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Primary *Fibromyalgia* (Fibrositis): Clinical Study of 50 Patients With Matched Normal Controls

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FIBROSITIS or fibromyalgia is a form of nonarticular rheumatism characterized by chronic aches, pains, and stiffness in multiple areas of the musculoskeletal system, including articular and periarticular areas, muscles, ligaments, tendon insertions, subcutaneous tissues and bony prominences, accompanied by increased tenderness at specific anatomical sites known as tender or trigger points.[1,2] The latter term was coined because of production of pain at a distant site following pressure on a tender point, analogous to distant action of a gun on pulling its trigger. However, such distant pain is not always produced and *tenderpoint* is therefore more precise. Symptoms are usually aggravated by cold, humid weather, tension and inactivity, and eased by heat, moderate activity or vacation.[1,3]

The syndrome is considered *primary* when no known cause or associated contributory disorder is present, and all laboratory investigations and roentgenographic studies are normal. Since no evidence of inflammation is present in the primary condition, the nomenclature *primary fibromyalgia* is more accurate. Fibrositis may be secondary to trauma, various rheumatic diseases, e.g., osteoarthritis and rheumatoid arthritis, various connective tissue diseases, and a variety of nonrheumatic disorders, e.g., hypothyroidism and malignancy.[1,4,5] Some secondary conditions producing the syndrome may be inflammatory and hence the term *secondary fibrositis* may be used.

Fibrositis or fibromyalgia and other forms of nonarticular rheumatism are a common cause of disability, resulting in a high proportion of absences from work.[6] Many rheumatologists regard primary fibromyalgia as one of the most common rheumatic conditions.[7-9]

The term fibrositis was first used by Sir William Gowers in 1904, in an article on lumbago.[10] He hypothesized an inflammatory change in the fibrous tissues of the muscles of the back which produced "muscular rheumatism" with or without a history of trauma. The presence of edema or proliferated fibrous tissue in muscle biopsy of tender areas of such patients was first described by Stockman.[11] However, other investigators failed to show significant presence of inflammatory cells by microscopic examination[12-14] hence the term "inflammatory reaction,"[11] may be misleading.

In spite of its long heritage, this condition is not generally recognized among physicians. Numerous studies have been assembled on such myofascial pain syndromes since 1900, including a recent review with 85 references.[15] However,

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relatively few of these reports deal with primary fibromyalgia per se. Contributing to the poor recognition or acceptance of primary fibromyalgia as an entity is the absence of standardized criteria for diagnosis. The condition has been variously described, e.g., fibrositis syndrome, fibromyositis, fibromyalgia, myofibrositis, interstitial myofibrositis, myofascial pain syndrome, myofascitis, muscular rheumatism, nonarticular rheumatism, and tension rheumatism. Although a separate entity, many fibromyalgia patients are diagnosed as having psychogenic rheumatism.[1]

Although many reports[1,3,7,10,16,17] have described various features of primary fibromyalgia, e.g., its relationship to weather and physical activities, sites of symptoms, and locations of "trigger points", none provides precise criteria for the patients selected, detailed quantitative clinical data on the patients studied, or controls to compare various manifestations in this disorder.

Many clinicians have dealt with only limited aspects of the disease, e.g., "trigger points",[18,19] or with "localized" fibrositis involving certain anatomical sites.[20,21] Previous reports of laboratory results in "primary" fibromyalgia cannot be fully accepted, either because of insufficient information to exclude secondary causes[22] or no quantitative data.[1,17] Though primary fibromyalgia has recently been well-described and criteria for diagnosis have been suggested,[1,2] no detailed quantitative description of this syndrome is available based upon longitudinally derived data, and the suggested criteria are based on anecdotal experience only.

No controlled studies are available either on various features of primary fibromyalgia or on the presence of tender points in the normal population. Thus, while fatigue[2,7,10,17] and anxiety[2,3] have been described in primary fibromyalgia, their frequency as compared to a normal population is not reported. Similarly, despite many reports on "trigger points" as reviewed by Simons[15] their frequency in normal controls is not available.

Hence, we believe that a detailed, controlled study of this common rheumatic condition will provide valuable data on its clinical characterization.

MATERIALS AND METHODS

Patient Selection

Fifty consecutive patients diagnosed as having primary fibromyalgia were seen over a period extending from July 1977 to August 1978, at a private outpatient clinic in a Division of Rheumatology. All were referred by other physicians, predominantly general internists, family physicians, pediatricians and orthopedic surgeons. Criteria for diagnosis were similar to those suggested by Smythe.[1] All patients had symptoms of either generalized aching or stiffness, involving 3 or more areas, for a minimum of 3 mo duration, and at least 4 well-defined tender points (see below). All relevant investigations including roentgenographs were normal. Patients with aches and pains thought to be related to trauma (obvious or due to repetitive use) were excluded. No patient had clinical evidence of any organic systemic illness, and physical examination, including joint examination and muscle strength, was normal except for tender points, areas of muscle spasm (in some patients), and a tender colon due to irritable bowel syndrome.

Since we had previously observed many primary fibromyalgia patients to have irritable bowel syndrome and headaches, we estimated the frequency of these clinical associations in primary fibromyalgia in this study.

Tender Points

Tender points were defined as areas of prominent localized tenderness elicited on firm palpation of specific anatomic sites. Similar amount of pressure did not elicit significant discomfort in other sites in the same patient, often including contralateral locations. An area of tenderness was accepted as a tender point only if there was evident verbal response to pain ("oh, it *really* hurts"), physical withdrawal of the part, expression of pain on the face, or the characteristic recoil out of proportion to the amount of pressure exerted by the examiner, i.e., the "jump sign."[23]

Irritable Bowel Syndrome (IBS)

This was characterized by periodically altered bowel habits associated with lower abdominal pain or distension, usually relieved by bowel movements.[24] The majority of patients also had characteristic small or thin stools with or without mucus and none had blood in the stools or weight loss. In many patients, symptoms were related to emotional stress. No history of an organic bowel disease was present.

Headaches

Patients with migraine had typical severe, throbbing, episodic "sick headache", unilateral or bilateral, associated with visual symptoms and nausea or vomiting.[25] In all 11 such patients, symptoms began in early adolescence; eight had taken an ergot preparation. "Tension headaches" were defined as steady, bothersome, episodic headaches (diffuse, frontal or occipital), often experienced during a period of emotional stress, and without visual or gastrointestinal symptoms of migraine.[26]

Control Subjects

Fifty age, sex, and race matched normal volunteer subjects without significant musculoskeletal symptoms (43 females and 7 males), either students, clerical or administrative staff, and their children were recruited. Age was matched within 5 yr, and all persons were in excellent health. The same protocol for history taking and physical examination was used as in patients.

Laboratory and Roentgenographic Studies

Complete blood count including white cell count (WBC) and hemoglobin (Hb) was done by Coulter counter and erythrocyte sedimentation rate (ESR) by the Westergren method. The latex fixation method was used for rheumatoid factor[27] and antinuclear antibody (ANA) was done by the indirect fluorescence method using rat liver as a substrate.[28] Chemistry profile which included serum calcium, phosphorous, glucose, blood urea nitrogen (BUN), uric acid, cholesterol, total protein, albumin, globulin, bilirubin, alkaline phosphatase, lactic dehydrogenase (LDH) and serum glutamic oxaloacetic transaminase (SGOT), was done by an automated continuous flow procedure. Creatinine phosphokinase (CPK) was measured by using Beckman CK reagent. All but seven patients had roentgenograms of the involved sites.

Statistical Methods

Differences between patient subgroups in proportionate frequencies of dichotomous (yes/no) variables were evaluated using the Chi-square or Fisher exact test. Frequency distributions of continuous variables were evaluated for modality, skewness and kurtosis. Continuous variables were then dichotomized at critical levels and subjected to Chi-square or Fisher exact test analysis, as mentioned above. Classical R-type factor analysis was performed to examine possible variable interrelationships.[29]

RESULTS

Age, Sex, and Race

The age range of patients at presentation was from 14–61 yr, with a mean and median of 34 yr (Table 1). The onset age ranged from 9–55 yr with a mean and median of 29 yr. The most frequent age group both for onset and presentation was 26–35 yr. Fourteen percent were juveniles at presentation. Forty-three patients (86%) were females and 7 (14%) were males, with no age difference found between the sexes. All patients and controls were white Americans.

Frequency of Symptoms

The patients had a high frequency of rheumatic symptoms, i.e., generalized aches and pains (98%), stiffness (84%) and subjective feeling of swelling in articular or periarticular areas (32%) which were significantly greater than among the matched controls (Table 2). One patient denied having aches and pains, but complained of marked stiffness.

