Approach to patients with suspected muscle disease

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Objectives

• Provide an overview of clinical approach to muscle disease based on patterns of weakness
• Discuss the role of different diagnostic tests in muscle disease

Goals of evaluation

• What is the site of the lesion?
  – Is it muscle?
  – Where in the muscle?
• What is the cause of the myopathy?
  – Hereditary: MD; Myotonias; Metabolic; Mitochondrial
  – Acquired: Inflammatory; Endocrine; Toxic; Systemic illness
• What is the treatment?
### Shot gun approach

- Time constrains “Reality of the practice of medicine”!
- Focused & systematic approach is the most efficient approach
- “Good history and examination ..can not be replaced”
- Search for clues in the H &P

### History of present illness

- **Age at symptom onset**
  - Birth vs. childhood vs. adulthood
  - Mild childhood sx. are usually missed
- **Evolution of symptoms**
  - Acute/sub-acute vs. Chronic vs. Static
- **Weakness**
  - Proximal vs. Distal vs. Cranial
- **Fatigue & exercise intolerance**
  - Metabolic and mitochondrial myopathies
  - Cardiopulmonary; depression; systemic illness
- **Myoglobinuria**

### Chief complaint

- **Negative sx.**
  - Weakness
  - Fatigue
  - Atrophy
  - Exercise intolerance
  - Periodic paralysis
- **Positive sx.**
  - Myalgia
  - Cramp
  - Contracture
  - Myotonia

### More History

- **PMH**
  - Thyroid, parathyroid, adrenal, GH, cancer, HIV
  - Cardiac, pulmonary, musculoskeletal
- **FH**
  - X-linked, AD, AR, maternal transmission
- **SH**
  - Smoking >> paraneoplastic
- **Meds**
  - Statins, amiodarone, chloroquine, Colchicine, prednisone
Examination

- Pattern of weakness (6 major patterns)
  - Symmetry
  - Location (proximal/distal)
  - Cranial (ocular, facial, pharyngeal)
- Calf hypertrophy
  - True vs. pseudo
- Other features
  - Frontal balding, cataract, face muscle wasting
  - Dysmorphic features
  - Rash
  - Liver enlargement

“Limb-Girdle” Proximal Weakness Pattern

- Most common
- Symmetric
- Proximal; Proximal >> Distal
- Neck muscle involvement
- Remember to examine muscles against gravity
- Examples
  - Acquired: PM, DM, endocrine and toxic myopathies
  - Hereditary: DMD, BMD, LGMD, Pompe disease
- Mimickers
  - SMA, LEMS, CIDP

Vignette 1

- 45 y/o WF
  - Weakness
  - Difficulty going up steps
  - Facial and knuckles rash
  - Swelling around the eyes
  - Difficulty swallowing
  - Recent h/o ovarian cancer
  - CK normal

Dermatomyositis

- Idiopathic inflammatory myopathy (IIM)
  - PM, IBM, NM
- Adults and children
- F > M
- Onset: Wks - Months
- Weakness: Symmetric; Proximal & Distal
- Myalgia
- Facial weakness
- Dysphagia ~30%
- Rash
### Dermatomyositis Rash

- Diffuse erythematous rash on face & scalp
- Erythematous macular rash on neck & anterior chest (V-sign)
- Gottron's sign: scaly lesions over knuckles and elbows
- Erythematous rash – post. Upper back & shoulder (shawl sign)
- Helliotrope rash: refer to purplish (brown) eyelid discoloration often with periorbital edema

### Muscle Enzymes

Wong et al. Am J Clin Path. 83
- 1537 subjects
- High CK group (52-520 U/L)
  - Black men
- Intermediate CK group (25-345 U/L)
  - Black women
  - Non-black men
- Low CK group (25-145 U/L)
  - Non-black women

Amato et al. Ann Neurol 96
- CK in normal in 10% Dermatomyositis pts
- Should be elevated in all PM and NM pts
- CK level doesn't correlate with weakness
- AST, ALT, LDH elevation
  - GGT to follow liver disease

Normal CK in slowly progressive myopathies

### Calcification

- Calcifications in subcutaneous tissues
- Pressure points (buttocks, knees, and elbows)
- Tend to occur in inadequately treated patients
- More in children (30-70%)
- Difficult to treat

