

CME Report

Fibromyalgia *Diagnostic and Treatment Strategies for Family Physicians*

An Evidence-based Consensus Recommendation from an Expert Panel

There has been much debate and controversy in the medical community surrounding fibromyalgia (FM). At one extreme, some clinicians believe FM is a primary diagnosable disorder¹ while others do not believe it even exists.²

Although differences of opinion advance scholarly debate, these controversies can interfere with a Family Physician's ability to focus on patient issues. Some physicians still view the disorder skeptically and consider people presenting with a variety of FM symptoms as psychiatrically impaired or else simply lazy.³ In a 2008 survey of primary care clinicians (including physicians, nurse practitioners, and physician assistants), less than 10% (12 respondents out of 130) said they treat the pain associated with FM aggressively, and almost half (66 out of 136) said they did not want to treat the disorder in their practice.⁴

Although FM is, in fact, recognized as a legitimate clinical disorder by the American Medical Association, the National Institutes of Health, and other well-respected organizations, it is often misdiagnosed and improperly treated. It takes an average of 5 years for patients to get an accurate diagnosis,⁵ usually in a primary care setting.⁶ An accurate diagnosis and treatment plan is crucial since FM can significantly impair a patient's quality of life.⁷

Debates aside, advances in research are unraveling the neurobiological underpinnings of FM and revealing effective approaches to its management. Today there over 4,000 scientific journal articles on

fibromyalgia studies, and much of what researchers are learning can be applied in the clinical environment.⁸

In order to help Family Physicians feel more confident about diagnosing and treating patients with fibromyalgia, the New Jersey Academy of Family Physicians (NJAFP) recently convened a panel of experts to discuss diagnosis and treatment strategies. They reviewed the symptoms of FM, various comorbidities associated with the disorder, and the ways to differentiate FM from similar conditions. They also identified recent evidence regarding the pathophysiology of the disorder and discussed how to integrate evidence-based diagnostic and treatment guidelines into patient assessments.

The information contained in this monograph is designed to enable Family Physicians to recognize and effectively treat FM to help their patients manage pain and achieve a higher quality of life.

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General Objectives

To develop up-to-date scientific and clinical education that Family Physicians can utilize in their practice to improve their diagnostic, treatment, and management strategies for their patients with FM.

Learning Objectives

At the end of this program, participants will be able to:

- *Recognize the symptoms of FM and differentiate them from those of similar conditions*
- *Describe the recent evidence from genetic, biochemical, and imaging studies that shed insight on potential etiologies of FM symptoms*
- *Integrate evidence-based diagnostic and treatment guidelines for FM into patient assessments*
- *Evaluate and address comorbidities in patients with FM*
- *Employ pharmacologic and nonpharmacologic treatments in the management of FM*

Physician Accreditation Statements

This activity has been reviewed and is acceptable for up to 2.5 Prescribed credit(s) by the American Academy of Family Physicians. AAFP accreditation begins May 1, 2010. Term of approval is for two year(s) from this date, with option for yearly renewal.

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Defining Fibromyalgia

Although some physicians still question its existence, the history of medicine shows that fibromyalgia (although known by different names) is not a new condition. Over the years, advances in research have redefined the disorder, as reflected in the following brief history.

European medical literature contains descriptions from physicians in the late 16th century of clinical manifestations of musculoskeletal aches and pains.⁹

In 1904 Sir William Gowers coined the term “fibrositis” to describe the common muscular pain clinicians were seeing at the time. The term “fibrositis” suggested the cause of the condition was inflammation of the fibrous muscle tissue.¹⁰

In 1975, Dr. Harvey Moldofsky found that patients with fibrositis demonstrated abnormal brain activity during sleep. Patients had alterations in the patterns of slow-wave sleep, the deepest stage of sleep, and Dr. Moldofsky recommended redefining the disorder as a “non-restorative sleep syndrome.”¹¹

In 1981, the term “fibromyalgia” was used for the first time in a scientific publication. Yunus and colleagues believed the term fibromyalgia was more accurate than fibrositis because there was no evidence of inflammation or any other pathologic change in the muscles of patients with the disorder.¹²

In 1990, the American College of Rheumatology (ACR) established research classification criteria for fibromyalgia using tender points on specific body sites to help facilitate research on the condition.¹ In the absence of clinical diagnostic criteria, the research classification criteria found its way into clinical practice. While imperfect, the ACR criteria are the most common method of identifying fibromyalgia today.

Our concept of FM, and the best means by which to diagnose it, continues to be refined. In 2009, the lead author on the article that established the original classification criteria (Wolfe et al, 1990) and his colleagues proposed a set of clinical criteria that do not rely on the ACR tender point examination. The new diagnostic criteria instead rely on an index of widespread pain and a scale rating patient-reported somatic symptoms, including unrefreshing sleep, fatigue, and cognitive difficulties.¹³

Incidence/Prevalence

Fibromyalgia affects about 3% to 6% of the world population and an estimated 10 million Americans. Although the incidence increases with age, people are usually diagnosed between the ages of 20 and 50.¹⁴ By age 80, approximately 8% of women have FM.^{14,15}

Women, especially between the ages of 35 and 55, represent 75% to 90% of FM clinical cases.¹⁴ Although a disproportionate number of patients with FM are women, the disorder also occurs in men, children, and adolescents in all races, ethnic groups, and cultures. Studies indicate an increased prevalence in families, which appears to indicate a genetic component.¹⁴

Economic Burden

The economic burden of FM to both society and the individual is substantial. For example, the yearly cost to the US economy is \$12 to \$14 billion, and FM accounts for a loss of 1% to 2% of the nation’s overall productivity.¹⁶

For patients with FM, managing the disorder can be costly, resulting in a disproportionate consumption of health care and social resources. According to the National Fibromyalgia Association, 34% of FM patients spend between \$100 and \$1,000 per month above their insurance costs to see a health care professional.¹⁶ Like other chronic pain conditions, such as osteoarthritis, fibromyalgia can be disabling, and mounting medical bills make patients’ financial situations worse.

In addition to increasing out-of-pocket expenses, FM can also result in lost income. Patients with FM frequently change jobs or reduce their hours because of muscle pain or inability to focus.¹⁷

Etiology/Pathophysiology

Although there are several hypotheses regarding the etiology of FM, there is as yet insufficient evidence to support any single cause. Research suggests that a confluence of factors leads to the presentation of FM, including biochemical, metabolic, and immunoregulatory abnormalities.

Several factors appear to influence a person’s risk of developing FM, including familial/genetic predisposition, exposure to environmental stressors, altered sleep architecture, and changes in the function of such systems as the hypothalamic-pituitary-adrenal

(HPA) axis, autonomic nervous system (ANS), and central pain processing systems. There also appears to be a role for cognitive, behavioral, and psychological factors in the development of FM.

FAMILIAL/GENETIC PREDISPOSITION

FM runs in families, which suggests that there are important genetic factors that influence the development of the disorder. In a study of genetic factors among patients with FM and rheumatoid arthritis (RA), researchers found that compared with patients with RA, patients with FM had an eight times greater likelihood of a first-degree relative having a condition like FM.¹⁸ In addition, family members had a significantly higher number of tender points (specific sites on the body that cause pain when pressed), a significantly lower total myalgic score, and a greater risk of developing a major mood disorder than did the controls with RA.

ENVIRONMENTAL STRESSORS AS TRIGGERS

Environmental and psychological factors can trigger, maintain, or exacerbate FM in genetically predisposed individuals. Although researchers have tried to find specific types of stressors, there does not appear to be a single cause of this disorder.

Some of the stressors for which case studies have been reported include the following: other pain syndromes (eg, RA, osteoarthritis, systemic lupus erythematosus), physical trauma (eg, auto accidents), certain catastrophic events, some infections, and psychological stress/distress.^{10,19}

There is also evidence that physical trauma, such as a neck injury, can result in “posttraumatic” FM. For example, in a controlled study designed to examine the relationship between cervical spine injuries and the onset of FM, researchers compared patients with neck injuries to patients with leg fractures. They found that almost all FM symptoms were more common and severe in the neck injury group 3.2 months after the trauma. Researchers reported that FM is 13 times more likely to occur following a neck injury than an injury to the lower extremities.²⁰

Past trauma and abuse are prevalent among FM patients. Beck and colleagues²¹ administered a variety of validated self-report measures to 184 FM patients. When patients were asked: “Have you ever been in a severe accident, suffered the loss of a child, spouse, or suffered severe emotional trauma from some other life event?” almost 75% answered yes. Over half said they had been abused emotionally, physically, or sexually.