Sites of Symptoms

Aches, pains, or stiffness, were localized mainly in the articular and periarticular areas (Table 3). The following sites were commonly involved, in order of decreasing frequency: knees, low back, shoulders, hands, (MCP's 16%, PIP's 16%, "fingers" 12%, DIP's 2%, not specified 18%), hips, neck, elbows, ankles, feet, upper and mid-back, wrists, gluteal areas, thighs and legs. Uncommon sites were arms (10%), toes (8%), anterior chest wall (8%), "tailbone" (6%), "shoulder blades" (4%), ears (2%), and eyeball (2%). The number of anatomical sites of symptoms in a patient ranged from 3–31 with a mean of 9.8 (median 9). Only 2 patients had symptoms in 3 anatomical sites. Each interphalangeal and MCP joint of the hand, a finger, foot, neck, upper back, mid-back, and low back were each counted as one anatomical site.

Duration of Symptoms

Duration of symptoms ranged from 6 mo–23 yr with a mean and median of 5 yr at presenta-

Table 1. Sex and Age Distribution of Primary Fibromyalgia Patients at Onset and Presentation

Age	Female		Male		Total	
	Onset	Presentation	Onset	Presentation	Onset	Presentation
<15*	13	6	1	1	14 (28%)	7 (14%)
16–25	6	6	0	0	6 (12%)	6 (12%)
26–35	12	12	4	3	16 (32%)	15 (30%)
36–45	6	8	1	2	7 (14%)	10 (20%)
46–55	6	7	1	1	7 (14%)	8 (16%)
56–61	0	4	0	0	0 0	4 (8%)
	43	43	7	7	50 (100%)	50 (100%)

*Youngest onset age was 9 and presentation age was 14.

Table 2. Percent Frequency of Selected Manifestations in 50 Primary Fibromyalgia Patients and Matched Controls

Manifestations	Patients	Controls	*P* Value
Symptoms			
Generalized aches and pains	98	—*	
Tiredness	92	10	< 0.001
Stiffness	84	—*	
Anxiety	70	18	< 0.001
Sleep problem	56	12	< 0.001
Bothersome headaches	44	16	< 0.01
Irritable bowel symptoms	34	8	< 0.01
Subjective swelling†	32	6	< 0.01
Numbness	26	4	< 0.01
Tender Points			
One or more found	100	48	< 0.001
Mean number	12	1.1	< 0.001
Range	4–38	0–4	

*Individuals with significant aches, pains or stiffness were excluded from control group.

†Periarticular, or diffusely in the fingers.

tion. One-fifth had symptoms for more than 10 yr.

Diurnal Variation of Symptoms

In 48%, aches, pains or stiffness were most prominent both in the morning and in the evening, usually on rest after a day's work. In 28%, these symptoms occurred mostly or only in the morning, in 14%, mostly or only in the evening, in 6%, at no particular time, and in 4%, throughout the day. (Table 3)

Stiffness

Eight patients had no stiffness and four patients had stiffness only in the evenings, after a day's work. Two patients consistently complained of stiffness "all the time." In the remaining 36 patients, the duration of morning stiffness ranged from 5–240 min, with a median of 40 min (mean of 63 min). Some patients had both morning and evening stiffness. No correlation was found between the duration of morning stiffness and the number of trigger points.

Subjective Swelling

A feeling of swelling was described by 16 patients, although no objective evidence of swelling was documented in any of them. The sites involved were mostly articular and periarticular, but frequently patients reported the swelling feeling in the whole hand or the fingers.

Nonrheumatic Symptoms

Frequent nonrheumatic symptoms described by patients, were marked tiredness (92% in total and spontaneously described in 60%), anxiety (70%), endogenous sleep problem (56%), headache (44% total; 22% migrainous and 22% nonmigrainous), irritable bowel syndrome (34%), and numbness (26%), which were all significantly greater than among controls (Table 2). Seven of the 16 patients with IBS had had a normal barium enema examination, and one other had a normal sigmoidoscopic examination. No other bowel disease was diagnosed in these patients.

Numbness was usually, but not exclusively, in the upper extremities and not obviously related to hyperventilation or a state of anxiety. All 13 patients with numbness had a complete and normal neurological examination and six of them were also seen by a neurologist. One patient complained of constant earache and dizziness with normal otologic evaluation. The symptoms were relieved by injection of Xylocaine plus corticosteroid in a pronounced trigger point at the ipsilateral, adjacent sternomastoid muscle insertion.

Modulating Factors

Symptoms were characteristically made worse by cold or humid weather, fatigue, sedentary state, anxiety and overactivity (Table 4). Other aggravating factors mentioned spontaneously were poor sleep (8%) and alcohol use, exposure to air conditioned areas, menstrual period, and the weather change before rain, each occurring in 4% of patients. Symptoms were characteristically relieved (often temporarily) by a hot shower, being moderately active, warm, dry weather and massage. Other ameliorating factors, spon-

Table 3. Percent Frequency of Aches, Pains or Stiffness at Common Articular or Periarticular Areas in 50 Primary Fibromyalgia Patients

Area	Percent	Area	Percent
Knees	66	Ankles	22
Low back	66	Feet	18
Shoulders	54	Upper & mid back	16
Hands	52	Wrists	14
Hips	38	Gluteal areas	14
Neck	34	Thighs	14
Elbows	24	Legs	14

Table 4. Percent of Primary Fibromyalgia Patients Who Reported Modulating Factors on Symptoms

Aggravating Factors	Percent	Relieving Factors	Percent
Cold or humid weather	92	Hot shower	92
Fatigue	78	Being active	82
Sedentary state	78	Warm, dry weather	80
Anxiety	68	Massage	64
Overactivity	62		

taneously mentioned, were vacation (8%), nap (8%), general rest (8%), swimming (6%), alcohol ingestion (4%), pregnancy (4%), and exercise (4%). One or more modulating factors (considering both aggravating and relieving factors) were present in all patients and 5 or more such factors were present in 90%.

Though 32% had no preference for season, symptoms were milder in the summer in 32% and in both spring and summer in 12%. Two patients preferred the fall and one both the fall and spring. Only one patient consistently preferred the winter season. Symptoms were present for less than a year in 16%; and seasonal choice was not determined.

Articular Examination and Tender Points

The articular examination was normal without evidence of joint swelling in any patient as was the complete musculoskeletal system evaluation, except for the presence of tender points or muscle spasm. Tender points were noted in all patients (Table 2). They were persistently evident at individual sites on follow-up, unless they were injected with corticosteroids and Xylocaine. These sites were remarkedly consistent in an individual patient. The total number of tender

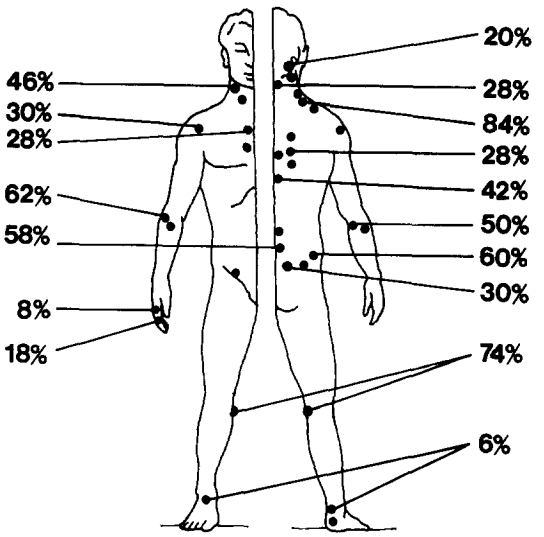

Fig. 1. Common sites of tender points in primary fibromyalgia patients.

points in a patient ranged from 4–33, with a median and mean of 12. Only two patients had as few as 4 tender points, the minimum number required for study entry.

The common sites of tender points (Fig. 1 and Table 5) in decreasing frequency were upper, middle border of the trapezius muscles, near the "fatty pad" at the medial aspect of knees, lateral epicondylar area of the elbows, posterior iliac crests, lumbar spinal prominences or adjacent areas, medial epicondylar area of the elbows, sternocleidomastoid muscle at either its mastoid insertion or mid-point, dorsal spine areas, costochondral junctions, bicipital tendons, sacroiliac joint region, cervical spine, medial border of the scapulae, greater trochanter of the hip and suboccipital muscle insertions. The less common sites were proximal interphalangeal (PIP) joints

Table 5. Percent Frequency of Common Sites of Tender Points in 50 Primary Fibromyalgia Patients Compared to 50 Normal Matched Controls*

	Patients	Controls		Patient	Controls
Upper border of trapezei	84	16	Costochondral Junction	32	0
Medial part of knees	74	10	Bicipital tendon area	30	0
Lateral border of elbows	62	26	Sacroiliac joint area	30	0
Posterior iliac crest	60	10	Cervical spine	28	2
Lumbar spine area	58	0	Medial border of scapulae	28	0
Medial part of elbows	50	2	Greater trochanter of hip	24	0
Sternomastoid muscles	46	16	Suboccipital muscle insertion area	20	2
Dorsal spine area	42	0			

*All differences were statistically significant at the $P < 0.001$ level, except sternomastoid muscles ($P < 0.01$).

of the hands (18%), sternoclavicular joints, masseter muscles near the temporomandibular joints and the pectoral muscles (each 12%), MCP joints of hands and wrists (each 8%), subdeltoid areas, ankles and the feet (each 6%), inguinal ligaments, gluteal muscles and achilles tendons (each 4%), and wrists (2%).