### High aldolase with normal creatine kinase in serum predicts a myopathy with perimysial pathology

K. Nigral, A. Pfeiffer
- 12 pts
- Muscle discomfort 92%
- P & D weakness 50%
- Joint pain 75%
- Pulmonary involvement 50%
- Negative Jo-1 in five tested
- EMG: Normal 36%; irritable myopathy 18%; non-irritable 45%
- Bx.
  - Perimysial pathology (92%)
  - Acid phosphatase positive cellularity (83%)
### EMG

| Fibs & PSW | Myopathic MUPs |

### Other Laboratory work up

- ANA positive
  - DM 24-60%
- ESR normal
- Auto-antibodies
  - Jo-1 20% IIM
  - Anti-SRP Myocarditis and NM
  - Mi-2 15-20% DM

### Muscle MRI

- Abnormal signal
  - Edema
  - Inflammation
  - Fatty replacement
    - Chronic disease
- Muscle atrophy
- Current use
  - Identify biopsy side
  - Known myositis & normal CK
  - Flare vs. steroid

### DM-Muscle Biopsy

- Multifocal
- Severity vary within muscle specimen
- Characteristic feature is perifascicular atrophy
  - Seen in 50%-75%
- Perivascular inflammation
  - Macrophages
  - B-cells
  - CD4+ >>PDCS
- Gene microarray studies
  - Increase expression of type 1 interferon & proteins they regulate

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Amato AA, Russel JA 2008
Malignancy

- Increased incidence of malignancy
- Usually after age 40
- Highest near time of diagnosis (1-3 year)
- Still some risk after 3 year
- Presence of malignancy doesn’t correlate with disease severity
- Types of associated cancer
  - Breast, ovary, lung, pancreas, non-Hodgkin’s, stomach, colorectal, melanoma
  - Nasopharyngeal (Asia)
- Treatment of malignancy may improve myositis

Evaluation

- Suspected inflammatory myopathy
- ck
- TSH
- Autoimmune screen
- Jo-1
- CBC
- INR
- EMG
  - myopathy
  - irritability
  - exclude mimickers ex. myotonia
  - Multiple proximal and distal muscles
  - Thoracic paraspinal
- Muscle Biopsy
- Baseline Dexa scan
- Malignancy screen (> 40)
  - Examination
    - General/skin
  - Ct chest
  - Lung fibrosis
  - Ct abdomen/pelvis
  - Mammogram
  - Colonoscopy
  - Prostate
  - Swallow evaluation

Treatment Summary

- RCT are rare
- Corticosteroids is considered 1st line Rx
- IVIG is a costly Rx of DM
- There is a role for steroid and IVIG sparing agents
  - Methotrexate, cyclosporine, mycophenolate mofetil
- Patients should be encouraged to participate in research trials

Distal weakness Pattern

- Make sure neuropathy (sensory) & MND (asymmetry) are excluded
- Examples
  - Myotonic dystrophy
  - Distal myopathies
  - Myofibrillar myopathy
Vignette

- 42 y/o female
- Stiffness of the hands x 5 years
- Swallowing difficulty
- Cataract surgery age 20
- Pacemaker
- Excess daytime sleepiness

Myotonic Dystrophy 1 (DM1)

- Most common adult muscular dystrophy
- AD inheritance
- Single locus in chromosome 19q13.3
dystrophia myotonica protein kinase (DMPK)
- 3' untranslated region with increase in trinucleotide CTG repeats
- Multisystem disease
  - Cardiac conduction defects ....Pacemaker
  - Cardiomyopathy
  - Hypersomnia
  - Cognitive Impairment
  - Gastrointestinal symptoms
  - Insulin insensitivity

Myotonic Dystrophy 2 (DM2)

- Share many DM1 features
  - >>> hip flexor weakness
  - <<< facial weakness
- AD inheritance
- Single locus at chromosome 3q 21.3
- Zinc finger protein 9 gene (ZNF9)
- CCTG repeat expansion in intron 1
- Disease severity independent of number of repeats
- Screening for cardiac and pulmonary abnormalities similar to DM1

