

FIBROMYALGIA: ABSTRACTS 2003 FROM ARTICLES IN MEDICAL JOURNALS

The abstracts in this collection are intended to provide doctors and other health professionals with a convenient overview of trends in research on fibromyalgia published in medical journals in the year 2003. The studies were selected from the extensive literature on fibromyalgia so as to cover a wide range of subjects in limited space.

Abstracts for 2004 will be posted at intervals during the year. Similar collections of abstracts produced annually from 1999 on can be found on the website of the National Fibromyalgia Partnership: www.fmpartnership.org.

The abstracts are arranged in alphabetical order by lead author.

Aaron LA, Buchwald D

Chronic diffuse musculoskeletal pain, fibromyalgia and co-morbid unexplained clinical conditions

This chapter reviews our current knowledge on the presence of overlapping syndromes in one form of chronic diffuse pain, fibromyalgia. Patients with fibromyalgia often present with signs and symptoms of other unexplained clinical conditions, including chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorders, and multiple chemical sensitivities. **The high prevalence, impact on function and opportunities for treatment underscore the need for clinicians and researchers to screen routinely for co-morbid unexplained clinical conditions among persons with fibromyalgia.** We, therefore, describe a simple approach to screening for such conditions in accordance with published criteria. Interventions should directly address both fibromyalgia symptoms and co-morbid unexplained clinical conditions, as well as the multiple factors that propagate pain, fatigue and limitations in function.

Best Pract Res Clin Rheumatol 2003 Aug; 17(4):563–74

Al-Allaf AW, Mole PA, Paterson CR, Pullar T

Bone health in patients with fibromyalgia

OBJECTIVES: To determine whether women with fibromyalgia are at increased risk of developing osteoporosis or osteomalacia. **METHODS:** Forty premenopausal women with fibromyalgia and 37 age-matched female controls were studied. Broadband ultrasound attenuation (BUA) and velocity of sound (VOS) were measured at the calcaneum and bone mineral density was measured at the

forearm and lumbar spine using dual-energy X-ray absorptiometry. Serum calcium, alkaline phosphatase, gamma-glutamyl transferase, 25-hydroxyvitamin D and plasma viscosity were measured in all subjects and parathyroid hormone was measured in subjects recruited in the latter part of the study. **RESULTS:** Seventeen patients with fibromyalgia syndrome and seven controls had 25-hydroxyvitamin D concentrations < 20 nmol/l ($P < 0.015$) and in three FMS patients serum parathyroid hormone was raised. Bone density in fibromyalgia patients was slightly lower at the mid-distal forearm but comparable to that in controls at other sites. **CONCLUSIONS:** **There is no reason to recommend routine bone densitometry in fibromyalgia patients.** However, vitamin D subnutrition is common in these patients and this should be sought.

Rheumatology (Oxford) 2003 Oct; 42(10): 1202–6

Amel Kashipaz MR, Swinden D, Todd I, Powell RJ

Normal production of inflammatory cytokines in chronic fatigue and fibromyalgia syndromes determined by intracellular cytokine staining in short-term cultured blood mononuclear cells

It has been proposed that cytokines play a role in the pathogenesis of chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS). However, different studies have reported conflicting results using enzyme-linked immunosorbent assay or polymerase chain reaction to detect cytokines in these conditions. In the present study, for the first time, the production of inflammatory [interleukin (IL)-1alpha, IL-6, and TNF-alpha] and anti-inflammatory (IL-10) cytokines by CD14+ and CD14- peripheral blood mononuclear cells (PBMC) from chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) patients and sex- and age-matched normal subjects was investigated at the level of individual cells using the technique of intracellular cytokine staining and flow cytometry. Cultures were carried out in the presence of polymyxin B to inhibit the effect of endotoxins on cytokine production by monocytes. The mean intensity of fluorescence (MIF) and percentage of CD14+ (monocytes) and CD14- (lymphocytes) cytokine-producing mononuclear cells were comparable in patients and controls in either unstimulated or IFN-gamma-stimulated conditions. **Our study indicates that dysregulation of cytokine production by circulating monocytes or non-monocytic cells (lymphocytes) is not a dominant factor in the pathogenesis of CFS/FMS.**

Clin Exp Immunol 2003 May; 132(2):360–5

Assefi NP, Coy TV, Uslan D, Smith WR, Buchwald D

Financial, occupational, and personal consequences of disability in patients with chronic fatigue syndrome and fibromyalgia compared to other fatiguing conditions

OBJECTIVE: To examine the nature and degree of self-reported disability in patients with chronic fatigue syndrome (CFS) and its associated conditions, fibromyalgia (FM) and subsyndromal fatigue (CF), compared with a chronically fatiguing but unrelated medical condition (MED). **METHODS:** Six hundred and thirty patients evaluated at the University of Washington Chronic Fatigue Clinic were sent questionnaires asking them to identify the financial, occupational, and personal consequences of their fatiguing illness. Thorough medical evaluations had previously applied accepted criteria for defining CFS, FM, and CF. **RESULTS:** The FM groups (those with and without CFS) were among the least employed. Likewise, the FM and CFS groups, more frequently than the other groups, endorsed loss of material possessions (such as car), loss of job, and loss of support by friends and family, as well as recreational activities as a result of their fatiguing illness. There were no reliable differences between groups in use of disability benefits. **CONCLUSION:** **There is substantial illness-related disability among those evaluated at a specialized chronic fatigue clinic. Those reporting the most pervasive disability met criteria for FM either alone or in conjunction with CFS.** Employers and personal relations of patients with chronic fatigue should make a greater effort to accommodate the illness-related limitations of these conditions, especially for those with FM and CFS.

J Rheumatol 2003 Apr; 30(4):804–8

Astin JA, Berman BM, Bausell B, Lee WL, Hochberg M, Forsys KL

The efficacy of mindfulness meditation plus Qigong movement therapy in the treatment of fibromyalgia: a randomized controlled trial

OBJECTIVE: To test the short- and long-term benefits of an 8-week mind-body intervention that combined training in mindfulness meditation with Qigong movement therapy for individuals with fibromyalgia syndrome (FM). **METHODS:** A total of 128 individuals with FM were randomly assigned to the mind-body training program or an education support group that served as the control. Outcome measures were pain, disability (Fibromyalgia Impact Questionnaire), depression, myalgic score (number and severity of tender points), 6-minute walk time, and coping strategies, which were assessed at baseline and at 8, 16, and 24 weeks. **RESULTS:** Both groups registered statistically significant improvements across time for the Fibromyalgia Impact Questionnaire, Total Myalgic Score, Pain, and Depression, and no improvement in the number of feet traversed in the 6 minute walk. However, there was no difference in either the rate or magnitude

of these changes between the mind-body training group and the education control group. Salutory changes occurring by the eighth week (which corresponded to the end of the mind-body and education control group sessions) were largely maintained by both groups throughout the 6 month followup period. **CONCLUSION:** While both groups showed improvement on a number of outcome variables, **there was no evidence that the multimodal mind-body intervention for FM was superior to education and support as a treatment option.** Additional randomized controlled trials are needed before interventions of this kind can be recommended for treatment of FM.