CENTRAL PAIN PROCESSING SYSTEMS

There is considerable evidence that FM is related to central nervous system (CNS) anomalies in pain processing and/or modulation leading to generalized heightened pain sensitivity. Pain testing studies suggest that people with FM have evidence of enhanced wind-up, that is, a progressive increase in pain perception following repetitive stimulation from the periphery such as the musculature sending repetitive nociceptive signals to the CNS for processing.²²

Data from functional neuroimaging studies demonstrate that the pain experienced by patients with FM is real and support the concept of centrally augmented pain processing. In a groundbreaking study, researchers used functional magnetic resonance imaging (fMRI) to evaluate the pattern of cerebral activation involved with pain processing in 16 FM patients and 16 matched controls while pressure was applied to their left thumbnail.²³ Although equal perceived pain intensity produced similar areas of activation, FM patients needed much less pressure than did controls to activate the cerebral pain matrix.

Several important abnormalities in levels of some key neurochemicals within the central nervous system (ie, spinal cord and brain) have also been identified in FM.

- *Substance P is a neurochemical agent that excites the afferent transmission of nociceptive signals to the brain. Russell and colleagues found that concentrations of substance P were three times higher in the cerebrospinal fluid (CSF) of FM patients than of normal controls.²⁴ This finding has been replicated by at least three other research groups. Since elevated levels of substance P are also found in other chronic pain syndromes, this might be a biological marker for the presence of chronic pain.¹⁰*
- *Glutamate is another important neurotransmitter in pain processing. Researchers found evidence that patients with FM have higher levels of glutamate and other excitatory amino acids in their CSF in comparison with controls.²⁵*
- *Abnormally low levels of serotonin, norepinephrine, and dopamine (all of which modify the experience of pain) have also been found in patients with FM.²⁶*
- *Evidence from studies using positron emission tomography (PET) demonstrates abnormalities related to brain dopamine in patients with FM, including reduced synthesis at baseline within several areas of the brain in which dopamine plays a role in pain perception²⁷ and attenuated release in response to painful stimulation specifically within the basal ganglia.²⁸*

Another central mechanism that likely contributes to enhanced pain perception in patients with FM is the observed lack of diffuse noxious inhibitory controls, or DNIC.¹⁰ DNIC describes the generalized whole-body analgesia that is produced in healthy people after 2 to 5 minutes of an intense, painful stimulus. The triggering of natural pain killers accounts for the effects of DNIC in healthy people but seems to be missing in some individuals with FM.

HPA AND ANS

Subtle alterations in the function of the HPA axis and ANS have been described in subsets of patients with FM.^{29,30} Because environmental stressors can influence the function of these systems, it has been suggested that set points or changes in these systems might participate in the development of FM in some people.

One consistent finding in FM is the presence of abnormal heart rate variability and exaggerated sympathetic activity.^{30,31} People with FM tend to have a significantly higher heart rate at rest and significantly lower heart rate variability compared with controls (eg, hyporesponsivity to environmental demands).

ALTERED SLEEP STAGE ARCHITECTURE

In healthy people, the most restorative part of the sleep cycle occurs during the deepest stages of non-rapid eye movement (NREM) sleep.³¹ NREM has three stages, and it is during stage 3 that people's breathing slows down, their blood pressure drops, energy is restored, and many substances such as growth hormones, antibodies, and other neurochemicals are synthesized.^{32,33}

Laboratory studies reveal that most people with FM show arousal disturbance in their EEG sleep physiology during stage 3 NREM sleep.³⁴ Since FM patients are constantly interrupted by bursts of awake-like brain activity, they spend a limited amount of time in the deeper, more refreshing, sleep cycles. The intrusion of arousal patterns into deep sleep has been suggested as the basis for the unrefreshing sleep experienced in FM patients.

COGNITIVE, BEHAVIORAL, AND PSYCHOLOGICAL FACTORS

While depression and anxiety often accompany FM, FM can occur in the absence of a psychiatric disorder. A clear distinction needs to be made between the presence of a psychiatric disorder such as depression or anxiety and the presence of psychological factors, any of which can worsen the experience of pain.

One psychological factor that appears to have importance for FM is the perception of control over pain, also known as pain "locus of control."³⁵ People with an internal locus of control believe they are able to influence events, whereas people with an external locus of control think that outcomes depend largely on factors that are beyond their personal control. Unfortunately, people with FM tend to have an external locus of control and do not believe that they have control over their pain. Such a belief is wholly understandable in the context of living with a form of persistent pain. Gradually introducing successful experiences associated with actually controlling pain through personal effort can help to alter this belief. A belief in internal locus of pain control has been associated with cerebral brain structures responsible for pain processing and modulation.³⁶

Another cognitive factor that influences pain in patients with FM is known as catastrophizing, or interpreting experiences in terms of worst possible outcomes.³⁷ People who catastrophize often describe their pain as "awful," "horrible," or "unbearable" and have a hard time shifting their attention away from the painful stimuli. While understandable, catastrophizing may actually make the pain worse. Again, neuroimaging studies suggest that catastrophizing also influences pain processing and modulation because brain regions activated by these interpretations overlap with cerebral areas in the pain matrix.

Patient Evaluation: Diagnosis

Since FM is diagnosed mainly in primary care settings, it is imperative for family physicians to know how to properly recognize and diagnose the disorder. As FM researchers Millea and Holloway wrote in an article in *American Family Physician*, "the family physician is ideally suited to treat FM because its management calls for a longitudinal relationship, a willingness to try different therapeutic modalities, and an understanding of the interrelationship of the biopsychosocial aspects of health."³⁸

CLINICAL PRESENTATION

Although there are no laboratory tests to confirm the diagnosis, most patients with FM present with widespread pain, physical findings, and comorbid conditions.³⁸ The symptoms of FM can result in severe disability comparable to that seen in other rheumatic diseases such as osteoarthritis or rheumatoid arthritis.

Patients with FM typically present with chronic pain. They have a heightened sensitivity to pain that is not restricted to only tender points but is widespread. "I feel like I've been run over by a truck" or "I hurt all

over all the time” are common complaints. Although the pain may be constant, it can be unpredictable—that is, the pain can change location and intensity from day to day.^{17,39}

Different patients describe pain in a variety of terms, such as burning, gnawing, a flu-like achiness, or stiffness. The stiffness is typically worse when they get up in the morning or after being still and usually improves as the day progresses.⁴⁰ In a qualitative study of FM patients, participants reported that although they experienced a window of less pain, usually from 10:00AM to 3:00PM, they seldom had 2 or 3 days in a row without symptoms.¹⁷

Certain daily activities seem to make the pain worse. These activities usually involve the repetitive use of muscles or prolonged tensing of a muscle.¹⁹ For example, patients may complain that the muscles in their upper back hurt after sitting at the computer for a period of time.

Patients may also present with comorbidities that are common to FM, especially irritable bowel syndrome, restless legs syndrome, and headaches/temporomandibular joint disorder (TMJD).⁴⁰ Comorbidities are discussed later in this course.

