Clinical Manifestations and Diagnosis of Fibromyalgia

Robert M. Bennett, MD, FRCP, MACR

The basic clinical manifestations of fibromyalgia (FM), in terms of pain, fatigue, dysfunctional sleep, and tenderness were described by Smythe and Moldofsky in 1977 and elaborated by Yunus and colleagues in 1981. The 1990 American College of Rheumatology (ACR) fibromyalgia classification paper listed many other symptoms that were commonly reported by FM patients (paresthesia, anxiety, headaches, irritable bowel, urinary urgency, sicca symptoms, noise and cold intolerance, dysmenorrhea, depression, low back pain, neck pain, Raynaud phenomenon, and weather-related effects). An Internet survey conducted by the National Fibromyalgia Association (NFA) on 2569 people who have diagnosed fibromyalgia reported the rank order of symptoms as: morning stiffness, fatigue, nonrestorative sleep, pain, forgetfulness, poor concentration, difficulty falling asleep, muscle spasms, anxiety, and depression (Table 1). A similar questionnaire from the German Fibromyalgia Association (DFV) was mailed to 3996 patients and was completed by 699 patients; the rank order of the most frequent symptoms was: muscle pain, morning stiffness, nonrestorative sleep, poor concentration, lack of energy, low productivity, and forgetfulness. Since that time, many of these symptoms have been subject to further study and the patients’ perspective has been more rigorously evaluated as part of the OMERACT (Outcome Measures in Rheumatology Clinical Trials) process.

PAIN

The core symptom of FM, according to the 1990 ACR classification criteria, is chronic widespread pain (WSP). FM patients usually describe their pain as arising from muscle and joints, and the majority of FM patients also have tender skin. Fibromyalgia pain typically waxes and wanes in intensity; flares are associated with unaccustomed exertion, prolonged inactivity, soft tissue injuries, surgery, poor sleep, cold exposure, long car trips, and psychological stressors. Many FM patients describe...
increased pain with cold, damp weather and low barometric pressure.\textsuperscript{4} FM pain is predominantly axial in distribution, but pain in the hands and feet is not uncommon and may lead to a misdiagnosis of early rheumatoid arthritis (RA).\textsuperscript{8} Staud and colleagues\textsuperscript{9} has surmised that “peripheral factors account for most of the variance of overall clinical FM pain, suggesting that the input of pain by the peripheral tissues is clinically relevant.” Many patients describe a feeling of swelling in their soft tissues; this is often localized to the area of joints, which may lead to self-diagnosis of arthritis and referral to a rheumatologist. Martinez-Lavin and colleagues\textsuperscript{7} reported that many FM symptoms are similar to those experienced by patients with neuropathic pain syndromes; these neuropathic symptoms refer mainly to changes in skin sensation. Fibromyalgia pain and stiffness typically have a diurnal variation, with a nadir from about 11:00 AM to 3:00 PM.\textsuperscript{10} Fibromyalgia often occurs in the setting of other pain syndromes, such as RA, systemic lupus erythematosus (SLE), osteoarthritis, and so forth. There has been a profusion of sophisticated psychoneurophysiological and imaging studies indicating that FM pain is a result of disordered sensory processing.\textsuperscript{11}

### FATIGUE

Fatigue is one of the most common symptoms encountered in patients seeking medical care, with a prevalence of 24% in one report.\textsuperscript{12} The association of fatigue and pain has a long history and was a prominent feature of neurasthenia as described in the late nineteenth century.\textsuperscript{13} The differential diagnosis of fatigue includes many medical illnesses, but a well-defined diagnosis is only found in about 5% of fatigued patients presenting in primary care.\textsuperscript{14} The OMERACT 8 patient Delphi rated fatigue as the third most important symptom after two pain-related items; it was endorsed by 96% of participants. In the NFA and DFV surveys, it was rated as the second most troublesome symptom (see Table 1). The Fibromyalgia Impact Questionnaire (FIQ) includes “How tired have you been?” with anchors of “No tiredness” and

