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**

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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

Chief complaint

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

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

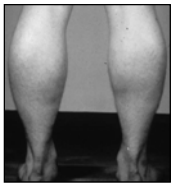
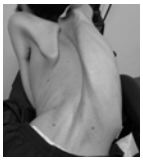
More History

- 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

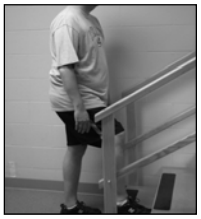
- Pattern of weakness (6 major patterns)
  - Symmetry
  - Location (proximal/distal)
  - Cranial (ocular, facial, pharyngeal)
- Calf hypertrophy
  - True vs. pseudo
- Other features
  - Frontal balding, cataract, face muscle wasting
  - Dysmorphic features
  - Rash
  - Liver enlargement



" 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



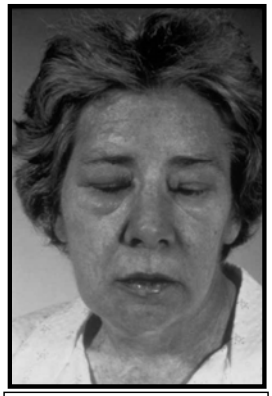
Vignette 1

- 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

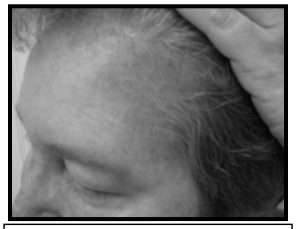
Dermatomyositis

- 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

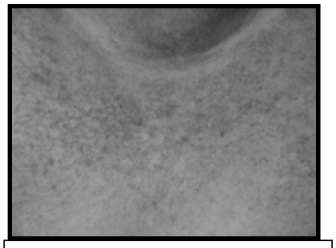
Dermatomyositis rash



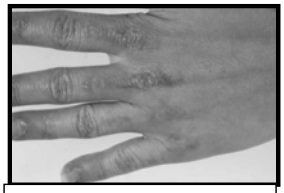
Heliotrope rash refer to purplish (brown) eyelids discoloration often with periorbital edema



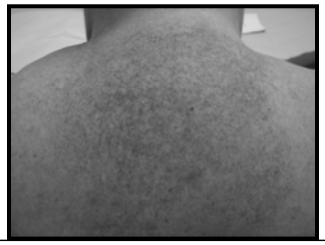
Diffuse erythematous rash on face & scalp



Erythematous macular rash neck & anterior chest (V-sign)



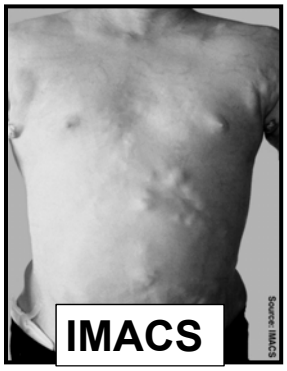
Gottron's sign scaly lesions over knuckles and elbows

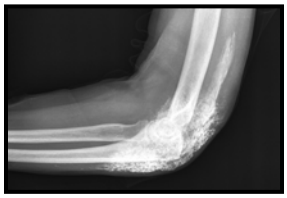


Erythematous rash – post. Upper back & shoulder (shawl sign)

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





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

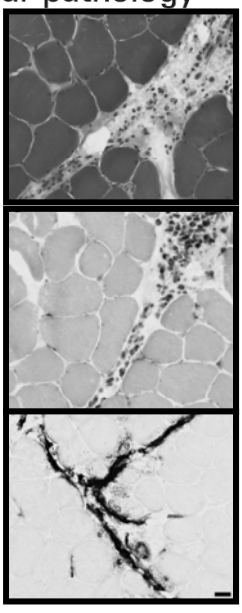
- Amato et al. Ann Neurol 96
  - DM (9 pts) 758 (± 6929)
  - PM (22 pts) 5097 (± 7706)
  - sIBM (15 pts) 698 (± 430)
- CK in normal in 10% Dermatomyositis pts
- Should be elevated in all PM and NM pts
- CK level doesn't correlate with weakness
- AST,ALT, LDH elevation
  - GGT to follow liver disease

