

LRA by ELISA/ACT® CLINICAL UPDATE # 10

Fibromyalgia and Chronic Pain

What are the major symptoms of fibromyalgia and how is the diagnosis made?

Fibromyalgia (FM) is an autoimmune syndrome characterized by widespread aching and musculoskeletal pain, disturbed sleep patterns, fatigue, morning stiffness, and local tenderness. Although Hench et al coined the term *fibromyalgia* in 1976, it was not until 1990 that a consensus committee actually adopted the term (22). It was recommended that the older term, fibrositis, be dropped since inflammation is not typically observed.

Other symptoms frequently associated with FM include headache, depression, paresthesias, bowel and bladder disturbances, subjective soft tissue swelling, Raynaud's phenomenon, and more recently rhinitis, bruxism, bursitis, sciatica, temporal mandibular joint dysfunction, and allergies (21). Most patients also report that stress, anxiety, poor sleep, humidity, warmth, cold, and weather changes significantly exacerbate their symptoms. Despite the symptoms, physical, laboratory, and radiologic studies are normal. However, a large percentage of patients typically demonstrate electroencephalographic non-REM sleep anomalies (13,15,21, 25). Unlike rheumatoid arthritis, this rheumatic disorder is not associated with any deformity or inflammation of the joints. Thus, the diagnosis has been one of subjectivity rather than objectivity.

This lack of objective signs has made the diagnosis of FM difficult. In the past FM has been found in association with irritable bowel syndrome, chronic fatigue syndrome, thyroid disease, local myofascial pain, and rheumatoid arthritis (15,20,24). However, in 1986, 16 medical centers in the United States and Canada participated in a criteria study of patients

with FM. Patient data from these centers were compiled, and a committee from the American College of Rheumatology (ACR) developed specific criteria for classifying such patients (21,22). As a result of defining these criteria, patients with FM can be identified with good sensitivity (88.4%) and specificity (81.1%) (22). Table 1 below provides the criteria for classification and details of the tender point site locations. Figure 1 depicts the tender point locations.

Table 1. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia syndrome (FM).

1. History of widespread pain.

Definition. Pain is considered widespread when all of the following are present:

- pain in the left side of the body,
- pain in the right side of the body,
- pain above the waist
- pain below the waist.

In addition, axial skeletal pain (cervical spine or anterior chest or thoracic & spine or low back) must be present. In this definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.

2. Pain in 11 of 18 tender point sites on digital palpation.

Definition. Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:

Occiput: bilateral, at the suboccipital muscle insertions.

Low cervical: bilateral, at the anterior or aspects of the intertransverse spaces at C5-C7.

Table 1. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia syndrome (FM).

Trapezius: bilateral, at the midpoint of the upper border.

Supraspinatus: bilateral, at origins, above the scapula spine near the medial border.

Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces.

Lateral epicondyle: bilateral, 2 cm distal to the epicondyles.

Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle.

Greater trochanter: bilateral, posterior to the trochanteric prominence.

Knee: bilateral, at the medial fat pad proximal to the joint line.

Digital palpation should be performed with an approximate force of 4 kg.

For a tender point to be considered "positive", the subject must state that the palpation was painful. "Tender" is not to be considered "painful."

*For classification purposes, patients will be said to have FM if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a 2nd clinical disorder does not exclude the diagnosis of FM (Reference 22).

INDEX

Diagnosis of Fibromyalgia.....	1
Prevalence of Fibromyalgia	2
Conditions Precipitating.....	2
Approaches to Treat Fibromyalgia	3
Role of LRA by ELISA/ACT	3

Since developing these criteria, the diagnosis has been significantly improved, whereas in the past, many patients had not been diagnosed until after many years of living with pain (15,19,25). Now when a patient reports symptoms associated with FM, the physician can verify the criteria, obtain a thorough history, conduct a physical examination, and request several laboratory tests. These include complete blood counts, liver enzymes, antinuclear antibodies, thyroid function tests, erythrocyte sedimentation rate, urinalysis, and rheumatoid factor (19). The patient with only FM should have normal laboratory tests, whereas abnormal results may indicate a concomitant disease. In sum, using the criteria set forth by the ACR and objective data to rule out other coexisting diseases, allows the physician to diagnose FM with a high level of confidence.