Tender points were exclusively or predominantely present on one side of the body in 14%. Of 16 patients with tender points at the costochondral junctions, four with chest pain, not typical of angina, had electrocardiograms which were normal. Injection of tender points with local Xylocaine and corticosteroids relieved or significantly decreased the chest pain in these patients.

Marked cutaneous erythema following pressure over the tender point areas was observed. This phenomenon was not quantitated, either in patients or controls.

Subcutaneous "Fibrositic" Nodules

Though not specifically quantitated, "fibrositic" nodules were frequently observed during the examination, mostly in the sacral and posterior iliac crest regions. The subcutaneous nodules were firm, mobile and usually tender. One nodule was biopsied by the referring physician with histological demonstration of fibro-fatty tissue without inflammation.

Laboratory Results

The mean values and 2 S.D. of white blood cell count (WBC), hemoglobin, hematocrit, erythrocyte sedimentation rate (ESR), uric acid, SGOT, LDH and CPK are shown in Table 8. The results were within normal limits. The remainder of the chemistry profile was also within normal limits. Rheumatoid factor and ANA were negative in all 50 patients.

All but seven patients had roentgenographs of prominently involved sites. All patients above the age of 30 having symptoms in their neck or back had their spine invariably X-rayed. Five of these seven patients without roentgenographs were less than 30 yr of age. The other two had predominant symptoms in areas not usually involved by osteoarthritis, e.g., wrists, elbows, or costochondral areas. Only one of the patients X-rayed had minimal evidence of osteoarthritis of the cervical spine, but had generalized symptoms and 13 tender points with only four in the cervical region and the trapezius muscles. Thus, it is unlikely that any of the seven patients without roentgenographs had significant osteoarthritis.

Preceding Consultations and Diagnoses

Patients were seen by a median of three previous physicians (mean of 3.5), with a range of 1–11. More than half the patients (52%) did not have a referring diagnosis (Table 6). "Fibrositis" was diagnosed in only three patients, whereas "psychogenic pain" was diagnosed in 16%. Patients were usually dissatisfied with their previous medical consultations, and the lack of a firm diagnosis appeared to be a major reason for their apprehension. All patients diagnosed or implied to have "psychogenic pain" emphatically said that they knew the pain was not "all in the head."

Unwarranted and often distressing investigations were carried out during previous consultations in 12 (24%) of the primary fibromyalgia patients. They included myelogram (8%), arthrogram (6%), cancer investigation (4%), adrenal evaluation (4%), and intravenous pyelogram (2%). One unfortunate young girl with primary fibrositis had an ankle arthrodesis.

Report of a Case With Primary Fibromyalgia

A 30-yr-old white female presented with "aches all over," especially in low back, upper gluteal regions, knees, neck, shoulders and hands, for the past 10 yr. She also complained of stiffness in the morning and evening. In general, her symptoms were aggravated by inactivity, damp and cold weather, mental stress and excess physical activities, and relieved by warm weather, moderate activities and a hot bath. She felt tired and over-worked as a housewife, and admitted that she was a somewhat anxious person. She slept poorly and had occipital head-

Table 6. Frequency of Previous Diagnoses Made on Primary Fibromyalgia Patients Before Referral to This Study

Previous Diagnoses	Number	Percent
None	26	52
Fibrositis	3	6
Muscle spasm	6	12
Psychogenic pain	8	16
Rheumatoid arthritis	4	8
Ankylosing spondylitis	2	4
Osteoarthritis	1	2

aches. She also gave a history of constipation and lower abdominal pain. The barium enema examination was negative. She was seen by three previous physicians, and one of them diagnosed "mild rheumatoid arthritis" 5 yr ago. Physical examination showed completely normal joint findings, but areas of pronounced tenderness at specific sites (tender points) in elbows, middle of trapezius muscles, suboccipital muscle insertion areas, 2nd to 4th costochondral junctions, sacroiliac joint areas, posterior iliac crest regions and medial aspect of the knees. All laboratory tests including erythrocyte sedimentation rate, rheumatoid factor, antinuclear antibodies, and muscle enzymes were normal. Treatment included reassurance regarding the benign nature of primary fibromyalgia, salicylate therapy for pain, and Elavil 25 mg at bedtime for better sleep. On follow-up after 6 wk, she reported some improvement. The sites of tender points were the same as at the first visit but less tender. After 4 mo of follow-up, her symptoms were significantly improved, and after 8 mo she remained only mildly symptomatic.

Intercorrelation and Factor Analysis of Clinical Variables

Important intercorrelations are shown in Table 7. Particular characteristics predominated in certain age groups. In the group with onset age of 15 or less, subjective swelling and aches in the metacarpophalangeal (MCP) joints as well as ankles were particularly more common ($P < 0.005$). Patients under age 30, in contrast to older patients, had significantly more frequent involvement of their fingers and ankles as sites of symptoms ($P < 0.05$). Subjective feeling of swelling was also more common in the younger patients ($P < 0.05$) as was numbness ($P < 0.05$). The older patients had more frequent involvement of their shoulders ($P < 0.05$).

Patients with anxiety were more likely to have sleep problems ($P < 0.05$), headaches ($P < 0.05$), symptoms made worse by fatigue ($P < 0.05$), irritable bowel syndrome ($P < 0.05$), low backache ($P < 0.01$), and tender points at the posterior iliac crests (<0.001) and lumbar spine area ($P < 0.05$) than patients who denied anxiety. Patients with headaches were more anxious ($P < 0.05$) and more likely to have tender point(s) in the upper cervical region or at the occipital attachment of the neck extensor muscles ($P < 0.01$).

Associations were found among symptoms at certain sites. Thus, MCP joint related aching or stiffness was more likely to be involved along with PIP joint related symptoms ($P < 0.001$). Symptoms in the gluteal areas, thighs and legs

Table 7. Intercorrelation of Clinical Features in 50 Primary Fibromyalgia Patients

Major Feature	Correlation With	*P* Value
Onset age 15 or less	Subjective swelling	<0.005
	Metacarpophalangeal aches	<0.005
	Ankle aches	<0.005
Anxiety	Sleep problems	<0.05
	Headaches	<0.05
	Symptoms worsened by fatigue	<0.05
	Irritable colon	<0.05
	Low back pain	<0.01
	Tender points at:	
	Posterior iliac crest	<0.001
	Lumbar spine (L. spine) area	<0.05
Headaches	Anxiety	<0.05
	Tender points at:	
	Upper cervical spine	<0.01
	Suboccipital region	<0.01
12+ tender points	Symptoms for >5 yr	<0.05
	Fatigue	<0.05
Sleep problems	Headaches	<0.05
	Anxiety	<0.05
	Symptoms better by:	
	Vacation	<0.01
	Nap	<0.01
	L. spine area trigger point	<0.05

associated with each other ($P < 0.001$), as did the hips and shoulders ($P < 0.001$). Similiarly, a correlation was found between tender points at the medial border of the scapula and the sacroiliac joint area ($P < 0.01$), as well as between those at the sternocleidomastoid muscle and the upper border of the trapezius muscle ($P < 0.05$).

Patients with 12 or more tender points more frequently had symptom duration longer than 5 yr ($P < 0.05$), fatigue ($P < 0.05$), and tender points at sternocleidomastoid muscle insertion(s) ($P < 0.05$) as well as at the lateral border of the elbows ($P < 0.01$). Patients with less than 12 tender points tended to have more irritable bowel syndrome ($P < 0.05$).

Patients with sleep problems more likely had headaches ($P < 0.05$), anxiety ($P < 0.05$), symptoms improved by vacation and nap ($P < 0.01$), and tender point(s) in the lumbar spine area ($P < 0.05$). They also had irritable bowel syndrome more frequently ($P < 0.05$).

A correlation was found between certain symptom sites and tender points in those same areas. These were knees ($P < 0.01$), cervical ($P < 0.001$), dorsal ($P < 0.05$), and lumbar ($P < 0.001$) spine areas. Low back pain and tender points at the posterior iliac crest correlated ($P < 0.05$) also.

Controls

Elicited symptoms were all significantly less frequent among the control subjects than the primary fibromyalgia patients (Table 2). Among the controls, anxiety and numbness were correlated ($P < 0.05$). This correlation was not observed among the patients. As with the patients, a correlation was found between anxiety and tender points at the lateral epicondylar area of the elbows ($P < 0.05$).

Among the 50 matched controls, 24 (48%) had tender points, all females. The number ranged from one to four, with a mean of 1.1 (Table 5). Eight controls had one tender point, six had two, four had three and six had four tender points.

