Fibromyalgia: Neuropathic or Not

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30 years ago:

- pain in absence of pathology or lesion
  - Work or insurance compensation (malingers)
  - Opioid seekers (liars)
  - Psychiatric disease (hysters)
Always looking for the “pain generator”

La Columna Rota • 1944
Mexican painter Frida Kahlo
FMS NEW definitions
NEW perceptions

- Mechanisms and pathways associated with FMS and central sensitization clearly exist

- FMS shares same pathways as many of the neuropathic pain syndromes (IBS, Interstitial cystitis, CRPS)

Variable Pain Mechanisms

- Nociceptive pain – generated by noxious stimuli
- Inflammatory pain – produced by tissue injury / immune cell activation
- Neuropathic pain – due to a lesion of the nervous system

- Pain with no clear etiological factor:
  - Central sensitization
  - Hereditary component in developing central sensitization in particular system patterns
    (fibromyalgia, Temporomandibular joint disease, tension headache, irritable bowel)
FMS….one or many?

- Chronic Lyme disease
- Post-traumatic stress disorder
- Chronic fatigue syndrome
- Gulf war syndrome
- Multiple chemical sensitivity

Commonly used Terms

1) Chronic Widespread Pain (CWP)
   - > 3 months
   - Lt & Rt side of body + axial skeleton
   - 4 - 15% of population

2) Fibromyalgia (FMS)
   - Defined by ACR in 1990
   - CWP + 11 of 18 TP's
   - 1 to 4% of population
   - Redefined by ACR in 2010 without TP's

3) Myofascial Pain Syndrome (MPS)

*NO biological difference between any of the above*
+ TP’s = Fibromyalgia ?

"Tell me if this hurts."

Tender Points

The gold standard?

“New” = NOT gold standard
Signs and Symptoms Among Unselected FMS Patients

- 20 consecutive patients at initial visit

(Wilke W. Clev Clin 2005)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor sleep</td>
<td>20 (100)</td>
</tr>
<tr>
<td>Low energy</td>
<td>20 (100)</td>
</tr>
<tr>
<td>IBS</td>
<td>17 (85)</td>
</tr>
<tr>
<td>Sound</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Odor</td>
<td>13 (65)</td>
</tr>
<tr>
<td>Light</td>
<td>13 (65)</td>
</tr>
<tr>
<td>Urinary FQ</td>
<td>17 (85)</td>
</tr>
<tr>
<td>Orthostatic</td>
<td>17 (85)</td>
</tr>
</tbody>
</table>

ACR (1990) Criteria

- Compared signs and symptoms of 293 FMS patients (Dx’d by “experts”) vs 265 control pain patients (OA, CTD).

- The symptom of widespread pain for at least three month’s duration and the presence of 11/18 tender points (4 KG) (initially examined 24) provided sensitivity of 88% and specificity of 81% for TPs.

Diagnosis of Fibromyalgia

- Criteria:
  - Diffuse pain of ≥ 3 months
  - Tenderness at palpation in ≥ 11 of 18 “tender points”*

*These anatomic areas are normally more tender. Use 4 kgm pressure.

The Spectrum

- WSP
  - Better:
    - WSP Alone
  - Worse:
    - WSP + TPs
    - WSP + TPs + Fatigue
ACR (1990) wanted to simplify definition

- ACR = pain + TP (fatigue was not included)

New Definition

- severity of pain
- severity of fatigue
- diffuse pain > 3 months
- Sleep difficulties
- Stress – anxiety / depression
- TP likely (but # irrelevant)

“New” = Symptom Intensity Scale (ACR 2010)

- Developed by Wolfe and Rasker (2006): 25,417 patients with various rheumatic diseases
  - found that a “Symptom Intensity scale score” > 5.75 differentiated FMS from other rheumatic diseases
  - it identified 95% of the FMS (from usual ACR definition) AND was predictive for general health among all rheumatic disease patients.

Correlates with patient perceived pain, depression and disability.

