



Elusive syndromes: Treating the biologic basis of fibromyalgia and related syndromes

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■ ABSTRACT

Newer theories suggest that patients with fibromyalgia have a biologic predisposition to perceiving pain with more sensitivity than people without fibromyalgia. Several biologic triggers are implicated as possibly initiating or worsening the symptoms of fibromyalgia. Treatments to manage pain, help with sleep, and, when needed, treat cognitive disturbances show some success.

FIBROMYALGIA may have a stronger physiologic basis than previously thought, and its symptoms can be alleviated. Yet it remains elusive to definition and understanding and difficult to treat.

According to different criteria, fibromyalgia and related syndromes such as chronic fatigue syndrome affect between 2% and 10% of the population in industrialized countries.¹ The wide range reflects the difficulty of differentiating fibromyalgia from other syndromes that present with similar combinations of symptoms, such as chronic fatigue syndrome and multiple chemical sensitivity.

The difficulty of treating fibromyalgia is compounded by our still-poor understanding of its underlying mechanisms. Many physicians persist in thinking of fibromyalgia and

related syndromes as largely imaginary. Treatment is therefore often compromised from the outset because of the strained doctor-patient relationship that develops between a frustrated patient and a disbelieving physician.

■ CLINICAL FEATURES OF FIBROMYALGIA

According to the criteria set by the American College of Rheumatology (ACR) in 1990,² the clinical features that define fibromyalgia are:

- Chronic widespread pain in all four quadrants of the body and in the axial skeleton, and
- Tender points—points that are painful to touch using 4 kg (9 pounds) of pressure—in 11 of 18 designated areas.

On the basis of these criteria, 2% to 4% of the population in industrialized countries have fibromyalgia.² However, clinical experience and population studies suggest that these criteria have limitations.

■ LIMITATIONS OF TENDER POINTS AND OTHER CRITERIA

Tender points do not define the typical pain of fibromyalgia

Recent data show that the emphasis on tender points as indicating tenderness in discrete regions of the body does not adequately define the pain that people with fibromyalgia feel. Rather, people with fibromyalgia are more sensitive to pain throughout their entire body.^{3,4}

Other studies indicate a high correlation between the number of tender points reported by a patient and measures of anxiety, distress, and depression. In light of this correlation,

To treat fibromyalgia effectively, you must believe it is real

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 **PATIENT INFORMATION**
Living with fibromyalgia, page 837

tender points have been called a “sedimentation rate for distress,” ie, a sensitive but non-specific finding that may suggest a variety of diagnoses.⁵

This is not to say that the symptoms of fibromyalgia are not physically real. Rather, understanding is growing that patients who present with symptoms of fibromyalgia or similar conditions may be perceiving pain abnormally. In addition, physicians in clinical practice often do not examine the tender points accurately, using too little pressure or applying pressure in the wrong area.

Many people have chronic widespread pain

In clinical practice, many more people present with symptoms of chronic widespread pain than these criteria reflect. Of the US population, an estimated:

- 10% have chronic widespread pain
- 20% have chronic regional pain
- 15% have severe fatigue
- 15% have irritable bowel syndrome
- 10% have migraines
- 50% to 60% have tension headaches.^{1,6}

These symptoms tend to aggregate in individuals, so that people with any one of these symptoms tend to have more of the other symptoms than do others in the general population. This is one reason that there is considerable overlap among systemic conditions such as fibromyalgia, chronic fatigue syndrome, multiple chemical sensitivity, and Gulf War syndrome, as well as among “organ-specific” diagnoses such as irritable bowel syndrome, migraine, and tension headaches.⁷

Fibromyalgia: the end of a continuum?

A better way of understanding this syndrome, therefore, may be to consider fibromyalgia as the end of a continuum. Based on this theory, many people experience some pain, fatigue, and tenderness, but not enough to meet the established criteria for conditions such as fibromyalgia and chronic fatigue syndrome.

■ WHAT CAUSES FIBROMYALGIA?

What causes fibromyalgia is not clear. Many theories over the years point to the influence of both genetics and environment. Some current theories suggest fibromyalgia and similar

syndromes are due to:

- **A low threshold of pain** and heightened perception of internal and external stimuli. This could be due to psychological factors, such as hypervigilance, or to aberrant sensory processing in the spinal cord or brain. This latter theory is supported by findings of high levels of pro-nociceptive substances such as substance P and nerve growth factor in spinal fluid and by abnormalities in pain processing structures on cerebral SPECT scanning.⁸

Of note, this type of central or non-nociceptive pain is minimally responsive to drugs that act primarily in the periphery, such as nonsteroidal anti-inflammatory drugs or narcotics, and more responsive to tricyclic compounds and newer classes of drugs.

