are worsened by exercise or unaccustomed activity (postexertional malaise). The sleep complaints include difficulty falling asleep, difficulty staying asleep, and early-morning awakening. Regardless of the specific complaint, patients awake feeling unrefreshed. Patients with FM may meet criteria for restless legs syndrome and sleep-disordered breathing; frank sleep apnea can also be documented. Cognitive issues are characterized as slowness in processing, difficulties with attention or concentration, problems with word retrieval, and short-term memory loss. Studies have demonstrated altered cognitive function in these domains in patients with FM, though speed of processing is age-appropriate. Symptoms of anxiety and depression are common, and the lifetime prevalence of mood disorders in patients with FM approaches 80%. Although depression is neither necessary nor sufficient for the diagnosis of FM, it is important to screen for major depressive disorders by querying for depressed mood and anhedonia. Analysis of genetic factors that are likely to predispose to FM reveals shared neurobiologic pathways with mood disorders, providing the basis for comorbidity (see later in this chapter).

Overlapping Syndromes Because FM can overlap in presentation with other chronic pain conditions, review of systems often reveals headaches, facial/jaw pain, regional myofascial pain particularly involving the neck or back, and arthritis. Visceral pain involving the gastrointestinal tract, bladder, and pelvic or perineal region is often present as well. Patients may or may not meet defined criteria for specific syndromes. It is important for patients to understand that shared pathways may mediate symptoms and that treatment strategies effective for one condition may help with global symptom management.

Comorbid Conditions FM is often comorbid with chronic musculoskeletal, infectious, metabolic, or psychiatric conditions. Whereas FM affects only 2–5% of the general population, it occurs in 20% or more of patients with degenerative or inflammatory rheumatic disorders, likely because these conditions serve as peripheral pain generators to alter central pain-processing pathways. Similarly, chronic infectious, metabolic, or psychiatric diseases associated with musculoskeletal pain can mimic FM and/or serve as a trigger for the development of FM. It is particularly important for clinicians to be sensitive to pain management of these comorbid conditions so that when FM emerges—characterized by pain outside the boundaries of what could reasonably be explained by the triggering condition, development of neuropsychological symptoms, or tenderness on physical examination—treatment of central pain processes will be undertaken as opposed to a continued focus on treatment of peripheral or inflammatory causes of pain.

Psychosocial Considerations Symptoms of FM often have their onset and are exacerbated during periods of high-level real or perceived stress. This pattern may reflect an interaction among central stress physiology, vigilance or anxiety, and central pain-processing pathways. An understanding of current psychosocial stressors will aid in patient management, as many factors that exacerbate symptoms cannot be addressed by pharmacologic approaches. Furthermore, there is a high prevalence of exposure to previous interpersonal and other forms of violence in patients with FM and related conditions. If posttraumatic stress disorder is an issue, the clinician should be aware of it and consider treatment options.

Functional Impairment It is crucial to evaluate the impact of FM symptoms on function and role fulfillment. In defining the success of a management strategy, improved function is a key measure. Functional assessment should include physical, mental, and social domains. A recognition of the ways in which role functioning falls short will be helpful in the establishment of treatment goals.

DIFFERENTIAL DIAGNOSIS

Because musculoskeletal pain is such a common complaint, the differential diagnosis of FM is broad. Table 396-1 lists some of the more common conditions that should be considered. Patients with inflammatory causes for widespread pain should be identifiable on the basis of specific history, physical findings, and laboratory or radiographic tests.

TABLE 396-1 COMMON CONDITIONS IN THE DIFFERENTIAL DIAGNOSIS OF FIBROMYALGIA

Inflammatory
Polymyalgia rheumatica
Inflammatory arthritis: rheumatoid arthritis, spondyloarthritides
Connective tissue diseases: systemic lupus erythematosus, Sjögren's syndrome
Infectious
Hepatitis C
HIV infection
Lyme disease
Parvovirus B19 infection
Epstein-Barr virus infection
Noninflammatory
Degenerative joint/spine/disk disease
Myofascial pain syndromes
Bursitis, tendinitis, repetitive strain injuries
Endocrine
Hypo- or hyperthyroidism
Hyperparathyroidism
Neurologic Diseases
Multiple sclerosis
Neuropathic pain syndromes
Psychiatric Disease
Major depressive disorder
Drugs
Statins
Aromatase inhibitors

LABORATORY OR RADIOGRAPHIC TESTING

Routine laboratory and radiographic tests yield normal results in FM. Thus diagnostic testing is focused on exclusion of other diagnoses and evaluation for pain generators or comorbid conditions (Table 396-2). Most patients with new chronic widespread pain should be assessed for the most common entities in the differential diagnosis. Radiographic testing should be used sparingly and only for diagnosis of inflammatory arthritis. After the patient has been evaluated thoroughly, repeat testing is discouraged unless the symptom complex changes. Particularly to be discouraged is advanced imaging (MRI) of the spine unless there are features suggesting inflammatory spine disease or neurologic symptoms.

GENETICS AND PHYSIOLOGY

As in most complex diseases, it is likely that a number of genes contribute to vulnerability to the development of FM. To date, these genes appear to be in pathways controlling pain and stress

TABLE 396-2 LABORATORY AND RADIOGRAPHIC TESTING IN PATIENTS WITH FIBROMYALGIA SYMPTOMS

Routine
Erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP)
Complete blood count (CBC)
Thyroid-stimulating hormone (TSH)
Guided by History and Physical Examination
Complete metabolic panel
Antinuclear antibody (ANA)
Anti-SSA (anti–Sjögren's syndrome A) and anti-SSB
Rheumatoid factor and anti–cyclic citrullinated peptide (anti-CCP)
Creatine phosphokinase (CPK)
Viral and bacterial serologies
Spine and joint radiographs

Source: LM Arnold et al: J Women's Health 21:231, 2012; MA Fitzcharles et al: J Rheumatol 40:1388, 2013.