NOW part of a new ACR classification for FMS
Questionnaire in 2 parts (patient completes in 5 minutes):

1) Widespread PAIN index (WPI):
   - number of painful anatomic areas (possible 19 areas)
     - jaw, chest, abdomen, upper leg, lower leg, upper arm, forearm, upper back, lower back, shoulder, hip
   - patient response is YES or NO and indicating LEFT or RIGHT side
   - Score will be between 0 and 19

2) Symptom SEVERITY scale (SS score):
   - Fatigue
   - Waking unrefreshed
   - Cognitive symptoms

   Rate each of these over the past week:
   0= no problem
   1= slight or mild problems
   2= moderate, considerable problems, often present and or at moderate levels
   3= severe, pervasive, continuous, life disturbing

Considering somatic symptoms in general indicate whether the patient has:

   0= no symptoms
   1= few symptoms
   2= moderate number of symptoms
   3= a great deal of symptoms

The SS scale score is the sum of the severity of the:
3 symptoms (fatigue, waking, cognitive) +
the extent / severity of somatic symptoms in general

The final score is between 0 and 12
NEW Survey criteria for Fibromyalgia (ACR)

- WPI pain scale $\geq 7$
- Symptom Severity (SS) Scale $\geq 5$

OR

- WPI pain scale 3-6
- Symptom Severity (SS) Scale $\geq 9$

Clinical Features of Fibromyalgia

**WIDESPREAD PAIN**
- Chronic, widespread pain is the defining feature of FM
- Patient descriptors of pain include: aching, exhausting, nagging, and hurting
- Presence of tender points

**SLEEP DISTURBANCES**
- Characterized by nonrestorative sleep and increased awakenings
- Abnormalities in the continuity of sleep and sleep architecture
- Reduced slow-wave sleep
- Abnormal alpha wave intrusion in non-REM sleep

**FATIGUE/STIFFNESS**
- Morning stiffness and fatigue are common characteristics of FM
FMS – MIMICS, COMPLICATES other diseases

- Can occur with auto immune diseases (RA, SLE, Sjogren’s) = fatigue, HA, joint stiffness out of proportion to other measures of autoimmune disease activity

- In FMS (vs. CTD):
  - Diffuse pain at rest
  - Poor sleep
  - Joint pain without swelling
  - HA and depression

In the absence of other signs and symptoms

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Frequency of FMS in “Connective Tissue Disease”

<table>
<thead>
<tr>
<th>First Author</th>
<th>Disease</th>
<th>No. Patients</th>
<th>% FMS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morand</td>
<td>SLE</td>
<td>87</td>
<td>5</td>
</tr>
<tr>
<td>Gladman</td>
<td>SLE</td>
<td>119</td>
<td>21</td>
</tr>
<tr>
<td>Middleton</td>
<td>SLE</td>
<td>102</td>
<td>22</td>
</tr>
<tr>
<td>Wallace</td>
<td>SLE</td>
<td>464</td>
<td>22</td>
</tr>
<tr>
<td>Handa*</td>
<td>SLE</td>
<td>158</td>
<td>8</td>
</tr>
<tr>
<td>Vitali</td>
<td>SS</td>
<td>30</td>
<td>47</td>
</tr>
<tr>
<td>Wolfe</td>
<td>RA</td>
<td>280</td>
<td>13</td>
</tr>
<tr>
<td>Buskila</td>
<td>IBD**</td>
<td>113</td>
<td>30</td>
</tr>
</tbody>
</table>

*study performed in India
**CD 49%, UC 19%, controls 0%
Fibromyalgia: Because Pain Threshold is Low (Not Pain Tolerance)

- Arthritis
- Bursitis
- Tendinitis
- Neuropathy

Produce More Severe Pain

Overlapping Conditions with Widespread Secondary Hyperalgesia Allodynia

- Chronic fatigue syndrome
- Irritable bowel (IBS)
- Temporomandibular joint disorder (TMJD)
- Vulvodynia
- Headache (tension/migraine)
- Idiopathic low back pain
- Whiplash associated disorder