Various factors can aggravate a person’s symptoms. About 60% to 79% of patients with FM report that their symptoms are affected by poor sleep, fatigue, anxiety, stress, humidity, cold, warmth, and weather changes.¹ At the same time, chronic fatigue, stiffness, and sleep disturbance are mentioned by 75% of FM patients as part of the spectrum of related symptoms that, with pain, make up the so-called “fibromyalgia syndrome.”¹

Sleep disturbances affect most FM patients. Patients have trouble falling asleep and staying asleep and complain of waking up feeling tired and unrefreshed. Their pain makes sleeping more difficult, and lack of sleep makes the pain worse.³⁴ Sleep studies confirm that most people with FM have arousal disturbance in their sleep EEG. It is this disordered sleep physiology that is generally considered to be the basis of their un-refreshing sleep experience.¹¹

“I can’t do what I used to do” is another common complaint. Patients report that fatigue (or lack of energy) is one of the worst symptoms associated with FM.¹⁷ More than just being tired after a sleepless night or a busy day, the fatigue of FM is an all-encompassing exhaustion that can interfere with the person’s quality of life. There is a decreased physical functioning, and patients feel the need to pace themselves to get through their day. The fatigue can

be mental as well as physical, and resting does not seem to make it better. Like pain, the fatigue can be constant and incapacitating, and the amount of fatigue is disproportionate to the amount of activity or exertion levels.

Another debilitating symptom of FM is the cognitive or memory impairment that is sometimes called “fibro fog.”¹⁷ People have trouble concentrating or expressing themselves clearly. Lack of focus and memory problems can impact some patients’ ability to drive since they forget where they are going and have trouble focusing on the task of driving.¹⁷ Park and colleagues⁴¹ determined that the cognitive impairment found in FM patients, particularly memory and vocabulary deficits, are not age appropriate and concluded that FM may be a disorder that mimics premature mental aging.

Depression and anxiety are also not unusual symptoms for people with FM. Lack of social acceptance of the disorder or problems due to cognitive impairments can make some patients feel isolated, frustrated, or embarrassed. Patients also report that high levels of stress can make the symptoms more difficult to manage¹⁷ and can precipitate flare-ups.³⁸

The constant nature of FM symptoms can significantly impair patients’ quality of life and have a negative impact on their social and occupational function.¹⁷ The severity and unpredictability of the symptoms makes it hard to function at work or at social or leisure activities. Since the disorder has no visible signs, patients’ families, friends, coworkers, or physicians may not take the symptoms seriously, leading to patients’ feelings of frustration and isolation. This lack of understanding or general acceptance of the disorder can result in patients becoming socially withdrawn.

DIAGNOSTIC CRITERIA

Since laboratory tests are usually normal and people with FM tend to look healthy, it takes a Family Physician who is knowledgeable about FM to make a diagnosis. According to the National Fibromyalgia Association, FM should be diagnosed by its own characteristic features and should not be a diagnosis of exclusion.⁵ Patients are classified as having FM based on history, physical exam, and a manual tender point examination.

In 1990 the ACR established research criteria for the classification of FM.¹ Since there are no clinical diagnostic criteria available, the ACR criteria are the most common method used to identify FM today.

The ACR classification focuses on pain and tenderness, the defining characteristics of FM, and in-

cludes two basic criterion.¹ The first criterion is that a patient must have widespread pain for at least 3 months. Pain is considered widespread when it is in all four quadrants of the body, affecting both sides of the body, and above and below the waist. Axial skeletal pain (cervical spine, anterior chest, thoracic spine, or low back pain) must also be present.

The second criterion is that the patient must also experience pain or tenderness in 11 of 18 tender point sites on digital palpitation. Tender points are specific sites on the body that cause pain when pressed. The tender points have no underlying pathology—they are simply areas where we are all more tender but not typically painful except in cases of FM and other central pain states.

Coding

There is no specific single code for FM. According to the Centers for Disease Control and Prevention (CDC), FM is classified as a type of arthritis and is coded 729.1, which is labeled “Myositis and Myalgia, unspecified” and can include other conditions.⁴²

The code for unexplained fatigue is 780.79, while the code for Chronic Fatigue syndrome is 780.71. There are a variety of codes for sleep disturbance, depending on whether it is associated with a diagnosable condition (such as obstructive sleep apnea). The code for insomnia NEC is 307.40.⁴³

PHYSICAL EXAM/TENDER POINT EXAMINATION

Chronic widespread pain is not “normal” in generally healthy individuals, so its presence should prompt a Family Physician to conduct a tender point examination, a central component of identifying FM. Digital palpation of the defined tender points should be performed with the thumb by applying 4 kg of force (or about 9 pounds), increasing in intensity by 1 kg/second. This is generally considered to be just enough pressure to blanch the thumbnail of the examiner’s dominant hand.⁴⁰

According to ACR criteria, a tender point should be both painful and tender upon palpation. Although the ACR guidelines are considered the gold standard in research, the Expert Faculty agreed that if a patient is tender at less than 4 kg, there is no need to apply the full 4 kg of force.

Originally developed for research purposes, the ACR guidelines require pain at 11 or more of the 18 tender

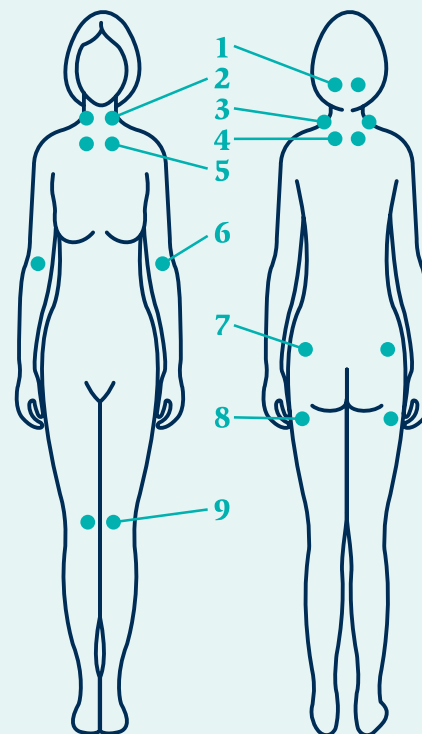
Figure 1. ACR Tender Points

American College of Rheumatology Diagnostic Criteria for Fibromyalgia

I. Widespread pain for at least three months, defined as the presence of all of the following:

- Pain on the right and left sides of the body
- Pain above and below the waist (including shoulder and buttock pain)
- Pain in the axial skeleton (cervical, thoracic or lumbar spine, or anterior chest)

II. Pain on palpation with a 4 -kg force in 11 of 18 sites.



Source: Wolfe et al Arthritis and Rheumatism 33(2):1:760 (1990)

Tender points are located in nine pairs, one point on each side of the body, for a total of 18 points. These pairs are located:

- 1) At the back of the neck behind the ear, where the neck muscles attach to the base of the skull
- 2) About halfway between the base of the neck and the tip of the shoulder
- 3) At the spot where the back muscles attach to the shoulder blade
- 4) On the front of the neck above the collarbone
- 5) Just to the right and left of the breastbone (sternum) about 2 inches below the collarbone.
- 6) On each forearm just below and to the outside of the crease of the elbow
- 7) Just above and to the outside of each buttock
- 8) On the outer upper leg just behind the bony part of the hip (this point is easier to find when standing)
- 9) On the inside of each knee

points for a clear classification.¹ In clinical practice, however, clinicians often soften the criteria and use a lower level of specificity to identify FM. It is also important to note that the severity of painful symptoms can vary from day to day, such that a person with FM might have pain at 13 tender points one day but only at 8 tender points the next. Even if a patient does not have 11 tender points, he or she can be considered to suffer from FM if there is disproportionate

amplified pain or tenderness in the absence of laboratory abnormalities.³⁸

During the physical exam, you are likely to notice two things about people with FM:

- *Although there are areas of pain on palpation, the classic inflammatory signs of redness, swelling, or heat in the joints and soft tissue are absent.*³⁸
- *Patients with FM display abnormalities in pain perception.*

Patients with FM are highly sensitive both to painful and nonpainful stimuli. During a physical exam, patients with FM typically have evidence of diffuse hyperalgesia, that is, increased pain perception in response to painful stimuli such that the pain is magnified and perceived with higher intensity than it would be by unaffected persons.¹⁰ They might also have allodynia, or pain in response to stimuli that would not be perceived as painful by healthy individuals.

