THE FIBROMYALGIA SYNDROME:
HOW FAR HAVE WE COME
IN OUR UNDERSTANDING & MANAGEMENT

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Nothing to Disclose
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.

• Recommend evidence based pharmacological & non-pharmacological options for management.
Fibromyalgia Syndrome

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

Diagnosis of exclusion, of unknown cause.

Psychosomatic
Fibromyalgia is a chronic condition characterized by widespread pain:

- Genetic predisposition.
- Environmental trigger that increases the brain’s susceptibility to pain signals.

It appears to affect certain neurotransmitters in the brain, over activating its pain receptors.

- chronic fatigue
- IBS, IC, TMJ
- mood disorders (depression/anxiety)
- headaches >50%
- abnormal/non-restorative sleep
- restless leg syndrome
- cognitive dysfunction "fibrofog"
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.
History

• **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)
Pathophysiology

- 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 disregulation in certain neurotransmitters, 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.
Use of fMRI to identify differences in brain of FM patient and healthy controls


• 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.
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.

WOKE UP STIFF

A mnemonic for the ACR criteria

- 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: upperborder midpoint
- Intertransverse spaces @ C5-C7, anterior aspects
- Femoral greater trochantor: posterior to prominence
- Four kg: approximate force on digital palpation
1. History of wide-spread pain (>3 months):
   Right & Left side of the body.
   Above & Below the waist.
   Axial skeleton.

2. 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

Objectives:

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

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

2) WPI 3-6 & SS ≥ 9

Correctly classifies 88.1% of FM cases classified by the 1990 ACR classification criteria.
Widespread Pain Index
Total (0-19) # of areas that the patient has had pain in the last week.

Symptom Severity Scale
Sum (0-12) of the severity of 3 symptoms (fatigue, waking un-refreshed, cognitive symptoms) & the level of somatic symptoms over the last week.
Widespread Pain Index (WPI)
In how many areas has the patient had pain in the last week?
Score = 0-19

Symptom Severity Scale (SS)
What was the level of symptom severity in the last week?
Score = 0-12
0 (no problem), 1 (slight), 2 (moderate), 3 (severe)

Fatigue; Waking unrefreshed; Cognitive disturbances; General somatic symptoms

Shoulder (L/R); Upper arm (L/R); Lower arm (L/R);
Jaw (L/R); Neck; Buttock; Hip trochanter (L/R);
Upper leg (L/R); Lower leg (L/R); Upper back;
Lower back; Chest; Abdomen

Patient satisfies the 2010 Fibromyalgia Clinical Diagnostic Criteria if
WPI ≥ 7 and SS score ≥ 5
or
WPI between 3-6 and SS score ≥ 9
### Table 3. The American College of Rheumatology 2010 diagnostic criteria for fibromyalgia

**Criteria**

A patient satisfies the diagnostic criteria for fibromyalgia if the following three conditions are met:

1. Widespread pain index (WPI) ≥ 7 and symptom severity (SS) scale score ≥ 5 or WPI 3–6 and SS scale score ≥ 9
2. Symptoms have been present at a similar level for at least 3 months
3. The patient does not have a disorder that would otherwise explain the pain

**Ascertainment**

1. **WPI**

   Note the number of areas in which the patient has had pain over the last week. In how many areas has the patient had pain? The score will be between 0 and 19.

<table>
<thead>
<tr>
<th>Shoulder girdle, left</th>
<th>Hip (buttock, trochanter), left</th>
<th>Jaw, left</th>
<th>Upper back</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Hip (buttock, trochanter), right</td>
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</tr>
<tr>
<td>Upper arm, left</td>
<td>Upper leg, left</td>
<td>Chest</td>
<td>Neck</td>
</tr>
<tr>
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<td>Upper leg, right</td>
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2. **SS scale score**

   - Fatigue
   - Waking unrefreshed
   - Cognitive symptoms

   For each of the three symptoms above, indicate the level of severity over the past week using the following scale:
   
   0 = no problem
   1 = slight or mild problems, generally mild or intermittent
   2 = moderate, considerable problems, often present and/or at a moderate level
   3 = severe: pervasive, continuous, life-disturbing problems

   Considering somatic symptoms in general, indicate whether the patient has:
   
   0 = no symptoms
   1 = few symptoms
   2 = a moderate number of symptoms
   3 = a great deal of symptoms

   The SS scale score is the sum of the severity of the three symptoms plus the extent (severity) of somatic symptoms in general. The final score is between 0 and 12.

Adapted from Wolfe F et al.29
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.

