The Fibromyalgia Syndrome: Updates in Diagnosis & Management
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No Disclosures

What American’s Know About Science
- H2O is Hot Water, CO2 is Cold Water
- Water is composed of two gins, oxygen and hydrogen. Oxygen is pure gin and Hydrogen is gin & water.
- Three kinds if blood vessels: arteries, veins and caterpillars.
- Gonads are a tribe of wondering desert people.
- How does one keep milk from turning sour, keep it in the cow.
Objectives

- Verbalize what is currently known about the pathophysiology of fibromyalgia.
- Identify patients at risk, making the correct diagnosis.
- Prioritize the use of pharmacological management, through identification of risks, benefits and side effects.
- Identify evidenced-based, non-pharmacological strategies for management.

Fibromyalgia Syndrome

A prevalent chronic pain syndrome, characterized by widespread pain all four quadrants of the body and the presence of tenderness @ 11+/18 specific muscle-tendon sites.

Diagnosis of exclusion, of unknown cause.

Psychosomatic.

Fibromyalgia Syndrome

Fibromyalgia is a chronic condition characterized by widespread pain:
- Genetic predisposition.
- Environmental trigger that increases the brain's susceptibility to pain signals.
- Dyregulation of neurotransmitters in the brain, over activation of its pain receptors.
- Chronic fatigue
- IBS, IC, TMJ
- Headaches - >50%
- Abnormal/non-restorative sleep
- Restless leg syndrome
- Cognitive dysfunction “fibro-fog”
- Mood disorders (depression/anxiety)
Fibromyalgia

- 2-6% US population, women>men 7:1
- Average 5 years diagnosis.
- FM is difficult to diagnose because it's the result of a neural distribution rather than a discrete physical injury.
- Direct cost > $20 billion annually.
- Indirect costs = years of pain and suffering, poor quality of life & possible decreased in life expectancy.
- 2-4% managed in primary care. >95% referred to specialty care: orthopedics, pain medicine, rheumatology, neurology, psychology, gastroenterology, urology, etc.

History

- 16th Century medical literature contains descriptions of clinical manifestations of musculoskeletal pain.
- 1904: Sir William Gowers coins the term "fibrositis"
- 1975: Dr. Harvey Moldofsky recommends redefining the disorder as "non-restorative sleep syndrome"
- 1981: Yunas et.al. use the term "fibromyalgia" for the first time in scientific literature.
- 1987: AMA acknowledges fibromyalgia as a true illness.

- 1990 ACR classification criteria used for diagnosis.
- 1992 WHO finally recognized FM as a disease.
- 2000+ fMRI findings demonstrate that neurobiological factors may contribute to the pathology of 'central' pain states such as fibromyalgia.
- 2006 @ The FM & CNS Symposium in Oregon, hypothesized that FM may be more than just a myofascial disease.
- 2007-2009 new pharmaceutical agents approved by FDA.
- 2010 ACR introduces new diagnostic criteria for FM.
Pathophysiology

- 1976 Fibromyalgia = fibro (fibrous tissue), my (muscles), al (pain), & gia (condition of).

- 2000+ Fibromyalgia Syndrome
  - Central Nervous System
    - Biochemical (↓ serotonin, ↑ substance P)
    - Metabolic (↑ oxidative stress, ↑ cytokines)
    - Immuno-regulatory (dysfxn HPA, ↓ GH, hypothyroidism)
  - Central Sensitization/wind-up (whole body hypersensitivity to pain)

Injury activates peripheral nerves.

Excitatory signals from PNS to CNS = PAIN

Inhibitory signals turn off pain response & rest CNS/PNS to baseline.

Dysregulation of excitatory & inhibitory signals results in the central sensitization seen in FMS.