DISCUSSION

Primary Fibromyalgia—A Neglected Entity

Although primary fibromyalgia is a common condition, perhaps as frequent as rheumatoid arthritis,[30] its existence as an entity remains controversial.[2,30,31] This study supports the belief, expressed by others,[1,3,30,32] that primary fibromyalgia is generally poorly recognized by the medical profession. Only 6% of our patients were referred with a diagnosis of primary fibromyalgia, although another 12% were believed to have muscle spasm. Sixteen percent of patients were told they had a psychological syndrome, and was implied in many others without a definite diagnosis. Such ambiguity and lack of assertion of a definite diagnosis increased patient anxiety and contributed to morbidity. At the other extreme, 12% of our patients were diagnosed to have a potentially crippling disease. In one patient, gold therapy was recommended by her physician who had diagnosed her condition as rheumatoid arthritis. The patient, however, wanted a second opinion before agreeing to such therapy. One of our young and bright patients was refused a scholarship from the Air Force, since the physician involved in certification of medical fitness had never heard of fibromyalgia or fibrositis. Despite explanation of the disorder, the physician was unconvinced that primary fibromyalgia was not a crippling condition.

Two popular textbooks of Internal Medicine mention fibrositis in only a few lines each.[31,33] These same texts describe irritable bowel syndrome as an entity in great detail,[24,34] though primary fibromyalgia is probably as common as irritable bowel syndrome, causes as much disability and has similar functional manifestations, e.g., anxiety, and muscle spasm[1,18,24,34] as part of its presumed mechanism. Both share an absence of specific abnormal laboratory tests at the present time. Despite these similarities, including anxiety factors, primarily fibromyalgia is scarcely recognized compared to irritable bowel syndrome.

Reasons may be suspected for the poor acceptance and apathy towards primary fibromyalgia. These include lack of diagnostic guidelines, neglect by academic medicine, lack of critical descriptive and controlled studies, and absence of laboratory tests which might indicate a physical abnormality.

Prevalence of Primary Fibromyalgia

Precise data on the prevalence of primary fibromyalgia are not available. A British study of disability[6] showed that 10.9% of absences from work were due to rheumatic complaints,

and 50% of these were due to nonarticular rheumatism. Some rheumatologists have expressed the opinion that primary fibromyalgia is the most common rheumatic condition.[7,8] A recent report by the American Rheumatism Association Committee on Rheumatologic Practice[9] indicated that "fibrositis" constituted 7% of new patients seen in a sample month by four rheumatologists in four different referral centers; "fibrositis" being the third most common rheumatic condition, after rheumatoid arthritis (14%) and osteoarthritis (13%). However, "fibrositis" was defined as a syndrome of persistent pain limited to the neck, upper back and the shoulders only, thus underestimating the true prevalence.

From our own experience, primary fibromyalgia is one of the commonest rheumatic conditions, accounting for the second most frequent cause for referral to the rheumatologist. Of 285 new patients seen at our rheumatology outpatient referral clinic over a period of one year in a subsequent survey, 29% had osteoarthritis, 20% primary fibromyalgia and 16% rheumatoid arthritis. However, primary fibromyalgia was the commonest diagnosis (30%) in patients under age 50.

Primary Fibromyalgia as Recognizable Entity

Our study has demonstrated that primary fibromyalgia is a recognizable syndrome with a particular pattern of symptoms, i.e., generalized musculoskeletal aches, pains, and stiffness, characteristically aggravated or improved by certain factors, e.g., weather, physical and emotional stress, quantity and quality of sleep, and degree of activity, to mention a few. Subjective feeling of swelling in articular or periarticular areas may occur but articular examination is typically normal.

The rheumatic manifestations are typically associated with many extraarticular complaints, e.g., tiredness, anxiety, sleep problems, headaches (migrainous and nonmigrainous), irritable bowel syndrome and numbness. These latter features were significantly more frequent than in a control group (Table 2). Primary fibromyalgia is not synonymous with psychogenic rheumatism though anxiety may play a role in the pathophysiologic mechanism.

The characteristic physical finding in primary fibromyalgia is the presence of multiple tender points, as previously defined, and the absence of arthritis. Although tender points were found in about 50% of our controls, they occurred in significantly lower frequency, an average of one per person with a maximum number of four, as compared to an average of 12 in the fibromyalgia patients (range of 4–38).

Clinical Features

Although primary fibromyalgia has been reported to be more frequent among middle aged women,[1,2,30] women in their climacteric and in their fifth decade[3] only Klinefelter[3] provides demographic data. In our study, the most frequent age of onset and presentation was 26–35 yr. This has been observed before, albeit without quantitation.[35] The older middle age preponderance of Klinefelter's patients may be explained by the inclusion of some with osteoarthritis, since not all of his patients were x-rayed to exclude this condition (personal communication). The frequent occurrence of primary fibromyalgia in the pediatric age group has not been appreciated, though Long[36] states that a careful history may discover the onset of the disease in childhood. Bates and Grunwaldt[37] described 62 children aged 3–18 years with "trigger points" among 85 juveniles with myofascial pain caused by a variety of underlying illnesses and injuries. The youngest age at presentation of our patients was 14 yr, but 28% had onset of symptoms between the ages of 9 and 15.

Generalized aches and pains, as well as stiffness, are the most common rheumatic symptoms of primary fibromyalgia as have been noted by various authors. In our study, stiffness was present in 84% of patients and one patient had only stiffness without aching. Since eight (16%) of our patients did not have stiffness at any time, we do not believe that stiffness is a necessary criterion for diagnosis. All of those eight patients had aching as well as other characteristic features of primary fibromyalgia. Our experience, consistent with that of others, is that gelling phenomenon occurs frequently in primary fibromyalgia.[1,3,36] Morning stiffness has been suggested as a criterion, but unlike rheumatoid arthritis, the duration of morning stiffness was not found to be a measure of disease activity in this study. Eight percent of our patients had stiffness in the evenings only, usually after a tiring day's work, as they relaxed (probaby the gelling phenomenon).

Though aching and stiffness obviously increased with mental stress in some patients, these symptoms were more impressively related to weather change in others. Some patients denied worrying, as well as its relationship to symptoms, but prided themselves in being able to forecast a weather change by worsening of symptoms the previous day. The effect of chilling, cold, or humid weather on fibrositic pain has been recognized since the time of Gowers.[1,3,10,16] The beneficial effect of local heat (such as a hot shower) in primary fibromyalgia is probably analogous to that in other rheumatic conditions, e.g., osteoarthritis and rheumatoid arthritis.[32] The mechanism of the weather effect in rheumatic disorders has been reviewed.[38]

Unlike psychogenic rheumatism, as described by various authors,[1,3,4] symptoms of primary fibromyalgia were characteristically influenced by weather and physical activities. In fibromyalgia, symptoms were made worse by inactivity in 78%, and by overactivity in 62%, while they were improved by moderate activity in 82% of our patients. A sedentary state may worsen symptoms by virtue of the gelling phenomenon. Also, diversional activities (recreational or otherwise) may distract attention from the aches and pains. Many patients volunteered this explanation for feeling better while being active. However, excessive physical activities probably worsen symptoms by producing fatigue and mechanical stress on ligaments, soft tissues and tendinous attachments. Though not quantitated, overworked patients had symptomatic improvement when they slowed down and took more rest and sleep. Four of our patients volunteered that vacation improved their symptoms, as did four other patients who improved with a nap. Similarly, only 4 patients volunteered that poor sleep aggravated their symptoms. This is likely to be a gross underestimation. Subsequent to this study, direct questioning showed that a greater proportion of patients had aggravation of symptoms by poor sleep and benefit from restful sleep and relaxation, especially those who sleep poorly and are physically exhausted. The observation that particular activities influence fibromyalgia symptoms has practical implications in patient management. Generally, patients should be encouraged to be active and continue their employment. In some patients, however, modification of a physically strenuous job responsibility may be advisable.

Subjective feeling of articular, periarticular, or diffuse finger or hand swelling was described in about 33% of our patients. To our knowledge, this has not been reported previously in primary fibromyalgia, and it is important to recognize its presence, since this symptom may mislead a physican to make an incorrect diagnosis of arthritis. Three of the four patients diagnosed by referring physicians to have rheumatoid arthritis had such complaints. Many patients volunteered that it was difficult for them to take rings off their fingers early in the morning, but they were not examined at such times. None of our patients had objective evidence of swelling, even though the majority with subjective complaints maintained at the time of examination that certain joint areas felt swollen.

Swelling symptoms were localized mainly in the hands, both around the joints and diffusely in the fingers or the whole hand, and less commonly in the knees. Younger patients more often had such complaints. The mechanism of this symptom in primary fibromyalgia is unknown. No correlation was found between subjective swelling and anxiety. Sola and Williams have observed skin changes in the areas of tender points, e.g., variations in temperature and edema, which they attributed to an altered vasomotor activity.[39] Altered physiologic function may play a part in producing a sensation of puffiness in fibromyalgia patients.

