



Fibromyalgia: a Distinct Entity or a Biopsychosocial Syndrome?

Introductory moderator remarks

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Fibromyalgia is defined as a chronic musculoskeletal disorder characterized by widespread pain, exquisite tenderness at specific anatomic sites ("tender points"), and other clinical manifestations such as fatigue, sleep disturbance, and irritable bowel syndrome [1]. Although fibromyalgia has been recognized for decades with descriptive terms such as fibrositis and psychogenic rheumatism, only after 1990, with the publication of the American College of Rheumatology criteria, did a burst of research and publications on fibromyalgia begin, which is still ongoing.

However, there is much debate and controversy about this condition. On the one side are those who deny the mere existence of fibromyalgia and consider it an artificial summation of unrelated symptoms [2]. Notably, if fibromyalgia is not a clinical entity but an expression of low self-esteem and unhappiness as discussed below by Prof. Rubinow, we should change our approach and deal with the patients in psychological and sociological terms. Moreover, the burden of these chronic unsatisfied patients would shift from rheumatology and pain clinics to multidisciplinary teams led by social workers and psychologists. On the other side are many clinicians and researchers who define fibromyalgia as a distinct clinico-pathologic disorder, and even claim that is a genetically based disease with an autosomal-dominant transmission [3]. Prof Buskila will discuss the various findings – including genetic,

neuroendocrine, specific sleep and functional brain abnormalities – that might point to fibromyalgia as a distinct pain syndrome. That is, if fibromyalgia has a genetically based molecular basis affecting pain regulation, more in-depth and thorough research is required to elucidate the pathogenesis and determine specific treatment for this very common disabling syndrome.

Both discussants present excellent and convincing data in favor of either approach. We hope that the data presented will provide readers with tools to more knowledgeably approach the care of patients with fibromyalgia.

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Fibromyalgia: A Distinct Entity?

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"Tenderness is the sedimentation rate of stress"

Fred Wolfe

Fibromyalgia is a contentious diagnostic label applied to individuals who complain of widespread muscular-skeletal pain and who on physical examination exhibit increased sensitivity when pressure

is applied to specific anatomic sites called "tender points." Although recognized as a chronic pain syndrome, affected patients display a myriad of additional symptoms, including fatigue (exhaustion), poor sleep, headaches, irritable bowel, numbness and tingling, cold extremities, dry mouth as well as memory and cognitive impairment. The overall impact of these features is a

marked subjective decrease in functional capacity [1]. Despite the publication of classification criteria by the American College of Rheumatology, controversy prevails as to whether fibromyalgia is a defined disease entity or a waste-paper basket diagnosis that is loosely applied to anyone with symptoms not explained by disease [2,3]. This brief report will attempt to question some of the widely held beliefs surrounding this syndrome and suggest which healthcare professionals are most equipped to care for individuals with fibromyalgia.

Fibromyalgia is not a muscular-skeletal disorder. Despite its obscure pathogenesis, it is not a systemic inflammatory disease. Diffuse widespread pain is the hallmark of the condition but no structural changes have been observed in the synovium, cartilage, bone, tendons or muscles. Although pressure-induced tenderness at typical tender point sites is regarded as a *sine qua non* of the disorder, it is not specific for fibromyalgia. Their locations do not correspond to anatomically defined tendon or myofascial insertion sites. In the original study from which the above-mentioned ACR guidelines were formulated, 19% of individuals who met ACR criteria (more than 11 of 18 tender points) did not have widespread pain and, conversely, there were subjects with diffuse pain who exhibited tenderness at less than the required 11 of 18 tender point sites.

Fibromyalgia is not the result of a specific sleep disturbance. Alpha-wave intrusion of normal delta (stage 4), non-REM restorative sleep has been reported in a number of situations. These include tension headaches, irritable bowel syndrome, chronic pain, rheumatoid arthritis, depression, sleep apnea, coffee and alcohol abuse, and emotional and physical trauma. Furthermore, the notion that the sleep pattern abnormality is a primary causative factor and not chronic pain or other factors has not been demonstrated conclusively.

Fibromyalgia is not a mental disorder. Psychopathology is not the primary explanation for the symptoms of fibromyalgia. Chronic pain modifies mental behavior, impairs cognitive function and subsequent depression may result. However, the incidence of mental problems in patients with fibromyalgia is not greater than in other chronic pain syndromes.

Fibromyalgia is not a genetic disorder. Preliminary studies suggested that T102C polymorphism of the serotonin transporter gene, *5HT2A*, may be associated with fibromyalgia [4]. Additional investigations have shown that although this holds true for patients with underlying psychiatric disease who meet fibromyalgia criteria, it is absent in the more frequently encountered mentally healthy subset of patients [5]. Buskila et al. [6] have reported aggregation of fibromyalgia within families as well as transmission of the symptoms from mothers to their daughters. These observations can be readily attributed to environmental and sociocultural factors related to prolonged (from childhood) exposure to diverse reactions to stress, distress and discontent within the family circle.