J Rheumatol 2003 Oct; 30(10): 2257–62

Bennett RM, Kamin M, Karim R, Rosenthal N

Tramadol and acetaminophen combination tablets in the treatment of fibromyalgia pain: a double-blind, randomized, placebo-controlled study

PURPOSE: To evaluate the efficacy and safety of a combination analgesic tablet (37.5 mg tramadol/325 mg acetaminophen) for the treatment of fibromyalgia pain. **METHODS:** This 91-day, multicenter, double-blind, randomized, placebo-controlled study compared tramadol/acetaminophen combination tablets with placebo. The primary outcome variable was cumulative time to discontinuation (Kaplan-Meier analysis). Secondary measures at the end of the study included pain, pain relief, total tender points, myalgia, health status, and Fibromyalgia Impact Questionnaire scores. **RESULTS:** Of the 315 subjects who were enrolled in the study, 313 (294 women [94%], mean [± SD] age, 50 ± 10 years) completed at least one postrandomization efficacy assessment (tramadol/acetaminophen: n = 156; placebo: n = 157). Discontinuation of treatment for any reason was less common in those treated with tramadol/acetaminophen compared with placebo (48% vs. 62%, P = 0.004). Tramadol/acetaminophen-treated subjects also had significantly less pain at the end of the study (53 ± 32 vs. 65 ± 29 on a visual analog scale of 0 to 100, P <0.001), and better pain relief (1.7 ± 1.4 vs. 0.8 ± 1.3 on a scale of -1 to 4, P <0.001) and Fibromyalgia Impact Questionnaire scores (P = 0.008). Indexes of physical functioning, role-physical, body pain, health transition, and physical component summary all improved significantly in the tramadol/acetaminophen-treated subjects. Discontinuation due to adverse events occurred in 19% (n = 29) of tramadol/acetaminophen-treated subjects and 12% (n = 18) of placebo-treated subjects (P = 0.09). The mean dose of tramadol/acetaminophen was 4.0 ± 1.8 tablets per day. **CONCLUSION: A tramadol/acetaminophen combination tablet was effective for the treatment of fibromyalgia pain without any serious adverse effects.**

Am J Med 2003 May; 114(7):537–45

Buskila D, Press J, Abu-Shakra M

Fibromyalgia in systemic lupus erythematosus: prevalence and clinical implications

Fibromyalgia (FM) is common in SLE patients, and is the source of many of the symptoms and much of the disability in these patients. The association of FM and SLE may pose diagnostic dilemmas. **Fibromyalgia does not correlate with SLE disease activity, but the clinical features of FM in these patients may contribute to a misinterpretation of lupus activity.** The recognition of the association between SLE and FM is relevant to every physician who treats lupus patients.

Clin Rev Allergy Immunol 2003 Aug; 25(1):25–8

Chang L, Berman S, Mayer EA, Suyenobu B, Derbyshire S, Naliboff B, Vogt B, FitzGerald L, Mandelkern MA

Brain responses to visceral and somatic stimuli in patients with irritable bowel syndrome with and without fibromyalgia

OBJECTIVE: Symptoms of irritable bowel syndrome (IBS) and fibromyalgia (FM) commonly coexist. We hypothesized that one of the mechanisms underlying this comorbidity is increased activation of brain regions concerned with the processing and modulation of visceral and somatic afferent information, in particular subregions of the anterior cingulate cortex (ACC). METHODS: Regional cerebral blood flow (rCBF) was assessed in age-matched female IBS (n = 10) and IBS + FM (n = 10) subjects using H(2)(15)O positron emission tomography during noxious visceral (rectal) and somatic pressure stimuli. RESULTS: GI symptom severity was significantly higher in the IBS patients compared with the IBS + FM patients (p < 0.05). In addition, IBS + FM patients rated somatic pain as more intense than their abdominal pain (p < 0.05). Whereas the somatic stimulus was less unpleasant than the visceral stimulus for IBS patients without FM, the somatic and visceral stimuli were equally unpleasant in the IBS + FM group. Group differences in regional brain activation were entirely within the middle subregion of the ACC. There was a greater rCBF increase in response to noxious visceral stimuli in IBS patients and to somatic stimuli in IBS + FM patients. CONCLUSION: **Chronic stimulus-specific enhancement of ACC responses to sensory stimuli in both syndromes may be associated with cognitive enhancement of either visceral (IBS) or somatic (IBS + FM) sensory input and may play a key pathophysiologic role in these chronic pain syndromes.**

Am J Gastroenterol 2003 Jun; 98(6):1354–61

Currey SS, Rao JK, Winfield JB, Callahan LF

Performance of a generic health-related quality of life measure in a clinic population with rheumatic disease

OBJECTIVE: To assess the performance of a generic health-related quality of life (HRQOL) measure in a rheumatology clinic population. **METHODS:** Participants (n = 619) with fibromyalgia, rheumatoid arthritis, or osteoarthritis receiving care from rheumatologists completed mailed questionnaires that included the Behavioral Risk Factor Surveillance System (BRFSS) HRQOL measure and condition-specific measures assessing disability, pain, fatigue, and helplessness. The BRFSS assesses global health and number of days in the past 30 of poor physical or mental health or activity limitation. The overall sample was described, followed by comparison of adjusted scores on all HRQOL measures by diagnosis. **RESULTS:** Participants reported mild difficulty with activities of daily living, marked pain and fatigue, and moderate helplessness. Participants reported a mean of 8 or more days out of 30 of poor physical and mental health and activity limitations; more than 40% reported poor or fair health. Participants with fibromyalgia reported more ill health on condition-specific measures and the BRFSS HRQOL measures than did participants with osteoarthritis or rheumatoid arthritis. **CONCLUSION:** **The BRFSS HRQOL measure is a brief, easily administered, generic health indicator that shows differences among rheumatic disease diagnoses.**

Arthritis Rheum 2003 Oct 15; 49(5): 658–64

Dobkin PL, De Civita M, Bernatsky S, Kang H, Baron M

Does psychological vulnerability determine health-care utilization in fibromyalgia?

OBJECTIVES: Patients with fibromyalgia (FM) undergo multiple testing and referral to specialists, and often use complementary/alternative medicine (CAM) services. The objectives of the study were: (i) to document health service utilization, and (ii) to examine whether psychological vulnerability was associated with visits to physicians and CAM providers. **METHODS:** Women (N = 178) with a diagnosis of primary FM completed a psychosocial test measuring pain, perceived stress, global psychological distress, sexual abuse history, co-morbidity and disability due to FM. Subjects also completed a health services questionnaire, documenting visits to physicians and CAM providers during the previous 6 months. Psychological vulnerability was operationalized as obtaining high scores on psychological distress, perceived stress and reporting at least one abusive event. **RESULTS:** The average number of visits was 7.2 to physicians and 11.3 to CAM providers. **CONCLUSIONS:** The number of physician visits was significantly associated with more co-morbidity. **Psychologically vulnerable subjects were more likely to use CAM services than those not so classified.**

Rheumatology (Oxford) 2003 Nov; 42(11): 1324–31

Endresen GK

Mycoplasma blood infection in chronic fatigue and fibromyalgia syndromes

Chronic fatigue syndrome (CFS) and fibromyalgia syndrome (FMS) are characterised by a lack of consistent laboratory and clinical abnormalities. Although they are distinguishable as separate syndromes based on established criteria, a great number of patients are diagnosed with both. **In studies using polymerase chain reaction methods, mycoplasma blood infection has been detected in about 50% of patients with CFS and/or FMS, including patients with Gulf War illnesses and symptoms that overlap with one or both syndromes.** Such infection is detected in only about 10% of healthy individuals, significantly less than in patients. Most patients with CFS/FMS who have mycoplasma infection appear to recover and reach their pre-illness state after long-term antibiotic therapy with doxycycline, and the infection can not be detected after recovery. By means of [determining] causation and therapy, mycoplasma blood infection may permit a further subclassification of CFS and FMS. It is not clear whether mycoplasmas are associated with CFS/FMS as causal agents, cofactors, or opportunistic infections in patients with immune disturbances. Whether mycoplasma infection can be detected in about 50% of all patient populations with CFS and/or FMS is yet to be determined.

