Fibromyalgia & Chronic Fatigue Syndrome
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Objectives

Definition
• Fibromyalgia (FM) = disorder of chronic widespread pain with associated:
  • fatigue
  • cognitive difficulties
  • poor sleep
  • stiffness
  • multiple somatic symptoms
  • anxiety and/or depression.

Other Common FM Symptoms
• Weight fluctuations
• Allergic symptoms (eg, nasal congestion) & hypersensitivity to environmental stimuli (eg, odors, bright lights, loud noises) & medications
• Regional pains, including noncardiac chest pain, dyspepsia, headache, abdominal cramping (irritable bowel syndrome), temporomandibular pain, chronic pelvic pain, & others
  • Syncope or dizziness
  • Shortness of breath
• Urinary frequency & urgency (female urethral syndrome, interstitial cystitis)

Fibromyalgia Pain
• radiates diffusely from the axial skeleton over large areas of the body, predominantly involving muscles & musculoskeletal junctions, but also in joints (arthralgia w/o actual synovitis) & most commonly described:
  – Exhausting
  – Burning
  – Miserable
  – Unbearable.
  – may also be multifocal, can wax & wane in a migratory fashion
  – “Pain all over” is a common patient description

Fibromyalgia & Chronic Fatigue Syndrome (CFS)

- Fatigue & chronic lack of sleep = almost universal in all FM patients therefore meeting the criteria for CFS

Cognitive problems

- "fibrofog" may be a primary symptom of fibromyalgia = impairments in working, episodic, & semantic memory that are roughly equivalent to 20 years of aging


New classification

- new classification: central sensitivity syndrome (CSS)
- now considered a neurosensory disorder characterized, in part, by abnormalities in CNS pain processing
- Increased understanding of the biological bases underlying fibromyalgia rapidly leading to new era of specific pharmacologic therapy for the condition
- Some practitioners still consider it a "waste basket illness" & not a true diagnosis that is treatable

More widespread & overlapping with

- Other central sensitivity syndromes (eg, chronic fatigue syndrome, irritable bowel syndrome, chronic pelvic pain syndrome/primary dysmenorrhea, temporomandibular joint pain, tension-type headaches/migraine, posttraumatic stress disorder [PTSD], multiple chemical sensitivity, periodic limb movement disorder/restless legs syndrome, interstitial cystitis)
- Other regional pain syndromes
- Mood & anxiety disorders


Current FM Paradigm

- certain vulnerability elements (female sex, genes, abuse or other adverse experiences during childhood when the brain is still developing) & persistent stress or distress
- psychologic variables (eg, distress, mood & anxiety disorders, personality traits and disorders, catastrophizing, coping, self-efficacy for pain control) = central role in the pain experience, overall morbidity, & prognosis in patients with fibromyalgia

International Association for the Study of Pain: Pain Definition

- "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merskey, 1994).

Neurophysiological

- Pain experience comes from a complex sensation-perception interaction involving the simultaneous parallel processing of nociceptive input from the spinal cord to multiple regions of the brain.

Pain Experience in FM

- Sensory-discriminative elements of nociception & afferent input from somatic reflexes.
- Major contributions from pathways & regions of the brain that are associated with emotional, motivational, & cognitive aspects of pain are evident & determine the subjective intensity of pain.
- Two principal effectors of the stress response, the hypothalamic-pituitary-adrenocortical (HPA) axis & the sympathetic nervous system (SNS), are also activated.

Stress Response

- Stress response may become maladaptive in patients with chronic pain & fatigue syndromes, eg fibromyalgia.
- Negative emotions (eg, depression & anxiety), other negative psychologic factors (eg, loss of control, unpredictability in one’s environment), certain cognitive aspects (eg, negative beliefs & attributions, catastrophizing) all function as stressors.
- Negative emotions, eg anger & sadness, have been shown to be direct amplifiers of pain in women w/ & w/o fibromyalgia.

Negative Emotional, Motivational, & Cognitive Stressors

- May dominate the clinical picture, potentially leading to a self-sustaining neuroendocrine cascade that contributes to flu-like symptoms, depressed mood, fatigue, myalgias, cognitive difficulties, & poor sleep.
- Biologic elements include proinflammatory cytokines, HPA axis, other neuroendocrine axes, & autonomic nervous system. Growth-hormone abnormalities also thought to contribute to symptomatology in fibromyalgia.