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<tr>
<th>OMERACT 7 Patient Delphi</th>
<th>NFA Survey</th>
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<tr>
<td>Pain or physical discomfort</td>
<td>Morning stiffness</td>
<td>Pain</td>
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<td>Joint pain or aching</td>
<td>Fatigue</td>
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<td>Fatigue or lack of energy</td>
<td>Nonrestorative sleep</td>
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<td>Poor sleep</td>
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<td>Fibro-fog</td>
<td>Forgetfulness</td>
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<td>Stiffness</td>
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<td>Disorganized thinking</td>
<td>Difficulty falling asleep</td>
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<td>Difficulty with moving</td>
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<td>Having to push yourself to accomplish things</td>
<td>Anxiety</td>
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<td>Problems with setting goals and completing tasks</td>
<td>Depression</td>
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<td>Tenderness to touch</td>
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<td>Feeling hands are swollen</td>
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<td>Depression</td>
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<td>Limitations in normal daily activities</td>
<td>Restless legs</td>
<td>Headaches</td>
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<td>Poor memory</td>
<td>Abdominal pain</td>
<td>Visual disturbances</td>
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Table 1
A comparison of the major patient-perceived manifestations of fibromyalgia

Bennett\textsuperscript{216}
“Very tired” on a 0–10 visual analog scale (VAS); it is often used a surrogate measure of fatigue. However, exactly what is meant by “fatigue” must be considered. Sleepiness and fatigue are interrelated—but-distinct phenomena that are often reported in the context of medical disorders, psychiatric disorders, and primary sleep disorders. Sleepiness and fatigue usually have different implications in terms of diagnosis and treatment; however, they are often used interchangeably or merged under the more general lay term of “feeling tired.” Most FM patients describe their fatigue as a weariness of mind and body that impairs their productivity and enjoyment of life.

A careful analysis is required in the evaluation of the fatigued patient to determine the possible cause of the symptoms and the patient’s reaction to being fatigued. Wessely conceptualized four components of fatigue: behavior (effects of fatigue), feeling (subjective experience), mechanisms, and context (environment, attitudes). He stresses that even when a discrete cause for fatigue is identified, such as chronic infection or multiple sclerosis, the social, behavioral, and psychological variables are still important in the comprehensive evaluation of a patient’s fatigue. Arnold emphasized the wide range of symptoms that can masquerade as fatigue; she divides fatigue into three major domains: (1) Physical (eg, reduced activity, low energy, tiredness, decreased physical endurance, increased effort with physical tasks and with overcoming inactivity, general weakness, heaviness, slowness or sluggishness, nonrestorative sleep, and sleepiness); (2) Cognitive (eg, decreased concentration, decreased attention, decreased mental endurance, and slowed thinking); and (3) Emotional (eg, decreased motivation or initiative, decreased interest, feeling overwhelmed, feeling bored, aversion to effort, and feeling low). In FM patients, the two most obvious contributors to fatigue are depression and nonrestorative sleep. However, although antidepressant therapy often results in a modest improvement in fatigue scales, they are seldom curative of this symptom. Furthermore, improvements in nonrestorative sleep do not necessarily translate into absence of fatigue. In the 2009 sodium oxybate study, the overall improvement of sleep was about 30% (Jenkins sleep questionnaire) and tiredness (FIQ) was reduced by about 25%.

Chronic pain itself appears to have a fatiguing effect. This is probably the result of comorbidities such as insomnia, deconditioning, and depression. However, there is increasing interest in the notion that the fatigue/pain association may be a direct result of chronic pain modulating the release of inflammatory cytokines from pain-activated astrocytes and microglia within the brain, inducing a “sickness syndrome.”

