Fibromyalgia
Past, Present, and Future

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Conflicts of Interest

- Consultant for Depomed
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Introduction

• Fibromyalgia
  • Chronic pain disorder which results in
    • Widespread hypersensitivity
    • Sleep disorders
    • Abnormal thinking
    • Fatigue
  • Can also result in
    • Depression/anxiety
    • IBS or GI complaints
    • Pelvic pain
    • Migraine/tension headaches
    • Irritable bladder
    • TMJ
History

- Guillaume de Baillou circa 1592
  - Rheumatism
    - Muscular pain and acute rheumatic fever
- 1700’s
  - Articular rheumatism
    - Painful deforming condition of joints
  - Muscular rheumatism
    - Painful nondeforming soft tissue disorders
Articular vs. non articular rheumatism

http://www.google.com/url?sa=i&rct=j&q=&esrc=s&source=images&cd=&cad=rja&uact=8&docid=FIt0MAkfiKzi2M&tbnid=E6Q9 _G5yWKAZjM:ved=0CAQQjBo&url=http%3A%2F%2Fwww.arthriti s.co.za%2Frheumatoid%2520arthritis%2520an%2520update.html&ei=x05lI8eSFYWZyASPvYKwAg&bvm=bv.65788261,d.aWw&p sig=AFQjCNGB-BgizYFhizs873q6uUOT9WVvw&ust=1399234603281410

19th century

- Literature published on muscular rheumatism from German, Scandinavian, and British physicians
- William Balfour
  - 1815 Nodules were the result of inflammation in muscle connective tissue
  - 1824 Focal tenderness in muscles first referred to as tender points
- François Valleix
  - 1841 painful points in the body referred to other areas on palpation
  - Suggested muscular rheumatism as a form of neuralgia
19th century

- Inman
  - 1858 trigger point radiation independent of nerves
  - Functional change due to spasm
- Beard
  - 1880 relation of widespread pain, fatigue, and psychological disturbance
  - Neurasthenia
  - Myelasthenia
  - Attributed to stresses of modern life
19th century

http://www.mdjunction.com/forums/fibromyalgia-me-discussions/general-support/1046518-tender-point-locations

http://championschiropractic.com/archives/268
20th century

- Cornelius
  - 1903 local tender points from hyperactive nerve endings called nerve points
- Hyperactivity due to external stimuli
  - Climate
  - Emotional
  - Exertion
Fibrositis

- Sir William Gowers
  - 1904 “We are thus compelled to regard lumbago in particular, and muscular rheumatism in general, as a form of inflammation of the fibrous tissues of the muscles...(and thus)...we may conveniently follow the analogy of ‘cellulitis’ and term it ‘fibrositis’.”
    - Spontaneous pain
    - Sensitivity to compression
    - Fatigue
    - Sleep disturbance
    - Exaggeration by acute/chronic cold and overstrain
Fibrositis

- **Treatment**
  - Manipulation
  - Counterirritation
  - Cocaine injections
  - Failure of salicylates

- **Stockman**
  - 1904 Provided pathologic basis for Gowers inflammation theory from myalgic muscle biopsies

- Mayo clinic physicians reexamined Stockman sections and could not corroborate the findings
Pain Clinic Initial Evaluation:

Name

Main Complaint:  **Pain**

Age 68  Sex:  

History of Present Illness:  surgury spinal stimaus of lumbar region.  Dr. Stephen Bostick, here on 8/3/2010, I have a rod 8 4 screws.

1) What caused your pain?  (circle one): Work Injury/MVA/Other  

   Explain:  my spine is tested tightening

2) When did it start?  1904

3) Draw where your pain is on the diagram below:

4) Rate your pain by putting a "X" on the line below:

   No Pain  

5) Pain Relieved By:  Norco 10mg 325mg per 8-10 hours

Exacerbated By:
Fibrositis

- Sir William Osler
  - 1909 Fibrositis was nothing more than neuralgia of sensory nerves of the muscles
  - Lack of laboratory tests
  - Uncertain histologic changes
  - Uncertain physical findings
    - Led to non recognition by north American physicians

- Kellgren
  - 1937 injected hypertonic saline into muscle groups and interspinous ligaments and proved radiating patterns
Fibrositis

- Kelly
  - 1941 proposed the somatovisceral reflex theory
  - Information from tender points caused a CNS reflex of deep pain and hyperalgesia
  - Suggested local anesthetic injection

- Travell and Rinzler
  - 1940’s published work on myofascial trigger points and myofascial pain syndrome
  - Described myofascial trigger point referral patterns
Fibrositis