Rheumatol Int 2003 Sep; 23(5):211–5

Fitzcharles MA, Costa DD, Poyhia R

A study of standard care in fibromyalgia syndrome: a favorable outcome

OBJECTIVE: A longitudinal prospective study was undertaken to examine the outcome of fibromyalgia (FM) with standard medical care, as well as factors that might either predict or influence this outcome. **METHODS:** Eighty-two women with clinical FM were evaluated at baseline and 70 were followed for a mean of 40 months. Patients continued their usual management for FM as prescribed by their own physicians. The primary outcome variable was patient's overall status compared to baseline on a 7 point Likert scale (range 1 = much worse, 7 = much better). Secondary outcome measures included measurements for pain, fatigue, and patient and physician global assessment on a visual analog scale. Additional functional measures were the disease-specific Fibromyalgia Impact Questionnaire (FIQ), and the generic Health Assessment Questionnaire (HAQ). **RESULTS:** Of 70 (85%) patients who were followed up at 3 years, 33 (47%) reported overall moderate to marked improvement, and the remaining 53% reported either slight improvement, no change, or deterioration. The improved group (n = 33) compared to those that remained the same or worsened (n = 37) showed significant differ-

ences for change of score from baseline for tender point count, patient global assessment, sleep disturbance, fatigue, pain, FIQ and HAQ, and were younger, 46 versus 51 years. No other baseline demographic or disease variables discriminated between the 2 groups. **The only baseline predictors for a favorable outcome were younger age and less sleep disturbance.** CONCLUSION: The overall outcome in this group was favorable, with almost half the sample reporting clinically meaningful improvement in overall FM status. These findings are discussed in terms of their implications regarding current theory on the pathogenesis of FM.

J Rheumatol 2003 Jan; 30(1):154–9

Fitzcharles MA, Boulos P

Inaccuracy in the diagnosis of fibromyalgia syndrome: analysis of referrals

OBJECTIVE: To examine prospectively the accuracy of an initial diagnosis for fibromyalgia (FM). METHODS: All patients newly referred for rheumatology consultation in a 6-month period were evaluated prospectively for either a preceding, current or subsequent diagnosis of FM. Clinical characteristics, previous and subsequent management and health care utilization were assessed. The final diagnosis at 6 months was verified and accuracy regarding the diagnosis of FM was assessed. RESULTS: Seventy-six (12%) of all new patients were either referred with a question of FM or finally diagnosed with FM. At the final evaluation the accuracy of the diagnosis regarding FM by either the referring physician or by the rheumatologist at the time of the initial visit was correct in 34% of patients. The FM group in comparison with those with some other rheumatological diagnosis had more tender points (12.5 vs 4) and were more fatigued. In contrast, prolonged early morning stiffness and limitation of lumbar spinal mobility in more than one plane was more common in the non-FM group. CONCLUSION: **There is a disturbing inaccuracy, mostly observed to be overdiagnosis, in the diagnosis of FM by referring physicians. This finding may help explain the current high reported rates of FM and caution physicians to consider other diagnostic possibilities when addressing diffuse musculoskeletal pain.**

Rheumatology (Oxford) 2003 Feb; 42(2):263–7

Giesecke T, Williams DA, Harris RE, Cupps TR, Tian X, Tian TX, Gracely RH, Clauw DJ

Subgrouping of fibromyalgia patients on the basis of pressure-pain thresholds and psychological factors

OBJECTIVE: Although the American College of Rheumatology (ACR) criteria for fibromyalgia are used to identify individuals with both widespread pain and

tenderness, individuals who meet these criteria are not a homogeneous group. Patients differ in their accompanying clinical symptoms, as well as in the relative contributions of biologic, psychological, and cognitive factors to their symptom expression. Therefore, it seems useful to identify subsets of fibromyalgia patients on the basis of which of these factors are present. Previous attempts at identifying subsets have been based solely on psychological and cognitive features. In this study, we attempt to identify patient subsets by incorporating these features as well as the degree of hyperalgesia/tenderness, which is a key neurobiologic feature of this illness. METHODS: Ninety-seven individuals meeting the ACR criteria for fibromyalgia finished the same battery of self-report and evoked-pain testing. Analyzed variables were obtained from several domains, consisting of 1) mood (evaluated by the Center for Epidemiologic Studies Depression Scale [for depression] and the State-Trait Personality Inventory [for symptoms of trait-related anxiety]), 2) cognition (by the catastrophizing and control of pain subscales of the Coping Strategies Questionnaire), and 3) hyperalgesia/tenderness (by dolorimetry and random pressure-pain applied at suprathreshold values). Cluster analytic procedures were used to distinguish subgroups of fibromyalgia patients based on these domains. RESULTS: Three clusters best fit the data. Multivariate analysis of variance (ANOVA) confirmed that each variable was differentiated by the cluster solution (Wilks' lambda [degrees of freedom 6,89] = 0.123, $P < 0.0001$), with univariate ANOVAs also indicating significant differences (all $P < 0.05$). One subgroup of patients ($n = 50$) was characterized by moderate mood ratings, moderate levels of catastrophizing and perceived control over pain, and low levels of tenderness. A second subgroup ($n = 31$) displayed significantly elevated values on the mood assessments, the highest values on the catastrophizing subscale, the lowest values for perceived control over pain, and high levels of tenderness. The third group ($n = 16$) had normal mood ratings, very low levels of catastrophizing, and the highest level of perceived control over pain, but these subjects showed extreme tenderness on evoked-pain testing. CONCLUSION: These data help support the clinical impression that there are distinct subgroups of patients with fibromyalgia. **There appears to be a group of fibromyalgia patients who exhibit extreme tenderness but lack any associated psychological/cognitive factors, an intermediate group who display moderate tenderness and have normal mood, and a group in whom mood and cognitive factors may be significantly influencing the symptom report.**

Arthritis Rheum 2003 Oct; 48(10): 291–22

Gronemann ST, Ribel-Madsen S, Bartels EM,
Danneskiold-Samsøe B, Bliddal H

Collagen and muscle pathology in fibromyalgia patients

OBJECTIVE: To measure collagen concentration and search for muscle pathology in muscle non-tender-point areas from fibromyalgia (FM) patients. METHODS:

Muscle biopsies were obtained from m. vastus lateralis of 27 carefully selected, female fibromyalgia patients, and from eight age-matched female control subjects. Amino acids were determined by HPLC, and electron microscopy was performed. RESULTS: The FM patients had lower hydroxyproline and lower total concentration of the major amino acids of collagen than the controls. No significant difference was seen in the concentration of the major amino acids of myosin or of total protein. Electron microscopy showed no significant differences between FM patients and controls although atrophied muscle fibrils occurred in FM patients only, but frequencies were not significantly different. CONCLUSION: **Fibromyalgia patients had a significantly lower amount of intramuscular collagen. This may lower the threshold for muscle micro-injury and thereby result in non-specific signs of muscle pathology.**

Rheumatology (Oxford); 2003 Jul 16

Holdcraft LC, Assefi N, Buchwald D

Complementary and alternative medicine in fibromyalgia and related syndromes

Complementary and alternative medicine (CAM) has gained increasing popularity, particularly among individuals with fibromyalgia syndrome (FMS) for which traditional medicine has generally been ineffective. A systematic review of randomized controlled trials (RCTs) and non-RCTs on CAM studies for FMS was conducted to evaluate the empirical evidence for their effectiveness. Few RCTs achieved high scores on the CONSORT, a standardized evaluation of the quality of methodology reporting. **Acupuncture, some herbal and nutritional supplements (magnesium, SAMe) and massage therapy have the best evidence for effectiveness with FMS.** Other CAM therapies have either been evaluated in only one RCT with positive results (Chlorella, biofeedback, relaxation), in multiple RCTs with mixed results (magnet therapies), or have positive results from studies with methodological flaws (homeopathy, botanical oils, balneotherapy, anthocyanidins, dietary modifications). Lastly, other CAM therapies have neither well-designed studies nor positive results and are not currently recommended for FMS treatment (chiropractic care).