**STIFFNESS**

Stiffness is a prominent condition in many musculoskeletal disorders. Patients in the NFA online survey rated morning stiffness as their most troublesome symptom; German FM patients rated it as their fourth most important symptom (see Table 1). In the OMERACT 8 Delphi, stiffness was reported by 91% of participants and was rated the sixth most important symptom. The combination of stiffness with the common FM experience of joint pain raises questions about a diagnosis of an early inflammatory arthritis; many patients who have early FM request to be seen by a rheumatologist. Stiffness is an item on the FIQ, and thus an indication of its relevance can be found in the many studies that have used the FIQ. There have not been any physiologic studies of stiffness in FM. Muscle stiffness is a combination of the intrinsic properties of muscle tissue (mainly nonelastic connective tissue) and resting muscle tone. There is an increase in this nonelastic tissue with aging, and muscle tissue displays thixotropic properties (ie, it stiffens with increasing rest and vice versa); this may be relevant to the benefits of exercise in FM. On the other hand, exercise-induced muscle
damage increases muscle stiffness,\textsuperscript{27} thus the need for restraint in the prescription of vigorous exercise in FM patients.\textsuperscript{28} Muscle stiffness may be a prominent early symptom of several disorders; for instance, stiffness is a feature of severe hypothyroidism (Hoffman’s syndrome)\textsuperscript{29} and is often an early symptom of Parkinson disease.\textsuperscript{30} It is quite evident that a greater understanding of stiffness in FM patients should yield important clues as to clinically relevant changes in muscle composition, muscle tone, and deconditioning.

**DISORDERED SLEEP**

Fibromyalgia patients usually report disturbed sleep.\textsuperscript{31,32} They often have problems with sleep initiation and maintenance; the most notable feature is feeling tired upon awakening. This is usually referred to as nonrestorative sleep (NRS) and typically causes greater daytime impairment than does difficulty initiating or maintaining sleep.\textsuperscript{33,34} There is no definitive classification of NRS; Stone and colleagues\textsuperscript{35} suggested this definition: “a report of persistently feeling unrefreshed upon awakening in the presence of normal sleep duration, occurring in the absence of a sleep disorder.” This is partly captured in the FIQ question on sleep: “How have you felt when you get up in the morning?” with the 0–10 VAS ranging between “Awoke well rested” and “Awoke very tired.” NRS has been associated with certain EEG changes. In the 1970s, alpha intrusion into the delta rhythm of non–rapid eye movement (NREM) sleep was initially described in psychiatric subjects,\textsuperscript{36} and shortly thereafter Moldofsky and colleagues\textsuperscript{37} described a similar abnormality in “fibrositis” subjects. It is now apparent that alpha–delta sleep is not always found in FM subjects and does not always correlate with the symptom of NRS.\textsuperscript{38} More recently, other abnormal EEG patterns have been found in FM subjects. Rizzi and colleagues\textsuperscript{39} reported that a cyclic alternating pattern of sleep correlated with FM symptoms, and Roizenblatt and associates\textsuperscript{40} reported that alpha intrusion had several different patterns, with a phasic pattern correlating most closely with FM symptoms. Landis and colleagues\textsuperscript{41} reported that female FM subjects had fewer spindles during NREM stage 2 sleep and a lower spindle time per epoch of NREM stage 2 sleep.

In the clinical evaluation of disturbed sleep in FM subjects, the most important issue is the determination as to whether a patient has a primary sleep disorder. By far the most common is restless leg syndrome (RLS), which is associated with periodic limb movement disorder in most cases.\textsuperscript{42} A 2008 study found a 64\% prevalence of RLS in 3302 women who have fibromyalgia and noted that these subjects experienced more sleep disturbances and pronounced daytime sleepiness.\textsuperscript{43} The history and response to a dopamine agonist are so typical that a formal sleep study is often unnecessary to diagnose RLS unless comorbid sleep apnea is suspected. However, it is suggested that patients who have RLS have a ferritin level, as there is a relationship of RLS with iron deficiency.\textsuperscript{44} This iron deficiency seems similar to the iron deficiency of chronic disease and is often unresponsive to oral iron supplements. Interestingly, patients who have RLS have been reported to have low levels of iron in the substantia nigra and putamen;\textsuperscript{45} neuropathological studies have led to the notion that RLS may be a functional disorder resulting from impaired iron acquisition by the neuromelanin cells.\textsuperscript{46} There are no large studies of sleep apnea prevalence in FM; one study of 50 subjects attending a sleep clinic found the prevalence of FM was 10 times higher in subjects who have sleep apnea/hypopnea compared with the reported prevalence of FM in the general population.\textsuperscript{47} Upper-airway resistance syndrome (UARS) is increasingly being diagnosed in patients who have dysfunctional sleep; this diagnosis will be missed unless additional channels are incorporated into the polysomnography
testing. UARS was found in 26 out of 28 female FM subjects attending a sleep clinic; only one subject had obstructive sleep apnea. A continuous positive airway pressure machine resulted in an improvement in functional symptoms ranging from 23% to 47%. If these results were confirmed in a larger sample, there would be a good rationale for including polysomnography in the routine evaluation of FM patients.

