The term fibromyalgia refers to a collection of symptoms with no clear physiologic cause, but the symptoms together constitute a clearly recognizable and distinct pathologic entity. The diagnosis is made through the examiner’s clinical observations. The differential diagnosis must include other somatic syndromes as well as disease entities, including hepatitis, hypothyroidism, diabetes mellitus, electrolyte imbalance, multiple sclerosis, and cancer. Diagnostic criteria serve as guidelines for diagnosis, not as absolute requirements. Treatment of fibromyalgia, which is an ongoing process, remains individualized, relying on a good physician-patient relationship. It is goal-oriented, directed at helping patients get restorative sleep, alleviating the somatic pains, keeping patients productive, and regulating schedules. It can be achieved through a goal-oriented agreement between patient and provider. Because fibromyalgia is chronic and may affect all areas of an individual’s functioning, the physician needs to also evaluate the social support systems of patients with fibromyalgia. The approach to treatment should integrate patient education as well as non-pharmacologic and pharmacologic modalities. To keep patients well educated and involved in their healthcare, physicians should provide patients with adequate sources for reliable information.

(Key words: fibromyalgia, tender points, chronic fatigue syndrome, somatic dysfunction)

Fibromyalgia is a chronic pain syndrome of unknown etiology. It is characterized by the presence of widespread and diffuse pain as well as many other associated symptoms of irregular sleep patterns, irritability, chronic fatigue, cognitive dysfunction, bladder irritability, numbness and tingling of the extremities, and headaches. It is also associated with symptoms of alternating diarrhea and constipation often seen in irritable bowel syndrome (IBS). The incidence of fibromyalgia has been estimated as high as 1% to 4% in the general population. It affects approximately 3.7 million people in the United States.1 Women are affected three times more often than men.2 Although this condition most commonly manifests in the third to the sixth decade, it has been described in both children and senior citizens.1-4 Diagnostic criteria for fibromyalgia were developed in 1990 and published by the American College of Rheumatology (Figure 1).5 Patients are generally classified as having the condition if they fulfill the diagnostic criteria of widespread pain lasting more than 3 months along with at least 11 of 18 tender points (Figure 2). These tender points are evaluated with manual pressure by an examiner using approximately 4 kg of pressure (enough pressure to turn the patient’s nail bed white). Although this classification is useful in a research setting to properly identify patients affected with the condition, real world experience may differ. Recent studies have suggested that most patients with fibromyalgia have a more generalized palpable tenderness not confined to the designated tender points of fibromyalgia.6 Furthermore, the sensitivity at specific tender points may be influenced by weather changes, mood, fitness level, and hormonal changes.

Pathophysiology
Although no one pathophysiologic mechanism is completely accepted as the mechanism for fibromyalgia, several have been explored and may have significance in this condition. It has been postulated that individuals with fibromyalgia have an abnormality in pain processing. This abnormality in turn produces the extreme sensitivity in tender points as well as visceral pain seen in IBS, noncardiac chest pain, headaches, and bladder irritability. Some evidence has supported the construct that peripheral nociceptors are involved.10 Other studies have suggested a central mechanism for the aberrant pain processing such as a decrease in circulating neurotransmitters such as serotonin or insulin-like growth factor I.11-13 Furthermore, researchers have demonstrated a decrease in blood flow to the thalamus and caudate nucleus in patients with fibromyalgia.14 These areas are in the brain which control pain, and this finding may have clinical significance in the heightened pain response seen in these patients.

Sleep disorders have been well documented in fibromyalgia.15,16 Affected individuals have a documented alpha wave intrusion into delta wave non–rapid eye movement sleep. This manifests as light sleep with frequent night awakening. Although the sleep abnormality is almost universal in patients with fibromyalgia, it is also seen in a large proportion of individuals without fibromyalgia and thus may be a symptom rather than a causative factor of the condition.17 Although many patients can associate the onset of symptoms to a particular illness or event, the causative role of trauma or infection has not been supported.
Fibromyalgia symptoms have been reported to occur after viral illnesses, Lyme disease infection, or physical injuries such as motor vehicle accidents. It is believed that these events may trigger or aggravate symptoms, but no evidence has supported the causative role of these events in the development of fibromyalgia.

