, and people are diagnosed earlier in their illness, more individuals with fibromyalgia will go into remission, or at least partial remission, and feel better.”<sup>41</sup>

## References

- 1) Yunus MB. What's New In Fibromyalgia Syndrome? A Review Of Abstracts Presented In The 1996 American College Of Rheumatology Annual Scientific Meeting: Part 1. *The Fibromyalgia Times* 1997;1(4):4.
- 2) Roizenblatt S, Moldofsky H, et al. Alpha Sleep Characteristics In Fibromyalgia. *Arthritis & Rheumatism* 2001;44:222-30.
- 3) Mountz JM, Bradley LA, et al. Fibromyalgia In Women. Abnormalities Of Regional Cerebral Blood Flow In The Thalamus And The Caudate Nucleus Are Associated With Low Pain Threshold Levels. *Arthritis & Rheumatism* 1995;38:926-38.
- 4) Clauw, DJ. Update On The Physiology And Management Of Fibromyalgia Syndrome. Presentation hosted by the National Fibromyalgia Partnership, on 11/10/97, Bethesda, MD.
- 5) Clauw DJ, Schmidt M, et al. The Relationship Between Fibromyalgia And Interstitial Cystitis. *J. Psychiatr. Res.* 1997;31(125):1.
- 6) See Thoracic Pain and Dysfunction. *Fibromyalgia Frontiers* 1997;5(2).
- 7) Ibid. Clauw, DJ. Update On The Physiology And Management Of Fibromyalgia Syndrome.
- 8) Bou-Holaigah I, et al. Provocation Of Hypotension And Pain During Upright Tilt Table Testing In Adults With Fibromyalgia. *Clinical and Experimental Rheumatology* 1997;15:239-246.
- 9) Yunus MB. Fibromyalgia And Other Overlapping Syndromes: The Concept Of Dysregulation Spectrum Syndrome. Presentation hosted by the National Fibromyalgia Partnership on 11/10/97, Bethesda, MD.
- 10) Clauw DJ. New Insights Into Fibromyalgia. *Fibromyalgia Frontiers* 1994; 2(4):7.
- 11) Wolfe F, et al. The American College Of Rheumatology 1990 Criteria For The Classification Of Fibromyalgia: Report Of A Multicenter Criteria Committee. *Arthritis & Rheumatism* 1990;33(2):160-172.
- 12) Ibid.
- 13) Clauw DJ. New Insights Into Fibromyalgia. Ibid, p.1.
- 14) Granges G, Littlejohn G. Pressure Pain Threshold In Pain-Free Subjects, In Patients With Chronic Regional Pain Syndromes, And In Patients With Fibromyalgia. *Arthritis & Rheumatism* 1993;36(65):642-6.
- 15) Staud R. The Abnormal Central Pain Processing Mechanism In Patients With Fibromyalgia. *Fibromyalgia Frontiers* 2002;10(3):18.
- 16) Crofford LJ, Clauw DJ. Fibromyalgia: Where Are We A Decade After The American College Of Rheumatology Classification Criteria Were Developed? Editorial. *Arthritis & Rheumatism* 2002;46(5):1136-7.
- 17) Russell IJ. Fibromyalgia Syndrome Sub-Groups. Editorial. *Journal of Musculoskeletal Pain* 2002;10(3):1-2.
- 18) For example, in 1999, NIAMS/NIH awarded a grant to Case Western Reserve University (Cleveland, OH) to the late researcher Jane Olson, Ph.D., for her project, "Mapping Genes for Fibromyalgia Syndrome".
- 19) See also: Arnold LM. Genetic Linkage Of Fibromyalgia To The Serotonin Receptor 2A Region On Chromosome 13 and the HLA Region On Chromosome 6. Abstract #505, presented at the 2003 Annual Meeting of the American College of Rheumatology, Orlando, FL.