TENDERNESS

FM patients typically report that they are more sensitive to touch, and experience pain on relatively minor contact (see Table 1). Skin roll tenderness (from the interscapular area) was incorporated into an early diagnostic definition of FM. Some 95% of FM subjects endorsed the Leeds neuropathic pain question, “Does your pain make the affected skin abnormally sensitive to touch?” Superficial pressure pain thresholds using von Frey hairs were found to be less in FM than in healthy controls, as were deep pressure pain thresholds and tourniquet test tolerance. Another feature of some FM patients that suggests cutaneous sensitization is dermatographia, which is reactive hyperemia, that is, increased local blood flow and edema that occur on mechanical or chemical stimulation of the skin. It results from the local release of histamine from mast cells and the antidromic release of substance P, neurokinin A, and calcitonin gene-related peptide from the peripheral endings. Dermatographia was one of the six clinical features used in FM diagnosis in the 1976 paper reporting on NREM sleep changes in subjects who had “fibrositis syndrome.” Littlejohn and colleagues subsequently reported that FM subjects had an exaggerated skin flare response to both mechanical and chemical (capsaicin) stimulation and a positive correlation between the size of the flare and the number of tender points. It was suggested that the exaggerated skin response reflected increased activity of polymodal nociceptors of afferent nerves and that this may play a role in FM-related skin tenderness. These observations were largely forgotten until Salemi and colleagues found that the skin biopsies of about 30% of FM subjects had demonstrable amounts of messenger RNA coding for IL-1β, IL-6, and TNF-α, whereas no cytokine-coding mRNA was found in skin biopsies from healthy controls. This finding was surmised to be a result of neurogenic inflammation. Supportive of this explanation was the finding of dermal deposits of IgG and increased numbers of mast cells in FM compared with controls. Interestingly, there is one report of experimental slow-wave sleep disruption being related to an exaggerated skin response and a reduced pain threshold. This is a currently neglected area of FM research that may be of relevance in relation to the initiation and maintenance of central sensitization.

COGNITIVE DYSFUNCTION

Difficulties with memory, concentration, and dual tasking are major problems of many fibromyalgia patients, according to self-reports. On three self-rating surveys (see Table 1), dyscognition was the fifth most distressing symptom. Patients commonly describe difficulties with short-term memory, concentration, logical analysis, and motivation. This decrease in cognitive performance has been estimated to be equivalent to 20 years of aging. Defects have been described in terms of working memory, episodic memory, and verbal fluency. Short-term memory problems have been linked to a disproportionate interference from distraction influences. Some investigators have noted that cognitive defects in FM may be a result of associated fatigue, pain, and depression, and others have failed to find significant defects using automated neuropsychological assessment. Newer imaging technology may provide some explanation for these deficits. For instance, a proton magnetic resonance
spectroscopy study showed lower levels of $N$-acetylaspartate in the hippocampus of FM subjects. The hippocampus is important in the formation of new memories; thus, its dysfunction may be implicated in short-term memory loss. There are several recent studies reporting a reduction in hippocampal volume in chronically stressed subjects. Using the relatively new technique of magnetic resonance diffusion-tensor imaging and MR imaging of voxel-based morphometry, defects in neuronal circuitry were noted in FM subjects along with decreases in gray matter volume in the postcentral gyri, amygdalae, hippocampi, superior frontal gyri, and anterior cingulate gyri. Luering and colleagues reported that cognitive deficits in nonverbal working memory were positively correlated with gray matter values in the left dorso-lateral prefrontal cortex, whereas working memory was positively correlated with gray matter values in the supplementary motor cortex.