Diffuse numbness has received little attention as a symptom in primary fibromyalgia. Kelly mentioned paresthesiae in his report on the neural theory of "fibrositis".[40] However, he described patients with localized neuralgias, e.g., after local trauma, rather than primary fibromyalgia. Smythe, in his discussion of the pathogenesis of fibromyalgia pain, mentioned numbness and suggested that the character of pain may change from "achiness" in proximal central sites to "numbness" in the extremities, and draws an analogy with anginal pain.[1,2] Numbness was observed in 26% of our patients. In 22% it occurred in nonradicular distribution (usually hands and forearms), though in one patient each it followed the ulnar and sciatic nerve distributions.

All patients had completely normal neurologi-

cal examinations and no evidence of radiological abnormality of the cervical or lumbar spine. It does not appear that numbness is simply a psychogenic manifestation in these patients. Anxiety and numbness correlated among the normal controls, but not at all in the patients. Diffuse muscle spasm may contribute to a degree of nerve compression. A single muscle or muscle group may be involved, e.g., the pyriform muscle, and produce sciatica-type pain.[5,18,41,42] Sciatica does not necessarily mean disc disease, according to Pace and Nagle.[42] Our observations support the opinion that diffuse numbness in primary fibromyalgia does not mean malingering or hysteria.[2]

Tiredness or fatigue has been described often in "fibrositis" patients.[2,7,10,17] Tiredness was usually present in our series; a patient typically complains, "I am always tired." Usually this symptom occurs either in the morning on arising or in the evening on relaxing after a day's work. One may question the diagnosis of primary fibromyalgia in the absence of tiredness. Although fatigue correlated significantly with the variable "symptoms worsened by anxiety", it was not associated with the variable "do you regard yourself as an anxious person." Fatigue should not be interpreted simply as a manifestation of anxiety or depression alone, as has been suggested.[15] Surprisingly, fatigue and patient's poor sleep did not correlate in this study. Fatigue was increased in many patients by excessive physical exertion, e.g., by laboring long hours, which then accentuated musculoskeletal symptoms. Thus, fatigue may be both a symptom and an aggravating factor.

Poor sleep in primary fibromyalgia has been observed previously.[15,32] Fifty-six percent of our patients admitted to sleeping poorly, which was not attributed to aches or pains. This symptom was, however, attributed to aches and pains, in other patients. Seventy-three percent of subsequent sample of 30 primary fibromyalgia patients admitted to having poor sleep irrespective of cause, and an additional four patients (13%) had morning tiredness but did not admit to having poor sleep. Waking up tired and achy may be the only manifestation of poor sleep, though patients may deny poor sleep per se. It is likely that most fibromyalgia patients fail to have deep, restorative sleep (stage 4) irrespective of the reasons, though this may not be realized by the patients. In one series of ten fibromyalgia patients, all had electroencephalographic (EEG) evidence of spontaneous intrusion of alpha waves, (i.e., waves associated with arousal response) into their slow-wave rhythm (non-REM deep sleep), suggesting a lack of deep, restful sleep.[43]

Seven normal volunteers whose non-REM (deep) sleep was disturbed by a buzzer showed a similar alpha wave intrusion and developed overwhelming tiredness and muscle tenderness the following day. Moldofsky, et al,[43] suggested that the EEG disturbance is due to an endogenous arousal system which may be provoked by stress and tension in the fibromyalgia patients. In our study poor sleep correlated with anxiety ($P < 0.05$). In subsequent studies, Moldofsky and Warsh found an inverse relationship between plasma free tryptophan and severity of pain symptoms in primary fibrositis.[44] They suggested that a metabolic disorder, possibly related to reduced brain serotonin contributed to the sleep disturbance. Correlation was found between self assessed nervous disposition, poor sleep and tiredness in a population study involving 2446 subjects.[45]

Headaches, with or without a history of migraine, were present in 44%. Most migrainous attacks occurred in the distant past, during the patient's younger ages. Non-migrainous headaches occurred in nearly a quarter of the patients. This was described as a dull, pressure-like ache over the occipital area, or diffusely in the skull. Non-migrainous headaches were previously found to be associated with "trigger points" in the suboccipital muscle insertion areas, other muscles in the scalp and deep cervical ligaments.[20] Our study too showed a correlation between headaches and tender points on the occiput at the insertion area of the suboccipital muscles ($P < 0.01$). Travell has mapped "trigger points" with their patterns of radiation to various parts of the scalp.[46,47] Headaches were significantly more common among self-assessed anxious patients in our study ($P < 0.05$).

While headaches are generally recognized to be a feature in primary fibromyalgia,[7,17,20] symptoms of irritable bowel syndrome (IBS) are not. Traut[17] stated that a history of "colitis" is frequent in "primary fibrositis" but without

elaborating on its frequency. Reynolds[58] observed functional colon symptoms in many patients with "psychogenic rheumatism." It appears that he included a number of primary fibromyalgia patients in his study. One-third of our patients had symptoms of IBS. A similar proportion (30%) of our subsequent 40 primary fibromyalgia patients also studied prospectively had IBS. One of our patients had multiple simultaneous attacks of IBS and increased fibromyalgia pain. The simultaneous pattern was so consistent that he was convinced of a common operative factor. His referring physician, however, was baffled by this association. Like headaches, IBS was significantly more frequent among patients who admitted to have anxiety ($P < 0.05$). Anxiety may, therefore, be a common operative factor in both primary fibromyalgia and IBS.

Anxiety is an important factor in primary fibrositis,[2] but unlike psychogenic rheumatism, evidence of emotional disturbance is not always present.[48] Seventy percent of our patients admitted to being unduly anxious, and in 68%, symptoms were made worse by anxiety and mental stress. Anxiety does not correlate with all manifestations of primary fibromyalgia. For example, it did not associate with stiffness, numbness, fatigue or subjective swelling.

"Trigger points" have received more attention in the literature than any other aspect of "fibrositis" since they were first described by Lange in 1931.[49] However, most articles were not written in the context of primary fibromyalgia.[18,19,46,47,50,51] Although "trigger points" have been related to localized fibrositic syndromes, psychogenic stress and general fatigue,[47] Smythe[1] is probably the first one to emphasize their diagnostic importance in primary fibromyalgia. His original criteria included a minimum of three "trigger points."[1] However, subsequently, Smythe and Moldofsky suggested that the minimum number of "trigger points" for a diagnosis of primary fibromyalgia should be twelve.[52] The mean number of tender points in our patients was 12, and no impressive overall difference was found in the pattern of manifestations between the patients with fewer than 12 (4–11) versus 12 or greater (12–38) tender points. The 50% of our patients who had a smaller number of tender points (less than 12) had typical characteristics of primary fibromyalgia and should not be excluded from this diagnosis. However, for classification purposes, a minimum number would be helpful to differentiate primary fibromyalgia from less specific musculoskeletal reactive syndromes, e.g., those which follow sporadic episodes of fatigue, over-exertion, localized trauma, and poor sleep, that remit promptly on correction of the precipitating or causative factor(s). Diffuse tenderness should be discriminated from multiple discrete tender points in characteristic locations since the former may occur in many rheumatic and nonrheumatic conditions. Requiring the finding of 12 tender points would probably not help to exclude secondary causes, e.g., post-viral infections or polymyalgia rheumatica, as suggested by others.[52]

From our control study, six normal subjects (12%) had as many as four tender points whereas only two patients (4%) had as few as four tender points. Thus, we believe that a minimum of five or six typical tender points is adequate for the diagnosis of primary fibromyalgia. The jump sign[23] is characteristic but not essential for diagnosis.

As emphasized by Smythe[1,2] and observed among our control subjects, many areas where tender points are found tend normally to be tender. An observer is therefore advised to learn by practice and experience the normal degree of tenderness at characteristic sites using standard palpation techniques in individuals without musculoskeletal symptoms.

The common sites of tender points are quantitatively described in this study. Since tender points correlated with pain symptoms only in the knees, back and neck, one should examine systematically the typical sites in suspected fibromyalgia patients. This view is consistent with those of others.[1,2,53] Fourteen percent of our patients had tender points predominantly or exclusively on one side of the body. Also, Klinefelter mentioned asymmetry of symptoms in some primary fibromyalgia patients.[3]

Many puzzling symptoms may occur in fibromyalgia patients. These include anterior chest wall syndrome mimicking cardiac or pleural pain,[7,18,41] sciatica,[5,41,42] vertigo related to tender points in the sternocleidomastoid muscle,[15] and, as described by Travell,[51,54] temporomandibular joint syndrome, toothache, earache, tinnitus, excessive lacrimation and groin pain. All these

symptoms can usually be attributed to specific tender points with pain referred to their reference zone areas.[51,54] In our study, four patients had anterior chest wall pain and one each had earache, pain in the jaw, pain in the eye ball, and pain in the groin.