PATIENT EVALUATION

Although patients with FM do not have readily demonstrated objective physical or laboratory abnormalities, it does not mean they are “well” or in no distress. And while chronic widespread pain is usually what brings an FM patient to a doctor, there are other core features of the disorder that can include:

- *Excessive tenderness*
- *Profound fatigue*
- *Morning stiffness*
- *Sleep disturbance*
- *Decreased physical functioning*
- *Cognitive difficulties with associated impairment of function and quality of life*
- *Mood disorders (depression, anxiety, anger)*

During the patient evaluation, it is important to ask the right questions that will not only determine the total spectrum of symptoms and their impact on the patient’s life, but also the patient’s opinion about what is causing the symptoms and what may be making the illness worse. For example, the patient’s chief complaint may be pain in one area of the body, but a careful history will most likely uncover additional areas of pain or additional problems associated with FM.

When evaluating a patient:

- *Identify the chief complaint—is it pain? Insomnia? Fatigue?*

- *Question the patient about the distribution of pain—is it regional or generalized, migratory or stationary?*
- *Ask about the type of pain—is it burning, tender, sore, aching, sharp, radiating, a bruised sensation, or flu-like aching?*
- *Determine the duration and onset of pain—is it insidious or did it come on suddenly as the result of a triggering event; do symptoms change from day to day?*
- *Inquire about aggravating and alleviating factors—is the pain affected by cold/humid weather, sleep problems, physical and mental fatigue, excessive physical activity, physical inactivity, anxiety, and stress?*⁴⁴
- *Ask about sleeping habits/patterns—how long does it take to fall asleep, how many times does the patient wake up? Is the sleep refreshing or restorative, is it associated with nightmares or bruxism, does the sleep partner complain about snoring or kicking?*
- *Obtain information about medications, exercise, and fatigue levels—many of the symptoms a patient is complaining about may be attributed to side effects of medication, including constipation (anticholinergics, opioids, calcium channel blockers), restless legs or sleep bruxism (selective serotonin reuptake inhibitors [SSRIs], tricyclic antidepressants [TCAs]), and fatigue (a wide variety of medications).*
- *Screen for common comorbidities or conditions that might aggravate symptoms or impact treatment (eg, obstructive sleep apnea [OSA], restless leg syndrome, irritable bowel syndrome, temporomandibular joint disorder, etc.)—ask if the patient has uncomfortable or unpleasant leg sensations when sitting or lying down? Feels worried, anxious, or nervous? Has been told there are pauses in his or her breathing while asleep? Has problems with memory, concentration, or mental clarity?*
- *Determine if there is a history of trauma, childhood abuse, anxiety, depression, sleep disorder, or a family history of FM or other painful conditions and psychiatric illnesses, including alcoholism, bipolar affective disorder, and substance abuse.*

In addition to the ACR tender point exam, it may be helpful to use another type of pain measure during the evaluation to assess different aspects of pain (ie, usual pain versus pain on palpation). There are several tools available for rating pain, but only one is specific for FM. (Each tool can be found in the Resources section.)

- *Revised Fibromyalgia Impact Questionnaire (FIQR)*—Revised in 2009, the FIQR is the only disease-specific outcome measure designed to capture the total spectrum of problems related to FM.⁴⁵ Filled in by patients prior to seeing their Family Physician, the FIQR can be a useful tool when trying to assess the impact of the disorder on a patient's functional abilities in daily life such as preparing meals, shopping, driving, and doing household chores. The questionnaire also asks patients about the overall impact of FM and to rate their level of pain, fatigue, stiffness, memory, depression and anxiety, tenderness, balance, and environmental sensitivity to loud noises, bright lights, etc.
- *Visual analog scale (VAS)*—The visual analog scale is a 10cm line on a piece of paper, marked 0-10 from left to right, with 0 being defined as “no pain” and 10 defined as “worst possible pain.” Patients rate their level of pain by pointing to a position on a straight line. This scale has been adapted for pediatrics and other special communication populations to a series of faces depicting expressions of pain.
- *Numerical Rating Scale*—Patients are asked to verbally choose a number from 0 to 10 that best describes their current pain. Zero means “no pain” and 10 means “worst possible pain.”

When evaluating patients, the Expert Faculty believe it is crucial to always ask about a person's problems with pain, sleep, and fatigue. If the patient has a problem with one, ask about the other. For example, even if sleep is the only presenting symptom, it is crucial to ask about pain and fatigue.

Common Comorbidities

FM frequently co-occurs with other medical conditions that can aggravate and perpetuate the patient's symptoms. Some patients may present with one comorbid condition, while others may present with several.³⁸

When considering common comorbidities in patients suspected of FM, keep in mind:

- *It is important to recognize and treat FM as a distinct disorder.*
- *The presence of other diseases does not rule out a diagnosis of FM.*
- *Although specific treatment for these conditions may be indicated, treating a comorbid condition should not be expected to alleviate all of the FM symptoms.*

Practice Recommendation #1

Focus pain assessment on type and quality of pain, pain intensity, source, location, duration, time course, pain affect, and effects on quality of life. Use self-report as the primary source of pain assessment, and use the same pain measurement tool at subsequent visits.

Source: Buckhardt CS, Goldenberg D, Crofford L, et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. Glenview, IL: American Pain Society; 2005.

Website: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=7298&nbr=4342

Strength of Evidence: Grade B recommendation. This means there are generally consistent findings from well-designed experimental studies; well-designed, quasi-experimental studies; or matched-case controlled studies and well-designed nonexperimental studies.

Most patients with FM have problems with sleep disturbance. It is up to the Family Physician to determine if the sleep problems are caused by FM or by OSA, restless legs syndrome, or teeth grinding. Patients with FM can have OSA but not meet the clinical stereotype. Since OSA not only happens in obese patients or in people with a double chin, the Expert Faculty recommends looking for it based on other clinical indicators such as nonrestorative sleep or the presence of self-reported cognitive difficulties.

Psychiatric disorders are common comorbidities found in patients with FM. Several psychological factors affect pain, including depressive symptoms, anxiety, and personality disorders. Although these can coexist with pain, they should not be confused with one another and each condition should be treated separately.¹⁰

Recognizing and treating the common comorbidities associated with FM will help alleviate the severity of the symptoms and may improve the patient's quality of life. A list of common comorbidities appears in *Table 1*.

Differential Diagnosis

A number of treatable conditions may present with symptoms resembling those of FM. (*See Table 2.*)

These conditions must be excluded before a definitive diagnosis of FM can be made. Making a differential diagnosis is especially difficult, however, since several of these illnesses can also affect patients with FM.

Table 1: Common Comorbidities^{19,38,40,42}

- *Chronic Fatigue Syndrome*
- *Irritable Bowel Syndrome*
- *Restless Leg Syndrome*
- *Migraine/tension headaches*
- *Mood and Anxiety Disorders - especially anxiety and depression*
- *Temporomandibular joint disorder (TMJD) / Sleep bruxism (teeth clenching/grinding)*
- *Chronic Pelvic Pain*
- *Premenstrual Syndrome*
- *Inflammatory Joint Disease (systemic lupus erythematosus, RA, ankylosing spondylitis, psoriatic arthritis)*
- *Raynaud's Phenomenon*
- *Positional cervical cord compression (some investigational evidence to suggest)*

Some of these illnesses and conditions are ruled out by clinical exam, while others can be ruled out by laboratory testing. Tests for a differential diagnosis include a complete blood count w/differential, thyroid stimulating hormone, metabolic panel (renal, hepatic function), muscle enzymes (creatine kinase), C-reactive protein, and sedimentation rate.⁵¹

Practice Recommendation #2

Begin the evaluation of people with FM with a complete history and physical examination, focusing on illnesses that may mimic or complicate FM, such as hypothyroidism or ankylosing spondylitis, or that can occur concurrently with FM, such as tendonitis, systemic lupus erythematosus, RA, or osteoarthritis. The clinician should perform a complete joint examination, manual muscle strength testing, and neurologic examination.

Source: Buckhardt CS, Goldenberg D, Crofford L, et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. Glenview, IL: American Pain Society; 2005.

Website: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=7298&nbr=4342

Strength of Evidence: Panel consensus (Practice recommended based on the opinions of experts in pain management.)