**DYSESTHESIA**

FM patients commonly report numbness and tingling in the extremities without any obvious cause coming to light upon further testing. In some patients this may be due to restless leg syndrome and in others an early peripheral neuropathy. Symptoms mimicking a neurologic disorder were first reported some 20 years ago. More recently, Martinez-Lavin postulated that fibromyalgia is a neuropathic pain syndrome and that dysesthetic sensations are evidence for this notion. To test this hypothesis, the Leeds neuropathic pain questionnaire was given to 20 FM subjects and 20 RA subjects. Sensory symptoms were more common in the FM cohort: dysesthetic (95% versus 30%), evoked (95% versus 35%), paroxysmal (90% versus 15%), and thermal (90% versus 20%). Another explanation for the experience of these neurologic-sounding symptoms is a conflict between sensory–motor central nervous processing and central sensitization syndrome.

**POOR BALANCE**

Poor balance is increasingly being recognized as a manifestation of fibromyalgia. In the NFA survey, balance problems were reported by 45% of participants. Jones and colleagues studied 32 FM subjects and 32 controls regarding number of falls, confidence about balance, and a clinical evaluation of physiologic dysfunctions (stability limits, anticipatory postural adjustments, reactive postural responses, sensory orientation, and stability in gait) relating to balancing. Over a 6-month period, FM subjects had 37 falls compared with six falls in the controls. FM subjects lacked confidence in their ability to do specific tasks with an increased fear of falling compared with controls. The reasons for this imbalance in FM is unclear at this time; relevant issues may include poor proprioception, vestibular dysfunction, disturbed spatiovisual orientation, lower limb weakness, concentration/distraction deficits, and orthostatic hypotension.

**RAYNAUD PHENOMENON**

FM patients often report being cold in situations whereas others are not; this phenomenon is often associated with changes in the color of their fingers. Symptoms suggestive of primary Raynaud’s have been reported in FM patients for the last 25 years, with a prevalence ranging from 8.8% to 53.3%. One study of nail-fold capillaroscopy in FM did not find any of the morphologic changes that have been described in connective tissue disorders, but did note sluggish circulation in those subjects who have Raynaud’s. Bennett and colleagues reported on quantitative evaluation of
cold-induced vasospasm in 29 FM subjects using the Nielsen test; 41% had an abnormal test and 38% had elevated levels of platelet $\alpha_2$-adrenergic receptors. There was a positive correlation between the percentage of change in finger systolic pressure on cooling (Nielsen test) and the number of $\alpha_2$-adrenergic receptors. Digital photoplethysmography did not reveal any changes suggestive of organic disease in the digital vessels. Thermosensory testing has uniformly found a reduced threshold for cold-induced pain.\(^{50,80,81}\) The relationship of cold intolerance and Raynaud phenomenon to the dysautonomia of FM and reduced perfusion of muscle warrants further research.\(^{82,83}\)

**ORAL AND OCULAR SYMPTOMS**

Dry mouth is a common symptom of FM patients, with estimates ranging from 18% to 71%.\(^{76,84}\) In some cases, this may be a result of side effects from tricyclic antidepressants,\(^{85}\) coexistent hepatitis C infection,\(^{86}\) or dysautonomia;\(^{87}\) but in the majority of cases, no obvious cause can be found.\(^{84}\) However, FM does appear to have a common association with Sjogren’s syndrome, with a 22% prevalence in one study,\(^{88}\) and is often the only diagnosis that can be made in patients who have keratoconjunctivitis sicca.\(^{89}\) On the other hand, a diagnosis of biopsy-proven Sjogren’s syndrome was only found in 7% of 72 FM patients.\(^{90}\) In a study of 67 FM subjects, a high prevalence of oral symptoms were recorded: xerostomia 70.9%, glossodynia 32.8%, dysphagia 37.3%, and dysgeusia, 34.2%.\(^{91}\) Blurred vision that cannot be corrected by prescription lenses is also a common phenomenon (R.M. Bennett, MD, unpublished data).