How prevalent is fibromyalgia and what groups of individuals appear to be at greatest risk?

Since 1990 when criteria for classifying persons with FM were accepted by the ACR, only a few studies have looked at the prevalence of FM. Earlier surveys indicate FM as the second or third most common disorder

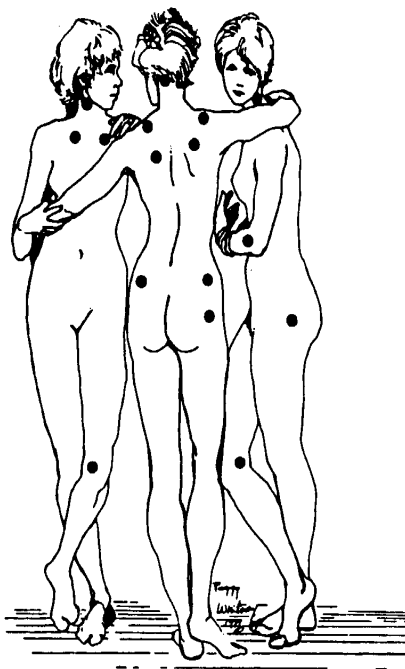


Figure 1. Tender point locations for the 1990 classification criteria for fibromyalgia (The Three Graces, after Baron Jean-Baptiste Regnault, 1973, Louvre Museum, Paris)

in rheumatology practices, with an overall frequency ranging from 15 to 19% (4,15,19). When patients entering general practice clinics/centers have been surveyed, 5 to 7% of patients are reported to have FM (4). Of those with FM, gender appears to be important. Approximately 80 to 95% of all cases are women, typically between the ages of 30 and 60 years (4,21). One survey conducted on a population of young and middle-aged women in Norway since development of the 1990 ACR criteria, found FM in 10.5% of the population (6). Thus, FM appears to be extremely prevalent, especially among women.

Other than age and gender, FM has been postulated to cut across all ethnic, socioeconomic, and educational backgrounds (21). However, what we know about the prevalence of FM comes from rheumatology and general medical clinics, where most patients are women (75 - 95%), and the proportion of non-Caucasians may be small. Thus, it remains to be seen whether FM occurs in African Americans, Hispanics, and/or Asians with the same frequency as in Caucasians.

Interestingly, FM is also found in children between the ages of 5 and 17. White females have been the primary target (20), but the prevalence of FM in this age group is unknown. The notion that it is hereditary has been considered (19,21), but remains only speculative. Clearly, more work is required before true prevalence of this syndrome can be determined.

What are some of the conditions precipitating fibromyalgia and what mechanisms are involved?

The question as to what causes FM or what the risk factors are for FM has not been conclusively answered. Moreover, since FM occurs in association with other clinical disorders, the other diseases are often presumed to have been the precipitating event. In particular, chronic fatigue syndrome and FM have similar clinical features (7). However, antibody titers of FM patients to Epstein Barr Virus are not different from controls (7).

Several theories have been offered by patients as to what they think preceded the onset of symptoms, including an unusually traumatic physical event, such as a fall or automobile accident (19). In other cases, emotional stress or a severe illness, such as a flu or viral illness, were cited as the precipitating events (15,19). However, a precipitating event is not always noted. Thus, a search for causes and mechanisms continues. Some of the proposed

mechanisms to explain the pathogenesis of FM are presented in Table 2

Table 2. Some Proposed Mechanisms of Fibromyalgia Pathology

Psychological Factors	Serotonin Metabolism
Abnormal Sleep	Muscle Pathology
Physical Trauma	Chronic Infection
Endocrinopathy	Hypoxia
Immunologic Abnormalities	Chronic Infection

Initially, FM was believed to be a psychiatric disease (15,19,22), but that notion has been put to rest by several excellent studies (10, 24). It is now well accepted that FM is an independent physical illness, and that the percentage of these patients with psychiatric disorders is similar to that found in general family practice centers (15,19). However, it is also acknowledged that many patients with FM are anxious and depressed, but that this is secondary to the illness (10,15,19).