Molecular genetic studies

Molecular genetic studies

### Vignette

- **23 y/o man**
  - Difficulty running and toe walking since age 3
  - No arm weakness or sensory symptoms
  - FH: Pos. with male to male transmission
  - Weak ankle dorsiflexor and big toe extensor
  - CK normal
  - EMG myopathic

### Distal myopathies

<table>
<thead>
<tr>
<th>Disease</th>
<th>Gene</th>
<th>Age at onset</th>
<th>Initial muscles</th>
<th>CK</th>
<th>Muscle Bi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Welander</td>
<td>2p 13</td>
<td>&gt; 40</td>
<td>Finger and wrist extensors</td>
<td>1-4 X</td>
<td>Rimmed vacuoles</td>
</tr>
<tr>
<td>Odd</td>
<td>TTN</td>
<td>&gt;35</td>
<td>Anterior leg compartment</td>
<td>1-4X</td>
<td>Rimmed vacuoles</td>
</tr>
<tr>
<td>Markesbery-Griggs</td>
<td>ZASP</td>
<td>&gt;40</td>
<td>Anterior leg compartment</td>
<td>1-2X</td>
<td>Vascular &amp; myofibrillar</td>
</tr>
<tr>
<td>Distal myo- myopathy</td>
<td>MYOT</td>
<td>&gt; 40</td>
<td>Posterior &gt; anterior leg</td>
<td>1-3X</td>
<td>Vascular &amp; myofibrillar</td>
</tr>
<tr>
<td>Laing (MPD1)</td>
<td>MTH1-7</td>
<td>&lt; 20</td>
<td>Anterior leg &amp; neck fascs</td>
<td>1-3X</td>
<td>Type 1 fiber atrophy</td>
</tr>
<tr>
<td>Vocal cord &amp; pharyngeal (MPD2)</td>
<td>MATR3</td>
<td>35-60</td>
<td>Asymmetric lower leg and hand; dysphonia</td>
<td>1-8X</td>
<td>Rimmed vacuoles</td>
</tr>
<tr>
<td>New Finnish (MPD3)</td>
<td>8 p22-q11 12q13-22</td>
<td>&gt;35</td>
<td>Hands or anterior leg</td>
<td>1-4X</td>
<td>Dystrophic; rimmed vacuoles</td>
</tr>
<tr>
<td>Nonaka</td>
<td>GNE</td>
<td>15-20</td>
<td>Anterior leg compartment</td>
<td>&gt; 10 times</td>
<td>Rimmed vacuoles</td>
</tr>
<tr>
<td>Miyoshi</td>
<td>DYSF</td>
<td>15-30</td>
<td>Posterior leg compartment</td>
<td>&gt; 10 times</td>
<td>Myopathic</td>
</tr>
</tbody>
</table>

### Proximal Arm Distal Leg Weakness Pattern (Scapuloperoneal)

- **Scapular winging**
- **Scapular stabilizer weakness**
- **Ankle stabilizer weakness**
- **Asymmetry**
- **Examples**
  - FSHD
  - LGMD
  - Acid maltase deficiency
  - Myofibrillar myopathy
  - Scapuloperoneal dystrophy
**Vignette**

- 32 y/o female
- Facial weakness
- Sleep eyes open
- Can’t whistle
- Difficulty raising arm above shoulder
- Shoulder pain
- Pos. FH

**Distal arm/Proximal Leg Weakness Pattern**

- Distal forearm (wrist and finger flexor) and quad (Knee extensor) weakness
- Asymmetric
- Facial weakness -mild
- Example
  - Inclusion body myositis

**Facioscapulohumeral dystrophy**

- 3rd most common MD
- Autosomal dominant linked to 4q35
- Deletion of 3.3 kb repeated sequence (D4Z4)
- Symptoms begin < age 20 in ~ 80%
- *Typically* begins in face; subtle or absent~4%
- Shoulder weakness, pain presenting c/o in 80%
- ~20% asymptomatic at dx
- CK mildly elevated
- 15% will require use of wheel chair