FM Pain Derives

- Partly from a generalized decrease in the pain perception threshold, reflecting discrimination of a nociceptive quality from a nonnociceptive quality (eg, touch, warmth, cold), & the threshold for pain tolerance, reflecting an unwillingness to receive more-intense stimulation.
- Phenomena can be demonstrated clinically by pressure algometry (dolorimetry) or in research settings with quantitative sensory testing (QST) using pressure, heat, cold, or electricity as stimuli.
**Demonstrated Abnormalities in FM Pain Processing**

- Excess excitatory (pronociceptive) neurotransmitters (e.g., substance P, glutamate levels in the insula)
- Low levels of inhibitory neurotransmitters (e.g., serotonin & norepinephrine) in descending antinociceptive pathways in the spinal cord
- Maintained enhancement of temporal summation of second pain
- Altered endogenous opioid analgesic activity in several brain regions known to play a role in pain modulation
- Dopamine dysregulation, & some others


**FM is a**

- Polygenic syndrome with multiple different underlying genetic polymorphisms, (genetic testing to tailor therapy and to predict response to therapy will soon become available).

**US FM & CFS Epidemiology**

- & persons of lower socioeconomic status=
- Prevalence of regional pain is 20%
- Widespread pain, 11%
- Fibromyalgia according to the American College of Rheumatology (ACR) criteria
- 3-5% in females & 0.5-1.6% in males
- Chronic fatigue, approximately 20%
- ACR criteria are relatively insensitive, the actual prevalence of fibromyalgia is higher.


**FM Epidemiology (continued)**

- Female-to-male ratio of approximately 9:1
- Males tend to have lower health perception & more physical limitations than females
- Females have greater pain sensitivity & may exhibit greater life interference due to pain
- Usually considered a disorder of women aged 20-50 years has been seen in pediatric populations (adolescents) & older patients
- ~25% of patients with RA 50% of patients with SLE also have fibromyalgia


**FM**

- Chronic relapsing condition.
- Academic medical centers, long-term follow-up care of patients with fibromyalgia reportedly averages 10 outpatient visits per year w 1 hospitalization every 3 years.
- Chronic pain & fatigue in fibromyalgia increases the risk for metabolic syndrome.
- Subset of fibromyalgia patients consider themselves more ill & impaired, reporting markedly abnormal scores for pain, functional disability, fatigue, sleep disturbance, & psychologic status
- They have significantly higher levels of comorbid illness & healthcare utilization and costs than matched controls
- Annual economic burden of fibromyalgia in 2005 was $10,199 (US dollars) per patient per year, nearly double that of matched controls

**History & Physical Details**

- Social & development history (abuse, alcoholism in a parent during childhood, past)
- Ongoing stressors
- Belief regarding triggers of illness
- Ongoing compensation claims, work status
- Previous treatment modalities & their efficacy
- Opioid prescription
History & Physical Details (Continued)

- signs of deconditioning, physical examination findings are normal
- pain, not just tenderness, at multiple fibromyalgia tender points when pressure (approximately 4 kg/cm²) is applied manually, with pressure increasing gradually at the rate of 1 kg per second over 4 seconds
- pain upon light pressure may not be restricted to specific tender points.
- feel pain virtually anywhere that pressure is applied, including control areas (eg, forehead, thumbnail) that are relatively insensitive to pain in healthy patients

Pressure/Pain Points

Pressure Algometer/Dolorimeter

- Provides rough quantitation of pain sensitivity

FM Etiology is Multifactorial

- Engel's biopsychosocial model of chronic illness (ie, health status & outcomes in chronic illness are influenced by the interaction of biologic, psychologic, & sociologic factors) provides a useful way to conceptualize fibromyalgia


Etiology: Biologic Variables

- none, as a single element, explains all facets of fibromyalgia
- Inheritance
- Female gender
- Age
- Sleep (most FM patients sleep poorly followed by painful day)
- Trauma as a trigger of fibromyalgia = highly contentious & medicolegally charged issue in American society (preponderance of current evidence does not support physical trauma as a significant causative factor)
- Physical deconditioning
- Central sensitization & abnormal central nociceptive processing
- Viruses or other infections NOT sole variable may contribute to exacerbation of symptoms
- Decreased collagen cross-linking, hypermobility, Chiari malformation, & environmental chemicals = UNCLEAR at this time
- Pain beliefs & attributions
- Hypervigilance
- Self-efficacy & coping
Etiology: Biologic Variables