- 20) Russell IJ, et al. Elevated Cerebrospinal Fluid Levels Of Substance P In Patients With The Fibromyalgia Syndrome. *Arthritis & Rheumatism* 1994;37(11):1593-1601. See also: Cerebrospinal Fluid (CSF) Substance P (SP) in Fibromyalgia (FM): Changes in CSP SP Over Time, Parallel Changes in Clinical Activity. *Arthritis & Rheumatism*, Abstract Supplement 1998;41(9).
- 21) Fransen J, Russell IJ. *The Fibromyalgia Help Book: Practical Guide to Living Better with Fibromyalgia*, St. Paul, MN: Smith House Press, 1996:25-26.
- 22) Yunus MB. Dysfunctional Spectrum Syndrome: A Unified Concept For Many Common Maladies. *Fibromyalgia Frontiers* 1996;4(4):3.
- 23) Crofford LJ, et al. Neurohormonal Perturbations In Fibromyalgia. *Baillieres Clin Rheumatology* 1996;10(2):365-78. See also: The Hypothalamic-Pituitary-Adrenal Stress Axis In The Fibromyalgia Syndrome. *Journal of Musculoskeletal Pain* 1996;4(1/2).
- 24) Abud-Mendoza C, et al. Hypothalamus-Hypophysis-Thyroid Axis Dysfunction In Patients With Refractory Fibromyalgia. *Arthritis & Rheumatism*, Abstract Supplement 1997;40(9).
- 25) Martínez-Lavín M. The Autonomic Nervous System And Fibromyalgia. *The Clinical Neurobiology Of Fibromyalgia And Myofascial Pain: Therapeutic Implications*. Binghamton, NY: The Haworth Press, 2002:221-228.
- 26) Ibid.
- 27) Graceley RH, Petzke F, Wolf JM, and Clauw DJ. Functional Magnetic Resonance Imaging Evidence Of Augmented Pain Processing In Fibromyalgia. *Arthritis & Rheumatism* 2002;46(5):1333-1343, and University Of Michigan Health System News Release 6/7/02: [www.med.umich.edu/opm/newspage/2002/fibromyalgia.htm](http://www.med.umich.edu/opm/newspage/2002/fibromyalgia.htm).
- 28) Ibid. Staud R., p. 20-21.
- 29) Buskila D, et al. Increased Rates Of Fibromyalgia Following Cervical Spine Injury: A Controlled Study Of 161 Cases of Traumatic Injury. *Arthritis & Rheumatism* 1997;40(3):446-52.
- 30) Donaldson S, et al. Fibromyalgia: A Retrospective Study Of 252 Consecutive Referrals. *Canadian Journal of Clinical Medicine*, June 1998.
- 31) Nicolson G. Co-Infections in Fibromyalgia, Chronic Fatigue Syndrome, And Other Chronic Illnesses. *Fibromyalgia Frontiers* 2002;10(3).
- 32) Yunus MB. Central Sensitivity Syndromes: A Unified Concept For Fibromyalgia And Other Similar Maladies. *JIRA* 2000;8(1).
- 33) Bennett R. Chronic Widespread Pain And The Fibromyalgia Construct. Website Of The Oregon Fibromyalgia Foundation: [www.myalgia.com](http://www.myalgia.com).
- 34) Meyer H. Presentation to the National Fibromyalgia Partnership on 3/7/98.
- 35) Muris S. Exploring Body Work For FM Self-Care. *Fibromyalgia Frontiers* 1996;4(3):4.
- 36) Esty ML. Neurotherapeutic Treatment Of Fibromyalgia Using EEG-Based Stimulation. *Fibromyalgia Frontiers* 2003;11(4):3-13.
- 37) Terrell ED. Chiropractic & Chronic Pain. *Fibromyalgia Frontiers* 1997;5(4):6.
- 38) Panel on Nutrition. Presentation to the National Fibromyalgia Partnership, on 6/4/97 featuring Virginia Inglese, M.A., R.D., CEDS; Sam Makoul, BCCN; Marti Pattishall, and Victoria Wood, M.P.H., R.D.
- 39) Website of the National Institutes of Health (NIH) National Center For Alternative And Complimentary Medicine (NCCAM): <http://nccam.nih.gov/health/acupuncture/#nccam>.
- 40) Ibid.
- 41) Rothenberg R. To The Newly Diagnosed Patient. *Fibromyalgia Frontiers* 1995;3(1):7.

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