Best Pract Res Clin Rheumatol 2003 Aug; 17(4):667–83

Kozanoglu E, Canataroglu A, Abayli B, Colakoglu S, Goncu K

Fibromyalgia syndrome in patients with hepatitis C infection

Fibromyalgia syndrome (FS) is characterized by widespread pain and tenderness at specific anatomic sites. Different theories have been proposed in the etiopathogenesis of this syndrome, and besides genetic, neuroendocrine, psychologic, and traumatic causes, infections have also been reported. The aim of the present

study was to evaluate the presence of FS in patients with hepatitis C virus (HCV) infection. Ninety-five patients with chronic HCV infection and 95 healthy controls were enrolled in the study. The 1990 American College of Rheumatology classification criteria were used for the diagnosis of FS. Tender point count, pain intensity, sleep disturbance, stiffness, headache, paresthesia, fatigue, irritable bowel syndrome (IBS), and sicca- and Raynaud-like symptoms were assessed. Fibromyalgia was found in 18.9% of patients and 5.3% of healthy controls. Mean tender point count, pain intensity scored on a visual analog scale (VAS), sleep disturbance, stiffness, paresthesia, and fatigue were higher in the HCV group. No significant relationship was observed between the two groups regarding headache, IBS, and sicca- and Raynaud-like symptoms. In addition, mean tender point count and pain intensity scores were also significantly higher in HCV patients with FS than in control subjects with FS. All of the symptoms except stiffness were not statistically significant between the HCV and control groups with FS. **Our results demonstrate a tendency toward higher prevalence of FS in patients with HCV infection.** Besides various extrahepatic features, musculoskeletal disorders including fibromyalgia might be expected in the progression of HCV infection. Detailed examination of the patients helps to differentiate FS from other musculoskeletal complications of HCV infection. This will provide appropriate management approaches and better quality of life for them.

Rheumatol Int 2003 Sep; 23(5):248–51

Maekawa K, Twe C, Lotaif A, Chiappelli F, Clark GT

Function of beta-adrenergic receptors on mononuclear cells in female patients with fibromyalgia

OBJECTIVE: To investigate the beta-adrenergic receptors (betaAR) in patients with chronic fibromyalgia syndrome (FM). These receptors are present on circulating mononuclear cells, and activation of G-protein coupled receptors like betaAR leads to an increase in the intracellular level of cyclic adenosine monophosphate (cAMP). Therefore, cAMP levels can be used to indirectly assess the functional status of the receptor. **METHODS:** Eight female patients with FM and 9 matched healthy female controls participated in this study. Blood samples were drawn from subjects' antecubital vein in the morning. Mononuclear cells were isolated from the whole blood according to Boyum's method. Basal and stimulated intracellular cAMP levels were determined by enzyme immunoassay. Aliquots of 10⁶ cells were incubated with or without stimulation of beta-agonist isoproterenol for 5 min. Two different concentrations of isoproterenol (10⁻³ M and 10⁻⁵ M) were utilized. **RESULTS:** The basal cAMP levels in patients with FM (3.02 +/- 0.44 pmol/10⁶ cells) were slightly more elevated (but not statistically different; p = 0.124, Mann-Whitney U test) than that of the control group (2.26 +/- 0.39 pmol/10⁶ cells). Proterenol 10⁻³ M stimulation significantly increased intracellular cAMP from the basal levels in both groups (FM group, p = 0.008;

control group, $p = 0.011$). However, isoproterenol 10^{-5} M did not increase mean intracellular cAMP levels in the FM group ($p = 0.74$), while a significant increase was observed in the control group ($p = 0.012$). **CONCLUSION: These preliminary results suggest that diminished betaAR function is associated with the chronic FM state.**

J Rheumatol 2003 Feb; 30(2):364–8

Mannerkorpi K, Iversen MD

Physical exercise in fibromyalgia and related syndromes

Fibromyalgia and related syndromes are characterized by chronic pain and fatigue. This chapter identifies the types of exercise that are effective for these patients and provides recommendations for exercise prescriptions. Based on a systematic review of randomized controlled studies of exercise, we suggest that low-intensity aerobic exercise, such as walking, can improve function and symptoms. Aerobic exercise performed twice a week at moderate intensity can improve aerobic capacity and reduce tenderness. Pool exercise can improve function, distress and symptoms. Strength training at adequate load can improve strength without exacerbation of symptoms. **Most patients tolerate low-intensity exercise. High-intensity exercise should be undertaken with caution.** Due to the large variability of functioning and symptom severity in patient populations, exercise prescriptions should be individualized and should include a long-term plan to maximize functioning and wellbeing. Studies with larger populations, allowing subgroup analyses regarding benefits and adverse effects of programmes, are needed.

Best Pract Res Clin Rheumatol 2003 Aug; 17(4):629–47

Marcus DA

Current trends in fibromyalgia research

The development of standardised criteria for the diagnosis of fibromyalgia in 1990 has allowed careful study of this chronically painful syndrome. Epidemiological studies show increased symptoms and disability in patients with fibromyalgia, compared with other conditions associated with chronic, widespread pain. In addition, prevalence and severity of fibromyalgia symptoms are increased in women. **Current studies have identified strong evidence for central sensitisation in fibromyalgia.** Data from these studies may expand effective treatment options for fibromyalgia.

Expert Opin Pharmacother 2003 Oct; 4(10): 1687–95

Martinez-Lavin M, Lopez S, Medina M, Nava A

Use of the Leeds assessment of neuropathic symptoms and signs questionnaire in patients with fibromyalgia

OBJECTIVE: Neuropathic pain syndrome is characterized by chronic, stimulus-independent pain sensation accompanied by hyperalgesia/allodynia and paresthesia. Fibromyalgia (FM) syndrome displays such features. The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) Pain Scale is an instrument developed and validated to recognize neuropathic pain and set it apart from nociceptive pain. **METHODS:** This study assessed the responses of patients with FM versus patients with rheumatoid arthritis (RA) to the LANSS Pain Scale questionnaire. Twenty patients with FM and 20 patients with RA answered the Fibromyalgia Impact Questionnaire and LANSS Pain Scale questions related to the following neuropathic sensory disturbance domains: dysesthetic, autonomic, evoked, paroxysmal, and thermal. **RESULTS:** Pain severity was similar in both groups according to visual analog scale values (5.3 +/- 3.0 for FM v 5.4 +/- 3.1 for RA). There were sharp differences between FM and RA groups in the percentage of affirmative responses to 4 of 5 sensory disturbance questions: dysesthetic (95 v 30), evoked (95 v 35), paroxysmal (90 v 15), and thermal (90 v 20); $P < .0001$ for each comparison. **CONCLUSIONS:** **The high prevalence of associated sensory disturbances supports the notion that FM is a neuropathic pain syndrome. Clinical Relevance: The LANSS Pain Scale items may become a useful, easily applied bedside test to differentiate FM pain from the nociceptive pain present in RA and in similar arthritic illnesses.**

Semin Arthritis Rheum 2003 Jun; 32(6):407-11

McCall-Hosenfeld JS, Goldenberg DL, Hurwitz S, Adler GK

Growth hormone and insulin-like growth factor-1 concentrations in women with fibromyalgia