= CONFUSING |
= MISLEADING |
= CAN LEAD DOWN WRONG PATH |
FMS: a clinical entity – not a disease

- Use FMS as a working hypothesis in which to group certain clinical features (sleep disturbance, diffuse pain, +/- TP, anxiety-stress, IBS etc)

- Determine what symptoms are FMS related and which are related to structural or systemic pathology
  = avoid intervention or surgery on functional and neuropathic symptoms

Case #1

- 40 yo female with history of rheumatoid arthritis. On disease modifying meds for her RA which is considered stable

- Chief complaint: pain in arms Right more than Left. Randomly occurring numbness in both hands mainly in D4 and D5. Symptoms worse as day progresses. Feels best in am. Midscapular and axial neck pain

- Hx of right carpal tunnel and right cubital tunnel release 1 year ago - transient benefit
Clinical exam

- Painful cervical ROM – mainly in extension
- Negative foraminal compression for referred UE symptoms
- Tender over right lateral and medial epicondyle, midtrapezius and both greater trochanters
- Pain with shoulder abduction and internal rotation - but negative impingement signs and strong rotator cuff
- Normal DTR’s in upper – lower extremities
- Negative Hoffman’s, Babinski
- Normal vibration and temperature discrimination
- Symmetrically weak proximally and distally to resistive testing

XR and Imaging

- Cervical spine showed disc space narrowing C4-5,C5-6, C6-7 with grade 1 listhesis at C4-5 and C5-6
- Cervical MRI showed mild central canal stenosis at C5-6 and neural foraminal stenosis moderate at C5-6 and C6-7
- EMG compatible with bilateral carpal tunnel syndrome
Clinical course

- Cervical epidural steroid injection - no benefit
- Left carpal tunnel injection - no change in symptoms
- No response to nighttime bracing
- Physical therapy – “feels worse”

Follow-up visits

- Difficulty falling asleep and nighttime awakening occasionally with pain
- Abdominal cramping periumbilical pain and constipation and occasional diarrhea. Negative upper GI, colonoscopy and abdominal CT other than gallbladder wall thickening
- Cramping in feet and restless leg feeling and during the day, feeling of “whole leg pain and weakness” unrelated to position or walking
Options

- General surgery consult for lap cholecystectomy
- Orthopedics consult for carpal tunnel and epicondylitis
- Spine surgery consult for spinal stenosis and radiculopathy
- Sleep medication
- Pain medication
- None of the above

Multifactorial pathogenesis

- Hypothalamic-pituitary-adrenal-axis abnormalities
- Central sensitization
- Increased levels of substance P & neurotrophins (spinal cord)
- Depression, anxiety
- Peripheral nociception, abnormal wind-up

Fibromyalgia pain
Pathogenesis: genetics + environment

1) Borderline Neurobiological factors:
   - General sensory augmentation
     - Heat, Cold, Noise, Smells and other sensory stimuli
   - Decreased activity of descending inhibitory pathways
     (deficit in serotonin, norepinephrine, dopamine)
   - Hypothalamic-Pituitary axis dysfunction
     = decreased cortisol response
**Pathogenesis:**

*genetics + environment*

- 2) Excessive nociceptive firing & central sensitization

![Diagram](image)

- Trauma
- Infection
- Sleep deprivation

> cytokines (secondary to decreased cortisol response)

> peripheral nociceptors

> via NMDA

Dorsal horn sensitization → allodynia → widespread pain

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**Pathogenesis:**

Pain → fear-avoidance → exercise / sleep → stress

Dysregulation monoamine pathways

Gate control dysfunction at dorsal horn

IL-6 cytokines

nociceptor sensitization
Pathogenesis

DEPRESSION / ANXIETY lead to:

Disruption of short wave sleep (SWS) i.e. stage 3 and 4 of non-REM sleep = disruption of synthesis of hormones and neurotransmitters that govern many organ systems and the CNS.

- Decreased activity of pituitary endorphins which modulate nerve excitability.
- Decreased Serotonin levels = increased nerve firing

Pain Comorbidities:
Sleep and Mood Alterations

Pain

Depression/ anxiety

Functional impairment

Sleep disturbances
Fibromyalgia Syndrome
how do we explain it?

