

## Fibromyalgia

### 1. Definition

American College of Rheumatology (ACR)  
Wolfe, F. et al Arthritis Rheum 1990; 33:160-72

Criteria:

1. Chronic, widespread pain (i.e. in at least 3 of 4 body quadrants for three months)
2. Presence of pain in 11 of 18 standardized "tender points" on palpation

81% sensitive

88% specific

### 2. Epidemiology

- 2-4 % of the world's population
- Evenly divided between industrialized and rural countries
- Predominately in women 3.4 %-10.5%, compared to men 0.5%  
Russell, IJ - CNS Spectr. 2008; 13(3 Suppl 5): 6-11  
Lawrence, R.C. Arthritis Rheum. 1998; 41(5): 778-799
- 5 million adults in US
- 200,000 in DFW metroplex

### 3. Pathophysiology

An interplay among genetic factors, environmental triggers, neuroendocrine abnormalities, and aberrant central pain processing

#### A. Genetics

1. Familial aggregation of FM patients i.e. with first degree female relatives found with greater number of tender points and low pressure scores to elicit pain Kato: Arthritis Rheum. 2006; 54(5): 1682-86
2. Swedish Twin Registry: 15, 950 pairs, genetics and shared environment each explained half the variation Kato-see above
3. Gene Encoding
  - FM linked to single nucleotide polymorphism in the serotonin 2A-receptor gene Neurobiol Dis. 1999; 6(5): 433-439
  - Increase risk of FM with MDD and diarrhea predominate IBS Arthritis Rheum 2002; 46(3): 845-847
  - Higher harm avoidance scores, lower novelty-seeking scores, a significant decrease in frequency of the dopamine D4 receptor allele with FM Mol. Psych. 2004; 9(8): 730-731
  - Increase combination of 2 COMT gene polymorphisms (have diminished mu-opioid response to pain) in FM patients Rheum. Int 2003; 23(3): 104-107

## B. Peripheral Tissue Abnormalities

- Increase nitric oxide: which may increase cell deaths;
- Decrease phosphocreatine/ATP (lower oxidative capacity)
- Increase sub. P, interleukin-1, DNA fragments (perfusion defects)
- In skin of FM patients vs. controls  
Increase NR2D receptors (glutamate an important pain modulator, binds to NR2 subunits of NMDA receptors) ((N-methyl D-aspartate)
- EM of unmyelinated fibers, Schwann cell ballooning, axonal peripheralization, smaller axonal size, simplified folding structure

## C. Biochemical Abnormalities

- Decrease serum serotonin/norepinephrine levels in FM (not found in all condition involving widespread pain)
- Decrease CSF serotonin precursors in FM
- Decrease CSF norepinephrine and dopamine metabolites in FM
- Increase CSF substance P, nerve growth factor, glutamate
- Decrease mu-opioid receptor availability

## D. Neuroendocrine Abnormalities

- Decrease ACTH/epinephrine to hypoglycemia
- Decrease peak cortical response to ACTH
- Decrease 11-deoxycortisol level in metyrapone test

## E. Functional Imaging

- Greater activation of brain in response to lower pain stimulation on fMRI
- Decrease metabolism of bifrontal lobes at rest: worse with overexertion

## F. Triggering Factors

- Emotional stress- early life trauma, PTSD(1/4) conditions found in military deployed Iraqi-Gulf War
- Physical stress- heavy lifting, repetitive motions, injuries especially cervical whiplash (8x increase vs. lumbar strains)
- Medical conditions: endometriosis 60%, hypothyroidism, diabetes, hepatitis C (2 fold increase)
- Autoimmune disorders: SS 50%, SLE 30%, RA 20%

## 4. Comorbid Conditions

Major depressive disorder

FM: 61.5% life time prevalence vs. 27.5% controls: with lifetime hx. depression, 4x increase in FM vs. controls

Muscular and migraine headaches

Panic Disorders

Generalized Anxiety Disorders

Post traumatic Stress Disorders

Bipolar Disorder

Irritable Bowel Syndrome

5. Symptoms commonly associated with FM

Neurological: cognitive dysfunction “fibrofog”,  
i.e. poor STM, WFD, attentional disorder, difficulty multitasking  
Psychiatric: anxiety, depression, fear, anger, guilt  
Gastrointestinal: abdominal pain, bloating, constipation, diarrhea  
Constitutional: fatigue, weakness, night sweats stiffness, swelling, postural  
dizziness  
Miscellaneous: widespread allodynia multiple chemical sensitivities  
Sleep: insomnia, RLS, unrefreshing sleep