Clinical presentation
Patients with fibromyalgia generally have a chief complaint of pain. Their pain is often described as “all over” or “from head to toe.” The pain is often so severe in that it interferes with their daily functioning. In addition to pain, generalized fatigue is often described. Many individuals describe their symptoms as being similar to a “flu-like illness” but without the viral infection. Patients with fibromyalgia often describe some degree of sleep disturbance, which can include difficulty falling asleep, frequent night awakenings, early awakening with difficulty returning to sleep, and morning fatigue with stiffness. One third to one half of patients with fibromyalgia relate the onset of their symptoms to a traumatic experience and can identify the day their symptoms began.

Other commonly associated symptoms include a type of Raynaud’s phenomenon with distal extremities turning blue in cold temperatures, urinary urgency, depression, anxiety, headache (mostly tension or muscular), nondermatomal paresthesias, and temporomandibular joint dysfunction. In one study, up to 66% of people with fibromyalgia were found to have allergic rhinitis. These patients may show a high degree of adverse reactions to drugs, chemicals, and other environmental stimuli such as bright lights or loud noises. Visceral organ dysfunction is not uncommon in this group of patients. Associations have been noted with the incidence of noncardiac chest pain, heartburn, palpitations, and interstitial cystitis. The frequent coexistence of fibromyalgia and IBS is well documented. Symptoms occur daily but may vary in severity. Although these patients are never symptom free, they may reach functional points during which time they require less or no medical intervention.

Physical examination and testing
Aside from the findings of multiple tender points, other findings of the physical examination are often normal. In some individuals, the findings of more localized myofascial pain may also be found in the cervical, thoracic, and lumbar region ( singly or in combination). Laboratory testing is most useful in elimination of other causes for the clinical findings. In fibromyalgia, results of laboratory testing are almost always normal. Extensive laboratory evaluation is usually not necessary, but basic testing should be limited to a complete blood cell count, chemistry profile, thyroid function, and an erythrocyte sedimentation rate or C-reactive protein level.

More detailed testing, including that for antinuclear antibody (ANA) and rheumatoid factor, should be reserved for only individuals with the appropriate history and physical findings to suggest either systemic lupus erythematosus (SLE) or rheumatoid arthritis. Interpretation of laboratory results must be done in the context of the patient’s clinical findings as some reports have found that some tests such as that for ANA may frequently be positive in this group of patients.

Although a history of sleep disorder is commonly present in patients with fibromyalgia, sleep studies should be reserved for patients with history suggestive of sleep apnea. Symptoms of paresthesias, although common, are generally in a nondermatomal or inconsistent distribution. Patients with paresthesias suggestive of neuropathy or radiculopathy should be further evaluated by electromyography and nerve conduction studies. Findings of weakness on examination, especially involving the proximal muscle groups, should prompt further evaluation for a muscle disorder such as myopathy, inflammatory myositis, or polymyositis. Fibromyalgia does not involve the joints. Findings on examination of joint tenderness or joint swelling should prompt further investigation of other conditions.

The coexistence of fibromyalgia with other autoimmune disorders is not uncommon. Many individuals with established rheumatoid arthritis, SLE, or ankylosing spondylitis will also fulfill the diagnostic criteria for fibromyalgia. In these cases, it is thought that fibromyalgia is a secondary condition possibly precipitated by the chronic pain of the underlying inflammatory disease. Fibromyalgia is not an inflammatory disease.

Treatment
Although fibromyalgia is a chronic condition and is not curable, symptomatic relief should be the goal of both patient and physician. The approach to treatment should integrate patient education as well as nonpharmacologic and pharmacologic modalities.

Patient education
Once the diagnosis of fibromyalgia is clearly established, adequate time should be allotted to explain the diagnosis to the patient. Along with being given a definition of the condition, the patient should be reassured that other more serious illness-
es have been excluded. A realistic prognosis should be given. Patients need to understand that this is a chronic condition, and though not curable, it is treatable. Responsibility for treatment must be shared by the patient as well as physician. Patients need to take an active role in their treatment and should be encouraged to seek out support groups and the “Fibromyalgia Self Help Course,” which has been developed by the Arthritis Foundation and often offered by local chapters in the community. Although the Internet has become a readily available source for medical information, it can be unreliable. Providing patients with adequate sources for reliable information will help to keep them well educated and involved in their healthcare.