- **Hyporeactivity of both the hypothalamic-pituitary-adrenal axis and the autonomic nervous system**, with attenuated response to stressors.⁷

- **Lack of sleep or exercise or both.** Studies suggest that both sleep and exercise deprivation can lead to fibromyalgia symptoms, and carefully designed exercise programs can represent effective treatment.

These varying theories suggest that fibromyalgia and similar syndromes are not homogeneous syndromes and are possibly due to a variety of factors. This increases the importance of identifying subsets of patients in whom the primary problem has yet to be adequately identified, such as problems in sensory processing, distress syndrome, neuroendocrine problems, or autonomic dysfunction.

Biologic triggers

Although a clear cause remains unknown, various biologic “stressors” are recognized as triggers for fibromyalgia and similar syndromes (TABLE 1)

Genetics plays a key role in how a person manages these biologic stressors, with strong evidence pointing to the importance of early life events and the development or lack of development of plasticity of neuroendocrine response systems to stress.

For all of these biologic stressors, an environment characterized by lack of control, unpredictability, and lack of support will amplify the adverse physiologic effects.

Aerobic exercise may be the most effective treatment for fibromyalgia



It is not all in the head

Ten to 15 years ago, care of patients with fibromyalgia focused on the psychiatric comorbidity that often presented with the physical symptoms. This emphasis, coupled with uncertainty about the cause of fibromyalgia, contributed to the belief by many health care practitioners that these syndromes are more psychological in origin than physical.

The focus has since shifted to the distress and dysfunction experienced by the patient, and to a greater understanding of how these syndromes may indicate a disturbance in the brain mechanisms that control sensory perception.

■ EFFECTIVE TREATMENT

To treat fibromyalgia effectively, health care practitioners need to believe that fibromyalgia and similar syndromes are real physical diseases. Treatment has several components.

Whatever treatment is used, it is critical to encourage patients to gain control over their environment and get sufficient support to look beyond the disabilities of the condition and toward what they can do to alleviate the symptoms and to function as normally as possible.

Education. Patients need to know that although the disease may not be curable, it is not fatal and can be managed. They also need to focus on wellness rather than illness, that is, to avoid thinking of themselves as victims and to concentrate on doing things to make themselves better (see patient information, “Living with fibromyalgia,” page 837).

Drug therapy can be effective to manage common problems with sleep, pain control, and irritable bowel. Tricyclic antidepressants such as amitriptyline (Elavil) or cyclobenzaprine (Flexeril) in low doses are the usual first-line drugs. Second-line antidepressant drugs may include venlafaxine (Effexor) or bupropion (Wellbutrin).

Aerobic exercise may be the most effective therapy and may work by affecting the neurochemicals serotonin, epinephrine, and endorphin.

Cognitive behavioral therapy, combined with drugs and exercise, can help people learn to manage chronic illnesses by recognizing

TABLE 1

Stressors that may trigger fibromyalgia and similar syndromes

- Catastrophic events (eg, war)
- Epstein-Barr virus infection
- Hormone alterations
- Hypothyroidism
- Lyme disease
- Parvovirus infection
- Physical trauma (eg, car accident)
- Psychological or emotional distress
- Q fever

and correcting “maladaptive illness behaviors”: patterns of behavior or cognition that worsen their symptoms or interfere with their recovery or improvement. For example, patients with chronic conditions often have “good” or “bad” days and develop a pattern of attempting to do too much on a good day, which leads to several bad days. Since these are behavioral rather than biologic processes, they do not respond to drug therapy.


Cognitive behavioral therapy has been shown to be effective in fibromyalgia, chronic fatigue syndrome, and in chronic medical illnesses such as cancer and rheumatoid arthritis, and after myocardial infarction. The best programs are “medicalized” and self-limited and address primarily cognitive processes and maladaptive illness behaviors rather than psychiatric issues.

Complementary approaches. Alternative or supplementary approaches, such as acupuncture, myofascial release therapy, trigger point injections, chiropractic manipulation, and biofeedback, are available and may help ease chronic pain and other symptoms of fibromyalgia.

Multimodal therapy. The more symptoms or the more advanced on the continuum of disease, the more multimodal therapy may be needed. For example, patients with more prominent psychosocial or behavioral symptoms may need cognitive behavioral therapy,

See patient information, page 837



whereas patients with more prominent abnormal sensory processing or autoimmune or hypothalamic pituitary adrenal dysfunction may best be treated with drugs. Patients with strong symptoms in both areas may need treatment with both drugs and cognitive behavioral therapy. 

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