FMS treatments ↓ excitatory sigs  ↑ inhibitory sigs

↑ NMDA – glutamate
↑ Substance P
↑ Nitric Oxide

↓ Norepinephrine
↓ Serotonin
↓ GABA & Opiates

Pathophysiology/Current Research

- FM is a chronic, central pain condition.
- Increase in the brain’s susceptibility to pain, possibly related to a deregulation in certain neuro-transmitters, which keep the brain in a heightened sense of sensitivity.
- FM is now believed to be, at least in part, a disorder of central pain processing that produces heightened response to painful stimuli (hyperalgesia) and painful responses to no painful stimuli (allodynia). Clauw, DJ 2010.
The first study to use fMRI in patients with FM. Exposed 16 patients and 16 controls to painful pressures during MRI. Found increases in the blood oxygen-level (hyper-activation) in those with FM.

Regions of increased activity included the primary and secondary somatosensory cortex, the insula, and the anterior cingulate.

"I think the main message clinically is that there are prominent central changes in pain processing and that the preponderance of evidence is that this is a central nervous system disease"

- Daniel J. Clauw, MD, Director of the Chronic Pain and Fatigue Research Center at the University of Michigan in Ann Arbor.

Diagnostic Guidelines


The ACR 1990 criteria for the classification of FM

- Seminal article on classification criteria.
- Gold Standard in FM diagnosis
- Continues to be used in research on FM/FMS.
Widespread Pain
Occiput: suboccipital muscle insertion
Knee: medial fat pad
Epicondyle: 2cm distal to lateral epicondyles
Upper outer quadrant of buttocks
Parasternal: second costochondral junction
Supraspinatus muscles: at origins, above scapular spine
Trapezius muscles: upper borderer midpoint
Intertransverse spaces @ C5-C7, anterior aspects
Femoral greater trochantor: posterior to prominence
Four kg: approximate force on digital palpation

American College of Rheumatology
1990 Criteria for the Classification Fibromyalgia
History of wide spread pain (>3 months):
- Right & Left side of the body.
- Above & Below the waist.
- Axial skeleton.
Pain in 11.18 tender points on digital palpation (4kg)
(occiput, low cervical, trapezius, supraspinatus, second rib, lateral epicondyle, gluteal, greater trochanter, knee)
88.4% sensitivity / 81.1% specificity

Diagnostic Guidelines
Objectives:
- Simple, practical diagnostic criteria
- Provide a severity scale FM symptoms
- Improve sensitivity/specificity of dx
**American College of Rheumatology 2010 Preliminary Diagnostic Criteria**

Widespread Pain Index (WPI) ≥ 7 &  
- Symptom Severity Scale (SS) ≥ 5

WPI 3-6 & SS ≥ 9

Correctly classifies 88.1% of FM cases classified by the 1990 ACR classification criteria.

<table>
<thead>
<tr>
<th>Widespread Pain Index</th>
<th>Total (0-19) # of areas that the patient has had pain in the last week.</th>
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<tbody>
<tr>
<td>Symptom Severity Scale</td>
<td>Sum (0-12) of the severity of 4 symptoms (fatigue, waking un-refreshed, cognitive symptoms &amp; the level of somatic symptoms) over the last week. Rate symptoms 0-3.</td>
</tr>
</tbody>
</table>

**Patient satisfies the 2010 Fibromyalgia Clinical Diagnostic Criteria if**

- WPI ≥ 7 and SS score ≥ 5
- WPI between 3-6 and SS score ≥ 9
Patients at Risk

Gender - female to male 7:1
Genetics - strong familial component, 8-fold increase risk in a first degree relative, genetic polymorphisms serotonin and dopamine receptors.
Environmental - physical trauma (especially involving the trunk), certain infections (hepatitis C, Epstein-Barr, Lyme disease), emotional stress, hormone alterations, drugs, vaccines.
Psychological Trauma - higher incidence in individuals with co-morbid hx depression, anxiety, PTSD.

• R/O other possible causes of symptoms: primary anemia, hypothyroidism, viral or bacterial dz, vitamin/nutrient deficiencies, primary muscle disorders.