**Nonpharmacologic therapy**

Exercise is an integral part of the treatment prescription for fibromyalgia. A number of studies evaluating the effect of aerobic training in fibromyalgia have reported improved outcomes. Exercise can be found to reduce pain as well as improve the patient’s overall sense of well-being. Low-impact aerobic exercise such as walking, bike riding, swimming, or water aerobics should be recommended. Warm-water exercises are often well tolerated, and the warm-water environment may help to reduce muscle pain or spasm. It should be emphasized that many of these patients may be poorly conditioned and prescribed exercise should be started at a level to correlate with the patient’s conditioning. Overexertion by the patient may exacerbate symptoms and provide a roadblock to further exercise. Supervised physical therapy is one option to help patients develop exercise programs if they have no previous conditioning or experience. It should be emphasized to patients that the physical therapy program is meant to help them develop a long-lasting independent exercise program. Too often, participation in organized programs is good but does not carry through to the independent home exercise program.

Cognitive behavioral therapy has been used with efficacy in many chronic pain conditions, including fibromyalgia. It can provide pain management techniques as well as tools that patients can incorporate into their individual coping mechanisms to reduce distress and gain control over their pain and illness. Cognitive behavioral therapy has also been shown to be an effective treatment for insomnia that is secondary to chronic pain. Limitations of this modality include the cost, which often is not covered by insurance, as well as the need for long-term treatment to teach and enforce positive behaviors.

Biofeedback has been evaluated in fibromyalgia and has been able to demonstrate a decrease in the number of tender points, decrease in overall pain, and decrease in morning stiffness. Effects have been shown to last up to 6 months after initiation of treatment.

**Pharmacologic therapy**

Because fibromyalgia is not an inflammatory disease, it is not surprising that anti-inflammatory medications are of no proven benefit. Neither nonsteroidal anti-inflammatory drugs (NSAIDs) nor corticosteroid preparations have consistently been found to be beneficial. It should be noted that some patients with fibromyalgia may have pain from more focal sources, such as osteoarthritis, headaches, or dysmenorrhea. For this reason, it is reasonable to consider a trial of an NSAID. If clinical efficacy is not achieved after a trial of 3 to 6 weeks, use of the drug should not be continued.

Tricyclic antidepressants have been the most widely advocated prescription medication used in the treatment of fibromyalgia. Both amitriptyline hydrochloride and cyclobenzaprine hydrochloride have been widely studied and have both demonstrated clinical improvement in fibromyalgia. The doses used in fibromyalgia are low and significantly below the doses used to treat depression. The mechanism of efficacy in pain and fibromyalgia are thought to be different. One possible explanation for the efficacy in treating pain is related to the ability to modify serotonin pro-
duction and block uptake or to increase or potentiate endogenous opioids (endorphins) in the brain (or both).\textsuperscript{38} Unfortunately, these medications are not effective in all patients, and in many, efficacy has been demonstrated to diminish over time.\textsuperscript{39,40} Other limitations include the side effects of this class of drugs, including dry mouth, sedation, weight gain,\textsuperscript{38} and cardiac arrhythmia. Tricyclic antidepressants are started at a very low dose (Table) and titrated at 2- to 4-week intervals to tolerance or efficacy. It is best to dose them 1 to 2 hours before bedtime to reduce the sedative “hangover” the next morning.

Other antidepressant medications have been used in fibromyalgia with variable success. Fluoxetine hydrochloride (Prozac), a selective serotonin reuptake inhibitor, has been one drug studied in this class of drugs with some efficacy in alleviating the symptoms of fibromyalgia. One study has reported success with the combination of fluoxetine dosed in the morning and amitriptyline dosed at bedtime.\textsuperscript{41}

Many other pharmacologic agents have been anecdotally endorsed. These agents include gabapentin (Neurontin) for neuropathic symptoms, and tizanidine hydrochloride (Zanaflex) as a pain reliever for muscle spasm. Alternative antidepressants may have benefit but have not been clinically studied. Analgesics may be needed long term to maintain a functional level. Tramadol hydrochloride (Ultram), a nonnarcotic analgesic has been shown anecdotally to have some benefit in control of chronic pain in fibromyalgia. Tramadol binds to the opioid pain receptor. It also has a metabolically active metabolite that complements its efficacy. If narcotics are necessary for pain control in fibromyalgia, they should be used for short periods in limited quantity. If long-term narcotic therapy is used, long-acting agents are favored in order to avoid peaks and valleys in drug level as well as the euphoria and high addiction potential of the shorter-acting narcotic analgesics.