- Decreased collagen cross-linking, hypermobility, Chiari malformation, & environmental chemicals = UNCLEAR at this time
- Pain beliefs & attributions
- Hypervigilance
- Self-efficacy & coping
- Depression & anxiety
- Personality traits & disorders (perfectionism-compulsiveness = most common)
- Self-sacrificing
- Wounded warrior

Pain behaviors = various signals that serve to communicate the pain experience to the outside world. May be non-verbal or verbal or both

FM patients = excessive use of medical services. Care seekers exhibit lower pain thresholds & greater psychiatric morbidity

Environmental & Sociocultural Variables

- Psychosocial experiences during childhood
- Spousal & family support
- Ethnological factors
- Focus on definable causes
- Media hype
- Primary & secondary gain
  - Eg: job satisfaction in a person who strains his or her back at work or negatively or physician who medicalizes a minor injury by diagnostic waffling & inappropriate diagnostic testing

Developmental Variables

- Psychosocial experiences during childhood (eg, school stress, role models, unhappy families, abuse) that shape the cognitive, affective, & behavioral aspects of pain in adults
- Some studies = 2/3 patients with chronic pain have first-degree relatives with chronic pain, 1/3 have a family member with an affective illness, & 1/3 have a family member with alcohol abuse.

Interpersonal Variables

- Spousal support may mitigate or adversely affect FM
  - Spousal reinforcement of pain behaviors
- Work environment & job satisfaction
  - Job satisfaction & healthy work environment lessen the emotional distress associated with chronic pain
  - Job dissatisfaction strongly predicts the progression of acute back pain to chronic low back pain. Similarly, workers' compensation & disability benefits can be significant disincentives for recovery from chronic pain.

Interpersonal Variables (continued)

- Sociocultural factors
  - The current epidemic of fibromyalgia, chronic fatigue syndrome, sick building syndrome, & multiple chemical sensitivity syndrome is arguably due, at least in part, to media hype, fear, suggestibility, & a focus on definable causes by patients and physicians
  - Other factors such as cultural pain experience & expression
Differential Diagnosis

- Addison Disease
- Anxiety Disorders
- Conversion Disorders
- Cushing Syndrome
- Depression
- Dysmenorrhea
- Dysthmic Disorder
- Endometriosis
- Factitious Disorder
- Growth Hormone Deficiency
- Gynecologic Pain
- Hashimoto Thyroiditis
- Hepatitis C
- Hyperparathyroidism
- Hypochondriasis
- Hypothyroidism
- Insomnia
- Intestinal Obstruction
- Irritable Bowel Syndrome
- Malnouring
- Mitral Valve Prolapse
- Opioid Abuse
- Panic Disorder
- Personality Disorders
- Polymyalgia Rheumatica
- Polymyalgia
- Posttraumatic Stress Disorder
- Rheumatoid Arthritis
- Sierren Syndrome
- Systemic Lupus Erythematosus

Laboratory Studies in Workup

- CBC w diff
- Metabolic panel
- UA
- Thyroid-stimulating hormone
- Creatinine phosphokinase (CPK)
- Erythrocyte sedimentation rate (ESR)
- Antinuclear antibodies (ANAs)
- Rheumatoid factor

Laboratory Studies in Workup (continued)

- Sleep study may be useful if not improved with conservative treatment
  - elimination of caffeine, prescription of hypnotics or nighttime tricyclics
- serum transferrin & serum ferritin in ages 40-60 years, especially those with small-joint arthropathy in the hands

Procedures

- self-report form that incorporates visual analog scales for pain & fatigue
- global self-assessment of how the patient is doing,
- validated scales for physical & psychologic health status (eg, modified Health Assessment Questionnaire, Fibromyalgia Impact Questionnaire,
- checklist of current symptoms, scales for helplessness & cognitive performance
- psychometric testing includes the Minnesota Multiphasic Personality Inventory, the Social Support Questionnaire, the Sickness Impact Profile, & the Multidimensional Pain Inventory (MPI)