FMS = Central Sensitization

- All nerves in FMS patients are more sensitive than they should be including the brain and spinal cord:
  - Difficulty with concentration / focus
  - Light, odors, sounds become intolerable
  - IBS
  - Interstitial cystitis
  - Autonomic dysfunction = vasovagal symptoms
Central Sensitisation

- Central sensitization readily induced in animal and human volunteers after activating nociceptors (e-stim, mustard oil, capsaicin, heat or UV burn, hypertonic saline injection) in skin, viscera or muscle.

- Sensitization phenomenon presents as:
  - Tactile allodynia
  - Hyperalgesia
  - Enhanced pressure and thermal sensitivity
  - Spreading to neighboring nonstimulated sites and remote regions

Central Sensitization: objective findings reproduced in volunteers and animal models

- Nociceptors can become sensitized after injury reducing their firing threshold.
- Low frequency action potentials (stimuli) into the CNS generate increased synaptic efficacy in nociceptive neurons in dorsal horn of spinal cord which persisted after the stimuli had ended (LTP = long term potentiation).
- This state of sensitization amplified subsequent responses to other non nociceptor fibers (i.e. A beta fibers mediating allodynia).
- Gain (is a measure of the ability of a circuit - often an amplifier - to increase the power or amplitude of a signal from the input to the output) of neurons in the pain pathway is increased thus non noxious stimuli can activate the pain pathway and pain is felt in the absence of a real noxious stimulus.
- Consequences of central sensitization can be measured by objective biomarkers (i.e. Functional MRI changes in the cortex).
- Centrally acting drugs may reduce central sensitization: Ketamine (NMDA antagonist), gabapentin reduces tactile allodynia, duloxetine, milnacipran, lamotrigene and Cox 2 inhibitors (if sensitization is triggered by peripheral inflammation).
Physiology of Pain Perception

- Transduction
- Transmission
- Modulation
- Perception
- Interpretation
- Behavior

Central sensitization

CSS

Descending Pathways

Peripheral Nerve

C-fiber
α-β Fiber
α-δ Fiber

Ascending Pathways

Spinal Cord

Brain

Limbic Forebrain System

Dorsal Root Ganglion

Dorsal Horn

Injury
Central sensitization

- Increased excitability of spinal cord neurons (dorsal column) from peripherally sensitized afferents
- Leads to increased duration (spontaneous firing) and enlarging area of response (wide dynamic range neurons and “wind up”)
- Leads to abnormal neuro - anatomical reorganization with connections between A beta, A delta and C fibers (sprouting) - which can spread thus involving multiple dermatomes = diffuse symptoms

= symptoms outlast the injurious stimuli (LTP=long term potentiation)

Normal Pain Pathways in the Dorsal Horn

Stimulus

Innocuous

Noxious

Noxious

Sensory information

Withdrawal reflex

Pain

Dorsal columns

Pathophysiology of Fibromyalgia: The Role of Central Sensitization

1. First, impulses from afferents depolarize dorsal horn neurons.
2. Then, extracellular Ca\(^{2+}\) and nitric oxide diffuse into neurons and cause exaggerated release of substance P and glutamate; this results in neuronal hyperexcitability.
3. Finally, a pain signal is sent to the brain from the dorsal horn.

• In FM, dorsal horn neurons become hyperresponsive to nociceptive and nonnociceptive somatic stimulation.
• This is known as central sensitization and is thought to result in hyperalgesia and allodynia.

Despite extensive research, the pathogenesis of pain in FM is not clearly understood. However, central sensitization has emerged as a leading theory of disease mechanism.


Central sensitization leads to non-nociceptive nerve impulses being perceived as painful (allodynia).

Wide dynamic range (WDR) neurons normally respond to input from both nociceptive and non-nociceptive nerves, with appropriate interpretation of touch or pain by brain. In central sensitization, impulses from non-nociceptive nerves (for example, touch) are perceived as being painful (allodynia).