Nodules were observed in "fibrositis" as early as 1915, by Llewellyn and Jones[16] and by numerous others since that time.[5,7,11,17,20,55] Though Stockman[11] described these nodules as being "inflammatory," his and other subsequent histologic studies failed to document presence of significant inflammatory cells.[11,12,13,21] "Fibrositic nodules" have been described clinically as being globular, spindle-shaped, or having the shape of a band or rope.[15] The different shapes of these nodules may depend upon the tissues and areas where they occur. Thus, they may be produced by fatty lumps, fibrous cords, muscle spasm or normal variations in muscle density.[1]

Well circumscribed, globular nodules are most likely to consist of fatty or fibrofatty tissue, as was found histologically in one of our patients. Subcutaneous nodules are common, and found in equal frequency among normal and "fibrositic" patients, especially in the lumbar and upper gluteal areas.[56] Fifty-two percent of our control subjects had palpable nodules which were nontender. However, tender nodules are found mostly in patients with "fibrositis."[56] Though quantification is not available, it is likely that tender nodules are present in both primary and secondary fibrositis. Llewellyn and Jones,[16] described such nodules in many forms of "fibrositis" and rheumatic disorders.

Diagnosis of Primary Fibromyalgia

The diagnosis of fibromyalgia in a typical patient may often be suspected by the wary physician within minutes of consultation. The typical patient is most often a young female who complains of muscle and joint pain at multiple discrete sites but who demonstrates no joint swelling, arthritis or skin manifestations of connective tissue disease. The characteristic symptoms and signs as outlined indicate a recognizable clinical syndrome which is currently termed primary fibromyalgia. Nevertheless, a careful history, physical examination and appropriate laboratory tests are mandatory, before the diagnosis is accepted, as is the case with irritable bowel syndrome.

Secondary causes of fibrositis may be distinguished by the associated features of the primary disease. Examination will often show diffuse tenderness in muscles or joint swelling in addition to tender points at typical sites. In interpreting laboratory data, it should be remembered that modest ESR elevation to 35 is not uncommon above the age of 60.[7] Follow-up is important, especially in those with atypical features. Thus, the diagnosis of primary fibromyalgia should be based upon both the characteristic positive findings as well as the absence of other recognizable disease, and not simply when all other rheumatic diagnoses are excluded.

Differential Diagnosis

Psychogenic rheumatism is often confused with primary fibromyalgia, but the former is notably different and has characteristic features as shown in Table 8 which has been modified from Klinefelter[3] and Beetham.[4] Psychogenic rheumatism has been clearly described by various authors.[1,3,48] Our experience with a number of psychogenic rheumatism patients supports its differentiation, in most cases, from primary fibromyalgia. Psychogenic rheumatism patients

Table 8. Differentiating Features of Psychogenic Rheumatism and Primary Fibromyalgia

	Psychogenic rheumatism	Primary Fibromyalgia
Symptoms	Bizarre (e.g., burning, cutting) with exaggerated descriptions	Aching, pain and gelling
Sites	Changing and vague	Definite anatomic areas
Diurnal variation	Rare	Worse in the morning and in evening
Modulating factors	Emotional	Physical (e.g., weather, activities)
Functional complaints	Almost always	Less common
Response to analgesics and physical therapy	Uncommon	Usual
Examination	Patients overreact with facial grimacing and "touch-me-not" withdrawal of any part of the body	Tender points at specific, anatomic sites, and may elicit the "jump sign"

have bizarre, emotionally loaded symptoms described with dramatic metaphors. Their symptoms are not mere aches, but excruciating pain that has the quality of severe burning like fire, and cutting through like a knife. On the other hand, the pain may be vaguely described as numbness, tightness, tingling, prickling, or pressure. Localization may be equally vague and inconsistent without recognizable anatomic boundaries. Thus, the patient may describe symptoms as "a terrible pain in the chest that cuts through the lungs and comes out through the back." Their symptoms characteristically do not vary with external factors such as weather or activity. Unlike primary fibromyalgia, gelling is not a feature of psychogenic rheumatism.[4]

One may expect to find indicators of significant psychological or emotional disorder in psychogenic rheumatism patients, e.g., psychoneurosis, depression, schizophrenia and psychopathic personality. Antiinflammatory drugs are ineffective. On examination they are tender diffusely and react with exaggerated grimacing, as contrasted to patients with fibromyalgia who characteristically have tender points at specific sites. An occasional patient, however, may have features of both primary fibromyalgia and psychogenic rheumatism. Differentiation between primary fibrositis and psychogenic rheumatism is important, since the latter is more difficult to treat and usually requires psychotherapy by a psychiatrist. From our own experience, we describe the following case with psychogenic rheumatism.

A 55-yr-old black male known to have suffered from anxiety and depression aggravated by recent divorce complained of pain from head to toe variously described as aches, burning like fire, pricking as needles and cutting as knife, for the past 8 yrs. He was unable to point to a specific site with most symptoms. The symptoms had no variation with activities and had a vague relation to weather. They were present days in, days out. He felt tired and dizzy and had continuous headaches and numbness all over the body. He slept poorly, blaming the muscle pains that kept him awake. He was taking Valium 20 mg daily. Aspirin and other nonsteroidal antiinflammatory drugs were tried without benefit. He added that "nothing can help my hopeless condition." Examination showed a talkative man with flitting ideas who was a continuous smoker. He looked calm despite terrible headaches and total body pains.

No specific areas of tender points were present, but there was generalized tenderness all over the body, virtually everywhere touched. Remainder of the examination and laboratory investigations were normal. He was reassured, prescribed Amitriptyline at night and a high dose of aspirin with no improvement after three months. Psychiatric evaluation had suggested a diagnosis of schizophrenia. After one year of follow-up his symptoms remains as severe as before.

Unfortunately, the term psychogenic rheumatism has not been used uniformly by all authors. Reynolds[58] for example, described 29 patients with this diagnosis simply on the basis of an associated emotional disturbance. However, this retrospective report does not quantitate aggravating or relieving factors (or lack of them). This report mentions "generalized tenderness" on physical examination, without reference to more specific tender points. Although more than 33% of these 29 patients had identifiable joint disease, it is likely that some of these patients had primary fibromyalgia.

Rheumatoid arthritis may be suggested by pain, stiffness and subjective swelling of joints; however, in primary fibromyalgia, examination will fail to discover objective joint swelling. Duration of morning stiffness tends to be shorter (less than 1 hr) in primary fibromyalgia than in rheumatoid arthritis (which is usually longer than 1 hr). Laboratory tests, e.g., WBC, Hb, ESR, rheumatoid factor and X-rays should help to differentiate between the two conditions. Rheumatoid arthritis may initially present only as morning stiffness before appearance of characteristic joint swelling, several months later.[4] Hence, patients with a recent onset of symptoms should be followed for a more secure diagnosis.

Palindromic rheumatism may be misdiagnosed as primary fibromyalgia since often there is no objective evidence of synovitis at the time of examination. Elevation of ESR during an attack, positive rheumatoid factor or both should alert a physician to suspect this diagnosis. Patients should be asked to come to the clinic during an attack when joint swelling can be documented.

Osteoarthritis affects an older age population and has characteristic roentgenographic find-

ings. Clinical examination usually shows evidence of arthritis, e.g., Heberden's nodes, crepitus or swelling of joints.

Childhood primary fibromyalgia may be misinterpreted as a form of chronic juvenile onset arthritis, but most syndromes typically demonstrate joint swelling and various systemic manifestations.[59]

Connective tissue diseases may simulate fibromyalgia symptomatically but have objective findings which allow their differentiation. Polymyalgia rheumatica is a disease of the elderly with a high ESR and other characteristic features of a systemic syndrome.[30] Polymyositis is diagnosed by muscle weakness and elevated muscle enzymes.[30] Systemic lupus erythematosus, polyarteritis nodosa and other forms of vasculitis, when suspected, can be confirmed by appropriate immunologic and histologic findings.[60,61]

Ankylosing spondylitis (AS) and other spondyloarthropathy syndromes may be confused with primary fibromyalgia because of backache and tenderness in the sacroiliac joint areas. Two of our patients were referred with the diagnosis of AS. However, these primary fibromyalgia patients did not fulfill criteria for AS and would not be expected to be HLA B27 positive, like AS.[62] Of course, primary fibromyalgia patients may have B27 positivity by virtue of a normal population expectation.

Inflammatory bowel disease with arthropathy may also be suspected initially in primary fibromyalgia patients because of the combined bowel and musculoskeletal symptoms. However, the history, physical examination and appropriate investigations, will differentiate the two conditions. In primary fibromyalgia, bowel symptoms are due to irritable bowel syndrome, not inflammatory bowel disease, and there will be no evidence of objective arthritis.