- World war II
  - Growing interest as 70% of british troops admitted to a hospital had fibrositis
  - 5.8% of American soldiers admitted diagnosed with fibrositis
- Copeman and Pugh
  - 500 soldiers seen whereby the number of nodules were equal between those with and without fibrositis
  - 10 times the amount of tender/trigger points in fibrositis pts. 30% vs. 3%
Fibrositis

- Traut
  - 1968 described first modern day description of Fibromyalgia (FMS)
    - Female gender
    - Generalized aching and stiffness
    - Fatigue
    - Headaches
    - Colitis
    - Poor sleep
    - “worry worts”
    - Tender points
  - Described mind-body interaction in pathogenesis of FMS
Fibrositis

- Smythe
  - Grandfather of modern day FMS
  - Late 70’s 10 page chapter in popular rheumatology text
  - First to describe as generalized pain syndrome
  - Described the tender points which would serve for the 1990 classification system
  - Published EEG sleep studies
    - Decreased stage 3 and interruption of NREM by alpha rhythms
    - Healthy control volunteers had their NREM interrupted by auditory stimuli
    - In the morning healthy volunteers had increased fatigue, aches and stiffness, tenderness, and worse mood symptoms
Fibromyalgia Syndrome (FMS)

• 1976 fibromyalgia began acceptance as the new term for fibrositis

• Yunus
  • 1981 first controlled study of clinical characteristics
  • In addition to the previously described symptoms, fibrositis patients showed:
    • Subjective swelling of tissues
    • Paresthesias
    • IBS
    • Tension type and migranous headaches
Fibromyalgia

- 1980’s histologic studies of muscle biopsies
  - Pathologists blinded
  - No histologic difference in trapezius muscle biopsies
- 1984 interrelation of central pain syndromes and their overlap was first suggested by Yunus
Central pain syndromes

- THS
- IBS
- Muscle spasm
- PDS
- PFS
Diagnostic criteria

- 1983 Campbell published diagnostic criteria in JAMA
  - 3 obligatory criteria:
    - Chronic, generalized aches, pains, or stiffness involving 3 or more anatomic sites for at least 3 months
    - Presence of multiple tender points at characteristic locations
    - Absence of another systemic condition that could account for the symptoms
  - Some combination of 6 minor criteria
    - Disturbed sleep
    - Generalized fatigue or tiredness
    - Subjective swelling and numbness
    - Pain in neck and shoulders
    - Chronic headaches
    - Irritable bowel symptoms
Diagnostic criteria

1990 ACR criteria

- Widespread pain occurring for greater than 3 months
- Above and below the waist
- Palpation of 4kg/cm²
- Pain in 11/18 standardized tender points
- Could not have another disease which could explain the symptoms
Central Sensitization

- 1992-4 Russell published data on neurotransmitter changes
  - Increased substance P in CSF
  - Decreased serotonin in CSF
- 1993 Granges and Littlejohn using innocuous electrical stimuli
  - Decreased spinal flexion reflex
  - Decreased pain threshold
    - Pressure
    - Hot
    - Cold
Central Sensitization

- 1993 Griep published data on alteration of the hypothalamic-pituitary-adrenal axis
  - Hyperactive release of ACTH
  - Hyporesponsiveness of adrenal cortex
- 1995 Mountz PET scanning brains in FMS
  - Decreased cerebral blood flow in thalamic and caudate nuclei
Central Sensitization

- 2000 Martinez-Lavin and Hermosillo role of autonomic nervous system
  - Sympathetic overactivity
- 2002 Gracely\(^3\) provided painful stimulus to FMS patients and controls
  - Measured cerebral activity using fMRI
  - Significantly increased signal in areas of brain not found in controls
Pain Clinic Follow Up:

Name

Age 32  Sex F

About how long ago were you seen in the pain clinic: 1/15/2010

Draw where your pain is on the diagram below:

Rate your pain by putting a "X" on the line below:

No Pain ———— Worst Pain Imaginable

Pain Relieved By: Morphine 15mg - 4 hr. relief

Exacerbated By: Pain Clinics - 6 hr. relief

Related Problems: Incontinence/Sleeping problems/Weakness/Numbness/(circle) Tingling/Fatigue/Anxiety/Depression/weight loss/weight gain/appetite changes/decreased libido/other

Any new treatment: Medications/surgery/nerve block/physical therapy/psychiatry

(circle) Other: Antral Stomach Test 1/19/2010
1990’s diagnostic criteria

- Numerous changes occurred over a 10 year period
- Tender point exam was difficult to perform
- Often missed clinically significant FMS
  - Men have less tender points than women
- Removed the criteria for a diagnosis of exclusion
- Removed the 18 classic points to just pain above and below the diaphragm
Current diagnostic criterion

- 2011 Wolfe studied the new ACR criteria in over 7 thousand FMS and other rheumatologic patients
  - Tender point exam had a lot of interprovider variation
  - Men tend to have less tender points
  - More emphasis of symptom severity
  - Created the widespread pain index
  - Created the symptom severity scale
Widespread pain index


To answer the following questions, patients should take into consideration:
- how you felt in the past week,
- while taking your current therapies and treatments, and
- exclude your pain or symptoms from other known illnesses such as arthritis, Lupus, Sjogren’s, etc.