6. Common Conditions Associated with Generalized Pain

- a. Rheumatological: ankylosis spondylitis, gout, MCTD, RA, SLE, Sjogren's, syndrome, scleroderma, polymyalgia rheumatica
- b. Endocrine: adrenal dysfunction  
Hypothyroidism  
Hyperparathyroidism
- c. Musculoskeletal: Myofascial pain syndrome  
Disorders      Statin-induced myopathy  
                         Cervical/Lumbar spondylosis  
                         Osteoarthritis
- d. Infectious: Hepatitis C  
                         HIV  
                         Lyme's disease
- e. Nutritional: Vitamin B12 deficiency  
                         Vitamin D deficiency
- f. Neurological: Chronic neuropathy  
                         Multiple Sclerosis  
                         Myasthenia gravis  
                         Polymyositis, metabolic myopathy  
                         Generalized dystonias
- g. Miscellaneous: CFS  
                         Occult malignancy  
                         Opioid-induced hyperalgesia  
                         Chronic Insomnia

7. Diagnosis and Treatment

- Identify history of chronic, widespread pain for greater than or equal to 3 months
- Conduct general physical examination, neurological examination, sleep and mood evaluation, selected laboratory testing (eg, ESR, thyroid tests; Vitamin D, Vitamin B12)
- Consider holding statins temporarily
- Rule out other conditions that may present with chronic widespread pain
- Confirm presence of tender points (ACR criteria require greater than 11)
- Confirm diagnosis of fibromyalgia

### Confirm diagnosis of fibromyalgia

- Identify symptom domains, their severity, and level of patient function
- Assess for comorbid medical and psychiatric disorders
- Assess psychosocial stressors, level of fitness, and barriers to treatment
- Provide fibromyalgia education( individual or group) and review treatment options

### Recommended treatment based on individual evaluation

- Conduct first-line trials with evidence-based medications, such as SNRIs, alpha-2-delta ligands, or if these do not work, SSRIs or TCAs
- Use appropriate multidrug therapy if partial response to monotherapy is observed
- Provide additional treatment for comorbid medical and psychiatric disorders

### Consider adjunctive nonpharmacologic approaches

- Refer for CBT in patients with psychosocial stressors, or difficulty coping or exercising
- Encourage exercise according to fitness level (eg. 30 to 60 minutes of low-to moderate-intensity aerobic exercise (walking, pool exercises, stationary bike) at least 2-3 times per week)
- Encourage participation in supervised or group exercise

### Pharmacologic Treatments in Fibromyalgia Syndrome

<u>Effectiveness</u>	<u>Pharmacologic Therapies</u>
Strong evidence	Amitriptyline Cyclobenzaprine Duloxetine Gabapentin Pregabalin Milnacipran
Moderate evidence	Fluoxetine Tramadol
No evidence	Benzodiazepines Corticosteroids NSAIDs Opioids

Novel: Use of low-dose Naltrexone  
Yunger et al. Pain medicine Vol. 10 #4 2009

### In the Trenches Pearls for FMS

- Trust and believe in your patients
- Treat each patient as your parent; if you like your parents
- Teach your patients. Doctor comes from “docere” in Latin and means teacher
- Take a detailed history and especially focus on the onset of clinical symptoms.
- Go slow on therapeutics- it’s a chronic disorder; it’s not going to be cured at all, and it may take 6-12 months for optimal management
- Focus on functionality
- Emphasize reasonable pain control i.e. VAS 4-5
- Control the big 3 symptoms, as simply and safely as possible – pain, insomnia, and fatigue
- Exercise to capability
- Find a good rheumatologist to evaluate/treat co-existing rheumatological disorders that may respond to specific therapy and secondarily improve the FM
- Successful treatment depends greatly on management of comorbid disorders especially psychiatric
- Analgesic misuse is common, forgivable, and can respond to education.
- True addiction i.e. 4 C’s, is fairly rare (Craving, Compulsive, loss of Control over use, Continued use despite knowledge of harmful Consequences)
- Understand the differences between misuse, physiological dependency, withdrawal syndrome, pseudoaddiction and addiction
- Educate and involve the extended family; don’t forget Vitamin D and statins
- Document everything.
- Take a short walk in the woods with enduring friends every Wednesday and finish at the 19<sup>th</sup> hole.