Bennett, Mayo Clin Proc. 1999

Central sensitization leads to nociceptive nerve impulses being perceived as more painful (hyperalgesia).
Neural Influences on Pain and Sensory Processing

Facilitation
- Substance P
- Glutamate and EAA
- Serotonin (5HT$_{2a, 3a}$)
- Nerve growth factor
- CCK

Inhibition
- Descending antinociceptive pathways
- Norepinephrine-serotonin (5HT$_{1a,b}$), dopamine
- Opioids
- GABA
- Cannabinoids
- Adenosine

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There is a Deficiency of Descending Analgesic Activity in FM$^{1,2}$ Which One?

<table>
<thead>
<tr>
<th>Opioids</th>
<th>Noradrenergic/Serotonergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal or high levels of CSF enkephalins$^3$</td>
<td>Low levels of biogenic monoamines in CSF in FM$^5$</td>
</tr>
<tr>
<td>Never been administered in RCT but most feel that opioids are ineffective or marginally effective</td>
<td>Nearly any class of drug that raises both serotonin and norepinephrine has demonstrated efficacy in FM</td>
</tr>
<tr>
<td>Harris recently used PET to show decreased mu opioid receptor binding in FM$^4$</td>
<td></td>
</tr>
</tbody>
</table>
FMS…What doesn’t Work

- TP injections
- Flexibility exercises
- Chiropractic
- Modalities (US, massage)
- Acupuncture
- Opioids
- Corticosteroids
- NSAI
- Benzodiazepines
- Melatonin
- Calcitonin
- Thyroid suppl
- Magnesium
**Transcranial Direct Current Stimulation (tDCS)**

Arthritis Rheum. 2006;54:3988-3998

**Transcranial Magnetic Stimulation (TMS)**

Passard et al Effects of unilateral repetitive transcranial magnetic stimulation of the motor cortex on chronic widespread pain in fibromyalgia.
Brain 2007;130(Pt 10):2661-70

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**Analgesic Drugs**

<table>
<thead>
<tr>
<th><strong>Mechanism of Action</strong></th>
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</thead>
<tbody>
<tr>
<td><strong>Analgesic Drugs</strong></td>
</tr>
<tr>
<td><strong>Acetaminophen</strong></td>
</tr>
<tr>
<td><strong>Nonselective NSAIDs</strong></td>
</tr>
<tr>
<td><strong>COX-2 selective inhibitors</strong></td>
</tr>
<tr>
<td><strong>Tramadol/Tapendalol</strong></td>
</tr>
<tr>
<td><strong>Opioids</strong></td>
</tr>
<tr>
<td><strong>Antidepressants</strong></td>
</tr>
<tr>
<td><strong>Anticonvulsants</strong></td>
</tr>
</tbody>
</table>
**Tramadol**

- Weak μ opioid agonists
- norepinephrine and serotonin reuptake inhibition
- ER= Lag in drug absorption; reaches peak in 12 to 15 hours; steady state in 4 days
- An adequate trial requires 4 wk at maximum dosage
- Initiate tramadol ER at 100 mg/d and increase every 5 days to maximum of 300 mg/d


**Tapendalol**

- Mu opioid agonist, serotonin /NE reuptake inhibition
- Adjustment for renal insufficiency
- Available in IR (50, 75, 100 mg) titrate up to
- Available in ER (50,100,150,200 mg) titrate up to
- Side effect and precautions as with all opioids, possible serotonin syndrome in combination with other serotonin reuptake inhibitors (duloxetine, TCA’s etc)
**Gabapentin and Pregabalin: Mechanism of Action**

- Binds to a subunit of voltage-gated calcium channels
  - Reduces Ca\(^{2+}\) influx during depolarization
  - Analgesic, anxiolytic, and anticonvulsant activity
- Reduces release of excitatory neurotransmitters, (glutamate, norepinephrine, substance P)
- Effective in trials of epilepsy, neuropathic pain, and generalized anxiety