Other hypotheses relate to alterations in either central or peripheral mechanisms of pain (2,13,15,19,25). Bennet et al (2) proposed that FM was a disease of peripheral pain amplification in which deconditioned muscles become traumatized. However, to date no good data supporting muscle abnormalities have been provided.

Support for a central defect in pain modulation was first presented by Moldofsky et al (13) who demonstrated alterations in serotonin metabolism (13). The findings of Russell et al (17,18) supported the central serotonin hypothesis. They (18) reported that serum serotonin levels were lower and binding of ³H-Imipramine (binds with high affinity to serotonin receptors in brain and platelets) to platelets was higher in patients with FM as compared to controls. Subsequently, other abnormalities in the central nervous system (CNS) have been documented and/or reconfirmed. These include elevated cerebral spinal fluid (CSF) substance P (19), lower CSF biogenic amine metabolites of serotonin, norepinephrine and dopamine (17), lower levels of serum tryptophan, somatomedin-C and other serum amino acids (2,18). In addition, specific alterations in sympathetic nervous system and hypothalamic pituitary adrenal activation have been demonstrated (8,19,25). Thus, the hypothesis of a central defect is gaining ground. In particular, the notion dominates that elevated levels of substance P and decreased levels of serotonin together cause an exaggerated perception of pain.

It has been proposed that FM is caused by a sleep disorder and actually relates to the serotonin hypothesis (13). Moldofsky et al

(13) described a distinct interruption of stage-4 sleep characterized by alpha-wave intrusion into the normal delta rhythm. They found that induction of this sleep abnormality in normal volunteers produced symptoms similar to those of patients with FM. Surprisingly, when three highly conditioned men were included as subjects, disruption of their stage-4 sleep did not induce FM-like symptoms. This finding has led investigators to hypothesize that

- *FM may not occur in persons who are physically conditioned.*
- *FM is a disease of deconditioning.*
- *FM is a muscle disorder.*

These hypotheses remain to be tested, but to date, no discernible defects in muscle have been uncovered (15,19). However, the physical fitness levels of FM patients, including both aerobic capacity and muscle strength, are extremely low (11,12).

Finally, although few investigations have focused on immune function as a causative factor, immunologic abnormalities have been reported in patients with FM (15,19,25). Natural killer cell activity has been shown to be lower in FM as compared to control patients (15,19). Moreover, some, but not all, investigators have noted deposits of immunoglobulin G at the dermal-epidermal junction in skin biopsies from FM patients. These findings are intriguing and demonstrate the need for future investigations to include measures of immunologic load and assessment of the integrity of the host defense systems.

What approaches have been used to treat fibromyalgia?

Interestingly, numerous therapies have been attempted with FM, but most studies have shown that FM is not responsive to medications commonly used for other rheumatic disorders. Nonsteroidal anti-inflammatory drugs such as aspirin, and corticosteroids are basically ineffective (23), whereas alprazolam appears to confer some benefit (16). Amitriptyline has also been used effectively in many patients (15,19). Thus, tricyclic antidepressants have been the therapy of choice. These agents are believed to confer benefit by increasing non-REM stage-4 sleep and inducing analgesia through serotonergic and noradrenergic synapses. However, not all patients with FM have altered stage-4 sleep. Moreover, only short-term studies have been carried out, and long-term side effects have not been considered.

Importantly, nonprescription therapies, including electroacupuncture, homeopathic remedies, 5-hydroxytryptophan, dietary interventions, and exercise programs have also been tested. Deluze et al (3) provided six sessions of electroacupuncture at four common acupuncture sites over a three-week period. They found that those receiving the treatments demonstrated significantly greater resolution of symptoms as compared to controls. These included regional pain scores, sleep quality, and pain threshold. Fisher et al (5) gave patients the homeopathic treatment, *Rhus toxicodendron 6x*, under double-blind, placebo-controlled, crossover conditions for one month. Again, FM patients under the active treatment did better on all variables as compared to the FM control patients. Finally, administration of 100 mg. of 5-HTP three times daily for 30 days significantly improved all clinical symptoms in patients with FM (1).

