INTRODUCTION — Fibromyalgia (FM) is a common cause of chronic musculoskeletal pain. It is one of a group of soft tissue pain disorders that affect muscles and soft tissues, such as tendons and ligaments. None of these conditions is associated with tissue inflammation and the etiology of the pain is not known.

FM, like other functional somatic syndromes, has been a controversial illness [1,2]. Patients look well, there are no obvious abnormalities on physical examination, and laboratory and radiologic studies are normal. Thus, the role of organic illness has been questioned, and FM has often been considered to be psychogenic or psychosomatic. Ongoing research has led to pathophysiologic concepts of FM that focus on alterations in central nervous system pain processing.

The clinical manifestations and diagnosis of FM will be reviewed here. The possible pathogenic mechanisms, differential diagnosis of widespread pain, and treatment of FM, as well as the clinical manifestations, diagnosis, and treatment of FM in children and adolescents, are discussed separately. (See "Pathogenesis of fibromyalgia" and "Differential diagnosis of fibromyalgia" and "Initial treatment of fibromyalgia in adults" and "Fibromyalgia in children and adolescents: Clinical manifestations and diagnosis".)

PREVALENCE — Fibromyalgia (FM), initially termed fibrositis, was described in France and England in the mid-19th century. By the end of the twentieth century, many rheumatologists recognized FM as a discrete syndrome. Diagnostic classification criteria were proposed, evaluated, and then validated. Using such criteria, FM is now considered to be the most common cause of generalized, musculoskeletal pain in women between ages of 20 and 55 years; in the United States and in other countries, the prevalence is approximately 2 percent and increases with age [1-4]. As an example, one report found a prevalence of 1.6 percent in France [5]. FM is six times more common in females in reports from specialty clinics, although the female
predominance is not as striking in the community [6,7]. More than 40 percent of patients referred to a tertiary pain clinic meet the diagnostic criteria for FM [8].

CLINICAL MANIFESTATIONS — Fibromyalgia (FM) is characterized by widespread musculoskeletal pain and fatigue, often accompanied by cognitive and mood disturbances [9]. Physical examination reveals tenderness in multiple soft tissue anatomic locations. Laboratory testing is normal in the absence of other illnesses (table 1).

Symptoms — The cardinal manifestation of FM is widespread musculoskeletal pain, involving both sides of the body and above and below the waist. However, the pain may initially be localized, often in the neck and shoulders. Common patient descriptions include "I feel as if I hurt all over," or "it feels as if I always have the flu." Patients typically describe pain predominantly throughout the muscles, but often state that their joints hurt, and sometimes describe joint swelling, although synovitis is not present on examination [10,11].

Patients also often report paresthesias, including numbness, tingling, burning, or creeping or crawling sensations, especially in both arms and both legs. However, unless a concurrent neurologic disorder, such as carpal tunnel syndrome or a cervical radiculopathy, is present, a detailed neurologic evaluation or formal testing is usually unremarkable.

The other universal symptom of FM is fatigue. This is especially notable when arising from sleep, but is also marked in the mid-afternoon. Seemingly minor activities aggravate the pain and fatigue, although prolonged inactivity also heightens symptoms. Patients are stiff in the morning and feel unrefreshed, even if they have slept 8 to 10 hours. Patients with FM characteristically sleep "lightly," waking frequently during the early morning and have difficulty getting back to sleep. A common quote is "No matter how much sleep I get, it feels like a truck ran me over in the morning."

Cognitive and mood disturbances are present in the majority of patients. The cognitive disturbances are often referred to as "fibro fog." Patients typically describe problems with attention and difficulty doing tasks that require rapid thought changes. Neuropsychological testing reveals abnormalities that are somewhat different than those found in mood disturbances [12].