**Onset and Resolution of Dizziness and Somnolence in Controlled Trials of Pregabalin in FM**

<table>
<thead>
<tr>
<th></th>
<th>Dizziness</th>
<th>Somnolence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence*</td>
<td>38%</td>
<td>20%</td>
</tr>
<tr>
<td>Discontinuation*</td>
<td>6 (85)</td>
<td>3 (52)</td>
</tr>
<tr>
<td>Median time to onset</td>
<td>2 days</td>
<td>3 days</td>
</tr>
<tr>
<td>Median time to resolution (completers)</td>
<td>17 days</td>
<td>34 days</td>
</tr>
</tbody>
</table>

*Among those patients who reported dizziness or somnolence 38% and 58%, respectively continued to experience the reported adverse event for the duration of the trial

*All pregabalin dose groups pooled (n=1,517)
**TCAs: Mechanisms**

- Relief of pain through serotonin and norepinephrine reuptake blockade\(^1\)
- Blockade of \(\alpha\)-adrenergic receptors\(^2\)
- Sodium and potassium channel modulation\(^1,2\)
- Modulation of monoamine neurotransmitters\(^1\)
- \(?\) NMDA-receptor antagonism\(^1\)


**TCAs: Adverse Effects**

- Commonly reported AEs (generally anticholinergic)
  - Blurred vision
  - Cognitive changes
  - Constipation
  - Dry mouth
  - Orthostatic hypotension
  - Sedation
  - Sexual dysfunction
  - Tachycardia
  - Urinary retention

- Fewest AEs
  - Desipramine
  - Nortriptyline (*Pamelor*)
  - Imipramine (*Tofranil*)
  - Doxepin (*Sinequan,Sinelor*)
  - Amitriptyline (*Elavil*)

- Most AEs
SNRIs

**Venlafaxine (Effexor)** and duloxetine (Cymbalta)

- Inhibit norepinephrine and serotonin reuptake and increase synaptic availability
- Results suggest safety, tolerability, and effectiveness in patients with painful DPN
- Minimal anticholinergic AEs

**Milnacipran** (Savella)

FDA approved in 1/2009 for FMS (used since 1998 in Europe for depression)

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Sodium Oxybate (Xyrem)

- Sodium salt of γ-hydroxybutyrate (GHB), an endogenous neurotransmitter and/or neuromodulator and metabolite of GABA \(^1\)
- Approved for treatment of narcolepsy symptoms (EU, US, Canada) \(^2\)
  - Schedule # 3 drug (potential for abuse)
- Approved in some EU countries as an IV anesthetic and for treatment of alcohol withdrawal
- Increases slow-wave-sleep and reduces sleep disruption \(^1\)

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**References**


- Sodium Oxybate (Xyrem) RCT, double blinded, placebo controlled showed improved function and pain Russell et al, Arthritis and Rheum.2009; 60(1):299-309
**Study Design - Sodium Oxybate for Fibromyalgia**

- **Design:** Randomized, double-blind, placebo-controlled, parallel-group design at 108 sites US and EU (n=573)

- **Treatment Groups:**
  - Sodium oxybate 4.5 g/night (SXB4.5g)
  - Sodium oxybate 6 g/night (SXB6g)
  - Placebo (PBO)

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**FIQ & PGIC Responders – Week 14**

**FIQ**

- >30% Improvement in FIQ
  - Placebo (n = 181)
  - SXB 4.5 g (n = 190)
  - SXB 6 g (n = 185)

- Proportion of Patients
  - Placebo: 29.8%
  - SXB 4.5 g: 50.0%*
  - SXB 6 g: 55.1%*

**PGIC**

- "Much Better" or "Very Much Better" on PGIC
  - Placebo (n = 181)
  - SXB 4.5 g (n = 190)
  - SXB 6 g (n = 179)

- Proportion of Patients
  - Placebo: 16.0%
  - SXB 4.5 g: 32.1%*
  - SXB 6 g: 39.7%*

Data on file, Jazz Pharmaceuticals, Inc.
Pain VAS Responders at Week 14

Data on file, Jazz Pharmaceuticals, Inc.