To date, the role of diet has not been carefully evaluated in FM even though dietary regimens have been used extensively in patients with rheumatoid arthritis. Interestingly, Hostmark et al (9) found that providing a vegetarian diet for three weeks significantly improved the subjective feelings of well-being in 70% of the volunteers. Moreover, Moreshead and Jaffe (14) found that when reactive foods, as determined by LRA by ELISA/ACT® testing, were removed from the diet, and other measures were used to enhance the immune system, patient remission was greater than 85%. These therapies appear promising.

With regard to exercise, only a couple of longitudinal studies have been conducted, but in general the effects are promising. Cardiovascular conditioning appears to confer significant benefit relative to improvements in pain threshold, aerobic fitness, and global assessment scores of both the patient and physician (11,12). Thus, a regular program of physical exercise may prove to be beneficial in the treatment of FM.

Other than these therapies, FM patients are told to avoid modulating factors, and are reassured that their condition is neither life threatening or crippling (15,19,25). Therapies are aimed at reducing the severity of the symptoms while the search for more effective treatments continues.

What role can LRA by ELISA/ACT serve in the treatment and possibly prevention of fibromyalgia?

It was once stated by Voltaire that the art of the medicine is the “ability to keep the patient entertained while the disease runs its inevitable course”. This should not and need not be the case if the LRA by ELISA/ACT program is used as the treatment for FM. LRA by ELISA/ACT program is a comprehensive, multifactorial, patient-specific therapy based on several key components:

- *a modified lymphocyte response assay (MLRA) to identify humoral and cellular hypersensitivities to as many as 400 common exposures, including medications, foods, additives and preservatives, therapeutic herbs, toxic minerals, molds, danders, hairs and feathers and a variety of environmental chemicals*
- *substituting immunoreactive substances with non-immunoreactive substances*
- *following an alkalising diet to enhance and promote immune repair*
- *determining nutritional and cofactor needs*
- *reducing the toxin load*
- *modifying lifestyle behaviors and attitudes to promote and support the human healing response*

To date this program has been used with remarkable success on many FM patients. In particular, three patients with symptoms lasting 5.5, 9.3, and 15.3 years who were unsuccessful on other medical therapies experienced 80 to 95% remission after being on the ELISA/ACT program for 1.5 to 3 months. These individuals have remained in remission (greater than five years) as long as they follow the program of avoiding currently identified reactive substances reported by the ELISA/ACT MLRA, and continue the adjunct therapies for host defense enhancement. It is our belief that ELISA/ACT is truly one of the most effective therapies currently available for people with FM, and that it should be tried with anyone who has had unresolved symptoms. The overall improvement in their quality of life is significant, and there are no adverse side effects. If you have any patients with FM, it is time to let them try an LRA by ELISA/ACT program.