**IMPAIRED FUNCTION**

Most FM patients report some limitations of function. Item 1 of the FIQ consists of 11 questions relating to function with an average value of between 40 and 50 (on a 0–100 VAS) in several recent pharmaceutical studies.\(^{18,92}\) Difficulty with moving and low productivity are prominent conditions (see Table 1). An analysis of the NFA survey data found that over 25% of female FM subjects reported difficulties in taking care of personal needs and the majority reported problems with light housework and negotiating one flight of stairs.\(^{93}\) The average FM patient in this sample was assessed as having less functional ability than a typical woman in her 80s. In general, reduced function was associated with higher levels of pain, fatigue, depression, balance problems, irritable bladder, restless legs, and muscle spasms. FM patients’ reports of reduced functioning have been correlated to reduced activity on electronic ambulatory monitoring.\(^{94}\) There is some evidence that depression plays a role in reduced daytime activity.\(^{95}\) Problems with physical function and cognitive defects may result in difficulties in sustained employment.\(^{96,97}\)

**SEXUALITY**

It is not surprising that chronic pain and fatigue have an adverse effect on sexuality. This is an area of clinical manifestations that has only recently been explored.\(^{98}\) Orel-Ianala and colleagues\(^{99}\) gave the Changes in Sexual Functioning Questionnaire to 31 FM subjects along with 20 healthy controls and 26 subjects who had RA. Sexual dysfunction was more frequent among FM subjects (97%) and RA subjects (84%) compared with controls. There was a major correlation of sexual dysfunction with intensity of depression. A similar association with depression was reported by Aydin and colleagues.\(^{100}\) On the other hand, a study using the Female Sexual Function Index
compared sexual dysfunction in 40 subjects who had FM only, 27 who had FM plus major depression, and 33 healthy controls found no association with depression.101 One prevalence study of vulvodynia reported that FM subjects have an increased odds ratio of 3.84 for having this problem.102 Pelvic pain syndrome is also common according to one study;103 its relationship to endometriosis in FM subjects needs further investigation.

HEADACHES

Headaches were prominently ranked in the NFA and DFV surveys, but not in the OMERACT Delphi (see Table 1). The prevalence of International Headache Society diagnoses in one study of FM subjects was: migraine without aura, 20%; migraine with aura, 23%; tension alone, 24%; combined tension and migraine, 22%; posttraumatic, 5%; and probable analgesic overuse syndrome, 8% alone (n = 15 with aura, n = 17 without aura); tension-type alone (n = 18); combined migraine and tension-type (n = 16); posttraumatic (n = 4); and probable analgesic overuse headache (n = 6).104 It was reported that FM/migraine subjects have more disabling headaches and have higher cerebrospinal fluid glutamate levels than migraine alone.105 Other investigators have also opined that migraine, daily chronic headache, and fibromyalgia are an expression of abnormal pain processing.106 Questions regarding headache should be part of the comprehensive evaluation of all FM patients.

PSYCHOLOGICAL DISTRESS

Self-reported depression is a common symptom in FM patients (see Table 1). As FM was once considered to be a psychiatric diagnosis, there have been numerous studies evaluating the psychological profiles of FM subjects. For instance, early studies noted elevations of certain scales on the Minnesota Multiphasic Personality Inventory (MMPI), especially the hypochondriasis, hysteria, and depression scales.107 Smythe108 noted that any patient who had chronic pain would give positive answers on the MMPI to questions relating to pain and somatic symptoms, and concluded that there was a 40% bias of labeling such a patient as being neurotic. There is a general consensus that depression, anxiety disorders, and PTSD are common in FM patients.109 Arnold and colleagues110 reported that the odds ratios for psychiatric diagnoses in individuals who have fibromyalgia versus individuals who have RA are: bipolar disorder, 153; major depressive disorder, 2.7; any anxiety disorder, 6.7; any eating disorder, 2.4; and any substance use disorder, 3.3. Contrary to popular misconceptions, personality disorders are not especially common in the FM population.111 Thieme and colleagues111 found a prevalence of 8.7% and Fietta and associates112 found a prevalence of 7%. The coexistence of anxiety and depression with FM generally has a negative influence on the expression of FM symptoms and functionality, but this association can be quite variable.113