OBJECTIVE: To determine activity of the growth hormone-insulin-like growth factor-1 (GH-IGF-1) axis in women with fibromyalgia (FM). **METHODS:** Premenopausal women with FM (n = 24) and premenopausal healthy women (n = 27) were studied. IGF-1 was measured in 23 patients with FM and 25 controls. GH was measured during a stepped hypoglycemic hyperinsulinemic clamp procedure (blood glucose decreased from 90 to 40 mg/dl every 30 min in 10 mg/dl decrements) in 12 FM and 13 control subjects. **RESULTS:** IGF-1 concentrations were similar in the FM (200 +/- 71 ng/ml, mean +/- SD) and control (184 +/- 70 ng/ml) groups. By multiple variable analysis, IGF-1 was negatively associated with age ($p = 0.0006$), body mass index (BMI) ($p = 0.006$), and 24 h urinary free cortisol ($p = 0.007$) in healthy controls. Even after accounting for these factors, there was no association between FM and IGF-1. The average peak GH achieved

during hypoglycemia was lower in patients with FM (range 5 to 58 ng/ml, median 13 ng/ml) versus controls (6 to 68 ng/ml, median 21 ng/ml) ($p = 0.04$). However, BMI was a significant predictor of average peak GH in FM ($r = -0.62$, $p < 0.01$) and control subjects ($r = -0.40$, $p = 0.06$). After considering BMI, there was no significant association between FM subjects and the average peak GH ($p = 0.20$). **CONCLUSION: In this sample of premenopausal women with FM, the activity of the GH-IGF-1 axis was similar to that of healthy controls. Increases in age and obesity were both strongly associated with lower activity of this axis, suggesting that these factors must be considered when studying activity of the GH-IGF-1 axis in FM.**

J Rheumatol 2003 Apr; 30(4):809–14

Neumann L, Buskila D

Epidemiology of fibromyalgia

Chronic widespread pain, the cardinal symptom of fibromyalgia (FM), is common in the general population, with comparable prevalence rates of 7.3% to 12.9% across different countries. The prevalence of FM in the general population was reported to range from 0.5% to 5% and up to 15.7% in the clinic. The common association of FM with other rheumatic disorders, chronic viral infections, and systemic illnesses has been well documented in several studies. Up to 65% of patients with systemic lupus erythematosus meet the criteria for FM. **FM is considered a member of the family of functional somatic syndromes. These syndromes are very common and share a similar phenomenology, epidemiologic characteristics, high rates of occurrence, a common pathogenesis, and similar management strategies.** A high prevalence of FM was demonstrated among relatives of patients with FM and it may be attributed to genetic and environmental factors.

Curr Pain Headache Rep 2003 Oct; 7(5): 362–8

Peres MF

Fibromyalgia, fatigue, and headache disorders

Fibromyalgia, chronic fatigue, and primary headaches are common and debilitating disorders, and their related symptoms of widespread pain, fatigue, and headache have complex interactions and different implications for classification, diagnosis, mechanisms, and treatment. **The “continuum” or “spectrum” idea and the modular headache theory are fundamental concepts in understanding these interactions.** The overlap between symptom-based conditions leads the reasons to consider them as “functional somatic syndromes.” Management of these patients includes a correct diagnosis, appropriate investigation for

associated conditions, adequate treatment, and considering the therapeutic opportunities and limitations the comorbid disorders may impose.

Curr Neurol Neurosci Rep 2003 Mar; 3(2):97–103

Pfeiffer A, Thompson JM, Nelson A, Tucker S, Luedtke C,
Finnie S, Sletten C, Postier J

Effects of a 1.5-day multidisciplinary outpatient treatment program for fibromyalgia: a pilot study

OBJECTIVE: The purpose of this pilot study was to determine the effect of a 1.5-day multidisciplinary fibromyalgia treatment program on impact of illness, depression, and life fulfillment. **DESIGN:** A sample of 100 consecutive enrollees in a 1.5-day multidisciplinary group outpatient fibromyalgia treatment program between February 14, 2000, and May 9, 2000, in a tertiary medical center was used for this study. The Fibromyalgia Impact Questionnaire, the Life Fulfillment and Satisfaction Scales, and the Center for Epidemiologic Studies Depression Scale were administered to subjects immediately preceding the treatment program and by mail 1 mo after completing the program. **RESULTS:** The 78 subjects who returned their surveys 1 mo after treatment demonstrated significant improvement in the area of the impact of illness as measured by the Fibromyalgia Impact Questionnaire total score (51.3–44.7, $P < 0.002$). There was no significant improvement in depressive symptoms ($P < 0.056$) or the level of life fulfillment ($P < 0.53$). Subjects with depression improved on the Fibromyalgia Impact Questionnaire to the same degree as those without depression. The 22 nonresponders did not differ significantly from the responders in the variables of sex, age, pretreatment Fibromyalgia Impact Questionnaire score, marital status, educational level, family income, duration of symptoms, or history of depression. **CONCLUSIONS:** **These results suggest that a 1.5-day multidisciplinary fibromyalgia treatment program does have a significant positive effect on the impact of illness among patients with fibromyalgia with or without concomitant depression and may be a cost-effective model for the treatment of these patients.**

Am J Phys Med Rehabil 2003 Mar; 82(3):186–91

Rains JC, Penzien DB

Sleep and chronic pain. Challenges to the alpha-EEG sleep pattern as a pain-specific sleep anomaly

OBJECTIVE: The alpha-EEG sleep anomaly has been associated with chronic benign pain syndromes. Although controversial, the anomaly is believed by some to be an important biologic correlate of certain otherwise poorly explained painful conditions (e.g., fibromyalgia and chronic fatigue syndrome). To shed further

light on this phenomenon, this study compared the sleep and psychological characteristics of chronic pain patients who exhibited the alpha-EEG sleep anomaly with pain-free psychiatric and medical patients who also were found to exhibit the alpha-EEG anomaly. **METHODS:** The alpha-EEG sleep was identified in the polysomnographic records of 5% of over 1000 consecutive sleep patients. Objective sleep parameters, daytime sleepiness and psychological characteristics (Minnesota Multiphasic Personality Inventory [MMPI] scores) of patients exhibiting this anomaly were examined. **RESULTS:** The alpha-EEG anomaly was identified in only 5% of the total patient sample. Patients with the alpha-EEG anomaly could be further classified into three diagnostic subgroups: chronic pain, psychiatric and other medical/sleep disorders. The subgroups were compared on sleep parameters and psychological characteristics. Less than 40% of the patients exhibiting the alpha-EEG anomaly experienced chronic pain. Chronic pain patients evidenced disturbed sleep patterns and psychological characteristics that were for the most part similar to those observed in some pain-free medical and psychiatric patients. Only the medical subgroup exhibited objective daytime sleepiness. The alpha-EEG sleep disturbance was not accounted for by psychological characteristics. **CONCLUSIONS: These findings challenge the notion that alpha-EEG sleep is of direct etiological significance in producing the pain complaint among patients with chronic pain since the alpha-EEG sleep was not a sufficient condition for pain.**

J Psychosom Res 2003 Jan; 54(1):77–83

Rhodus NL, Friction J, Carlson P, Messner R

Oral symptoms associated with fibromyalgia syndrome

OBJECTIVE: Studies have described oral problems associated with fibromyalgia syndrome (FM), including sicca, oral ulcerations, and orofacial pain. We evaluated the prevalence and profile of various oral symptoms in a population of patients diagnosed with FM. **METHODS:** Subjects diagnosed with FM by American College of Rheumatology criteria ($n = 67$; all women, mean age \pm SEM 47.6 \pm 2.3 yrs) were enrolled in the study after meeting strict exclusion criteria (i.e., oral mucosal conditions, Sjögren's syndrome, anemia, inflammatory bowel syndrome or other gastrointestinal disturbances, and other disorders that may manifest oral symptoms). Subjective oral evaluations were carried out for each subject, including oral pain (Melzack scale) for glossodynia, throbbing, aching, etc.; temporomandibular joint dysfunction (TMD); xerostomia (including intake of fluids, functional problems, etc.); dysphagia; dysgeusia; and information about frequent oral ulcerations or lesions. Psychological tests including Beck Depression Scale (BDS) and Spielberger Anxiety Scale (SAS) were administered. **RESULTS:** The results indicated a significant prevalence in some subjects' oral symptoms, compared to age and sex matched control data (mean \pm SEM) for xerostomia 70.9% vs 5.7% ($p < 0.001$); glossodynia 32.8% vs 1.1% ($p < 0.001$);

