Fibromyalgia

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Case Study

A 45-year-old woman presents with diffuse muscle pain, weakness, and significant fatigue.

- Symptoms for over 3 years that have become slightly worse in past 6 months. Generalized pain and fatigue that limit her ability to work.
- Increasing sleep difficulty due to the pain Denies major depression or anxiety but increasingly frustrated by symptoms and lack of a diagnosis.

- Previously suffered from migraine but no major headaches since menopause
- Told that she had irritable bowel syndrome 3 years ago
Case Study (cont)

- General physical examination is unremarkable
- Diffuse muscle tenderness is noted
- Some tenderness around the joints, but no synovitis
- No objective muscle weakness
- Normal neurologic examination
- CBC, ESR, and chemistry profile are normal
Fibromyalgia Controversies

- Is it real?
- Can it be reliably diagnosed?
- Is it physical or psychological?
- Is there any effective treatment?
- Is a diagnosis helpful or harmful?
Problems in Defining Fibromyalgia

- “Real” if no clear pathophysiologic basis?
- Gold standard is “expert opinion.”
- Tender points, symptoms are subjective.
- Fewer than 11 tender points?
- Symptoms are not dichotomous.
- Same diagnostic criteria and dilemma for any illness lacking objective biologic markers (depression, migraine, IBS, CFS).
## Functional Somatic Syndromes

<table>
<thead>
<tr>
<th>Field</th>
<th>Syndrome</th>
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<tbody>
<tr>
<td>Rheumatology</td>
<td>Fibromyalgia</td>
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<tr>
<td>Gastroenterology</td>
<td>Irritable bowel</td>
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<tr>
<td>Neurology</td>
<td>Tension headache</td>
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<tr>
<td>Infectious Disease</td>
<td>Chronic fatigue</td>
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<tr>
<td>Gynecology</td>
<td>Chronic pelvic pain</td>
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<tr>
<td>Cardiology</td>
<td>Non-cardiac chest pain</td>
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<tr>
<td>Urology</td>
<td>Irritable bladder (ICS)</td>
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<tr>
<td>Allergy</td>
<td>Multiple chemical sensitivity</td>
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<tr>
<td>ENT</td>
<td>TMJ</td>
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FMS and Mood Disorders

- At the time of FMS diagnosis, mood disorders are present in 30-50%, primarily depression.
- Increased prevalence of mood disorders is primarily in tertiary-referral patients.
- Increased lifetime and family history of mood disorders in FM vs RA (Odds = 2.0).
- FMS aggregates in families and co-aggregates with mood disorders. Odds of having FMS in relatives is 8.5 in FMS vs RA proband (Arnold, et al 2003).
Genetic Factors in Fibromyalgia

- Familial predisposition
  - Arnold\(^1\) found that if an individual has fibromyalgia there is >8 odds ratio (OR) for first-degree relatives to develop fibromyalgia

- Candidate Genes
  - 5-HT\(_{2A}\) receptor polymorphism T/T phenotype\(^2\)
  - Serotonin transporter\(^3\)
  - Dopamine D4 receptor exon III repeat polymorphism\(^4\)
  - COMT (catecholamine o-methyl transferase)\(^5\)
  - Heterozygous beta-3 adrenergic receptor allele\(^6\)

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Stress Susceptibility

Negative life experiences

Genetic set point

Positive life experiences
Is there any effective management of fibromyalgia?

- All patients
  - Reassurance re diagnosis
  - Give explanation, including, but not solely, psychological factors
  - Promote return to normal activity, exercise

- Most patients
  - Medication trial (esp antidepressants, anticonvulsants)
  - Cognitive behavior therapy, counseling
  - Physical rehabilitation
Medications in FMS

- **Strong evidence for efficacy:**
  - Amitriptyline, 25-50 mg at bedtime
  - Cyclobenzaprine, 10-30 mgs at bedtime
  - Pregabalin, 300-450 mg/day
  - Gabepentin, 1600-2400 mg/day
  - Duloxetine, 60-120 mg/day
  - Milnacipran, 100-200 mg/day

- **Modest evidence for efficacy:**
  - Tramadol, 200-300 mg/day
  - SSRIs (fluoxetine, sertraline)
Medications in FMS (cont)

- Weak evidence for efficacy: pramipexole, gamma hydroxybutyrate, growth hormone, 5-hydroxytryptamine, tropisetron, s-adenosylmethionine.

- No evidence: opioids, NSAIDS, benzodiazepene and nonbenzodiazepene hypnotics, melatonin, magnesium, DHEA, thyroid hormone, OTC including guaifenesin.

New Fibromyalgia Treatment Approaches

- Combination antidepressants (SSRI+TCA)
- Individualized dosing (fluoxetine)
- Dual reuptake inhibitors (venlafaxine, duloxetine, milnacipran)
- Antiepileptics (gabapentin, pregabalin)
- Patient subsets treated differently
- Combine non-medicinal with drug therapies
- Multi-disciplinary programs
Gabapentin in FM: 30% Reduction on BPI Pain Severity Score


This information concerns a use that has not been approved by the US Food and Drug Administration.
Changes in the Brief Pain Inventory Average Pain Severity Score: Duloxetine vs. Placebo

Stepwise Treatment of Fibromyalgia

1. Confirm diagnosis
2. Identify important symptom domains, their severity, and level of patient function
3. Evaluate for comorbid medical and psychiatric disorders
   - Assess psychosocial stressors, level of fitness, and barriers to treatment
   - Provide education about fibromyalgia
   - Review treatment options
   - May require referral to a specialist for full evaluation

Stepwise Treatment of Fibromyalgia (cont)

As a first-line approach for patients with moderate to severe pain, trial with evidence-based medications

Provide additional treatment for comorbid conditions

Adjunctive CBT for patients with prominent psychosocial stressors, and/or difficulty coping, and/or difficulty functioning

Encourage exercise according to fitness level

Therapies with No to Mixed Evidence in Fibromyalgia

No Evidence

- NSAIDs
- Corticosteroids
- Opiates
- Chiropractic
- Trigger or tender point injections
- TENS units

Mixed Evidence

- SSRIs
- Acupuncture
- Massage
- Strength exercises
- Hypnosis
- Biofeedback
- Balneotherapy

Rooks DR. *Curr Opin Rheumatol* 2007;19:111-117
Why isn’t FM outcome better with current medical care?

- Long delay in diagnosis, initial therapy.
- Patients are often led to believe they have an intractable disease for which treatment options are limited.
- Need Individual Rx plan with active patient participation.
- Patient subsets.
- Often best handled with multidisciplinary care.
Subgroups of FM Patients

Group 1 (n=50)
- Low depression/anxiety
- Not very tender
- Low catastrophizing
- Moderate control over pain

Psychological factors neutral

Group 2 (n=31)
- Tender
- High depression/anxiety
- Very high catastrophizing
- No control over pain

Psychological factors worsening symptoms

Group 3 (n=16)
- Extremely tender
- Low depression/anxiety
- Very low catastrophizing
- High control over pain

Psychological factors improving symptoms
Does the FM diagnostic label promote helplessness and disability?

- Recent studies: Diagnostic label is helpful.

- Diagnosis should be reassuring and end doctor shopping.

- Only if diagnosis is coupled with education.

- Causation: issue is contentious.