**Sporadic Inclusion Body Myositis**

- Commonest IIM after age 50
- Refractory PM
  - = IBM or dystrophy
  - More common in men
- Onset: Months-Years
- Dysphagia ~30-60%
- CK Mild to moderate
- Not responsive to immunosuppressive Rx
**Ptosis With or Without Ophthalmoplegia Pattern**

- Ptosis alone
  - Myotonic dystrophy
  - Cong. Myopathy
  - Myofibrillar Myopathies
- Ptosis and Ophthalmoplegia
  - OPMD
  - Mitochondrial myopathy Ex. CPEO
  - NMJ disorders Ex. MG

**Neck Extensor Weakness**

- Dropped head syndrome
- DD: ALS, MG, Parkinson’s
- Examples
  - INEM
  - Inflammatory myopathy
  - FSHD
  - MD
  - Congenital Myopathy

**Vignette**

- 35 y/o
- Droopy eyelids
- Progressive ophthalmoplegia
- Proximal weakness
- Short stature
- Third degree AV block

Kears-Sayre Syndrome

**Isolated Neck Extensor Myopathy**

- 7th decade or older
- Weakness over days to Wks.
- Dull or burning neck pain
- Some report deltoid weakness
- EMG changes limited to cervical (mid to lower) and upper thoracic spine
- MRI fatty replacement and atrophy of the paraspinal muscles.
**Take Home Message**

- Detailed history and exam are fundamental steps to reaching a specific diagnosis
- Muscle disease can be distinguished from other disorders causing weakness
- Pattern of weakness help guide the work up
- Normal CK does not exclude muscle disease
- EMG and muscle biopsy are valuable diagnostic tools
- Molecular genetic testing is emerging as a useful noninvasive diagnostic tool – not for fishing expedition
- Symptomatic management and screening for complications decrease morbidity and mortality in muscle disease pts
- Multidisciplinary team approach for MD pts is crucial

**Muscle Pain Epidemiology**

- Most common complaint in NM clinics
  - ~50% of referrals for muscle biopsy
- Prevalence of diffuse myalgia ~10%
  - ~20% prevalence of focal myalgia
- 20-50% complain of muscle tiredness
  - Up to 25% of primary care OP visits
- 90% of myalgia patients have fatigue
  - 95% of CFS patients have myalgia

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**Muscle Pain Problems for Clinician**

- Pain only symptom in many patients
  - No signs of disease (eg weakness)
  - Difficult to assess at bedside
- Myalgia may arise from many sources
  - Ortho, rheum, gen med, psych
  - May not be related to muscle disease
- Many patients are “undiagnosable” in the usual sense

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**The Patient with Myalgia: Myths, Muscle Diseases, and (A Little) Madness**

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Vice Chair for Clinical Affairs
Associate Professor of Clinical Neurology
Ohio State University
Diagnoses in Myalgia Patients

*Mills and Edwards, 1983*

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th># Pts.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enzyme defects</td>
<td>16</td>
<td>15%</td>
</tr>
<tr>
<td>Inflammatory myopathy</td>
<td>8</td>
<td>7%</td>
</tr>
<tr>
<td>Neurogenic disorders</td>
<td>7</td>
<td>6%</td>
</tr>
<tr>
<td>Endocrine &amp; metabolic disorders</td>
<td>6</td>
<td>6%</td>
</tr>
<tr>
<td>No diagnosis</td>
<td>72</td>
<td>66%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>109</td>
<td>100%</td>
</tr>
</tbody>
</table>

Approach to Patient with Myalgia

**Objectives**

- Basic approach myalgia patient
  - When to biopsy and when to not!
- Present overview of myalgia in general
  - Terminology & classification
  - Highlight mistakes & myths seen in clinic
- Discuss 4 muscle diseases with isolated generalized myalgia (i.e. no weakness)
  - Including the “F--- word” (fibromyalgia)

Filosto et al, Neurology 2007

- Many myalgia patients DO have biopsy abnormalities, but they are usually non-specific
  - They usually do NOT lead to a diagnosis
- Routine biopsy NOT indicated in patients with isolated myalgia; careful patient selection is needed
- Important info for referring doctors AND patients!