Alternative modes of therapy

As with other medical conditions without a universally acceptable treatment regimen or cure, fibromyalgia has become a fertile ground for advocates of alternative modes of medical therapy. People with fibromyalgia are more likely than the general population to seek out alternative medicine, with up to 91\% of these patients seeing alternative providers.\textsuperscript{42} Vitamin and herbal supplements have been advocated by some but without good scientific data to support the use. Other alternative modes of therapy used may include magnet therapy, acupuncture, chiropractic care, and guaifenesin. Well-controlled studies are lacking to support the use of these treatment methods.

Prognosis

Fibromyalgia is a chronic condition, and in most individuals, it has some continued

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**Figure 3. Resources for patient education on fibromyalgia.**

- National Fibromyalgia Partnership, Inc (NFP) (formerly the Fibromyalgia Association of Greater Washington)
  140 Zinn Way
  Linden, VA 22642-5609
  Phone: 866-725-4404 (toll-free)
  [www.fmpartnership.org](http://www.fmpartnership.org)

- Fibromyalgia Association of Texas
  3810 Keele Drive
  Garland, TX 75041
  Phone: 972-271-5085

- Fibromyalgia Network
  PO Box 31750
  Tucson, AZ 85751-1750
  [www.fmnetnews.com](http://www.fmnetnews.com)

- National Fibromyalgia Research Association
  PO Box 500
  Salem, OR 97308
  [www.teleport.com/~nfra/](http://www.teleport.com/~nfra/)

- Arthritis Foundation
  1330 West Peachtree Street
  Atlanta, GA 30309
  Phone: 404-872-7100
  [www.arthritis.org](http://www.arthritis.org)

- National Chronic Pain Outreach Association
  7979 Old Georgetown Road, #100
  Bethesda, MD 20814-2429
  Phone: 301-452-4928

- The National Arthritis, Musculoskeletal, and Skin Diseases Information Clearing House
  9000 Rockville Pike
  Box AMS
  Bethesda, MD 20892
  Phone: 301-495-4484 (Barbara Weldon)

- National Chronic Fatigue Syndrome & Fibromyalgia Association
  PO Box 18426
  Kansas City, MO 64133
  Phone: 826-313-2000

- Seattle Fibromyalgia Association
  PO Box 77373
  Seattle, WA 98177
  Phone: 206-362-2310

- Centers for Disease Control (CDC)
  Division of Vital Diseases
  Building 6 - Room 127
  Atlanta, GA 30333
impact on their quality of life. Many individuals remain employed and have little change in their daily life. On the contrary, some individuals become chronically work disabled with significant disruption in all their activities. Fibromyalgia patients in the United States have self-reported disability rates between 6.3% and 23%.43 Others have made job changes directly as a result of their condition. Symptoms associated with functional limitations included pain, poor-quality sleep, abnormal tiredness, muscle stiffness, and increased pain after muscle exertion.44

Comment
Fibromyalgia is a common cause of diffuse and widespread pain seen in clinical practice. Diagnosis is based on historical symptoms as well as physical findings of multiple tender points on physical examination. Treatment is most effective if the physician uses an integrative approach, including patient education and reassurance, exercise, and adjunctive medications as necessary.45 Alternative modes of therapy have been used with variable success. In many individuals, symptoms may persist but they are able to maintain an uninterrupted lifestyle. In a small proportion of individuals, the symptoms of fibromyalgia result in long-term disability.

References

Table Dosing of Tricyclic Antidepressants in Fibromyalgia

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Usual starting dose (mg/d)</th>
<th>Usual effective dose (mg/d)</th>
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<tr>
<td>Amitriptyline hydrochloride</td>
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