What then is fibromyalgia? Self-reported questionnaires have shown that affected individuals regard themselves as compulsive, perfectionist, over-achievers whose lifestyles render them unable

to relax. Usually very dedicated, their personalities and objective life-event circumstances clash, resulting in a breakdown of normal adaptive stress-coping strategies. They lose their self-esteem and feel useless and exploited. What ensues is a never-ending cycle of poor sleep, widespread pain, frustration and unhappiness. To be unhappy is not an illness but a complex of interactions between the environment, the body and the mind that may cause significant functional impairment. The fibromyalgia condition probably depicts the psychobiology and somatization of stress and discontent.

Which healthcare professionals should be providing care for individuals with fibromyalgia? Presently, 10% of all visits in a general medicine practice and 20% of patients seen in a rheumatology clinic carry the diagnosis of fibromyalgia. Rheumatologists are well trained in a wide spectrum of muscular-skeletal disorders, but, for the most part, few have amassed the necessary skills and expertise required to manage these patients. Prescription medications are usually not beneficial and appropriate treatment strategies should underscore stress management, enhance coping skills and self-efficacy as well as restore self-esteem. Consultations with this group of patients are time-consuming and frustrating for physician and patient alike. Long office visits with a rheumatologist are often counterproductive and at the expense of patients with systemic inflammatory disease in need of his/her expertise. Indeed, Michael Weinblatt, former president of the ACR stated: "It is unacceptable for patients with rheumatoid arthritis to wait months for an appointment with a rheumatologist. Rationing visits for those with non-systemic rheumatic illnesses (including fibromyalgia) may be required" [7]. Therefore, the "fibromyalgia state" is best managed by a team led by a clinical psychologist versed in both stress and pain management and aided by a rheumatologist as well as other professionals as dictated by the particular case. The absence of objective structural damage precludes defining affected individuals as physically and permanently impaired.

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Fibromyalgia: A Biopsychosocial Syndrome

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Fibromyalgia syndrome is a common disorder of diffuse aching and pain or stiffness in the muscles or joints, accompanied by tenderness on examination at specific, predictable anatomic sites known as tender points [1,2]. It affects mainly women. A constellation of ancillary symptoms may be present, including headache, fatigue sleep disturbances, paresthesias, irritable bowel syndrome, and other manifestations [3]. The currently accepted criteria for the classification of fibromyalgia are those set by the American College of Rheumatology in 1990 [4], and they include the presence of widespread pain in combination with tenderness at 11 or more of 18 specific tender point sites.

Despite intensive research, major gaps in our understanding of the pathogenesis of fibromyalgia still remain. Moreover, controversy reigns regarding diagnosis and treatment. There are those who contend that fibromyalgia does not exist [5,6], and that the diagnosis is entirely based on subjective reports of pain either obtained by history or elicited during physical examination of the tender points. These physicians feel uncomfortable and frustrated facing a patient with multiple complaints and normal laboratory tests. But, although there are no specific pathologic laboratory findings in patients with fibromyalgia, there are many objective findings. Thermal and mechanical hyperalgesia can be consistently detected in most patients with fibromyalgia [7,8]. Increased amplitude of the cerebral somatosensory potentials evoked by laser heat stimuli to the dorsal surface of the hand have been reported in these patients [9,10]. Temporal summation means a progressive increase in action potential discharge from nociceptive nerve cells in the dorsal horn in response to repetitive stimulation by identical stimuli. Staud et al. [11] recently showed that the amount of temporal summation was greater in fibromyalgia patients than in controls. Indeed, several recent studies obtained psychophysical evidence that input to central nociceptive pathways is abnormally processed in such patients [11–14].

Nearly all fibromyalgia patients describe non-restorative sleep and, indeed, the objective abnormality found in these patients is a disruption of deep sleep (stages 3 and 4) by a fast "waking" rhythm (alpha-delta sleep) on electroencephalograph recording [15].

Elevated cerebrospinal fluid levels of neurotransmitters have been demonstrated in fibromyalgia, with the most dramatic and consistent chemical abnormality being elevated CSF substance P [16]. Many recent studies have reported a dysregulation of the hypothalamic-pituitary axis in a subset of fibromyalgia patients, specifically impaired cortisol secretion stressors and impaired

growth hormone secretion [17,18]. Reduced regional cerebral blood flow has been reported in fibromyalgia [19,20]: namely, reduced thalamic blood flow and reduced activity in inferior pontine tegmentum and the right lentiform. Several groups of investigators, using heart rate variability analysis and tilt-table testing, have shown that autonomic nervous system dysfunction is frequent in patients with fibromyalgia [21,22]. It was suggested that dysautonomia may explain many of the multisystem features of fibromyalgia [22].

Finally, it was shown that fibromyalgia is more prevalent in relatives of fibromyalgia patients [23,24], suggesting that genetic factors may predispose a person to the disorder. Furthermore, a possible association of fibromyalgia with a polymorphism in the serotonin transporter gene regulatory region has been reported [25,26].

In conclusion, based on the numerous neurochemical, neuroendocrine and imaging abnormalities found in these patients, I argue that fibromyalgia is a biopsychosocial syndrome that results in chronic pain.

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CSF = cerebrospinal fluid

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