Patient with Myalgia

**Case Presentation**

68 yo male, 6 mos hx
- Severe myalgias, AM stiffness, ADL loss
  - “Walking in glue”
- “I don’t feel good!”
- Lost 10 pounds
- CK, EMG normal
- Referred for muscle bx. for presumed PM
Evaluation of Muscle Pain

Screening examination
Labs. CBC, ESR, TFTs, lytes

Neuro. eval - strength, endurance testing
Serum CK, electrodiagnostic studies

Normal  CK elevated  Weak, abn EMG, CK

Tender points present?  Tender points absent?

<5x nl  No other abn  >5x normal, other sx  FET, Genetic testing

FM  PMR, MAD Statins  Repeat  Biopsy  biopsy

Muscle Pain Terminology

Types of Pain

- “I don’t have any pain at all…it just hurts!”
- “Pain” can mean numbness, stiffness, tingling, restlessness, burning, swelling
- Useful to classify 4 types of muscle pain
  - Contractures
  - Cramps
  - Stiffness
  - Aching myalgia

The Patient with Muscle Pain

General Approach

- Careful history attending to type of pain
  - Consideration of localization/pathogenesis
  - Analysis of disease possibilities
- Exam. with attention to strength testing!
  - Most common source of error!!
- Judicious lab tests
  - Routine (e.g. CK and EMG)
  - Specialized (FET, biopsy, genetic testing)

Deep Aching - Localized

Muscle Differential Diagnosis

- Post-exercise myalgia (“weekend warrior”)
- Infiltrating processes (e.g. tumor, sarcoid)
- Focal pressure necrosis
- Trauma
- Localized infections (bacterial, parasitic)
- Venous occlusion
- Arterial ischemia (thrombotic or embolic)
- Referred “muscle” pain
Examples of Focal Myalgia

| Sarcoid Myopathy | Diabetic Thigh Infarct |

Deep Aching - Generalized

**Differential Diagnosis**

**With weakness**
- PM, DM (20-25%)
- Hypothyroidism
- Mitochondrial dx.
- Myotonic dystrophy 2
- Infectious myopathies
- Other rare myopathies

**Without weakness**
- Infectious myalgia (esp. viral)
- Toxic myopathies (eg lovastatin)
- MADD
- PMR
- Fibromyalgia

Diffuse Muscle Pain

**Inflammatory Muscle Disease***

*Only ~25% of PM/DM pts. have significant myalgias

Evaluation of Muscle Pain

- Screening examination
  - Labs. CBC, ESR, TFTs, lytes
- Neuro. eval - strength, endurance testing
  - Serum CK, electrodiagnostic studies

**Normal**
- Tender points present?
  - FM

**CK elevated**
- Tender points absent?
  - PMR, MAD Dos
  - <5x nl
  - >5x normal, other sx

**Weak, abn EMG, CK**
- Repeat
  - Biopsy
  - FET, Genetic testing

*Only ~25% of PM/DM pts. have significant myalgias
Statin Myopathy
Terminology & Epidemiology

ACC & AHA & NHLBI list 4 entities (2002)

- Statin myopathy – ANY muscle complaint
  - Up to 15-25% (including isolated CK rise ?)
- Statin myalgia – pain without CK rise
  - 2-9% overall (up to 20% in some series)
- Statin myositis – pain/weakness/CK rise
  - Rare with biopsy proven inflammation, < 0.2% cases
- Statin rhabdomyolysis – CK > 10x normal
  - < 1 per million scripts for all but cerivastatin (Baycol)
  - SO
- Since 105 million patients should be on statins
  - 5-6 million new statin myopathy cases!? Underestimate!