Normal CK in slowly progressive myopathies

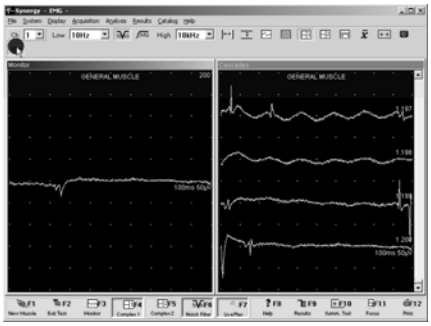
High aldolase with normal creatine kinase in serum predicts a myopathy with perimysial pathology

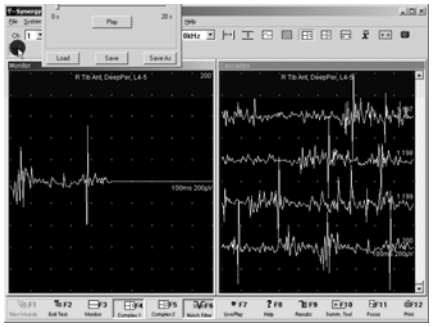
K Nozaki, A Pestronk

- 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



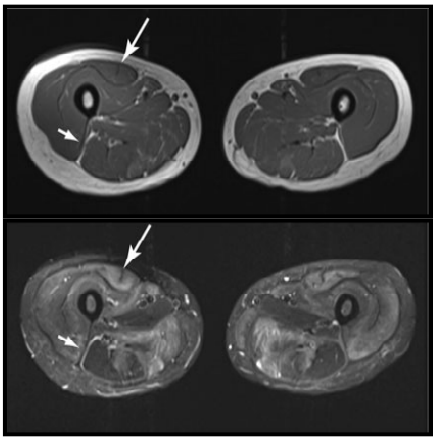


Fibs & PSW

Myopathic MUPs

Muscle MRI

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



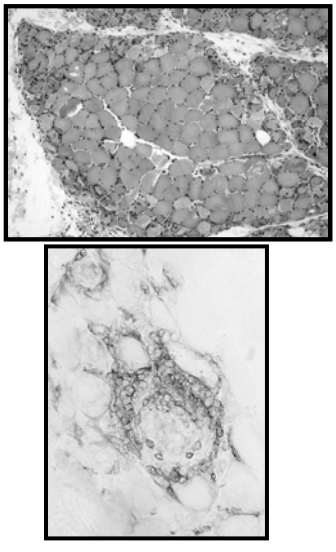
Mammen A. Ann. N. Y. Acad. Sci. 2009

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

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



Amato AA, Russel JA 2008

Malignancy

- Increased incidence of malignancy
- Usually after age 40
- Highest near time of diagnosis (1-3year)
- 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

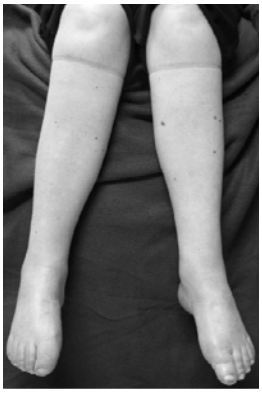
- Suspected inflammatory myopathy
- √ ck √ TSH
- √ Autoimmune screen
- √ Jo-1 √ CBC √INR
- EMG
  - √ myopathy √ mm irritability √ exclude mimickers ex. myotonia
  - Multiple proximal and distal muscles
  - Thoracic paraspinal
- Muscle Biopsy
- Baseline Dexa scan
- Malignancy screen (> 40)
  - Examination
    - *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

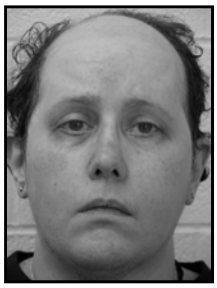
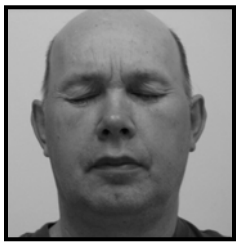
Distal weakness Pattern