Approaches to Management in General

- anspatic attitude of healthcare providers
- assess possible causal or perpetuating factors
- avoid diagnostic waftling, frightening testing, excessive use of physical therapy modalities after minor trauma, excessive activity limitation, & overly liberal work release
- be aware of confounders to recovery, such as pending litigation or compensation claims
- nociceptive pain coexists with the diffuse chronic pain of fibromyalgia, manage pharmacologically w analgesics using stepwise approach used for acute pain
- multifaceted treatment plan incorporating adjuvant medicines, aerobic exercise, & psychologic & behavioral approaches to reduce distress & promote self-efficacy & self-management (eg, relaxation training, activity pacing, visual imagery, distraction)
- Cognitive-behavioral therapy (CBT) & operant-behavioral therapy (OBT)

Approaches to Management in General (continued)

- relaxation training, activity pacing, guided imagery, written emotional disclosure, & distraction strategies. Instruction in proper sleep hygiene is beneficial
- Physical therapy/physical modalities
  - (eg, low-impact aerobics, walking, water aerobics, stationary bicycle) should start gently & progress gradually to endurance
  - aquatic therapy (in a warm pool) 3 times per week
  - heat, massage, & other treatments useful, diffuse & regional pain improved by strategies such as sauna, hot baths, showers, & hot mud
- Encouragement & positive reinforcement can improve compliance. Obesity, poor posture, & overloading activities at work & at home should be addressed.
Approaches to Management in General (continued)

- Trigger-point injections, acupuncture, chiropractic manipulation, & myofascial release – passive modalities of questionable efficacy and should be avoided. Furthermore, they do not promote self-efficacy for pain control
- Some electromagnetic wave devices appear to be efficacious in treating pain in fibromyalgia. A complex neural pulse stimulation (CNP) device that uses magnetic pulse applied to the cranium through a headset daily for 40 minutes for a few days to a few weeks is most promising because the treatment is self-administered.

Medications

- Opioids, hypnotics, anxiolytics, & certain skeletal-muscle relaxants must be used with caution because of the potential for abuse
- Tricyclic antidepressants (TCAs) are of proven benefit in treating pain in fibromyalgia. A complex neural pulse stimulation (CNP) device that uses magnetic pulse applied to the cranium through a headset daily for 40 minutes for a few days to a few weeks is most promising because the treatment is self-administered.

Medications (continued)

- Benzodiazepines (eg, alprazolam [Xanax]; half-life, < 12 h), temazepam [Restoril; half-life, 10-15 h], clonazepam [Klonopin; half-life, 25-100 h], buspirone [BuSpar], trazodone [Desyrel]

Medications

- Beta-blockers &/or increased fluid & sodium/potassium intake may benefit a subset of patients w/FM who have orthostatic hypotension, palpitation, & vasoconstriction
- Complementary and alternative medicine (CAM) – popular w/physicians in many locations
- Selective estrogen receptor modulator raloxifene (Evista) 60 mg qod is effective in improving pain, improving fatigue, reducing tender point count, & improving daily functioning in postmenopausal women w/fibromyalgia
- Modafinil (Provigil), approved for narcolepsy & shift work sleep disorder, 100-200 mg in the morning improves fatigue & cognitive disturbances
- Beta-adrenergic antagonists, eg, propranolol (Inderal), given in low doses at bedtime can also improve pain & agitation

Medications (continued)

- Centrally Acting Skeletal Muscle Relaxants
  - Cyclobenzaprine can be helpful for sleep & pain control as a single nighttime dose in combination with α-adrenergic/hypnotic agents
- Anti-inflammatory agents
  - Low-dose TCAs have proven short-term efficacy for pain control, improved sleep, improved sense of well-being in patients w/fibromyalgia, but adverse effects (eg, dry mouth, dizziness, weight gain) limit patient acceptance
  - Selective serotonin reuptake inhibitors (SSRIs), eg, fluoxetine (Prozac), citalopram (Celexa), escitalopram (Lexapro), paroxetine (Paxil), sertraline (Zoloft), improve symptoms in fibromyalgia but have largely been replaced as a treatment for pain by dual serotonin/norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine (Effexor), desvenlafaxine (Pristiq), milnacipran (Savella), which has recently been approved for fibromyalgia by the FDA, as a skeletal muscle relaxant


Approaches to Management in General (continued)