Table 2: Differential Diagnosis^{19,46-50}

- *Myofascial Pain Syndrome*
- *Chronic Fatigue Syndrome*
- *Hypothyroidism*
- *Rheumatological Disorders*
- *Hepatitis C*
- *Vitamin D Deficiency*
- *Positional Cervical Cord Compression*
- *Major Depressive Disorder*
- *Parkinson's Disease (Prodromal)*

Myofascial pain syndrome may occur in patients with FM and is defined by the presence of trigger (not tender) points in individual muscles.³⁸ Unlike FM, which is defined by widespread pain with changing areas of emphasis, consider myofascial pain syndrome if the patient's pain pattern is limited to a particular region over time.

Patients with FM may also have chronic fatigue syndrome, and both disorders manifest as chronic fatigue and pain. Unlike FM, which is not inflammatory, chronic fatigue syndrome is sometimes manifested by low-grade fever, enlarged lymph glands, and acute onset of the illness.⁴⁰

Treatment

Severity of symptoms and aggravating factors vary from patient to patient, and what works for one patient may not work for another. For this reason, FM requires both a multifaceted and an individualized approach to meet the complex needs of patients.

Although there is no universally accepted treatment or recognized cure for FM, clinical studies show that a variety of nonpharmacologic and pharmacologic strategies, offered in combination, are effective in reducing patients' symptoms.⁵² Treatment focuses on managing symptoms, changing patients' attitudes about the disease, and teaching adaptational behaviors to improve functional status and quality of life.

Appropriate management by a Family Physician can improve patients' daily function and quality of life.

Practice Recommendation #3

Use multiple strategies and include both pharmacologic and nonpharmacologic therapies in the management of FM.

Source: Buckhardt CS, Goldenberg D, Crofford L, et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. Glenview, IL: American Pain Society; 2005.

Website: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=7298&nbr=4342

Strength of Evidence: Grade A recommendation (This means there is strong, consistent evidence of effectiveness from meta-analysis of multiple well-designed controlled studies.)

NONPHARMACOLOGIC STRATEGIES

Depending on the patient's symptoms and overall health, there are several nonpharmacologic strategies available to help manage FM. A comprehensive literature review reported strong evidence to recommend incorporating two or more strategies to decrease pain and improve function in FM.⁵³

Nonpharmacologic interventions with the strongest evidence base supporting their use include the following:

- *Patient education*
- *Cognitive-behavioral therapy (CBT)*
- *Exercise*

There is strong evidence that patient education is critical to optimal management of FM.⁵² Patients should be instructed about the disorder itself. Family Physicians need to help patients understand that FM is not life-threatening and is not associated with deformity or early death.⁵⁴

Since the success of treatment can be influenced by patients' beliefs about their ability to control their symptoms, patients should have a clear understanding of the important role that they can play in their own care by partnering with their Family Physician. In an editorial in *American Family Physician*, respected FM researcher Daniel J. Clauw, MD, wrote that it is important to educate patients about the fact that "meaningful improvement rarely occurs without active participation on the patient's part—the patient must know that there is no "magic bullet" for treatment."⁵⁵

CBT is an evidence-based treatment that modifies patients' behavioral and thinking patterns to align them with good pain management. The therapy helps patients think and behave differently once they are able to see how thoughts, expectations, beliefs, and behaviors influence their symptoms.⁴⁰ Used for symptom management and lifestyle changes, CBT relies on a sound therapeutic alliance between the patient and the therapist.

The learning of a number of behavioral skills can help patients cope with their disorder. For example, completing common tasks may excessively tax sore muscles and lead to prolonged pain flare-ups. In such cases, time-based pacing can be helpful. Time-based pacing is a self-management strategy that involves taking brief regular rest breaks after a safe amount of work time (eg, 20 minutes).¹⁹ The work periods and the rest periods are controlled by time (eg, setting a watch to beep) rather than the completion of the task or in response to worsening pain. The rest breaks do not need to be long because the work periods are short and safe (eg, recovering from safe work not from a flare-up). Computer use is a good example in which time-based pacing can be easily applied.

Although pharmacologic approaches are available for treating sleep problems, sleep can also be managed with behavioral self-management skills.⁵⁶ For example, patients can be instructed regarding optimal sleep hygiene—to maintain regular bedtimes and awakening times thus establishing a more regular body rhythm. Maintaining an environment conducive to sleep may seem obvious but is rarely done (eg, sleeping in a room that is quiet, dark, relaxing, and not too hot or too cold). Additionally, the bed should be used only for sleeping and not for watching exciting TV, eating, or listening to music. Exercising a few hours before bed and avoiding large meals right before bed can also help.

Exercise should also be a key aspect of FM management. Since pain and fatigue cause inactivity and deconditioning, the goals of an exercise program are to combat deconditioning without triggering pain and to help patients maintain function in their everyday activities. The American Pain Society strongly recommends moderately intense aerobic exercise at least two or three times a week.⁶ People should slowly work up to this level by starting at a low level and gradually increasing their pace to avoid exercise-induced pain. A regular, low-impact program of gentle exercise and stretching should include strength training, aerobic conditioning, flexibility, and balance to help maintain muscle tone and reduce pain and stiffness.⁴⁰ Patients should focus on gentle aerobic exercises such as aquatic exercises, regular walking, or using a stationary bicycle and avoid

impact-loading exertion such as jogging, basketball, or high-impact aerobics.¹⁹

There is strong evidence that supervised aerobic and strength training exercise has beneficial effects on physical capacity and FM symptoms.⁵⁷ A Cochrane review of 34 studies concluded that 12 weeks of moderate intensity aerobic training “may improve overall well-being and physical function” but “probably leads to little or no difference in pain or tender points.” Twelve weeks of strength training, on the other hand, “may result in large reductions in pain, tender points and depression, and large improvement in overall well-being but may not lead to any difference in physical function.”

The benefits of exercise are enhanced when combined with CBT. A Mayo Institutional Review Board study evaluated data from a 1.5-day multidisciplinary program involving more than 2,600 FM patients.⁵⁸ The education portion focused on CBT to help participants with stress management, relaxation, sleep hygiene, and difficult day planning. Physical therapy sessions focused on the benefits of exercise, and occupational therapy sessions focused on activities of daily living. At the end of the program, patients reported an increase in their mental health and physical functioning, as well as a decrease in the overall impact of FM on all subscales of the Fibromyalgia Impact Questionnaire (FIQ) scores. The benefits were stable at a 12-month follow-up.

Unfortunately, many people including patients with FM may not be consistent at keeping up with regular exercise.³⁸ Regular exercise can be especially difficult for these patients since repetitive exertion can increase their pain and fatigue levels. Discussing ways to improve compliance with patients, such as choosing an exercise they enjoy or working out with a friend, may help them stick to an exercise program.

Pharmacologic Strategies

Certain antidepressants and anticonvulsants have been found to be useful in the treatment of the pain associated with FM. To understand how these drugs are thought to work, it is important to understand how pain is processed and modulated.

Pain is transmitted through many neural pathways and neurotransmitters within the central and peripheral nervous systems.⁵⁹ When an external stimulus activates nociceptors, it produces an electrical signal that is transmitted to the spinal cord along afferent nerve fibers. Once the signal reaches the dorsal horn of the spinal cord, pain

Practice Recommendation #4

Incorporate cognitive-behavioral therapy into a multimodal treatment approach to reduce pain, enhance self-efficacy, and improve function.

Source: Buckhardt CS, Goldenberg D, Crofford L, et al. Guideline for the management of fibromyalgia syndrome pain in adults and children. Glenview, IL: American Pain Society; 2005.

Website: http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=7298&nbr=4342

Strength of Evidence: Grade A recommendation (This means there is strong evidence from meta-analysis of multiple well-designed controlled studies.)

excitatory neurotransmitters, such as glutamate and substance P, are released. The nociceptive signal continues up the spinal cord to the brain where it is integrated with emotional and cognitive signals resulting in the experience of pain. The brain then releases inhibitory pain neurotransmitters, such as serotonin, norepinephrine, and gamma aminobutyric acid (GABA), through the descending pathways back to the spinal cord to inhibit additional nociceptive signals.