- 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

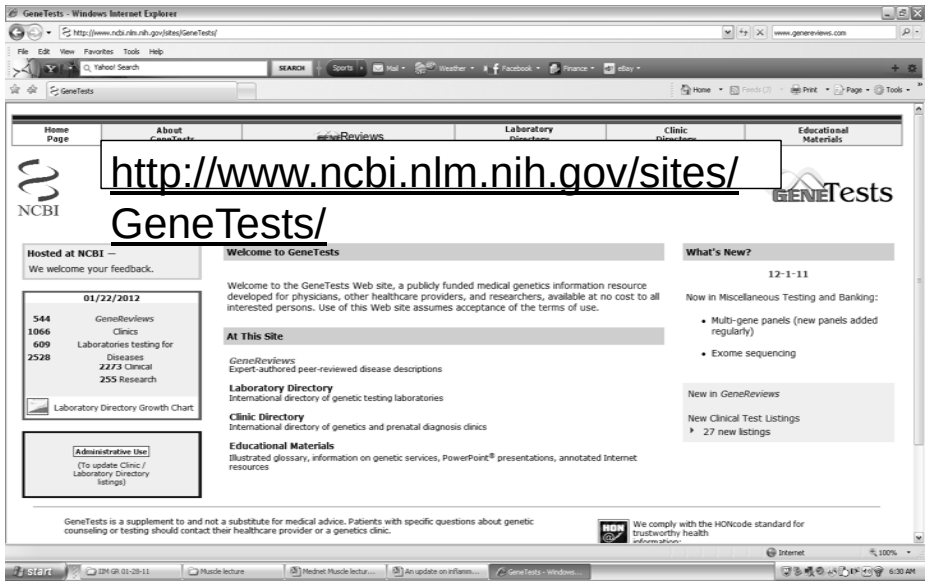

Myotonic Dystrophy 1 (DM1)

- 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

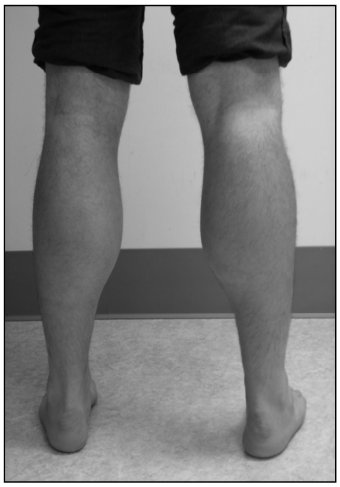
Molecular genetic studies



http://www.ncbi.nlm.nih.gov/sites/GeneTests/

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

Disease	Gene	Age at onset	Initial muscles	CK	Muscle Bx
Welander	2p 13	> 40	Finger and wrist extensors	1-4 X	Rimmed vacuoles
Udd	TTN	>35	Anterior leg compartment	1-4X	± Rimmed vacuoles
Markesbery-Griggs	ZASP	>40	Anterior leg compartment	1-3X	Vacuolar & myofibrillar
Distal myotlinopathy	MYOT	> 40	Posterior > anterior leg	1-3X	Vacuolar & myofibrillar
Laing (MPD1)	MYH 7	< 20	Anterior leg & neck flexors	1-3X	Type 1 fiber atrophy
Vocal cord & pharyngeal (MPD2)	MATR3	35-60	Asymmetric lower leg and hand; dysphonia	1-8 X	Rimmed vacuoles
New Finnish (MPD3)	8 p22-q11 12 q13-22	>30	Hands or anterior leg	1-4 X	Dystrophic; rimmed vacuoles
Nonaka	GNE	15-20	Anterior leg compartment	< 10 times	Rimmed vacuoles
Miyoshi	DYSF	15-30	Posterior leg compartment	> 10 times	Myopathic