ASSOCIATED DISORDERS

In addition to the numerous clinical manifestations of FM described here, many FM patients have an associated clinical syndrome such as irritable bowel, overactive bladder, restless legs, multiple chemical sensitivity, chronic fatigue syndrome, vulvodynia, and so forth. The association of these disorders with FM and between themselves is now considered to be a manifestation of widespread central sensitization and are increasingly being referred to as “central sensitivity syndromes.”73 (See the
The diagnosis of FM is usually based on the ACR’s classification criteria. This is certainly true for the entry of FM subjects into scientific research protocols. Although these criteria were intended for purposes of epidemiologic classification, the discussion section of the 1990 criteria paper noted that “the sensitivity of the criteria suggests that they may be useful for diagnosis as well as classification.”

These exact criteria are seldom used in the primary care setting, however, and are only used by about 50% of rheumatologists in their routine practice. The problem lies in performing the ACR-designated tender point evaluation, which requires training and experience that is lacking in most primary care settings and probably underestimates a diagnosis of FM in males. Thus, the question has arisen as to whether an office-based clinical diagnosis of FM can be made more simply.

**Using a History of Widespread Pain as a Diagnostic Criterion**

There are many epidemiologic studies of WSP reporting that most of the surveyed subjects have ACR-defined FM. Subjects who have WSP and FM are generally more symptomatic, dysfunctional, and depressed than those who have WSP without FM. On the other hand, there are several studies indicating that the finding of widespread allodynia is predictive of WSP. In general, there is a relationship between the number of tender points and changes in nociceptive processing in subjects who have WSP not fulfilling a diagnosis of FM. This has given rise to the concept that ACR-defined FM is at one end of a continuous spectrum of pain complaints.

Any new office-friendly definition of FM probably ought to be based on more than a history of WSP. A Swedish epidemiologic study of 9952 subjects found WSP without widespread allodynia in 4.5% of the population and ACR-defined FM in 2.5%. However, 50% of subjects who had WSP without FM had other diagnoses, such as inflammatory rheumatic disorders, stroke, whiplash-associated disorders, diabetic neuropathy, myopathy, herniated discs, and osteoarthritis. Conditions that may masquerade as WSP are given in Box 1.

As with any patient, the evaluation of a patient who has WSP must always consider the differential diagnosis, but the finding of another disorder or investigational abnormality does not necessarily rule out a diagnosis of FM. Indeed, it is very common for FM patients to have associated disorders such as rheumatoid arthritis, SLE, and other pain-related states. Considering these factors, diagnosing FM solely on the basis of WSP, though being valid in the majority of cases and a useful surrogate in epidemiologic studies, will lead to diagnostic errors that are unacceptable in the clinical setting.

**Using a Combination of Symptoms as Diagnostic Criteria**

FM patients have so many symptoms that, for years, many physicians were skeptical of FM as a distinct clinical disorder. However, it is now generally accepted that widespread central sensitization generates a wide array of symptoms. Unless a patient has another central sensitization syndrome, the wide range of seemingly unrelated FM symptoms could be useful in diagnosis, especially if combined with the history of WSP. In fact, such combinations were proposed by Yunus and colleagues in the 1980s and tested in the 1990 ACR criteria study. The 1990 ACR
criteria had a sensitivity of 88%, specificity of 81%, and accuracy of 85%, whereas the combination of WSP sine tender points and five or more of Yunus’s minor criteria (fatigue, aggravation of symptoms by physical activity, modulation of symptoms by weather changes, anxiety, chronic headaches, irritable bowel symptoms, subjective swelling, and numbness) had a sensitivity of 77%, a specificity of 76%, and an accuracy of 77%. Reducing the number of symptoms to just three (sleep disturbance, fatigue, and morning stiffness), resulted in a sensitivity of 81%, a specificity of 61%, and an accuracy of 72%. Hauser and colleagues\textsuperscript{126} suggested that a symptom-based diagnosis of FM without tender point examination is helpful for primary medical care, after exclusion of inflammatory rheumatoid, endocrinological, and neurologic diseases. From a cluster analysis of common symptoms in 533 German FM subjects compared with a representative population sample, the symptoms of limb pain and chronic fatigue were the most discriminatory symptoms. The authors concluded that “the survey method has the advantage that it does not require physical examination.” In a similar vein, Katz and colleagues\textsuperscript{127} have evaluated a combination of a fatigue VAS (0–10) and the regional pain score (0–19) as a possible simplified method for arriving at a diagnosis of FM. They evaluated 120 subjects with a clinical diagnosis of FM (clinician’s impression irrespective of ACR criteria) and found that clinical and survey criteria were concordant in 74.8% of cases, clinical criteria and ACR criteria were concordant in 75.2% of cases, and survey criteria and ACR criteria were concordant in 72.3% of cases.