Three drugs are currently FDA approved for the treatment of FM:

- *Pregabalin (Lyrica®)*—an anticonvulsant
- *Duloxetine (Cymbalta®)*—a serotonin–norepinephrine reuptake inhibitor
- *Milnacipran (Savella®)*—a norepinephrine–serotonin reuptake inhibitor

Before starting patients on any of these medications, make sure they understand the type of results they can reasonably expect, as well as the possible side effects that may occur.

Pregabalin

In June 2007, pregabalin became the first drug to receive FDA approval for neuropathic pain associated with FM. Two pivot trials involving about 1,800

Lyrica is a registered trademark of Pfizer Pharmaceuticals

Cymbalta is a registered trademark of Eli Lilly and Company

Savella is licensed from Pierre Fabre and Cypress Bioscience, Inc. and is a registered trademark of Forest Laboratories, Inc.

patients using doses of 300 or 450 mg/day supported FDA approval.⁶⁰

Pregabalin monotherapy has been shown to provide clinically meaningful benefit to patients with FM. A multicenter, double-blind, placebo-controlled trial randomly assigned 748 patients with FM to receive pregabalin 300, 450, or 600 mg/day (dosed twice daily) or a placebo for 13 weeks.⁶¹ Compared with patients receiving placebo, patients in the pregabalin groups showed statistically significant improvement in endpoint mean pain score and in Patient Global Impression of Change (PGI-C) response. The pregabalin groups' improvements in FIQ-Total Score were numerically but not significantly greater than those for the placebo group. Researchers reported that compared with placebo groups "all pregabalin treatment groups showed statistically significant improvement in assessments of sleep and in patients' impressions of their global improvement."

A Cochrane database review reported that pregabalin has proven efficacy for FM patients with neuropathic pain. The PGI-C rating of "much improved" or "very much improved" was 40% at daily doses of 300 to 600 mg.⁶² There is no evidence to support the use of pregabalin for the treatment of acute pain or in chronic pain conditions such as arthritis in which case the primary source of pain is not related to nerve damage.

Duloxetine and Milnacipran

Duloxetine and milnacipran both belong to the class of medication known as dual reuptake inhibitors, which block the reuptake of both serotonin and norepinephrine.

Duloxetine is a balanced reuptake inhibitor and is typically classified as a serotonin-norepinephrine reuptake inhibitor (SNRI), whereas milnacipran is thought to have greater noradrenergic activity and is classified as a norepinephrine-serotonin reuptake inhibitor (NSRI).

Increasing levels of these neurotransmitters in the brain has been proposed to be the basis of their utility in treating depression, whereas raising the levels of these chemicals in the brain and spinal cord is thought to reduce pain in people with FM. Although milnacipran is used as an antidepressant internationally, it has not been approved for the treatment of depression in the United States.

The approval of duloxetine for the treatment of FM by the FDA was based on the results of two randomized, placebo-controlled clinical trials. The first study was

3 months in duration and enrolled female patients only.⁶³ Compared with those taking placebo, patients taking duloxetine 60 mg either once or twice a day experienced significantly greater improvement on the Brief Pain Inventory (BPI) average pain severity score, with a significantly higher percentage of duloxetine-treated patients reporting at least a 30% reduction in pain as well as significantly greater improvement on several measures of overall function and quality of life.

The second study was a 6-month trial that enrolled male and female FM patients.⁶⁴ The co-primary outcome measures were the BPI average pain severity score and Patient Global Impressions of Improvement (PGI-I) score. Compared with placebo-treated patients, those patients treated with duloxetine 120 mg/day improved significantly more on the co-primary outcome measures at 3 months and at 6 months, whereas those treated with duloxetine 60 mg/day reported significant improvement in both measures at 3 months but only the BPI score at 6 months. Notably, neither study demonstrated superior benefit comparing 120 mg/day to 60 mg/day; however, the higher dose was associated with more adverse reactions and premature discontinuation of treatment.

Approval by the FDA of milnacipran for the treatment of FM was based on the results of two randomized, placebo-controlled studies. The first 6-month trial compared total daily doses of milnacipran 100 and 200 mg to placebo.⁶⁵ A significantly greater number of patients taking milnacipran than receiving placebo experienced at least a 30% reduction in pain as measured by the VAS and considered themselves to have experienced global improvement as measured by the PGI-C. The second 3-month trial also compared total daily doses of milnacipran 100 and 200 mg/day to placebo.⁶⁶ In this study, more subjects taking either dose of milnacipran experienced at least a 30% reduction in pain (as measured by VAS) and considered themselves globally improved (as measured by PGI-C) than did those taking placebo. Notably, both studies reported that treatment with milnacipran 200 mg/day did not confer greater benefit than treatment with milnacipran 100 mg/day.

The Expert Panel agreed that the choice to start newly diagnosed fibromyalgia patients on one of the above medications as initial therapy was a reasonable choice. It is the opinion of the expert faculty that those patients with comorbid depression, prominent cognitive complaints or fatigue might fare better on either duloxetine or milnacipran, whereas patients whose primary concerns are insomnia, those whose onset of symptoms may be related to cervical trauma, and those in whom anxiety is more promi-

ment than depression might fare better on an initial trial of pregabalin.

Tricyclic Antidepressants

In addition to SNRIs, other types of antidepressants are used off-label to treat FM whether or not the patient has depression.

A meta-analysis of 18 randomized controlled trials involving 1,427 participants determined that antidepressant medications (TCAs, SSRIs, SNRIs, and monoamine oxidase inhibitors [MAOIs]) are associated with improvements in pain, depression, fatigue, sleep disturbances, and health-related quality of life in patients with FM.⁶⁷

A review of 505 articles found the strongest evidence for efficacy is for TCAs, particularly amitriptyline and cyclobenzaprine.⁵² Although cyclobenzaprine is actually a centrally acting muscle relaxant, it is chemically related to the TCAs and possesses the structural and pharmacologic properties of other TCAs.

Because TCAs cause drowsiness, they can be helpful in promoting sleep. A meta-analysis of nine studies conducted by Arnold and coauthors found that TCAs were better than placebo for effectively treating FM symptoms, especially quality of sleep. The most modest improvement was found in measures of stiffness and tenderness.⁶⁸ Another meta-analysis of 13 studies found that antidepressants improved sleep, fatigue, pain, and sense of well-being. FM patients were more than four times as likely to report overall improvement.⁶⁹

When using TCAs to treat FM, it is common to use much smaller doses than would be necessary for the treatment of depression. For example, by taking 10 mg of amitriptyline at bedtime, FM patients experience the side effects of TCAs less frequently than people taking the same drugs at higher doses for depression.^{38,70} If, however, the patient has depression in addition to FM, the depression should be treated as a separate condition that may require a higher dose. However, the development of intolerable side effects may then limit this strategy.

Common side effects of amitriptyline include blurred vision, bowel problems, constipation, dry mouth, hair loss, problems urinating, rash, seizure, stroke, and water retention.⁷¹ Side effects of cyclobenzaprine include drowsiness, dizziness, and dry mouth.⁷²

The dosage of TCAs must be individualized for each patient. Although TCAs are effective in treating symptoms for some FM patients, a careful monitoring of symptoms is important once therapeutic blood lev-

els are reached because a significant number of FM patients have found their symptoms get worse while they are on antidepressants.³⁸

SSRI Antidepressants

SSRIs comprise another class of antidepressants that are frequently used to treat FM.

There is moderate evidence that fluoxetine may be effective in FM.⁵² For example, in a 12-week, double-blind, parallel-group, flexible-dose study, 60 women with FM reported improvement on FIQ total score and on subscores for pain, fatigue, and depression.⁷³

Another randomized, double-blind, crossover trial determined that combining fluoxetine (20 mg/day) and amitriptyline (25 mg/day) resulted in significantly improved scores on FIQ and on VAS for pain, global well-being, and sleep disturbances. The study also found the combination of the two medicines was more effective than either one alone.⁷⁴

Although there are data to support the use of fluoxetine either alone or in combination with amitriptyline, it is important to note that treatment failures have been shown with other SSRIs (eg, citalopram).⁷⁵

Analgesic Medications

Tramadol is a weak atypical opioid used to relieve mild to moderately severe pain. A review of 505 articles on FM treatment concluded that there is moderate evidence of tramadol's effectiveness in FM.⁵² Since nausea and dizziness are associated with high initial doses, the dose (50 to 100 mg two or three times daily) should be slowly increased over time and should be tapered gradually when discontinued.⁵³

Tramadol can be used alone or in combination with acetaminophen. A double-blind, randomized study of Ultracet, a tablet containing 37.5 mg of tramadol and 325 mg of acetaminophen, found that the combination was effective in reducing pain, decreasing the number of tender points, and lowering discontinuation rates.⁷⁶ Although some participants experienced nausea, dizziness, somnolence, and constipation, investigators found no serious adverse effects related to the study medication when compared with placebo.