Determining Your Widespread Pain Index (WPI)
The WPI Index score from Part 1 is between 0 and 19.

Check each area you have felt pain in over the past week:

- Shoulder girdle, left
- Shoulder girdle, right
- Upper arm, left
- Upper arm, right
- Lower arm, left
- Lower arm, right
- Hip (buttock) left
- Hip (buttock) right
- Upper leg left
- Upper leg right
- Lower leg left
- Lower leg right
- Jaw left
- Jaw right
- Chest
- Abdomen
- Neck
- Upper back
- Lower back
- None of these areas

Count up the number of areas checked and enter your Widespread Pain Index or WPI score here ___.
Symptom Severity Score

<table>
<thead>
<tr>
<th>Fatigue</th>
<th>Waking unrefreshed</th>
<th>Cognitive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ 0 = No problem</td>
<td>□ 0 = No problem</td>
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</tr>
<tr>
<td>□ 1 = Slight or mild problems; generally mild or intermittent</td>
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</tr>
<tr>
<td>□ 2 = Moderate; considerable problems; often present and/or at a moderate level</td>
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<td>□ 3 = Severe: pervasive, continuous, life disturbing problems</td>
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</tr>
</tbody>
</table>

Tally your score for Part 2a (not the number of checkmarks) and enter it here _____.

Indicate your level of symptom severity over the past week using the following scale.
Symptom Severity Score

Symptom Severity Score (SS score) - Part 2b

Check each of the following OTHER SYMPTOMS that you have experienced over the past week?

- Muscle pain
- Irritable bowel syndrome
- Fatigue/tiredness
- Thinking or remembering problem
- Muscle Weakness
- Headache
- Pain/cramps in abdomen
- Numbness/tingling
- Dizziness
- Insomnia
- Depression
- Constipation
- Pain in upper abdomen
- Nausea
- Nervousness
- Chest pain
- Blurred vision
- Fever
- Diarrhea
- Dry mouth
- Itching
- Wheezing
- Raynauld’s
- Hives/welts
- Ringing in ears
- Vomiting
- Heartburn
- Oral ulcers
- Loss/change in taste
- Seizures
- Dry eyes
- Shortness of breath
- Loss of appetite
- Rash
- Sun sensitivity
- Hearing difficulties
- Easy bruising
- Hair loss
- Frequent urination
- Painful urination
- Bladder spasms

Count up the number of symptoms checked above.

*If you tallied:
0 symptoms  Give yourself a score of 0
1 to 10      Give yourself a score of 1
11 to 24     Give yourself a score of 2
25 or more   Give yourself a score of 3

Enter your score for Part 2b here ____.

Now add Part 2a AND 2b scores, and enter ____.
This is your Symptom Severity Score (SS score), which can range from 0 to 12.
A patient meets the diagnostic criteria for fibromyalgia if the following 3 conditions are met:

1a. The WPI score (Part 1) is greater than or equal to 7 **AND** the SS score (Part 2a & b) is greater than or equal to 5.

**OR**

1b. The WPI score (Part 1) is from 3 to 6 **AND** the SS score (Part 2a & b) is greater than or equal to 9.

2. Symptoms have been present at a similar level for at least 3 months.

3. You do not have a disorder that would otherwise explain the pain.
Modern Day\textsuperscript{6}

- 2-8% of the population
- Female : male = 2 : 1
- Can develop at any age
- Similar prevalence in different
  - Countries
  - Cultures
  - Ethnic groups
- May occur with other chronic pain conditions
  - 10% - 30% of patients with OA, RA, SLE meet FMS criteria
May present or have history of other systemic complaints

- Headaches
- Dysmenorrhea
- Temporomandibular joint disorder
- Chronic fatigue
- Irritable bowel syndrome
- Other gastrointestinal complaints
- Regional pain syndromes
  - Back
  - neck
Modern Day

• Psychological, behavioral, and social issues
  • Contribute to the pathogenesis
  • Barriers to treatment
• More likely to have psychiatric disorders
  • Depression
  • Anxiety
  • Obsessive-compulsive disorder
  • Post traumatic stress disorder
Widespread complaints?
Treatment