Paradigm of Management

- Behavioral
  - Psychotherapy, CBT, sleep hygiene, biofeedback, relaxation techniques.
- Physical
  - Paced/graduated exercise, individualized PT, warm pool.
- Pharmaceutical
  - Antidepressants, Alpha-2-delta ligands, non-opioid analgesics, other.
- Nutritional
  - Antioxidants, low fat, low glycemic index


The European Union League Against Rheumatism evidenced-based recommendations for the management of FMS

A multidisciplinary task force of 19 experts in FMS representing 11 European countries.
  • Multimodal treatment
  • CBT
  • Tailored exercise program
  • Guided relaxation, biofeedback, heated pool
**Practical Applications**

- Realistic Goals
- Financial Considerations
- Personalize Activities
- Consider physical therapy for education.
- Reinforce positive behaviors/pacing.

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**Practical Applications**

- Education to avoid stigmatization
- Financial Considerations
- Personalize Therapy
- Reinforce positive behaviors/compliance.

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**Pharmaceutical**

Duloxetine (Cymbalta)
- 5- and norepinephrine reuptake inhibitor (SNRI)
- FDA approval 2008
- Fibromyalgia (FM) indication
  60mg qd

Milnacipran (Savella)
- SNRI
- FDA approval 2009
- FM indication 50mg bid
  (max 200mg qd)

Other:
- Tricyclic antidepressant
  (desipramine, amitriptyline, nortriptyline)
Pharmaceutical

Pregabalin (Lyrica)
FDA approval 2007
FM indication 150-225mg bid

Gabapentin (Neurontin)
NOT FDA approved for FM, but does have a clinical indication for neuropathic pain and PHN.
1200mg tid

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<tr>
<th>Drug</th>
<th>Side Effects</th>
<th>Comments</th>
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<tr>
<td>Pregabalin (Lyrica)</td>
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<th>Pharmaceutical</th>
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<tr>
<td>Pramipexole (Mirapex)</td>
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<tr>
<td>- Antiparkinsonian (dopamine agonist)</td>
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<tr>
<td>- NOT FDA approved for FMS</td>
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<tr>
<td>- For FM 4.5mg qhs</td>
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<td>(Holman &amp; Myers, 2005)</td>
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| Naltrexone |
| - Opiate antagonist |
| - NOT FDA approved for FMS |
| - For FM 4.5mg qhs |
| (Younger & Mackey, 2009) |

| Liothyronine (Cytomel (T3)) |
| - Synthetic thyroid replacement |
| - Currently under investigation |
| (Carroll & Younger) |
Muscle Relaxants
- tizanidine
- cyclobenzaprine
- baclofen

Non-narcotic analgesics
- NSAIDS
- ibuprofen
- tramadol

Sleep Aids
- zolpidem
- eszopiclone

Aim was to discover what was known from the scientific literature regarding FM and nutritional status.

Medline 1998-2008 (174 articles)
- Vegetarian/Vegan/low-allergenic diets.
- Weight control
- Increased antioxidant intake
- Low glycemic index (anti-inflammatory).
- Correct nutritional deficiencies (trace elements, Vit D)
- Tryptophan (AA), melatonin, Vit C

15 foods said to cause fibromyalgia flares
- Caffeine
- Refined sugar
- Aspartame
- High fructose corn syrup
- Simple carbohydrates
- Saturated fats
- Red meat
- Alcohol
- Processed foods
- Yeast
- Glutens
- Dairy
- Tomatoes
- Bell and chili peppers
- Eggplant
Nutraceutical product is a food or fortified food product that not only supplements the diet but also assists in treating or preventing disease (apart from anemia), so provides medical benefits.

The word nutraceutical is combined from the words nutrition and pharmaceutical.

Nutraceuticals are not tested and regulated to the extent of pharmaceutical drugs.

Check for deficiencies:
- Vitamin D, coenzyme Q10, carnitine.