Medications With No Proven Efficacy

Based on current evidence, several medications have no proven efficacy in treating patients with FM.

These include:

- *Nonsteroidal anti-inflammatory drugs (although they are commonly used for FM treatment)*⁴⁰
- *Benzodiazepine and nonbenzodiazepine sedatives, melatonin, calcitonin, thyroid hormone, guaifenesin, dehydroepiandrosterone, or magnesium*⁵²
- *Corticosteroids: there is very strong evidence against using these drugs unless there is concurrent joint, bursa, or tendon inflammation*⁵³

To date, there have been no randomized controlled clinical trials that have been published to support the use of traditional opioids (ie, hydrocodone, codeine, morphine) for the treatment of fibromyalgia pain. A review of 505 articles reported that although opioids are not typically recommended, they should be considered only after all other pharmaceutical and nonpharmaceutical strategies have been exhausted.⁵²

Our Expert Panel suggested narcotics be used for long-term pain only as a last resort for a very select population and for limited duration. Because of the high risk of tolerance and/or addiction, Family Physicians may feel more comfortable if opioids are used under the auspices of a pain clinic.

In the Pipeline

In addition to the medications discussed thus far, there are several others that have shown promise and/or are being evaluated for the treatment of FM.

One such agent is pramipexole, a drug that is FDA approved for the treatment of Parkinson's disease and restless legs syndrome (a common comorbidity in patients with FM). Although its use in FM is off-label, a controlled clinical trial by Holman and Myers⁷⁷ demonstrated that pramipexole improves both sleep and pain in a majority of study patients. Some of these study patients were already taking narcotic analgesics and were disabled, representing severely affected patients who would have typically been excluded from study participation. These researchers reported that, compared with placebo, 4.5 mg of pramipexole at bedtime significantly improved pain, fatigue, function, and global assessment with few side effects. As a result, the European League Against Rheumatism (EULAR) included pramipexole in its list of medications that should be considered in the treatment of FM.⁷⁸

Another medication that shows promise for the treatment of FM is sodium oxybate, a medication that facilitates restorative sleep and is an FDA-approved treatment of cataplexy (a sudden collapse

while awake) and excessive daytime sleepiness in patients with narcolepsy. In a multicenter, randomized, double-blind clinical trial, Russell and colleagues⁷⁹ found significant changes in the primary composite outcome measure (VAS, FIQ score, PGI-C, and pain rating) among patients treated with either 4.5 or 6 g of sodium oxybate compared with those receiving placebo. Sodium oxybate improved patients' quality of life and reduced their insomnia, fatigue, and severity of pain.

Alternative Therapies

Some studies show that alternative therapies may be effective when used as an adjunctive treatment for patients with FM.

- *There is strong evidence to suggest that balneotherapy (warm water therapy/therapeutic bathing) may be helpful for pain relief in patients with FM.*⁵³ *In a randomized study, the group that received 20-minute spa bathing once a day five times a week for 3 weeks saw an improvement in the number of tender points, VAS, Beck's Depression Index, and FIQ score compared with the control group.*⁸⁰
- *Modest evidence supports the use of acupuncture to relieve symptoms of FM.*⁵³ *A review of seven studies reported that acupuncture can relieve pain, increase pain thresholds, improve global ratings, and reduce morning stiffness in people with FM.*⁸¹ *The duration of the benefit following the acupuncture treatment series is not known. In addition, a randomized, double-blind study of 70 FM patients found that electroacupuncture resulted in a 70% improvement in pain threshold compared with only 4% in the control group.*⁸²
- *Modest evidence also supports the use of clinical hypnosis for pain relief.*⁵³ *In a controlled study, patients were randomly assigned to either hypnotherapy or physical therapy for 12 weeks with a follow-up at 24 weeks. The patients in the hypnotherapy group showed a significantly better outcome in pain, fatigue on awakening, sleep pattern, and global assessment than those in the physical therapy group.*⁸³

When To Refer

Depending on the severity of a patient's symptoms, the Family Physician may need to consider referral for specialty care. Potential resources/referrals include rheumatologists, pain management specialists, physical therapists, psychiatrists, and/or other behavioral medicine specialists (ie, therapists, counselors, and social workers).

Consider referring or consulting when:

- *The diagnosis is in doubt.*
- *The patient does not respond to initial treatments.*
- *Multiple comorbidities complicate management.*
- *Additional diagnostic procedures are indicated.*
- *Psychosocial burden is sufficient enough to require a behavioral specialist.*

Conclusion

FM is characterized by chronic widespread pain associated with a predictable pattern of tenderness. Patients also typically are affected by persistent fatigue and poor sleep, and frequently experience

a variety of other associated symptoms and comorbid conditions that can vary in their intensity and impair quality of life. FM is recognized as a legitimate, distinct clinical entity with specific diagnostic criteria.

While there is no universally effective treatment or “cure” for FM, there are evidence-based treatments for symptom management, including three FDA-approved medications. Successful management of FM requires a comprehensive approach with the ultimate goal of improvement in pain, function, and quality of life.

Family Physicians can help their patients by identifying and treating FM early before it leads to dysfunction and disability.

Professional Resources for Health Care Providers and Patients Related to the Diagnosis and Treatment of Fibromyalgia

RESOURCES	CONTACT INFORMATION	DESCRIPTION
American Pain Society — “Guide for Adults with Fibromyalgia Syndrome Pain”	Go to: http://www.ampainsoc.org/pub/pt_fibromyalgia.htm or call (847) 375-4715	<ul style="list-style-type: none"> • 16-page booklet designed to help patients live with fibromyalgia syndrome (FM) pain • Discusses how FM is diagnosed and outlines therapies and medicines used to alleviate the pain and other effects of FM • Suggests tools for rating pain intensity and for locating pain (e.g., a body map)
Revised Fibromyalgia Impact Questionnaire	http://arthritis-research.com/content/supplementary/ar2783-s1.pdf	<ul style="list-style-type: none"> • Questionnaire used to capture the total spectrum of FM related symptoms
The Manual Tender Point Survey Booklet and DVD	http://www.nfra.net/fibromyalgia_tender_point_dvd_57_prd0.htm	<ul style="list-style-type: none"> • Guides the user through each tender point site, providing information on the exact location, and describes and demonstrates both the patient’s and examiner’s positions during the examination • A booklet also includes a scoring sheet that can be copied and included in the patient’s medical file
National Fibromyalgia Association — The Physician Assistance, Information & Needs (P.A.I.N.)	Contact NFA at (714) 921-0150	<ul style="list-style-type: none"> • Kit was designed to assist medical professionals with the diagnosis and treatment of FM • Kit has resources for health care providers and information for patients
Visual analogue scale (VAS)	http://www.health.vic.gov.au/qualitycouncil/downloads/app1_pain_rating_scales	<ul style="list-style-type: none"> • Instructs patients to point to the position on the line between the faces to indicate how much pain they are currently feeling
Numerical rating scale (NRS)	http://www.health.vic.gov.au/qualitycouncil/downloads/app1_pain_rating_scales	<ul style="list-style-type: none"> • Instructs patients to choose a number from 0 to 10 that best describes their current pain

Case Study: Susan

Susan, 47, works as a secretary at a local real estate company. The company she works for is laying off people, and Susan is worried about losing her job. Although her two children are grown up and live outside the house, Susan's elderly mother lives with her and requires care because of crippling RA.