Hypothyroidism may closely mimic primary fibromyalgia because of musculoskeletal stiffness, often worsened by cold weather, and marked tiredness.[63,64] Other features of hypothyroidism mimicking primary fibromyalgia are constipation, headaches and numbness.[64] In fact, one of our patients, initially believed to have primary fibromyalgia was subsequently diagnosed primary hypothyroidism and excluded from this study. Middle-aged or elderly women presenting with features of primary fibromyalgia should especially be scrutinized for evidence of hypothyroidism.

Malignancy and myeloma may be the causes of secondary fibrositis and should be excluded by appropriate tests. Unlike those with malignancy, patients with primary fibromyalgia retain a good appetite and a good general musculature, without weight loss.

Idiopathic edema patients may have features similar to those of primary fibromyalgia. Recently, Pinals and his colleagues[65] reported six women, aged 24–53, who presented with diffuse aching, marked fatigue, morning stiffness and swelling of the hands, with puffiness of the face in the morning. They also had swelling of the legs which became marked with aching and purplish discoloration after periods of dependency. Nocturia was common and all slept poorly. Presence or absence of tender points was not mentioned but their joint examination was normal. All of them had orthostatic fluid retention, with maximum diurnal weight change ranging from 1.8–4.1 Kg. The musculoskeletal symptoms improved following treatment with diuretics, which produced a mean weight loss of 8 Kg. (range 2.5–12.0 Kg.).

This orthostatic edema syndrome has also been called idiopathic edema and its possible mechanisms, including water retention due to excessive vasopressin secretion, have been discussed in a review.[66] None of our patients reported either pedal edema or facial puffiness and these features were not found on examination. Since diurnal weight change was not recorded in our series, it is not possible to exclude idiopathic edema as a cause of symptoms in some of the patients. However, none of our patients were treated with diuretics and response was gratifying using other measures to be described (vide infra).

Localized forms of fibrositis, e.g., cervical fibrositis of taxi drivers, gluteal and back fibrositis of bus drivers and localized fibrositis due to trauma (obvious or due to repetitive use) may be recognized by history, involvement of limited (one or two) anatomic sites[1] and by the usual absence of non-musculoskeletal symptoms, e.g., fatigue, anxiety, or irritable bowel syndrome. Bursitis and tendonitis also have more well

defined areas of localization than is seen in primary fibromyalgia.

Mixed Fibromyalgia

We, as others,[67] have observed elderly patients with minimal or moderate osteoarthritis who have generalized aches and pains out of proportion to the degree of arthritis and radiologic findings alone. They may also have many features of primary fibromyalgia, e.g., prominent tiredness, poor sleep, anxiety, and a history of headaches or irritable bowel syndrome. Such patients may be considered to have mixed fibromyalgia since their musculoskeletal symptoms result from both osteoarthritis and fibromyalgia manifestations. Reynolds[58] observed that more than 33% of his 29 patients with "psychogenic rheumatism" had joint disease. The concept of mixed fibromyalgia is an important one, since successful management of the patient will depend upon appropriate attention to, and management of, the associated fibromyalgia syndrome in addition to the accepted arthritis disorder, i.e., osteoarthritis. Ten percent of 285 new patients seen at our rheumatology outpatient referral clinic over a period of one year in a subsequent survey had mixed fibromyalgia.

We agree with Smythe[2] that fibromyalgia may contribute to the persistent symptoms of many patients with inactive rheumatoid arthritis. In fact, this may occur in patients with any inflammatory arthropathy which has become inactive. During the period of this study, we observed six such fibromyalgia patients (not included in the study) with inactive arthritis (two had Reiter syndrome, three had adult rheumatoid arthritis and one juvenile rheumatoid arthritis). All had characteristic features of fibromyalgia with anxiety, fatigue and numbness which usually developed as their original arthritis became inactive. They had multiple tender points but little or no joint swelling.

These patients may also be classified mixed fibromyalgia, since their original disease may have some contribution to the continued symptoms. It is likely that an anxiety about their previously active arthritis contributed to the new fibromyalgia syndrome. Again, in agreement with Smythe,[2] we emphasize the need for recognition of this group of patients, since they may receive unwarranted and hazardous treatment directed at their original, now inactive, rheumatic disease. One of our above-mentioned patients had received, prior to her consultation with us, increasing doses of corticosteroids, which was not indicated.

SUGGESTED CRITERIA FOR DIAGNOSIS OF PRIMARY FIBROSITIS

On the basis of findings in this study, including normal control subjects, and results of other investigations, the following guidelines are offered for the diagnosis of primary fibromyalgia: (1) Obligatory Criteria: (A) Presence of generalized aches and pains or prominent stiffness, involving 3 or more anatomic sites, for at least 3 mo. (B) Absence of secondary causes, e.g., traumatic (due to repetitive or more direct trauma), other rheumatic (including degenerative), infective, endocrine or malignant, with normal laboratory tests (CBC, ESR, rheumatoid factor, ANA, muscle enzymes) and roentgenograms. (2) Major Criteria: presence of at least five typical and consistent tender points. (3) Minor Criteria: (A) modulation of symptoms by physical activity, (B) modulation of symptoms by weather factors, (C) aggravation of symptoms by anxiety or stress, (D) poor sleep, (E) general fatigue or tiredness, (F) anxiety, (G) chronic headache, (H) irritable bowel syndrome, (I) subjective swelling, and (J) numbness.

All primary fibromyalgia patients must satisfy the 2 obligatory criteria, by definition, as well as either the major criterion plus at least 3 minor criteria. If the patient has only 3 or 4 tender points, then 5 minor criteria are suggested.

All but 2 of the 50 patients and none of the 50 controls satisfied the above criteria, providing a sensitivity of 96%, and specificity of 100% against normal controls. Two patients not fulfilling the criteria had 4 tender points and 4 minor criteria each. Forty-three patients (86%) had 5 or more minor criteria as opposed to none of the controls. Three patients had 3 and 4 patients had 4 minor criteria.

The suggested requirement of 5 tender points as a major, and symptomatic involvement of 3 or more anatomic sites for 3 or more months as an obligatory criterion seems appropriate. Six of the 50 normal controls had as many as 4 tender points, but only 1 had 4 minor criteria, and thus did not satisfy the suggested criteria. Four controls had 3 tender points and none had as

many as 4 minor criteria. In our subsequent analysis of 40 primary fibromyalgia patients (not included in this study), only one patient had aches and pains in 2 anatomic sites, and another three had their symptom duration for less than 6 mo (2 for 3 mo and the other for 4 mo). These four patients had satisfied the above suggested criteria except for involvement of 2 sites (instead of 3) in one patient. Since localized form of "fibrositis" (e.g. by repetitive use) may involve 2 sites, inclusion of 3 or more symptom sites as an obligatory criterion in primary fibromyalgia appears justified. With further study and additional control groups, a greater number of tender points than 5 may be an advisable major criterion, but it is doubted that as many as 12 will be necessary.[52]

We do not believe that stiffness (in the morning or at other times) should be included as an obligatory criterion as has been suggested.[43,52] Sixteen percent of our patients did not have stiffness at any time. Critical comparison of the patients with and without stiffness showed no significant difference.

We did not study skin roll tenderness over the upper scapular region. This sign has been suggested as a criterion for diagnosis of primary fibromyalgia.[2] A multicenter controlled longitudinal study of primary fibromyalgia patients seems indicated in order to derive generally acceptable criteria for the diagnosis of this important and common rheumatic disorder.

Pathophysiology of Primary Fibromyalgia

Pain in primary fibromyalgia probably results from a number of interacting pathophysiologic mechanisms. It has been hypothesized that local factors in certain sites cause referred pain which may, in turn, sustain or aggravate the initial disorder, e.g., a pain → spasm → pain phenomenon.[2] It is likely that such sites are the lower cervical and lumbar spine where mechanical stresses in these curvature areas contribute to a state of deep hyperalgesia in pain sensitive tissues, e.g., the discs and apophyseal joints.[2,68] The cervical spine during sleeping and the lumbosacral area during upright posture are subjected to exaggerated stress.[2] Poor posture either because of bad habits or certain occupations, as well as repeated unrecognized trauma, e.g., from various occupations, may heighten and sustain this hyperalgesic state.