Check for allergies/sensitivities:
- Gluten, Diary.

Diet/nutrition Assessment:
- Poor dietary choices?
- Pro-inflammatory diet?

Supplements that can be used empirically:
- Fatigue – omega-3-ols, D-ribose.
- Neuropathy – acetyl L-carnitine, alpha-lipoic acid.
- Gastrointestinal – glutamine, probiotics.
- Sleep – valerian root, melatonin.
- Mood – SAMe, 5HTP, 1-tryptophan.

Other – magnesium, calcium, Vit. D, malic acid, phyto-inflammatories (Kaprex, Zyflament).

Dietary aspects in fibromyalgia patients: results of a survey on food awareness, allergies, & nutritional supplementation

Arranz Li, Canela MA, Rafecas M. - Faculty of Pharmacy, University of Barcelona, Barcelona, Spain. Rheumatol Int. 2011 Jul 22.

Design: Questionnaire (six questions regarding dietary habits, FAIs, and NS use). Patients recruited in local fibromyalgia associations. 101 ♀ suffering from FM, diagnosed for more than 6 months, mean age of 53.88 ± 7.76 years.

Our objective was to investigate the dietary awareness, food allergies and/or intolerances (FAIs), and nutritional supplement (NS) consumption of FM patients. Influence of advice from healthcare provider.

Findings:
- Magnesium was one of the supplements most recommended specifically for FM.
- Seventy-four percentage of these patients used NS following advice from health professionals.
- Once patients are diagnosed, they change their dietary habits and nutritional supplement intake, seeking nutritional strategies to improve their symptoms.
Evidence for the efficacy of complementary and alternative medicines in the management of fibromyalgia: a systematic review


**Design:** Review of available scientific/medical literature - Randomized controlled trials of FM using CAMs, in comparison with other treatments or placebo, published in English up to March 2009.

To critically evaluate the evidence regarding complementary and alternative medicines (CAMs) taken orally or applied topically for the treatment of FM.

**Findings:**
- There is insufficient evidence on any CAM, taken orally or applied topically, for FM.
- Further high-quality trials are necessary to determine whether these initial findings can be supported by a larger evidence base.
- Anthocyanidins (flavonoids), capsaicin and SAMe each showed at least one statistically significant improved outcome compared with placebo.

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**ALGORITHM FOR TX OF FM SYNDROME**

Confirm dx, explain condition, educate about stress reduction/exercise/sleep hygiene, offer TCA for sleep

Symptoms persist/worsen (no) → [Monitor ☺]
  (yes)

Refer to PT for paced exercise program & mental health for CBT

Symptoms persist/worsen (no) → [Monitor ☺]
  (yes)

Reevaluate/ Most persistent symptoms?

(PT injections, manual tx, acupuncture) Focal → PAIN → Generalized (tramadol, OTC, SNRIs, anticonvulsants)
**FATIGUE/ALTERED SLEEP?**

Review pacing activities, sleep hygiene, Refer for formal sleep evaluation
Treat like any primary sleep disturbance

MOOD DISTURBANCE?

Ψ Evaluation
Treat like any major mood disorder
Symptoms Persist → (no) [Monitor]
(yes)
Multidisciplinary Pain Management/Other Specialty Care

**Where Is The Research Going?**

Familial/Genetic Predisposition
Alteration in the Central Nervous System

FMRI

NEUROSENSORY DYSFUNCTION

CLINICAL SYMPTOMS

Substance P

“Wind-up Phenomenon”

Hyperalgesia

NEUROENDOCRINE DYSFUNCTION

NEUROTRANSMITTER DYSFUNCTION

Triggering Events

**Internet Resources**

Fibromyalgia Information: [http://fibromyalgia.ncf.ca/](http://fibromyalgia.ncf.ca/)


American Pain Foundation: [www.painfoundation.org](http://www.painfoundation.org)


Selected References


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