Susan comes to you complaining of aching, flu-like pain in her muscles and joints, especially in her shoulders and hips. The pain has steadily gotten worse over the past 3 months and is severe enough to make it difficult to get out of bed or to sit at the computer for several hours at work. She says she hurts every day. When asked to rank her average pain in the last week on a scale from 1 to 10, she tells you it's 7.5.

1) She says the constant pain makes it hard for her to concentrate and she's also having trouble remembering things. What should you do at this point?

- a) Ask about her sleep habits/patterns
- b) Determine if she has any coexisting conditions
- c) Ask about fatigue and her physical functioning
- d) All of the above

When asked about her sleep habits, Susan reports that she has a hard time falling and staying asleep. She wakes up feeling tired, and in general, feels too tired to do much of anything. She used to look forward to taking an hour-long walk every night after work "to change gears from work mode to taking-care-of-Mom mode" but she says she's so tired after her walk that now "it's not worth it." She's even stopped going out socially on weekends with her friends.

2) Although she denies feeling depressed, she's increasingly discouraged by her limitations. You recommend all of the following except:

- a) Sleep hygiene strategies
- b) Time-based pacing (ie, shorter walks)
- c) Bed rest
- d) Tricyclic antidepressants, primarily for sleep

You suspect FM and decide to do a tender point examination. During the exam, Susan has pain at 14 tender points. No specific triggering event for symptom onset is identified. However, she acknowledges that she's under a lot of stress from the combination of family- and work-related problems.

3) Which of the following could be a contributing factor in the development of FM?

- a) Genetic predisposition
- b) Physical trauma
- c) Psychosocial trauma/duress
- d) All of the above

During Susan's physical exam, you notice she displays several clinical signs that are common among people with FM.

4) The following are commonly found in FM except:

- a) FM patients have signs of inflammation in their joints and soft tissue.
- b) FM patients have diffuse hyperalgesia (increased pain to painful stimuli).
- c) FM patients have many comorbid conditions such as fatigue, sleep problems, and memory difficulties.
- d) FM patients have allodynia (pain from a normally nonpainful stimulus).

Susan tells you the OTC analgesic she's been taking hasn't provided any meaningful relief.

5) Which medications have little or no proven efficacy for fibromyalgia?

- a) Nonbenzodiazepine sedatives
- b) Nonsteroidal anti-inflammatory drugs
- c) Opioids
- d) All of the above

On her follow-up visit, Susan complains that the TCAs aren't helping. You give her samples of pregabalin, but 5 days later she makes an unscheduled visit complaining that the pills make her too sleepy. You start her on a trial of duloxetine 30 mg once a day for a week and then increased to 60 mg once a day, but she calls the office 2 weeks later saying she's having trouble with nausea and loss of appetite.

6) Which one of the following options would be considered best for Susan?

- a) Increase the dose of duloxetine to 120 mg/day
- b) Reduce the dosage to 30 mg until she adjusts
- c) Switch her back to pregabalin
- d) Add a benzodiazepine to her regimen

RESOLUTION: At the 6 month follow-up, Susan's pain level is at a 3 (on a scale of 1 to 10), and she has enough energy to return to her nightly walks. Susan says she's functioning better and is able to get more done during the day.

ANSWERS: SUSAN

- 1) The correct answer is d: All of the above.
- 2) The correct answer is c: Bed rest.
- 3) The correct answer is d: All of the above.
- 4) The correct answer is a: FM patients have signs of inflammation in their joints and soft tissue.
- 5) The correct answer is d: All of the above.
- 6) The correct answer is b: Reduce the dosage back to 30 mg until she adjusts.

Case Study: Robin

Robin, 33 years old, was in a car accident 9 months ago in which she was struck from behind. Her chief complaint is muscle spasms and back pain, and she describes her pain as 7 out of 10 on a numerical rating scale. Radiologic evaluation including cervical computed tomography performed in the emergency department was negative for bony fractures or vertebral disc abnormality. Her labs were normal except for an incidental finding of low vitamin D. She describes having been to physical therapy for a few weeks immediately following the accident, but she says it provided minimal relief from symptoms.

During the physical exam you determine that her neurologic examination, including sensation and deep-tendon reflexes, is normal, although her strength and range-of-motion testing of upper extremities is limited by pain. Palpation of her pectoral, paraspinal, and trapezius muscles demonstrates cord-like bands that are exquisitely tender and produce radiations when palpated.

You diagnose her with myofascial pain and prescribe a trial of cyclobenzaprine, supplemental vitamin D, and another round of physical therapy. On the follow-up exam, Robin reports limited benefit from the current regimen. The physical therapist notes indicate she has increased range-of-motion in her upper extremities but continued complaints of severe musculoskeletal pain. Subsequent examination shows resolution of previous muscle spasms. Robin complains of severe insomnia, which she attributes to pain and to “nerves” since the car accident. You suspect FM and decide to do a manual tender point survey.

1) How many tender points do the ACR guidelines require for a diagnosis of fibromyalgia?

- a) 7
- b) 11
- c) 15
- d) 18

Robin has dull pain on light palpation at 10 out of 18 ACR tender points. Although she doesn't technically meet the ACR guidelines of 11 tender points, you are cognizant that tenderness can vary over time and diagnose her with FM based on complaints of chronic widespread pain and a history consistent with the disorder.

2) Since she attributes the pain and insomnia to “nerves” following the car accident, which comorbidity do you test Robin for?

- a) Restless leg syndrome
- b) Premenstrual syndrome
- c) Irritable bowel syndrome
- d) Posttraumatic stress disorder

3) Some alternative therapies have proven effective or moderately effective when used as an adjunctive treatment for patients with FM. Which therapy might be helpful for Robin?

- a) Exercise
- b) Acupuncture
- c) Cognitive-behavioral therapy
- d) Any of the above

RESOLUTION: Robin is started on a trial of pregabalin at bedtime, increased as tolerated to twice a day. A follow-up examination shows resolution of the paresthesias in Robin's upper extremities, but the 450-mg dose of medication is causing problems with excessive daytime sleepiness. You adjust the dosing to load the majority of medication at bedtime. At the 3-month follow-up, Robin tells you she is tolerating the current regimen and has continued improvements in sleep and pain.

ANSWERS: ROBIN

- 1) The correct answer is b: 11.
- 2) The correct answer is d: Posttraumatic stress disorder
- 3) The correct answer is d: Any of the above



Faculty Disclosures

NJAFP adheres to the conflict-of-interest policy of the AAFP, as well as to the guidelines of the Accreditation Council for Continuing Medical Education and the AMA. Current guidelines state that participants in CME activities should be made aware of any affiliation or financial interest that may affect an author's article. The members of this Expert Panel have completed conflict-of-interest statements. Disclosures do not suggest bias but provide readers with information relevant to the evaluation of the contents of these recommendations.

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QUESTIONS

- 1) The ACR's tender point research classification criteria for FM is currently the only clinical diagnostic criteria used to diagnose FM.
 - a) *True*
 - b) *False*
- 2) While pain is often what drives the patient to seek help, those with FM will present with a spectrum of symptoms. Which are the most common FM symptoms?
 - a) *Stiffness*
 - b) *Sleep disturbance*
 - c) *Fatigue*
 - d) *Cognitive impairment*
 - e) *All of the above*
- 3) Which of the following is not useful in diagnosing FM?
 - a) *History*
 - b) *Physical exam*
 - c) *Tender point examination*
 - d) *Laboratory tests*
- 4) There are two basic requirements for the diagnosis of FM. They are:
 - a) *Disproportionate localized pain and disturbed sleep for 3 months*
 - b) *Widespread pain for at least 3 months and unrefreshing sleep*
 - c) *Pain/tenderness in 11 out of 18 tender point sites and disturbed sleep for 3 months*
 - d) *Widespread pain for at least 3 months and pain/tenderness in 11 out of 18 tender points*
- 5) A patient can be considered to have FM even when painful symptoms vary from day to day, pain severity varies from day to day, and there is demonstrated disproportionate amplified pain or tenderness in the absence of laboratory abnormalities.
 - a) *True*
 - b) *False*
- 6) Patients experiencing FM will present not only with pain on palpation but also with inflammatory signs of redness, swelling, or heat in the joints and soft tissue.
 - a) *True*
 - b) *False*



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