Depression and/or anxiety are present in 30 to 50 percent of patients at the time of diagnosis [1-3]. In a Canadian general population sample of 127,000, those 1635 subjects with FM were three times more likely to have depression compared with subjects without FM [13]. Twenty-two percent of the FM group had concurrent major depression. Depression in that group correlated with younger age, female gender, unmarried status, food insecurity, number of chronic conditions, and limitations in activities. Two-fifths of those with depression and FM had not discussed mental health concerns with any health professionals in the previous year.

Headaches are present in more than 50 percent and include migraine and muscular (tension) types [14]. In an ambulatory tertiary headache clinic, FM was present in 174 of 889 patients (20 percent), including 44 percent of those with chronic, tension-type headaches [15]. FM comorbidity correlated with frequency of headaches, anxiety, pericranial tenderness, poor sleep, and physical disability.

Patients also may have a variety of poorly understood pain symptoms, including abdominal and chest wall pain and symptoms suggestive of irritable bowel syndrome, pelvic pain and bladder symptoms of frequency and urgency suggestive of the interstitial cystitis/painful bladder syndrome (formerly female urethral syndrome) [3,14,16-19]. (See "Clinical manifestations and
Other common complaints include ocular dryness, multiple chemical sensitivity and "allergic" symptoms, palpitations, dyspnea, vulvodynia, dysmenorrhea, sexual dysfunction, weight fluctuations, night sweats, dysphagia, dysgeusia, and orthostatic intolerance [12,17,20].

Some individuals commonly report that particular weather conditions or changes in the weather may aggravate symptoms, but consistent effects of such conditions upon daily pain or fatigue have not been found in most studies [21-25]. As an example, a detailed study of the influence of weather on symptoms of pain and fatigue involving 403 women with FM found a statistically significant but small effect of weather upon either pain or fatigue [25].

Physical signs — In patients with FM, the only reproducible finding on physical examination is tenderness in soft-tissue anatomic locations (figure 1). The tender point examination requires that the examiner knows where to palpate and how much pressure to apply.

The nine pairs of tender points used for the 1990 American College of Rheumatology (ACR) Classification Criteria (see '1990 ACR classification criteria' below) are at locations that most primary care clinicians and specialists routinely evaluate in patients with soft tissue complaints. These locations include the upper mid-trapezius muscle, the lateral epicondyle (the so-called tennis elbow location), the second costochondral junction (the site of costochondritis), and the greater trochanter (the site of trochanteric bursitis of the hip). The amount of pressure should equal 4 kg/cm², which is enough to whiten the nail bed of the examiner's finger tip.

We advise that when evaluating the tenderness of the nine pairs of specific FM points that so-called control locations, such as over the thumb, the mid forearm or the forehead, also be palpated in a similar fashion, FM patients are typically not as tender in these control areas. A joint examination should always be done, looking for any synovitis and also palpating for tenderness over the joints themselves.

A complete physical examination, with a careful joint and neurologic examination, is necessary to exclude other illness presenting with similar symptoms. The neurologic evaluation may sometimes reveal minor sensory and motor abnormalities, in the absence of another condition [26].

DIAGNOSIS — The diagnosis of fibromyalgia (FM) is based primarily on the patient's symptoms of widespread pain. Patients report chronic myalgias and arthralgias, but have no evidence of joint or muscle inflammation on physical examination or laboratory testing. The physical examination reveals multiple tender points at soft tissue locations (figure 1). However, FM can be diagnosed without a specific number of tender points (see below).

There is no diagnostic laboratory test, or radiographic or pathologic finding, and testing should be kept to a minimum (see below). The diagnostic evaluation is usually straightforward and should never be a "fishing" expedition to exclude every potential cause of pain and fatigue (table 2 and algorithm 1) [27]. FM should be initially considered in any patient complaining that “I hurt all over” or “It feels like I always have the flu” (table 2). Often, subspecialty referral is more cost-effective than ordering multiple laboratory and imaging studies.

FM, like headache or irritable bowel syndrome, will continue to be a controversial diagnosis because of a lack of objective changes. Nevertheless, at least 10 percent of the general population has chronic widespread pain, and the majority of these individuals do not have any
specific disease or structural abnormality to account for the pain. Many such individuals have symptoms and findings compatible with the diagnosis of FM.