- No general surgical treatment at this time
- Consultations w/Rheumatologist, Neurologist, Dentist, Psychologist/Psychiatrist, or other specialist may be useful
- Diet
  - Promote sound nutrition
  - Vit D deficient in many w/FM
  - Opioids, hypnotics, anxiolytics, & certain skeletal muscle relaxants must be used with caution because of the potential for abuse

Medications (continued)

- Antidepressants & anticonvulsant drugs (both of which also have efficacy for anxiety and insomnia)
  - Venlafaxine (Effexor), desvenlafaxine (Pristiq), milnacipran (Savella) which has recently been approved for fibromyalgia in women pooled results from two randomized, placebo-controlled clinical trials. J Women's Health (Larchmt). Oct 2007;16(8):1145
  - Trazodone [Desyrel]
Medications (continued)

- Anticonvulsants
  - Useful for chronic pain states, including FM & related syndromes & various types of neuropathic pain, serve as adjunctive medications for disturbed sleep & depression eg, gabapentin (Neurontin), tiagabine (Gabitril), & recently released pregabalin (Lyrica), which has been particularly well-studied in fibromyalgia.

- Antihypertensives
  - Clonidine is helpful in controlling withdrawal symptoms during tapering of opioids, which may take 2-3 weeks or longer.


Observe for Complications

- Extreme alodynia with high levels of distress
- Opioid or alcohol dependence
- Marked functional impairment
- Severe depression and anxiety
- Obesity and physical deconditioning
- Metabolic syndrome

Prognosis

- Varies with patients & patient subsets
  - Response to therapy improves significantly in many patients if ongoing stressors are relieved & self-efficacy for pain control can be achieved. The treatment goal that responds least to therapy is improvement in daily functioning

Guarded Prognosis with

- High levels of distress
- Long-standing fibromyalgia
- Major psychiatric disease or severe depression and anxiety that responds poorly to treatment
- An ingrained pattern of work avoidance
- Marked functional impairment despite multidisciplinary approaches to treatment
- Opioid or alcohol dependence

Education of Patient & Support System

- Arthritis Foundation; MedlinePlus Health Information, a service of the US National Library of Medicine and the National Institutes of Health; American College of Rheumatology; Missouri Arthritis Rehabilitation Research and Training Center: A Physician’s Guide to Fibromyalgia Syndrome; The American Fibromyalgia Syndrome Association: Chronic Fatigue Syndrome and Fibromyalgia; Fibromyalgia.com; Health information for the whole family from the American Academy of Family Physicians; and Friends International Support. Local patient support groups

Chronic Fatigue Syndrome

- Have severe chronic fatigue of six months or longer duration with other known medical conditions excluded by clinical diagnosis; and
- Concurrently have four or more of the following symptoms: substantial impairment in short-term memory or concentration; sore throat; tender lymph nodes; muscle pain; multi-joint pain without swelling or redness; headaches of a new type, pattern or severity; unrefreshing sleep; & post-exertional malaise lasting more than 24 hours.
- The symptoms must have persisted or recurred during six or more consecutive months of illness & must not have predated the fatigue.
Chronic Fatigue Syndrome

- Similar conditions
  - FM, myalgic encephalomyelitis, neurasthenia, multiple chemical sensitivities, and chronic **mononucleosis**
- Risk Factors
  - All people, any age, ethnicity, sociocultural background
  - Females 4 times to 1 male
  - Most common in 40s-50s

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Chronic Fatigue Syndrome

CFS includes eight characteristic symptoms:
- postexertional malaise (relapse of symptoms after physical or mental exertion);
- unrefreshing sleep;
- substantial impairment in memory/concentration;
- muscle pain;
- pain in multiple joints;
- headaches of a new type, pattern or severity; sore throat;
- tender neck or armpit lymph nodes.
- Symptoms & consequences can be severe. CFS can be as disabling as **multiple sclerosis**, **lupus**, **rheumatoid arthritis**, **congestive heart failure**.
- Symptom severity varies from patient to patient & may vary over time for an individual patient.

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Chronic Fatigue Syndrome

- Diagnosis:
  - NO specific test
  - Disease of exclusion
- Treatment
  - No cure
  - No single treatment
  - Symptom management only
- Longer illness before treatment = increased complications
- Recovery rates vary widely 8-63%
- Cause unknown