Statin Myopathy Characteristics
Franc et al, 2003

Table 4. Time to onset of muscle pain

<table>
<thead>
<tr>
<th>Time to onset of muscle pain</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2 days</td>
<td>4.5% (n = 6)</td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>24.8% (n = 33)</td>
</tr>
<tr>
<td>1–3 months</td>
<td>9.8% (n = 13)</td>
</tr>
<tr>
<td>3–12 months</td>
<td>12% (n = 16)</td>
</tr>
<tr>
<td>&gt;12 months</td>
<td>24.8% (n = 33)</td>
</tr>
</tbody>
</table>

- Symptoms can occur at any time in course!
- Symptoms do NOT always resolve with drug DC

Statin Myopathy
Predisposing Factors

<table>
<thead>
<tr>
<th>Patient Factors</th>
<th>Medication Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased age</td>
<td>High statin dose</td>
</tr>
<tr>
<td>Female sex</td>
<td>Agent (eg lovastatin)</td>
</tr>
<tr>
<td>Small stature</td>
<td>Polypharmacy</td>
</tr>
<tr>
<td>Liver, kidney dysfunction</td>
<td>- Colchicine</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>- Erythromycin</td>
</tr>
<tr>
<td>Post-operative</td>
<td>- Cyclosporine</td>
</tr>
<tr>
<td>Diet (eg grapefruit juice)</td>
<td>- Niacin</td>
</tr>
<tr>
<td>Genetic predisposition</td>
<td>- Calcium channel blockers</td>
</tr>
<tr>
<td>Underlying myopathy</td>
<td>- Nefaxodone</td>
</tr>
<tr>
<td>Cause still unknown!</td>
<td>- Anti-fungals</td>
</tr>
<tr>
<td></td>
<td>- Fibric acids (gemfibrozil)</td>
</tr>
</tbody>
</table>

Statin Myopathy
Management

- Tricky, since the meds ARE helpful
  - Cannot just blindly stop in all patients
- Rechallenge with other drug may be option
  - Usually doesn’t work!
- Symptomatic treatment (gabapentin, PT, NSAIDs, short course steroids)
- Little evidence for aerobic exercise, CoQ10, carnitine
- “Tincture of time” sometimes best option
  - Some patients have persistent symptoms!
Grable-Esposito et al
Muscle & Nerve 2010

- 25 pts. on chronic statins (only 4 with pain)
  - Weakness, high CK after statins DCd
  - Necrotizing myopathy on muscle bx.
  - Responded to immunospressive drugs
  - 24 required multiple agents
  - 15 relapsed on withdrawal of agents

Patient with Myalgia
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  - “I don’t feel good!”
  - Lost 10 pounds
  - CK, EMG normal
  - Referred for muscle bx. for presumed PM

The Patient with Myalgia
Case Presentation

- Examination NORMAL, including strength
- Screening blood work normal
  - Including CK, aldolase
- EMG - completely normal (but painful)
- Muscle biopsy deferred
- ESR = 80 mm/hour; diagnosis of PMR
- Prednisone 40 mgs/day
  - Complete resolution in 2 days

Statin Myopathy Management

- Symptoms (myalgia, CK, weakness)
  - Sx. Resolve
  - DC Statin
  - Sx. Persist
  - Observe
  - Manage with diet, niacin, bile resins
  - Stable
  - Progression
  - Treat symptoms
  - Weakness
  - Higher CK
  - Resolve
  - Persist
  - Muscle bx.
Polymyalgia Rheumatica

Polymyalgia Rheumatica

**Epidemiology**

- Technically not muscle disease per se
- One of most common causes of myalgia
  - 600-1000/100,000 in patients > age 50
  - Incidence of ~50/100,000 per year
- Mean age of onset 70 (90% > age 60)
- Female predominance of 3:1
- 50% of giant cell arteritis (GCA) get PMR
  - 15-20% of PMR develop GCA

**Symptoms**

- Myalgia, stiffness, aching,
  - Neck, shoulders, hips
- Worse in AM, movement
  - Stiffness, “gelling”
- Systemic symptoms in 40%
  - Fevers, depression, wt. loss, poor sleep, anorexia, anemia, arthritis
  - Similar to FM
- Tenderness rare (ddx FM)

**Laboratory**

- CK and EMGs normal
- ESR very high (>100)
  - 15-20% - normal ESR
- Temporal artery bx. only in patients with GCA sx.
  - Not in isolated PMR
- Muscle bx. not indicated
  - Non-specific changes
  - Pathogenesis?
    - Synovial pain