I decided to take an aerobics class. I bent, twisted, gyrated and jumped up and down for an hour. But, by the time I got my leotard on, the class was over.
Practical Applications

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

“My therapy is quite simple: I wag my tail and lick your face until you feel good about yourself again.”
Duloxetine (Cymbalta)
- SNRI
- FDA approval 2008
- FM indication 60mg qd

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

Other:
- TCA (desipramine, amitriptyline, nortriptyline)
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
## AGENTS APPROVED FOR FIBROMYALGIA

<table>
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<tr>
<th>Agent</th>
<th>Side Effects</th>
<th>Comments</th>
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| Pregabalin (Lyrica) was the first FDA-approved agent for fibromyalgia (1987) | • Common side effects include ataxia, dizziness, sleepiness, and peripheral edema  
• Other side effects include blurred vision, constipation, general weakness, headache, neuropathy, pain, weight gain, and xerostomia  
• Pregabalin is contraindicated for patients with rhabdomyolysis | Pregabalin had been previously approved for seizure disorders, neuropathy, and pain associated with shingles (herpes zoster infection) |
| Duloxetine hydrochloride (Cymbalta), approved in 2008 | • Side-effect profile includes anorexia, constipation, diarrhea, dizziness, drowsiness, fatigue, hyperhidrosis, insomnia, nausea, and xerostomia  
• May increase the risk of suicide  
• Contraindicated for patients with narrow-angle glaucoma and serotonin syndrome | Previously approved for treating depression, anxiety, and diabetes-associated neuropathy |
| Milnacipran HCl (Savella), a selective serotonin and noradrenaline dual reuptake inhibitor, was approved in 2009 | • Nausea is the most frequently reported side effect  
• Other common effects include constipation, hyperhidrosis, vomiting, palpitations, increased heart rate, dry mouth, hypertension, and hot flashes  
• Use with caution in patients with a history of a seizures, mania, or narrow-angle glaucoma | Clinical trials assessed the agent across 3 domains, including pain, physical functioning, and general global assessment, with findings demonstrating effectiveness for all 3 domains |
Pharmaceutical

Pramipexole (Mirapex)
- Antiparkinsonian (dopamine agonist)
- NOT FDA approved for FMS
- For FMS 4.5mg qhs
(Holman & Myers, 2005)

Naltrexone
- Opiate antagonist
- NOT FDA approved for FMS
- For FMS 4.5mg qhs
(Younger & Mackey, 2009)

Liothyronine (Cytomel (T3))
- synthetic thyroid replacement
- currently under investigation
(Carroll & Younger)
Pharmaceutical

Muscle Relaxants
- tizanidine
- cyclobenaprine
- baclofen

Non-narcotic analgesics
- NSAIDS
- tylenol
- tramadol

Sleep Aids
- trazodone
- amitriptyline
- 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
Fibromyalgia Cookbook
A Daily Guide to Become Healthy Again

Revised Edition
WITH CONTRIBUTIONS FROM
William Crook, M.D.

Written By
MARY MOELLER, L.P.N., T.F.H.
Recovered Fibromyalgia and Chronic Fatigue Sufferer

The Fibromyalgia Cookbook
More Than 140 Easy and Delicious Recipes to Fight Chronic Fatigue
15 foods said to cause fibromyalgia flares

* Caffeine
* Refined sugar
* Aspartame
  (also known as NutraSweet)
* High fructose corn syrup
* Simple carbohydrates
  cake, white bread, potatoes, etc.
  (white sugar and white flour products)
* 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.

Nutraceuticals are not tested and regulated to the extent of pharmaceutical drugs. The word nutraceutical is combined from the words nutrition and pharmaceutical.
NUTRACEUTICALS

Supplements that can be used empirically:

• Check for deficiencies: vitamin D, Coenzyme Q10, carnitine.
• Check for allergies/sensitivities: gluten, diary.
• Diet/nutrition assessment: poor dietary choices? Pro-inflammatory diet?

Fatigue - omega-3 oils, D-ribose, CoQ10
Neuropathy - acetyl L-carnitine, alpha-lipoic acid
Gastrointestinal - glutamine, probiotics
Sleep - valerian root, melatonin
Mood - SAMe, 5HTP, 1-tryptophan

Other - magnesium, calcium, VitD, malic acid, phyto-inflammatories (Kaprex, Zyflamend).
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 ± 7.78 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

De Silva, V., El-Metwally, A., Ernst, E., et al., on behalf of the UK Arthritis Research Campaign working group on complementary and alternative medicines, United Kingdom.


**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.

- Anthocyanidins (flavinoids), capsaicin and SAMe each showed at least one statistically significant improved outcome compared with placebo.

- Further high-quality trials are necessary to determine whether these initial findings can be supported by a larger evidence base.
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?

(TP injections, manual tx, acupuncture) Focal ➡️ PAIN ➡️ Generalized
(tramadol, OTC, SNRI, 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

Manipulation of Biochemistry
Pharmacological Research

fMRI

NEUROSENSORY DYSFUNCTION

CLINICAL SYMPTOMS

Manipulation of Biochemistry
Pharmacological Research

Substance P

NEUROENDOCRINE DYSFUNCTION

NEUROTRANSMITTER DYSFUNCTION

“Wind-up Phenomenon”

↓

Hypergesia

Triggering Events
Internet Resources

- Fibromyalgia Information: http://fibromyalgia.ncf.ca/
- National Fibromyalgia Association: http://www.fmaware.org/
- American Pain Foundation: www.painfoundation.org
THANK YOU