TMD 67.6% vs 20% ($p < 0.01$); dysphagia 37.3% vs 0.4% ($p < 0.001$); dysgeusia 34.2% vs 1.0% ($p < 0.001$). Other findings were not significantly different from controls: oral ulcerations/lesions 5.1% vs 4.4% (NS); BDS 34% vs 30% (NS); SAS 21% vs 19% (NS). The average visual analog scale (100 mm) for burning pain was 53.0 +/- 5.6 ($p < 0.001$). Anxiety and depression scores were no different in the FM subjects compared to controls with chronic pain conditions. **CONCLUSION: These data indicate that patients with FM have significantly increased prevalence of xerostomia, glossodynia, dysphagia, dysgeusia, and TMD compared to controls, with no significant difference in clinical oral lesions or psychological status.**

J Rheumatol 2003 Aug; 30(8):1841-5

Robinson RL, Birnbaum HG, Morley MA, Sisitsky T, Greenberg PE, Claxton AJ

Economic cost and epidemiological characteristics of patients with fibromyalgia claims

OBJECTIVE: Fibromyalgia (FM) is characterized by widespread pain that can lead to significant patient disability, complex management decisions for physicians, and economic burden on society. We investigated the total costs of FM in an employer population. **METHODS:** Administrative claims data of a Fortune 100 manufacturer were used to quantify direct (i.e., medical and pharmaceutical claims) and indirect (i.e., disability claims and imputed absenteeism) costs associated with FM. A total of 4699 patients with at least one FM claim between 1996 and 1998 were contrasted with a 10% random sample of the overall beneficiary population. Employee-only subsets of both samples also were drawn. **RESULTS:** Medical utilization, receipt of prescription drugs, and annual total costs were proportionately similar yet significantly greater among FM claimants than the overall sample (all $p < 0.0001$). Total annual costs for FM claimants were \$5945 versus \$2486 for the typical beneficiary ($p < 0.0001$). Six percent of these costs were attributable to FM-specific claims. The prevalence of disability was twice as high among FM employees than overall employees ($p < 0.0001$). For every dollar spent on FM-specific claims, the employer spent another \$57 to \$143 on additional direct and indirect costs. **CONCLUSION:** Hidden costs of disability and comorbidities greatly increase the true burden of FM. **Regardless of the clinical understanding of FM, when a claim for FM is present, considerable costs are involved. Findings suggest that within the management of FM there may be large cost-offset opportunities for reductions in patient, physician, and employer burdens.**

J Rheumatol 2003 Jun; 30(6):1318-25

Roelofs J, Peters ML, McCracken L, Vlaeyen JW

The pain vigilance and awareness questionnaire (PVAQ): further psychometric evaluation in fibromyalgia and other chronic pain syndromes

In chronic pain patients, preoccupation with or attention to pain is associated with pain-related fear and perceived pain severity. The current study investigated psychometric properties of the pain vigilance and awareness questionnaire (PVAQ). An exploratory factor analysis on Dutch fibromyalgia patients indicated that a two-factor solution was most suitable. The first factor could be referred to as attention to pain and the second factor was interpreted as attention to changes in pain. A confirmatory factor analysis, testing three different factor structures in two independent samples (Dutch fibromyalgia patients and American pain patients with various diagnoses) showed that the goodness-of-fit indicators for all models were satisfactory. The existence of the previously reported intrusion subscale of the PVAQ as a unique construct within the PVAQ was discussed. This subscale should be further extended by non-reverse-keyed items. With regard to the convergent validity, the PVAQ was highly correlated with related constructs such as the pain catastrophizing scale (PCS), pain anxiety symptoms scale (PASS), and Tampa scale of kinesiophobia (TSK). The attention to pain subscale was significantly stronger associated with these pain-related measures than the attention to changes in pain subscale, indicating that **attention to changes in pain is a distinctive construct**. The uniqueness of the attention to changes in pain subscale was also supported by an exploratory factor analysis on all items of the PVAQ, PCS, PASS, and TSK which showed that all items from that scale loaded on one separate factor. Overall, the PVAQ showed good internal consistency. Implications for future research and treatment interventions are discussed.

Pain 2003 Feb; 101(3):299–306

Salemi S, Rethage J, Wollina U, Michel BA, Gay RE, Gay S, Sprött H

Detection of interleukin 1beta (IL-1beta), IL-6, and tumor necrosis factor-alpha in skin of patients with fibromyalgia

OBJECTIVE: To determine if abnormal collagen metabolism is correlated with neurogenic inflammation, a potential activator of collagen metabolism, in patients with fibromyalgia (FM). **METHODS:** The presence of inflammatory cytokines, interleukin (IL)-1beta, IL-6, and tumor necrosis factor (TNF)-a was investigated in skin tissues by using reverse transcription-polymerase chain reaction (RT-PCR) and immunohistochemistry. Fifty-three skin biopsies from female patients with FM (30-65 years of age) were examined and compared to skin biopsies of 10 age and sex matched healthy controls. Biopsies were obtained from the left deltoid

region. Rheumatoid arthritis synovial fibroblasts and tissues were used as positive controls for the expression of cytokines. Total RNA isolated from the tissue samples were reverse transcribed (RT) by random hexamers as the primer for RT followed by PCR amplification using specific primers for IL-1beta, IL-6 or TNF-a. Expression of IL-1beta, and TNF-a protein was investigated in the skin by immunohistochemistry using specific antibodies (avidin-biotin method). RESULTS: Positive signals (RT-PCR) were detected in skin tissues of 19/50 (38%) FM patients for IL-1beta, in 14/51 FM patients (27%) for IL-6, and in 17/53 patients (32%) for TNF-a. None of the cytokines could be detected in healthy control skin. Immunoreactivity for IL-1beta and TNF-a was demonstrated in certain skin tissues of our FM patients. CONCLUSION: **The detection of cytokines in FM skin indicates the presence of inflammatory foci (neurogenic inflammation) in the skin of certain patients (about 30% of FM patients), suggesting an inflammatory component in the induction of pain. This may explain the response to nonsteroidal anti-inflammatory therapy in a subset of FM patients.**

J Rheumatol 2003 Jan; 30(1):146–50

Sayar K, Aksu G, Ak I, Tosun M

Venlafaxine treatment of fibromyalgia

BACKGROUND: Although the pathophysiology of fibromyalgia is unknown, central monoaminergic transmission may play a role. Antidepressants have proved to be successful in alleviating symptoms of fibromyalgia. Medications that act on multiple neurotransmitters may be more effective in symptom management. OBJECTIVE: To assess the efficacy of venlafaxine, a potent inhibitor of both norepinephrine and serotonin reuptake, in the treatment of patients with fibromyalgia. METHODS: Fifteen patients with fibromyalgia were assessed prior to and after treatment with fixed-dose venlafaxine 75 mg/d. Before initiation of pharmacotherapy, patients were interviewed with the Structured Clinical Interview for Axis I disorders in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition. The study lasted for 12 weeks, and patients were evaluated in weeks 6 and 12. The primary outcome measures were the Fibromyalgia Impact Questionnaire (FIQ) total score and pain score. The anxiety and depression levels of the patients were measured with the Beck Depression, the Beck Anxiety, the Hamilton Anxiety, and the Hamilton Depression scales. RESULTS: There was a significant improvement in the mean intensity of pain ($F = 14.3$; $p = 0.0001$) and in the disability caused by fibromyalgia ($F = 42.7$; $p = 0.0001$) from baseline to week 12 of treatment. The depression and anxiety scores also decreased significantly from baseline to week 12. The improvement in the FIQ scores did not correlate with the decrease of scores in both patient- and physician-rated depression and anxiety inventories. Change in pain scores also was not correlated with the change in depression and anxiety scores. CONCLUSIONS: **Venlafaxine was quite promising in alleviating the pain and disability associated with**

fibromyalgia. This effect seems to be independent of its anxiolytic and anti-depressant properties. **Blockade of both norepinephrine and serotonin reuptake might be more effective than blockade of either neurotransmitter alone in the treatment of fibromyalgia.**