**Treatment**

- Prednisone (10-40 mg/day) causes immediate and dramatic improvement
  - Diagnostic as well as therapeutic
- GCA requires higher doses
  - 60-100 mg orally or 1.0 gm IV
- Treat symptoms and ESR
  - Taper slowly when sx. under control
  - Usually requires 1-2 years treatment
- 10% require treatment for over 10 years!
Fibromyalgia – The Madness

Epidemiology

• >3000 Medline articles since 1990!
• ~2% population in US – (3.4% F; 0.5% M)
  – 3-6 mil. people in U.S.
• 75-90% cases in women
• Any age (children); especially elderly (7% of women > age 60)
• 20% of rheum. patients; – 3rd most common (after OA, RA)

Fibromyalgia

Notable Quotes

• “I don’t know what that term means.”
• “It’s just a waste-basket term.”
• “That’s just a grab-bag diagnosis.”
• “Doctor’s diagnosticate that when they really don’t know what’s wrong with someone.”
• “I don’t think it’s a ‘real’ disease at all.”
• “All these people are just depressed.”
• “They’re all trying to get disability.”

Clinical Features

• Diffuse myalgia, stiffness, aching, joint pain
• Proximal predominance; can be anywhere
• Insidious onset (? post-infectious, trauma)
• Fatigue, morning stiffness, non-restorative sleep in 75%
  – Anxiety --Swelling --Headaches
  – IBS --Imbalance --Dysuria
  – Raynaud’s --Dysmenorrhea --Dysesthesias

New ACR Diagnostic Criteria

Arth Care Res 2010;62:600-10

• Widespread pain > 3 mos.; no other cause
• Widespread pain index (WPI) ≥ 7 and symptom severity (SS) scale score ≥ 5 OR
  – WPI 3-6 and SS score ≥ 9
• NO tender point exam! 88% correlation
**FM - Pathogenic Hypotheses**

**Summary**

- FM is NOT a muscle dx. (40 neg. studies)
- FM is NOT entirely psych (30-50% with dx.)
- FM is NOT a single disease (multiple studies)
- May be central up regulation of pain pathways (decreased subs. P in CSF)
  - Sorensen (1995) - improved with IV ketamine (NMDA ant.) in blinded, cont. trial of 31 pts.
  - No imp. with IV lidocaine or morphine
- May be variation of small fiber neuropathy

---

**Fibromyalgia**

**Tentative Conclusions**

1. FM is clearly NOT a primary muscle dx.
2. FM is a “real” syndrome, as valid as any other in which criteria are clinical only.
3. FM is valuable concept for patient care
   - Avoids unnecessary testing
   - Provides frame of reference for patient
   - Helps design therapeutic program
4. Diagnosis *not* diagnosis of exclusion

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**Fibromyalgia**

**Treatment**

<table>
<thead>
<tr>
<th>Beneficial</th>
<th>Possibly Beneficial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregabalin</td>
<td>Imipramine</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Fenfluramine</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>Fluoxetine</td>
</tr>
<tr>
<td>Exercise</td>
<td>NSAIDs (used alone)</td>
</tr>
<tr>
<td>BCT</td>
<td>Zolpidem</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>Cyclobenzaprine</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Alprazolam</td>
</tr>
</tbody>
</table>

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**Evaluation of Muscle Pain**

- Screen for pain
  - Labs. (CBC, ESR, TFTs, lytes)
  - Neuro. eval - strength, endurance testing
  - Serum CK, electrodiagnostic studies

- CK elevated
- No other abn

- FET, Genetic testing

- Biopsy

---

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## Muscle Pain

### Summary

- Consider carefully the type of pain
- Concentrate exam on strength testing!
  - Presence of tenderness
- Evaluate further with CK, EMG, ESR
- Do NOT automatically biopsy
  - Unrewarding most of the time!
  - Only in selected cases
- Consider statin myopathy, MADD, PMR, FM in patients with “normal everything”.

## Forearm Exercise Test

### Method

- IV in dominant antecubital vein (23 ga)
  - Kept open with heparin/saline boluses
- Draw baseline lactate and NH₃ (on ice!)
- Do not do ischemically
- Squeeze ball MAXIMALLY for 1 minute
  - Cuff deflated
- Lactate, NH₃ at 1, 2, 4, 6, & 10 min
- Do NOT do ischemically (contracture)!