There has also been controversy regarding the utility of the diagnosis of FM. Although some have argued that providing a diagnostic label to everyday symptoms increases illness behavior, there are now more studies suggesting that patients improve after a diagnosis and there is significant saving of health care dollars [28].

Laboratory testing — FM does not cause any abnormalities in laboratory testing or imaging. Thus, any testing is done primarily to exclude an associated disease or another illness that may mimic FM (table 2). We use the following approach to laboratory testing:

- We obtain a complete blood count (CBC) and an erythrocyte sedimentation rate (ESR) or a C-reactive protein (CRP), for initial laboratory evaluation. Since FM is not an inflammatory condition, normal acute phase reactants immediately provide confidence that an occult inflammatory disorder is unlikely.

- Serologic tests, such as antinuclear antibody and rheumatoid factor, should be obtained only if the history and physical examination suggest an inflammatory, systemic rheumatic disease. These tests are often positive in otherwise healthy people and have very poor predictive value unless there is significant clinical suspicion of a systemic rheumatic disease. (See "Measurement and clinical significance of antinuclear antibodies", section on 'Clinical limitations of ANA testing'.)

- In patients with any suspicion of thyroid disease or inflammatory muscle disease we order thyroid function tests or a creatine kinase, respectively.

- There is no evidence that ordering viral tests such as antibodies to the Epstein-Barr virus or ordering vitamin D levels are helpful in the diagnosis of FM.

Additional evaluation — We obtain a careful history from all patients with FM to identify primary sleep or mood disorders. Patients should be questioned for symptoms of sleep apnea and repetitive limb movements; if the history is suggestive, patients should be referred for an overnight polysomnogram [29]. Every FM patient should be questioned for symptoms of depression and anxiety, since at least one-third of FM patients have active mood disturbances at the time of their initial diagnosis. If a mood disorder is suspected, further evaluation and treatment by an expert experienced in these conditions is indicated. (See "Overview of obstructive sleep apnea in adults" and "Clinical manifestations and diagnosis of restless legs syndrome in adults" and "Unipolar depression in adults: Assessment and diagnosis".)

Autonomic nervous system dysfunction has been noted in patients with FM [30]. However, there are no appropriate screening tests other than blood pressure and heart rate readings when patients are recumbent and standing. In selected individuals in whom autonomic dysfunction is suspected on the basis of these findings, referral is indicated for further evaluation and, if needed, more formal tests such as tilt table testing. (See "Upright tilt table testing in the evaluation of syncope", section on 'Test procedure'.)

Diagnostic and classification criteria

1990 ACR classification criteria — In an attempt to provide some homogeneity in patient populations in clinical studies, various classification criteria for FM have been developed and tested. The American College of Rheumatology (ACR) Classification Criteria for Fibromyalgia
were published in 1990 and have been used in most clinical and therapeutic trials [31]. They are less useful for diagnosing FM in routine clinical practice.

The ACR criteria were based upon expert rheumatologists' opinions regarding the optimal historical and physical findings that could differentiate patients with FM from those with other rheumatic diseases and forms of chronic pain. These criteria were then field-tested in a number of academic rheumatology clinics and office practices.

The final 1990 ACR FM classification criteria included:

● Symptoms of widespread pain, occurring both above and below the waist and affecting both the right and left sides of the body
● Physical findings of at least 11 of 18 tender points

These simple criteria had greater than 85 percent sensitivity and specificity for differentiating patients with FM from those with other rheumatic diseases.

In office practice, the diagnosis of FM can be made even if fewer than 11 of 18 tender points are present, provided that the history is consistent with FM and that the major differential diagnoses have been excluded. The tender points represent heightened pain perception rather than sites of inflammation or tissue pathology. Thus, they are proxies for pain, and the exact number necessary to diagnose FM clinically is somewhat arbitrary. It is important to recognize that the classification criteria were validated for large patient populations and should be used primarily in clinical research and epidemiologic studies of FM.