Ann Pharmacother 2003 Nov; 37(11): 1561–5

Schachter CL, Busch AJ, Peloso PM, Sheppard MS

Effects of short versus long bouts of aerobic exercise in sedentary women with fibromyalgia: a randomized controlled trial

BACKGROUND AND PURPOSE: The purposes of this study were: (1) to assess the effectiveness of a 16-week progressive program of home-based, videotape-based, low-impact aerobic exercise on physical function and signs and symptoms of fibromyalgia in previously sedentary women aged 20 to 55 years and (2) to compare the effects of 1 long exercise bout versus 2 short exercise bouts per training day (fractionation) on physical function, signs and symptoms of fibromyalgia, and exercise adherence. SUBJECTS: One hundred forty-three sedentary women were randomly assigned to 1 of 3 groups: a group who trained using a long bout of exercise (LBE group, n=51), a group who trained using short bouts of exercise (SBE group, n=56), and a group who performed no exercise (NE group, n=36). METHODS: The SBE group exercised twice daily, and the LBE group worked out once daily. Both groups progressed in total daily training duration from 10 to 30 minutes, 3 to 5 times a week, for 16 weeks. Physical and psychological well-being, symptoms, and self-efficacy were evaluated using a multivariate analysis of variance. RESULTS: Dropout rates for the NE, SBE, and LBE groups were 14%, 38%, and 29%, respectively. The NE group differed from the LBE group in disease severity, self-efficacy, and psychological well-being (midtest, efficacy analysis) and from the SBE group in disease severity and self-efficacy (posttest, efficacy analysis). Exercise adherence was greater for the LBE group than for the SBE group between weeks 5 and 8 of the training program. No other differences between exercise groups were found. DISCUSSION AND CONCLUSION: **Progressive, home-based, low-impact aerobics improved physical function and fibromyalgia symptoms minimally in participants who completed at least two thirds of the recommended exercise. Fractionation of exercise training provided no advantage** in terms of exercise adherence, improvements in fibromyalgia symptoms or physical function. High attrition rates and problems with exercise adherence were experienced in both exercise groups.

Phys Ther 2003 Apr; 83(4):340–58

Scharf MB, Baumann M, Berkowitz DV

The effects of sodium oxybate on clinical symptoms and sleep patterns in patients with fibromyalgia

OBJECTIVE: Fibromyalgia (FM) is associated with the sleep phenomenon of alpha intrusion, and with low growth hormone secretion. Sodium oxybate has been shown to increase both slow-wave sleep and growth hormone levels. This double blind, randomized, placebo controlled crossover trial was conducted to evaluate the effects of sodium oxybate on the subjective symptoms of pain, fatigue, and sleep quality and the objective polysomnographic (PSG) sleep variables of alpha intrusion, slow-wave (stage 3/4) sleep, and sleep efficiency in patients with FM. **METHODS:** Patients received either 6.0 g/day sodium oxybate or placebo for 1 month, with an intervening 2 week washout period. Efficacy measures included PSG evaluations, tender point index (TPI), and subjective measurements from daily diary entries. Safety measures included clinical laboratory values, vital signs, and adverse events. **RESULTS:** Twenty-four female patients were included in the study; 18 completed the trial. TPI was decreased from baseline by 8.5, compared with an increase of 0.4 for placebo ($p = 0.0079$). Six of the 7 pain/fatigue scores (overall pain, pain at rest, pain during movement, end of day fatigue, overall fatigue, and morning fatigue) were relieved by 29% to 33% with sodium oxybate, compared with 6% to 10% relief with placebo ($p < 0.005$). Alpha intrusion, sleep latency, and rapid-eye-movement sleep were significantly decreased, while slow-wave (stage 3/4) sleep was significantly increased, compared with placebo ($p < 0.005$). Two of the 5 subjective sleep related variables were significantly different from placebo: morning alertness (improved by 18% with sodium oxybate, compared with 2% for placebo; $p = 0.0033$) and quality of sleep (improved by 33% and 10%, respectively; $p = 0.0003$). **CONCLUSION:** **Sodium oxybate effectively reduced the symptoms of pain and fatigue in patients with FM, and dramatically reduced the sleep abnormalities (alpha intrusion and decreased slow-wave sleep) associated with the nonrestorative sleep characteristic of this disorder.**

J Rheumatol 2003 May; 30(5):1070–4

Soderberg S, Strand M, Haapala M, Lundman B

Living with a woman with fibromyalgia from the perspective of the husband

BACKGROUND: Fibromyalgia (FM) is a chronic pain syndrome, which affects mostly middle-aged women. The syndrome is poorly understood and treatment is mainly palliative. The diagnosis is established from diagnostic criteria. Living with FM means living a life greatly influenced by the illness in various ways for people affected. **AIM of the study:** The aim of this study was to describe the

experiences of living with a woman with FM from the husband's perspective. METHODS: Five men married to women with FM were interviewed using a narrative approach. The interviews were analysed using qualitative thematic content analysis. FINDINGS: The analysis resulted in the following seven themes: increasing responsibility and work in the home; being an advocate for and supporting the wife; learning to see the woman's changing needs; changing relationship between spouses; changing relationship with friends and relatives; deepening relationship with the children and lacking information and knowledge about FM. The findings show that the women's illness had a great impact on husbands' lives, and that husbands lacked information about the woman's illness. CONCLUSION: **This study shows that it is not only the women with FM who experience a changed life; the whole family life is influenced and limited by FM.** The husband's role in the family changes, first and foremost concerning responsibility and workload within the family. This must be taken into consideration in care planning. **This study also highlighted the need of information and knowledge about FM expressed by the participants,** information that health care personnel have a great responsibility to give.

J Adv Nurs 2003 Apr; 42(2):143–50

Sprott H

What can rehabilitation interventions achieve in patients with primary fibromyalgia?

Symptoms of primary fibromyalgia (FM) persist for years, independent of applied therapy. That is the sad reality we have to deal with. But is that really true? The following review is a scan of literature from September 1, 2001 to August 31, 2002, concerning rehabilitation interventions for patients with FM, to find progress in this field and to ascertain state-of-the-art treatment strategies for the disease. The main problem when treating patients with FM successfully is the heterogeneity of the patients' group. Several investigators determined subgroups within FM patients diagnosed by the 1990 American College of Rheumatology classification criteria of FM. Therefore, uniform recommendations for treatment cannot be given. **Current treatment recommendations for FM include reassurance and explanation of the nature of the illness, evaluation and eradication of mechanical stressors as far as possible, symptomatic analgesic drug treatment, moderate individually adapted physical exercises, and adjuvant psychotherapeutic support in an interdisciplinary setting. Individually adapted measures are highly emphasized to differentially treat FM subgroups, as far as identified.** This review will focus on these points on the one hand, and provide an overview about the current symptomatically-oriented therapy on the other hand. This all occurs against the background of an unknown etiology of the disease so far. Experimental approaches will be noted as well. The demonstration

of a long-term effective intervention for managing the symptoms associated with FM is needed.