References

1. Caruso I, Puttini PS, Cazzola M, Azzolini V. Double-blind study of 5-hydroxy tryptophan versus placebo in the treatment of primary fibromyalgia syndrome. *J Inter Med Res* 1990;18:201-209.
2. Bennett RM, Clark SR, Campbell SM, Burckhardt CS. Low levels of somatomedin C in patients with the fibromyalgia syndrome. *Arthritis Rheum* 1992;35:1113-1116.
3. Deluze C, Bosia L, Zirbs A, Chantraine A, Vischer TL. Electroacupuncture in fibromyalgia: results of a controlled trial. *Br Med J* 1992;305:1249-1252.
4. Felson DT. Epidemiologic research in fibromyalgia. *J Rheumatol* 1989; 16(suppl 19):7-11.
5. Fisher P, Greenwood A, Huskisson EC, Turner P, Belon P. Effect of homeopathic treatment on fibrositis (primary fibromyalgia). *Br Med J* 1989; 299:365-366.
6. Forseth KO, Gran JT. The prevalence of fibromyalgia among women aged 20 to 49 years in Arendal, Norway. *Clin Rheum* 1992;21:74-78.
7. Goldenberg DL. Fibromyalgia and its relation to chronic fatigue syndrome, viral illness and immune abnormalities. *J Rheumatol* 1989; 16(suppl 19):91-93.
8. Griep EN, Boersma JW, de Klowt ER. Altered reactivity of the hypothalamic-pituitary-adrenal axis in the primary fibromyalgia syndrome. *J Rheumatol* 1993; 20:469-474.
9. Hostmark AT, Lystad E, Vellar OD, Hovi K, Berg JE. Reduced plasma fibrinogen, serum peroxides, lipids, and apolipoproteins after a 3-week vegetarian diet. *Plant Foods Human Nutr* 1993; 43:55-61.
10. Kirmayer LJ, Robbins MJ, Kapusta MA. Somatization and depression in fibromyalgia syndrome. *Am J Psych* 1988;145:950-954.
11. McCain GA, Bell DA, Mai FM, Halliday PD. A controlled study of the effects of a supervised cardiovascular fitness training program on the manifestations of primary fibromyalgia. *Arthritis Rheum* 1988; 31: 1135-1141.
12. Mengshoel AM, Komnaes HB, Forre O. The effect of 20 weeks of physical fitness training in female patients with fibromyalgia. *Clin Exp Rheumatol* 1992;10:345-349.
13. Moldofsky H, Scarisbrick P. Induction of neurasthenic musculoskeletal pain syndrome by selective sleep stage deprivation. *Psychosom Med* 1976;38:35-44.
14. Moreshead J and Jaffe R. *Fibromyalgia: Clinical success through enhanced Host Defenses*. AAPM&R Meeting, Miami, FL, 1 Nov 1993.
15. Powers, R. Fibromyalgia: An age-old malady begging for respect. *J Gen Intern Med* 1993; 8:93-105.
16. Russell IJ, Fletcher EM, Michalek JE, McBroom PC, Hester GG. Treatment of fibrositis/fibromyalgia syndrome with ibuprofen and alprazolam: A double-blind, placebo-controlled study. *Arthritis Rheum* 1991; 34:552-560.
17. Russell IJ, Vaeroy H, Javors M, Nyberg F. Cerebrospinal fluid biogenic amine metabolites in fibromyalgia/fibrositis syndrome and rheumatoid arthritis. *Arthritis Rheum*. 1992;35:550-556.
18. Russell IJ, Michalek JE, Vipraio GA, Fletcher EM, Javors MA, Bowden CA. Platelet ³H-Imipramine uptake receptor density and serum serotonin levels in patients with fibromyalgia/fibrositis syndrome. *J Rheumatol* 1992; 19:104-109.
19. Russell IJ. *Fibrositis/Fibromyalgia syndrome. Neocolonial and Scientific Basis of Myalgic Encephalomyelitis - Chronic Fatigue Syndrome*. Ed: B Hyde, Nightingale Research Foundation, Ottawa, Canada, 1992; pp663-690.
20. Walco GA, Ilowite NT. Cognitive-behavioral intervention for juvenile primary fibromyalgia syndrome. *J Rheumatol* 1992; 19:1617-1619.
21. Waylonis GW, Heck W. Fibromyalgia syndrome: New associations. *Am J Phys Med Rehab* 1992; 71:343-348.
22. Wolfe F, Smythe HA, Yunus MB, Bennett RM, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia: Report of the Multicenter Criteria Committee. *Arthritis Rheum* 1990; 33:160-172.
23. Yunus MB, Masi AT, Aldag JC. Ibuprofen in primary fibromyalgia (PFS): A double blind placebo controlled study. *Arthritis Rheum* 1989; 32(Suppl. 1): R28.
24. Yunus MB, Ahles TA, Aldag JC, Masi AT. Relationship of clinical features with psychological status in primary fibromyalgia. *Arthritis Rheum* 1991; 34:15-21.
25. Yunus MB. Research in fibromyalgia and myofascial pain syndromes: Current status, problems and future directions. *J Musculoskeletal Pain* 1993;1:23-41.

Contact

If you have any questions or would like more information about LRA by ELISA/ACT testing, please contact EAB's Client Services Department at 800-553-5472.