2010 ACR preliminary diagnostic criteria — Some investigators have advocated not using the tender point examination as part of the FM diagnostic criteria and relying only on symptoms [32,33]. This approach recognizes that most clinicians have not been trained in the technique for performing a tender point examination. Indeed, most rheumatologists make a diagnosis without a tender point examination. Furthermore, the tender points do not accurately reflect the underlying central pain pathophysiology involved in this disorder.

These considerations were important in developing the 2010 American College of Rheumatology (ACR) preliminary diagnostic criteria for FM (table 3). These criteria provide an alternative approach to diagnosis, which does not require a tender point examination, but does provide a scale for measurement of the severity of symptoms that are characteristic of FM [32]. These criteria were designed with the recognition that in practice, tender point counts are often not obtained, and the increased appreciation of the importance of cognitive problems and somatic symptoms in patients with FM that were not considered in the 1990 ACR classification criteria. The preliminary diagnostic criteria showed good correlation with the 1990 ACR criteria.

The preliminary diagnostic criteria that do not include a tender point examination may also help address concerns regarding the accuracy of the diagnosis by nonspecialists [34]. These criteria may be particularly useful for clinicians who are inexperienced in performing tender point examinations or as additional data points in difficult cases. However, the criteria require additional validation in different patient populations (e.g., primary care settings and patients with other rheumatic diseases). Since they can be self-administered, these new criteria will be more practical for population-based studies of chronic widespread pain.

The preliminary criteria may be used in patients with symptoms present at a similar level for at least three months, and no other disorder that would otherwise explain the pain. They combine a widespread pain index (WPI) and a symptom severity (SS) scale for making the diagnosis of FM
(table 3). The WPI is a measure of the number of painful body regions from a defined list of 19 areas. The SS score includes an estimate of the degree of fatigue, waking unrefreshed, and cognitive symptoms; and the number of somatic symptoms in general. The SS can also be used for the assessment of patients with current or previous FM or for longitudinal evaluation.

A simple modification of the 2010 criteria allows them to be used in epidemiologic and clinical studies without an examiner [35]; use of these modified criteria might help to reduce the need for rheumatology referral simply for the diagnosis of this common condition. In one study, the sensitivity and specificity of the modified 2010 diagnostic criteria for FM were 90.2 and 89.5 percent, respectively, among patients referred to a rheumatologist, typically for widespread pain, from a primary care practice [36]. Use of a total score of at least 13 rather than using two separate scores to define the cutoff for a diagnosis of FM was the most effective approach, with a sensitivity and specificity of 93.1 and 91.7 percent, respectively.

DIFFERENTIAL DIAGNOSIS — The multiple nonspecific symptoms of fibromyalgia (FM) can mimic many other conditions. However, the history and physical examination, as well as limited laboratory testing, are usually sufficient to differentiate FM from other conditions, such as systemic inflammatory arthropathies, spondyloarthropathy, autoimmune connective tissue disorders, polymyalgia rheumatica or myopathy (table 4). A detailed discussion of the differential diagnosis of FM is presented separately. (See "Differential diagnosis of fibromyalgia".)

COEXISTING DISORDERS — Since fibromyalgia (FM) is not uncommon in patients with rheumatic or systemic illness, it may be difficult to determine whether a patient's symptoms are related to that associated illness or to FM. This is especially important in inflammatory rheumatic disorders, but FM may also coexist with noninflammatory musculoskeletal conditions and a number of functional somatic syndromes.