Curr Opin Rheumatol 2003 Mar; 15(2):145–50

Staud R, Cannon RC, Mauderli AP, Robinson ME, Price DD, Vierck CJ

Temporal summation of pain from mechanical stimulation of muscle tissue in normal controls and subjects with fibromyalgia syndrome

Individuals diagnosed with fibromyalgia syndrome (FMS) report chronic pain that is frequently worsened by physical activity and improved by rest. Palpation of muscle and tendinous structures suggests that nociceptors in deep tissues are abnormally sensitive in FMS, but methods of controlled mechanical stimulation of muscles are needed to better characterize the sensitivity of deep tissue. Accordingly, force-controlled mechanical stimulation was applied to the flexor digitorum muscle of the forearm in a series of brief contacts (15 stimuli, each of 1s duration, at 3 or 5s interstimulus intervals). Repetitive stimulation was utilized to determine whether temporal summation of deep muscular pain would occur for normal subjects and would be enhanced for FMS subjects. Moderate temporal summation of deep pain was observed for normal controls (NC), and temporal summation was greatly exaggerated for FMS subjects. Temporal summation for FMS subjects occurred at substantially lower forces and at a lower frequency of stimulation. Furthermore, painful after-sensations were greater in amplitude and more prolonged for FMS subjects. These observations complement a previous demonstration that temporal summation of pain and after-sensations elicited by thermal stimulation of the skin are moderately enhanced for FMS subjects. **Abnormal input from muscle nociceptors appears to underlie production of central sensitization in FMS that generalizes to input from cutaneous nociceptors.**

Pain 2003 Mar; 102(1–2):87–95

Thompson ME, Barkhuizen A

Fibromyalgia, hepatitis C infection, and the cytokine connection

Fibromyalgia and chronic hepatitis C infection share many clinical features including prominent somatic complaints such as musculoskeletal pain and fatigue. There is a growing body of evidence supporting a link between cytokines and somatic complaints. This review discusses alterations of cytokines in fibromyalgia, including increased serum levels of interleukin (IL)-2, IL-2 receptor, IL-8, IL-1 receptor antagonist; increased IL-1 and IL-6 produced by stimulated peripheral blood mononuclear cell in patients with FM for longer than 2 years; increased gp130, which is a neutrophil cytokine transducing protein; increased

soluble IL-6 receptor and soluble IL-1 receptor antagonist only in patients with fibromyalgia who are depressed; and IL-1 beta, IL-6, and TNF-a by reverse transcriptase-polymerase chain reaction in skin biopsies of some patients with fibromyalgia. In addition, **this review describes the mechanism by which alterations in cytokines in fibromyalgia and chronic hepatitis C infection can produce hyperalgesia and other neurally mediated symptoms through the presence of cytokine receptors on glial cells and opiate receptors on lymphocytes and the influence of cytokines on the hypothalamus-pituitary-adrenal axis** such as IL-1, IL-6, and TNF-a activating and IL-2 and IFN-a down-regulating the HPA axis, respectively. The association between chronic hepatitis C infection and fibromyalgia is discussed, including a description of key cytokine changes in chronic hepatitis C infection. Future studies are encouraged to further characterize these immunologic alterations with potential pathophysiologic and therapeutic implications.

Curr Pain Headache Rep 2003 Oct; 7(5): 342-7

Velanovich V

The effect of chronic pain syndromes and psychoemotional disorders on symptomatic and quality-of-life outcomes of antireflux surgery

Psychoemotional disorders (PED) and chronic pain syndromes (CPS) are common problems. Many patients with these disorders also suffer from gastroesophageal reflux disease (GERD). It is unclear how PED/CPS affect outcomes of antireflux surgery; therefore, the purpose of this study was to determine if PED/CPS adversely affects the results of surgical therapy for GERD. All patients referred for surgical therapy for GERD completed both the GERD-HRQL symptom severity instrument and the SF-36 generic quality-of-life instrument prior to surgery. To be candidates for surgery, patients must have symptomatic GERD and objective evidence of pathologic reflux by upper endoscopy, esophageal manometry and 24-hour pH monitoring. Patients underwent either laparoscopic or open Nissen or Toupet fundoplication. Six to 24 months postoperatively, patients were evaluated for satisfaction and quality-of-life. Ninety-three percent of control patients compared to 25% of PED/CPS patients were satisfied with surgery ($P < 0.001$). Dissatisfaction in PED/CPS patients was generally due to persistent or new somatic complaints. Median total GERD-HRQL scores improved for both groups, although postoperative scores were worse in the PED/CPS group. PED/CPS patients had significantly worse SF-36 scores both preoperatively and postoperatively compared to control patients. SF-36 scores improved in four of eight domains in control patients and none in the PED/CPS patients. In conclusion, **PED/CPS patients are generally dissatisfied with antireflux surgery. Although some patients do benefit from surgery, careful patient selection is required.**

J Gastrointest Surg 2003 Jan; 7(1):53-8

Viane I, Crombez G, Eccleston C, Poppe C, Devulder J,
Van Houdenhove B, De Corte W

Acceptance of pain is an independent predictor of mental well-being in patients with chronic pain: empirical evidence and reappraisal

This paper reports upon: (1) the value of acceptance of pain in predicting well-being in patients suffering from chronic pain and (2) the construct validity of acceptance by comparing two questionnaires designed to measure acceptance (the Chronic Pain Acceptance Questionnaire, CPAQ, unpublished doctoral dissertation, University of Nevada, Reno, NV, 1992 and the Illness Cognitions Questionnaire, ICQ, *J Consult Clin Psychol* 69 (2001) 1026). The results of two independent cross-sectional studies are reported. Study 1 included 120 patients seeking help in tertiary care settings. In Study 2, 66 patients were recruited from a self-support group for fibromyalgia patients and from a pain clinic. Both studies revealed that acceptance of pain predicted mental well-being beyond pain severity and pain catastrophizing, but did not account for physical functioning. In both instruments, it was found that acceptance of pain was strongly related to engagement in normal life activities and the recognition that pain may not change. Acceptance in both instruments was strongly related to a cognitive control over pain. Study 2 further revealed that the correlation between the CPAQ and the ICQ is moderate, indicating that both instruments measured different aspects of acceptance. **It is concluded that acceptance of chronic pain is best conceived of as the shift away from pain to non-pain aspects of life, and the shift away from a search for a cure with an acknowledgement that pain may not change.**

Pain 2003 Nov; 106(1–2): 65–72

Wolfe F

Pain extent and diagnosis: development and validation of the regional pain scale in 12,799 patients with rheumatic disease

OBJECTIVE: To develop and validate a pain scale that measures the extent of body pain. **METHODS:** A total of 12,799 patients with rheumatoid arthritis (RA), osteoarthritis (OA), and fibromyalgia (FM) completed a mailed survey regarding the location and intensity of their pain in 38 articular and nonarticular regions. The data were analyzed using item response theory (IRT) by nonparametric Mokken analysis followed by Rasch analysis. The resultant scale was examined for its association with clinical severity variables and its ability to distinguish patients diagnosed with and without FM. **RESULTS:** The resultant 19 item regional pain scale (RPS) was composed primarily of nonarticular regions. The scale had strong scalability as measured by the Mokken H statistic ($H = 0.52$), and satisfied the Mokken monotonicity and double monotonicity criteria. The RPS

also fit the Rasch model and had satisfactory reliability and separation statistics. Of all clinical variables assessed by survey, the RPS best identified patients diagnosed with FM. In addition, the scale correlated with measures of clinical severity, regardless of diagnosis, and predicted measures of utilization. **CONCLUSION: The RPS is a valid scale of pain extent. It can be useful to identify patients with FM or can be used to develop a new definition of FM, even among patients with concomitant illnesses such as RA and OA.** In addition, it is a measure of pain extent that is disease independent, and works as well in RA and OA as in FM to identify patients with increased severity and resource utilization.

J Rheumatol 2003 Feb; 30(2):369–78