- Team based approach
- Mild symptoms can be managed in primary setting
- Referral for diagnostic uncertainty
- Refractory to therapy
- Treatment of underlying psychiatric disorder
- Education
  - Disease is not due to damage and not progressive
  - Engagement in self care
    - Stress reduction
    - Sleep
    - Exercise
Agents that reduce excitatory neurotransmitters
- Gabapentin (Neurontin)
- Pregabalin (Lyrica) FDA approved

Agents that increase inhibitory neurotransmitters like serotonin and norepinephrine
- Tricyclic antidepressents
  - Amitriptyline (Elavil)
  - Nortriptyline (Pamelor)
  - Cyclobenzaprine (Flexeril)
Drugs 1\textsuperscript{st} line

- Bicyclic antidepressants
  - Duloxetine (Cymbalta) FDA approved
  - Milnacipran (Savella) FDA approved
  - Venalafaxine (Effexor)
  - Desvenlafaxine (Pristiq)
  - Mirtazapine (Remeron)
Drugs 2\textsuperscript{nd} line

- Monocyclic antidepressants
  - Fluoxetine (Prozac)
  - Sertraline (Zoloft)
  - Paroxetine (Paxil)
- Opiate antagonists
  - Low dose naltrexone\textsuperscript{7}
  - 30\% reduction in pain
  - Improved general satisfaction with life
  - Improved mood
Drugs not helpful

- Non steroidal Antiinflammatory drugs
- Steroids
- OPIOIDS
  - Result in upregulation of NMDA receptor
  - NMDA receptor found to be related to hyperalgesia
  - Studies show opiates can worsen fibromyalgia related hyperalgesia and other central pain states
Non pharmacologic

- Magnitude of response greater than for the pharmacologic
- Greatest benefit in improved function
- Result in the most sustained improvement
- Adherence and access most important limitations
- Education
  - Some feel that the label of fibromyalgia may worsen the symptoms
  - Studies show that establishing the diagnosis can provide relief
Nonpharmacologic

• Cognitive behavioral therapy
  • Type of psychotherapy which addresses
    • Maladaptive behaviors
    • Dysfunctional emotions
    • Cognitive process
  • Problem focused
  • Action oriented
    • Some behaviors can't be controlled through rational thought
    • Select strategies to address issues
  • Poor acceptance when viewed as psychological intervention
Pain Clinic Initial Evaluation: 

Name: 

Age: 16

Sex: M

MRN: 

Main Complaint: Numbness/Tingling in (L) lower thigh.

History of Present Illness: Previous Treatment: 

1) What caused your pain? (circle one): Work injury/MTA/Other: 

2) When did it start? 

3) Draw where your pain is on the diagram below: 

4) Rate your pain by putting a "X" on the line below: 

No Pain ———— Wost Pain Imaginable

5) Pain relieved by: [ ] Walking [ ] Standing [ ] Sitting [ ] Laying

Examined by: [ ] Walking [ ] Standing [ ] Sitting [ ] Laying

Date of Evaluation: 8/31/2018

Referring Physician: 

[Diagram of body showing pain areas]
Non pharmacologic

- Exercise
  - Aerobic exercise the best studied
  - Strengthening and stretching of value
  - Inactivity leads to a snowball effect
    - Especially as we age
    - Exercise tolerance
  - Increasing daily activity may be better starting point
    - Walk a block daily for a week
    - Then 1.5 blocks daily for a week
  - Muscle strain can result in set backs
New Horizons

• **FM/a test**
  • Based on theory that there is a impaired immune response in FMS
  • Peripheral blood is taken and mononuclear cells isolated
  • Baseline cytokine levels measured
  • Subjected to mitogen activators
  • Stimulated cytokine levels are again drawn
  • FMS patients had significantly decreased cytokine levels post stimulation from controls
New Horizons

- FM/a test $744.00
- Would we see the same results in other pain disorders?
- Patients were selected who had no other comorbid disease states
  - No immune deficiencies
  - Not on steroids
  - No other rheumatologic disorder
- Small fiber polyneuropathy\(^8\)
  - Patients with FMS were 14 times more likely to have concomitant SFPN vs controls
  - 2 patients had HepC, 8 with immune disorder, 1 with genetic disorder
AV shunts in skin of women with fibromyalgia have increased sensory fiber innervation\(^9\)

- Alters sensory function in hands
- May alter muscle blood flow and explain fatigue and widespread muscle pain through ischemia
Works cited

5. Wide spread pain indes