Inflammatory rheumatic diseases — It is important to distinguish symptoms of FM from those of chronic rheumatic diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), because of the different implications for treatment. For example, FM should be considered as the cause of diffuse pain and fatigue in a patient with RA lacking active synovitis and elevated acute phase reactants, rather than escalating or reinstituting antinflammatory or immunosuppressive therapy for RA. There is also evidence that RA disease activity scores, such as the DAS28, can be overestimated in patients with coexisting FM [37]. Clinical, psychosocial, and illness severity variables predict the development of FM in patients with RA [38]. About 20 percent of RA patients meet criteria for FM at some point during long-term follow-up [38]. Multiple, inter-correlated factors including social disadvantage, psychological distress, comorbidity, RA severity, and FM variables correlated with the development of FM. FM is more common in all forms of chronic inflammatory polyarthritis and systemic rheumatic disease, including ankylosing spondylitis [39].

Noninflammatory musculoskeletal disorders — Other chronic noninflammatory pain disorders, such as osteoarthritis or lumbar spinal stenosis, may be present with or mimic FM; however, these disorders do not present with chronic widespread pain but rather more localized pain. In these conditions there is evidence of structural abnormalities on physical examination and imaging studies.

Functional somatic syndromes — The more challenging issue in differential diagnosis of FM is its association with other functional somatic syndromes. These include irritable bowel syndrome
(IBS), chronic fatigue syndrome (CFS), temporomandibular dysfunction, vulvodynia and irritable bladder.

Patients with FM may end up with multiple diagnoses according to subspecialty referral patterns, if the clinicians caring for the patient are diagnostic "splitters." On the other hand, the exact label may be less important if these functional illnesses are considered as part of a spectrum. For example, various studies have reported that 30 to 70 percent of patients with FM meet criteria for CFS and IBS [40,41]. Each of these somatic syndromes, like FM, has a set of proposed diagnostic criteria based on patients’ symptoms. (See "Clinical features and diagnosis of chronic fatigue syndrome" and "Clinical manifestations and diagnosis of irritable bowel syndrome in adults".)

Localized pain syndromes — Myofascial pain syndrome has often been differentiated from FM based on the more focal nature of the pain and the suggestion that trigger points with taut bands noted in myofascial pain can be distinguished from the tender points of FM [42]. Many investigators now believe that temporomandibular dysfunction and myofascial pain syndrome are localized forms of FM. Although these disorders have been linked in the past to abnormalities in the muscle and soft tissue in the head and neck, new research suggests that like FM, they are related to alterations in pain perception in the central nervous system. (See "Overview of soft tissue rheumatic disorders", section on 'Regional myofascial pain'.)

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Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

● Basics topic (see "Patient information: Fibromyalgia (The Basics))"

● Beyond the Basics topic (see "Patient information: Fibromyalgia (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

● We diagnose fibromyalgia (FM) in patients who present with chronic myalgias and arthralgias but who have no evidence of joint or muscle inflammation on physical examination or laboratory testing. (See 'Diagnosis' above.)

● The physical examination should reveal multiple tender points at specific soft tissue locations (figure 1). In clinical practice, a specific number of tender points are not required to make the diagnosis, and FM may be diagnosed without a specific tender point evaluation. (See 'Diagnosis' above.)

● Testing should be kept to a minimum, since there are no diagnostic laboratory tests for FM. We advise obtaining a complete blood count and testing for an acute phase reactant, such as the erythrocyte sedimentation rate or C-reactive protein, to exclude systemic inflammatory disease. Additional laboratory testing should be based upon clinical suspicion of a specific disorder, such
as a thyroid stimulating hormone test or a creatine kinase, if hypothyroidism or an inflammatory myopathy are suspected, respectively. (See 'Laboratory testing' above.)

● Additional evaluation should be considered for associated conditions if clinically suspected, including sleep disorders, such as obstructive sleep apnea or restless legs syndrome, and psychiatric disorders, such as depression or anxiety. (See 'Additional evaluation' above.)

● FM may coexist with other disorders, such as inflammatory rheumatic disease syndromes and noninflammatory musculoskeletal pain. Particular attention should be given to identifying the source of symptoms in such patients when making decisions regarding treatment. (See 'Coexisting disorders' above.)

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REFERENCES