\textbf{Using Tenderness as Diagnostic Criterion}

The ACR criteria use the combination of WSP and 11 or more out of 18 tender points, but the question arises as to whether it is possible to replace the ACR-defined tender point examination with a more simple test of widespread allodynia.\textsuperscript{128} There is now ample evidence that the 18 ACR tender points are not “special,” because FM subjects

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\textbf{Box 1} \\
A list of disorders that need to be considered in the differential diagnosis of widespread pain \\
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\textit{Disorder} \\
Polymyalgia rheumatica \\
Viral infections \\
Early stages of RA and SLE \\
Sjogren's syndrome \\
Polyarticular osteoarthritis \\
Early stages of a spondyloarthropathy \\
Severe vitamin D deficiency \\
Hypothyroidism \\
Statin therapy \\
Inflammatory myopathies \\
Metabolic myopathies \\
Joint hypermobility syndromes \\
Metastatic malignancies \\
Myotonic dystrophy type 2 \\
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have been shown to have widespread sensitivity to a number of neurophysiologic tests.\textsuperscript{129,130} In general, subjective reporting of tenderness to palpation has correlated with abnormal neurophysiological testing, but there is a variable component of psychological distress that colors the reporting of tenderness to palpation.\textsuperscript{131,132} A more limited evaluation of tenderness would probably suffice in the diagnosis of FM. For instance, Harden and colleagues\textsuperscript{119} found that, whereas an algometer-based scoring of ACR tender points differentiated FM from normals with 85.7\% accuracy, a single point had an accuracy of between 75\% and 89\%. Furthermore, it was reported that tenderness at three “sham” points (the glabella, the middle of the biceps, and the middle of the hamstring) differentiated FM from normals with 85.7\% classification accuracy. Using hierarchical cluster analysis, it was found that three points provided the same classification accuracy as all 18 points (Fig. 1). Vargas reported that 69\% of FM subjects had sphygmomanometry-evoked allodynia in contrast to 10\% of subjects who had osteoarthritis, 5\% who had rheumatoid arthritis, and 2\% of healthy subjects. The mean systolic blood pressure value for allodynia in FM was 143+/−40 mm Hg, whereas in the three other groups it was 176+/−11 mm Hg.\textsuperscript{133} Petzke and colleagues\textsuperscript{134} compared the diagnostic utility of dolorimetry-based pain thresholds at all 18 ACR tender points with a limited number of tender points. It was found that pain thresholds at two sets of three paired tender points (supraspinatus, epicondyle, occiput; and thumbnail, midtrapezius, epicondyle), had a diagnostic accuracy similar to all 18 tender points. Thus, it appears that a more simplified methodology for determining if a patient has widespread allodynia could be developed.

\textbf{SUMMARY}

Since the publication of the 1990 ACR Classification Criteria for Fibromyalgia, there has been an impressive advancement in our understanding of FM symptoms and their psychoneurologic underpinnings in terms of central sensitization and genetic influences. However, the roles of peripheral pain states, sleep disorders, psychopathology, and cytokines in initiating and perpetuating disordered sensory processing are less clear. There is now a general agreement that FM is a common disorder that...
causes much distress and dysfunction, but there is a need for a simplified office-based diagnostic evaluation. In this author’s opinion, a combination of a few key symptoms along with a simplified assessment of widespread allodynia, such as sphygmomanometer-induced tenderness, would be a reasonable point to start.

REFERENCES


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