Other options – non FDA approved

- **Dopamine agonist = Mirapex (pramipexole) 4.5 g @ bedtime**
  
  Holman et al – Randomized double blind, placebo controlled trial of pramipexole, a dopamine agonist, in the treatment of patients with fibromyalgia receiving concomitant medications. *Arthritis and Rheum.* 2005;52:2495-2505

- **Zanaflex (tizanidine) 4 mg at bedtime**
  
  Russell IJ et al. (2002) Therapy with a central alpha 2-adrenergic agonist (tizanidine) decreases cerebrospinal fluid substance P, and may reduce serum hyaluronic acid as it improves the clinical symptoms of the fibromyalgia syndrome. *Arthritis Rheum* 46: S614
**EULAR treatment recommendations (2008)**
(European League of Associations for Rheumatology)

- Multi disciplinary approach (pharmacological and behavioral)
- Heated pool treatment with or without exercise
- Individually tailored exercise (aerobic & strength training)
- Relaxation, physiotherapy, psychological support on case by case basis
- Tramadol / Tapendalol for the management of pain (no opioids or corticosteroids)
- Antidepressants (they noted only ONE trial lasting longer than 12 weeks and did not show improvement in pain compared to control)
- Pregabalin can reduce pain - should be considered (functional improvement not assessed in studies)

Recommendations based on FMS (ACR criteria only) literature review and expert review (19 experts from 11 countries)

**Ann Rheum Dis 2008: 67: 536-541**

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**Summary Treatment**

- Do not treat the symptoms of FMS

- Treat the pathogenic factors (depression, sleep disorders, distress)
  - CNS serotonin and norepinephrine reuptake inhibitors
  - TCA
  - Pregabalin
  - Aerobic exercise
  - Non pharmacological = meditation, biofeedback, aquatics, massage

- Treat “syndromes within the syndrome”:
  - IBS
  - Restless legs
  - Irritable bladder
  - Underlying triggers (focal areas of OA, nerve compression etc)
FACTORS WHICH EFFECT PROGNOSIS IN FIBROMYALGIA OUTCOME

<table>
<thead>
<tr>
<th>Better</th>
<th>Worse</th>
</tr>
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<tbody>
<tr>
<td>↑ Level of education</td>
<td>↑ Feelings of helplessness</td>
</tr>
<tr>
<td>↓ Age onset</td>
<td>↑ Severe initial symptoms</td>
</tr>
<tr>
<td>&lt; 5 years duration</td>
<td>↑ Depression</td>
</tr>
<tr>
<td>↑ Increased time spent in exercise</td>
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</tbody>
</table>

PROGNOSIS IN FIBROMYALGIA

- Some studies show little improvement over time.
- In one study of community treated patients evaluated after 2 years:
  - 46% no longer fulfilled criteria for FMS.
  - 22% achieved remission.

Granges:1994
Practical considerations

- Symptoms are important mediators of disability
- FMS patients frequently minimize psychological distress and describe HIGH levels of disability
- Repeated reassurance is frequently met by challenges to the physician’s judgment and competence
- Patient = symptoms are ominous
  Physician = symptoms have no basis in disease

- Mismatched outlooks
- Physician frustration
- Patient dissatisfaction

How can we best share the FMS diagnosis with our patients?
Practical considerations

- “You have a pain problem that is relatively common. It’s not harmful but it is very difficult to deal with. We don’t really understand it well. We know there are things we can do that will help but it’s unlikely that the symptoms will resolve or disappear. Some physicians refer to the combination of these symptoms as fibromyalgia but there is no known cause”.

- When fibromyalgia is present it changes the features of other diseases
- Understand the potential consequences of labeling a patient with FMS diagnosis – implications for work, SSD, litigation in accidents or post traumatic allegations.
- Recognition of depression will improve overall health (use of Wolfe’s ACR / Symptom intensity scale).

Avoid frustration....
If all else fails.....

GO FISHING !!!
(Colorado cutthroat trout)
Thank you