By a reflex mechanism, the pain is then felt in a widespread area, so that pain and tenderness may occur not only in the overlying structures, but distally in various parts of the limbs.[69] The referred pain zone may not follow a known segmental pattern.[70,71] The intensity of pain in the referred sites is not uniform, but tends to be exaggerated in those areas which are normally tender, e.g., epicondylar areas of the humerus or the upper border of the trapezius.[2]

We suspect that some of these "normally tender" areas are sites of increased mechanical stress, e.g., muscle origin or insertion locations. Our data showed a highly significant association of symptoms in the gluteal areas, thighs and the legs suggesting a common anatomical relationship of the pain. Following a disc protrusion, local tenderness may occur not only in the segmental lumbar spine but also in other muscle groups in the thighs and legs which cannot be explained entirely on nerve root compression mechanisms.[1]

Once the state of reflex hyperalgesia is established in the local and referred areas, other factors, e.g., trauma, sleep disturbance, weather, chronic tension state and mental depression could accentuate and perpetuate the symptoms. The extent to which these various factors operate in an individual is variable. Thus, in some individuals, anxiety and mental tension may be less important than physical stress or long working hours in a strenuous occupation. It is also conceivable that the state of deep hyperalgesia is only minimal in some patients with chronic symptoms resulting from a pain → spasm → pain mechanism,[1,51] the spasm being sustained by such factors as anxiety. Cold and humid weather, abuse of muscles, lack of adequate restful sleep, or other aggravating factors may also potentiate the chronic syndrome. Psychogenic factors also influence the degree of pain tolerance and the amount of restful sleep.[2]

Microscopic Findings

Many histologic studies have been reported in chronic and acute muscle pain syndromes,[11-14,72-74] not specifically in primary fibromyalgia. In these syndromes, muscle fibers showed fat-dusting along the fibrils,[14] increased sarcolemmal nuclei with pyknosis,[12,14,73] degenerative changes with loss of cross striations,[12] and interstitial edema.[11] In some acute cases, hyperemia

with mild to moderate infiltrates of lymphocytes and histiocytes were observed.[7,14] In one report,[13] no histological abnormality was found in "fibrositis" muscles, though criteria for diagnosis was not mentioned. More recently, Awad studied muscle tissue from tender, nodular areas of trapezei of 10 patients with undefined interstitial myofibrositis under both light and electron microscopy.[72] The most significant finding was the presence of massive amounts of metachromatic mucoid amorphous substance along with degranulating mast cells. Awad also reported abnormal serum LDH isoenzymes (with normal LDH) in these patients.[22] However, the significance of the above histological and biochemical findings in relation to primary fibromyalgia remains in doubt, both because of lack of adequate criteria for diagnosis and lack of control materials. None of our primary fibromyalgia patients in a subsequent study (to be reported separately) showed any light microscopic evidence of inflammation (but only minor fiber changes) in their tender trapezius muscles. The term primary fibromyalgia is therefore justified.

EMG Findings

A few EMG studies have been done in muscle pain syndrome,[23,72,75,76] but none of them can reliably be stated to have been primary fibromyalgia. The findings were normal in one study[23] and showed continued electrical activity in an area of muscle tenderness in others.[75,76] Awad[72] found increased numbers of polyphasic motor unit potentials in 6 of 10 patients with undefined myofibrositis.

Management of Primary Fibromyalgia: An Art Rather Than A Science

The first priority is to establish the diagnosis, ensuring that no other cause exists for the syndrome. However, unnecessary investigations should be avoided in this process. Once the diagnosis is made, patients should be reassured that the condition is benign, will not cripple, and may eventually remit. Exacerbations and remissions may also occur. It should be emphasized that the symptoms are not all in the head. Assurance alone will greatly help many patients. The origin of the pain and various interacting factors that perpetuate the symptoms should be explained to the patients in an understandable way. Then it will be easier for them to comprehend treatment and follow instructions.

Rest and relaxation is important for most patients, especially if they are tense and overworked. A well-deserved vacation may be helpful.[65] On the other hand, patients should be encouraged to keep themselves generally active and return to employment with necessary conditioning precautions if they have been off work for prolonged periods. A change to a lighter job may be advised. In some patients a change from a stressful life style is required. Keeping physically and mentally busy is beneficial to avoid gelling and to decrease fixation upon symptoms. Sufficient, restorative sleep is of great importance, and may be aided by medications such as Amitriptyline or Chlorpromazine. The latter drug increases the slow wave non-REM (deep) sleep and decrease muscular distress and tenderness.[77] An overworked housewife may find a nap useful. Four of our patients volunteered the information that a nap improved their symptoms.

Various stretching exercises are advised to keep the muscles supple.[7,17,23,78,79] These exercises have been elaborately described by Kraus.[79] Eight percent of our patients spontaneously described benefit from self-initiated nonstraining exercises, especially swimming. Avoidance of chill and use of heat in the form of a hot shower or hydrocollator packs relieve symptoms in most patients. Various forms of physical therapy such as massage,[7,78,90] diathermy,[7,17] and ultrasound[23] have all been found to be useful, though there is a paucity of controlled studies. Good posture[7] as well as weight loss in obese patients[5,15] should be emphasized.

For pain, salicylates may be useful,[81] and should be used first. Longer acting salicylates, such as salsalate, may allow increased patient compliance and cause fewer gastric side effects. Our experience has shown that other non-steroidal anti-inflammatory drugs, e.g., ibuprofen, naproxen, fenoprofen, indomethacin, tolmetin and sulindac are useful, and should be tried if adequate doses of salicylates fail to provide sufficient relief, or are not well tolerated. Similar observation has been made on the usefullness of these drugs in primary fibromyalgia.[4] Klinefelter[3] found phenylbutazone a useful drug in primary fibromyalgia. In view of potential toxicity, this drug may be used in resistant cases or

during a period of exacerbation of symptoms with careful monitoring of side-effects.

Injection of tender points with local analgesics such as procaine or Xylocaine have been helpful.[10,18,46,70,80,82] From our experience as well as that of others,[70] patients should be warned of possible increased pain occurring a few hours after the injection, but lasting less than 48 hr. Patients should further be advised to rest the injected areas for a few days. Local steroids have also been helpful.[18,68] We use both a local anesthetic mixed with a depo-corticosteroid preparation. The tender point is first located and then diffusely infiltrated with 3–5 cc of anesthetic, followed by injection of the mixture containing 20–40 mg of long acting corticosteroid in the same area.

A history of hypersensitivity reaction to Xylocaine should carefully be sought prior to injection, and one should make sure that no Xylocaine is inadvertently injected intravascularly. Some patients complain of lightheadedness following the injection, but more serious reactions may occur. Only a few most tender and symptomatic tender points should be injected at any one time. Ethyl chloride spray has been useful, especially in acute cases.[82,83] The detailed technique of the spray has been described by Travell.[82]

Systemic corticosteroids have also been claimed to be beneficial,[4,68] but without a controlled study. In a benign condition like primary fibromyalgia without evidence of inflammation, use of systemic corticosteriods cannot be justified in our opinion, with rare exceptions.

Acupuncture was found to be effective in an uncontrolled study.[35] Most patients were resistant to other modalities of treatment. Forty-six percent of patients claimed that acupuncture gave the best and longest lasting relief of symptoms of any type of treatment they had received.

Transcutaneous electric stimulation (TENS) has been used in the treatment of chronic pain due to various causes including myofascial syndrome[84] with variable degrees of relief. Biofeedback has been used in chronic tension headache,[85,86] localized form of myofascial pain such as temporomandibular syndrome,[87] as well as in chronic diffuse backache;[88] accordingly it may be beneficial in patients with primary fibromyalgia. However, as in acupuncture, no controlled study involving a large number of patients with primary fibromyalgia is available in TENS and biofeedback modalities.

Management of primary fibromyalgia is more than prescribing a drug or a certain type of physical therapy program. As stated earlier, it must never be implied that symptoms are all due to an anxiety state. However, the need for physical and mental relaxation should be emphasized. Some patients will require more emotional support than others. Tranquilizers in small doses may be required. The most important aspect of management is assurance and explanation of the probable pathophysiologic mechanisms involved. Management of primary fibromyalgia patients is a challenge and should be conceived as a comprehensive regimen, and can be most successful and gratifying.

SUMMARY

Detailed clinical study of 50 patients with primary fibromyalgia and 50 normal matched controls has shown a characteristic syndrome. Primary fibromyalgia patients are usually females, aged 25–40 yr, who complain of diffuse musculoskeletal aches, pains or stiffness associated with tiredness, anxiety, poor sleep, headaches, irritable bowel syndrome, subjective swelling in the articular and periarticular areas and numbness. Physical examination is characterized by presence of multiple tender points at specific sites and absence of joint swelling.

Symptoms are influenced by weather and activities, as well as by time of day (worse in the morning and the evening). In contrast, symptoms of psychogenic rheumatism patients have little fluctuation, if any, and are modulated by emotional rather than physical factors. In psychogenic rheumatism, there is diffuse tenderness rather than tender points at specific sites. Laboratory tests and roentgenologic findings in primary fibromyalgia are normal or negative. Primary fibromyalgia should be suspected by the presence of its own characteristic features, and not diagnosed just by the absence of other recognizable conditions.

This study has also shown that primary fibromyalgia is a poorly recognized condition. Patients were usually seen by many physicians who failed to provide a definite diagnosis despite frequent unnecessary investigations. A guideline

for diagnosis of primary fibromyalgia, based upon our observations, is suggested.

Management is usually gratifying in these frustrated patients. The most important aspects are a definite diagnosis, explanation of the various possible mechanisms responsible for the symptoms, and reassurance regarding the benign nature of this condition. A combination of reassurance, nonsteroidal antiinflammatory drugs, good sleep, local tender point injections, and various modes of physical therapy is successful in most cases.

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