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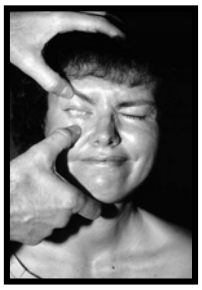
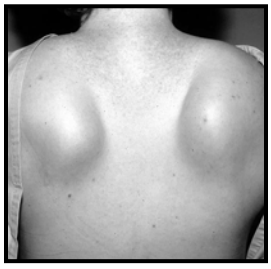
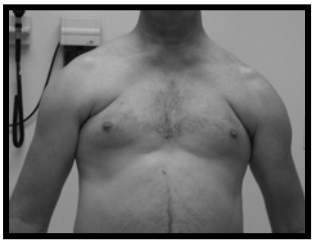
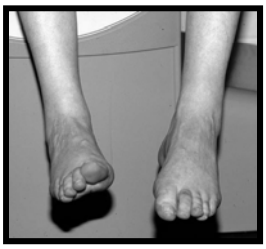
Proximal Arm Distal Leg Weakness Pattern (Scapuloperoneal)

- 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**

Facioscapulohumeral dystrophy

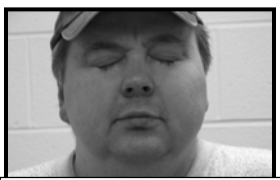
- 3rd most common MD
- Autosomal dominant linked to 4q35
- Deletion of 3.3 kb repeated sequence (D4Z4)
- Symptoms begin < age 20 in ~ 80%
- *Typically* begins in face; subtle or absent~4%
- Shoulder weakness, pain presenting c/o in 80%
- ~20% asymptomatic at dx
- CK mildly elevated
- 15% will require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

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

Sporadic Inclusion Body Myositis

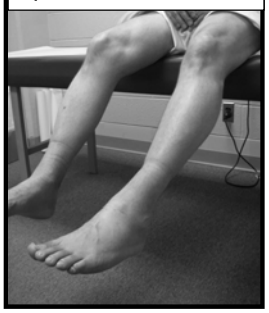
- Commonest IIM after age 50
- Refractory PM
- = IBM or dystrophy
- More common in men
- Onset: Months-Years
- Dysphagia ~30-60%
- CK Mild to moderate
- Not responsive to immunosuppressive Rx



Facial weakness 1/3

Forearm atrophy/ weakness

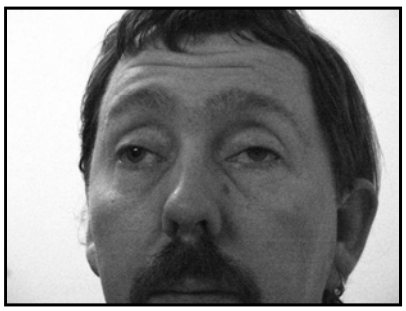
Quads weakness



Ptosis With or Without Ophthalmoplegia Pattern

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

Vignette

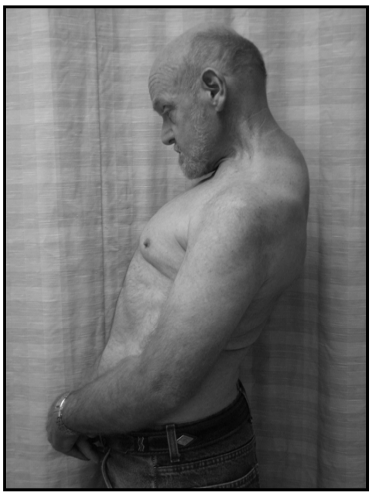


- 35 y/o
- Droopy eyelids
- Progressive ophthalmoplegia
- Proximal weakness
- Short stature
- Third degree AV block

Kearns-Sayre Syndrome

Neck Extensor Weakness

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



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

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

Miriam Freimer, MD
Department of Neurology
Vice Chair for Clinical Affairs
Associate Professor of Clinical Neurology
Ohio State University

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

Muscle Pain
Problems for Clinician

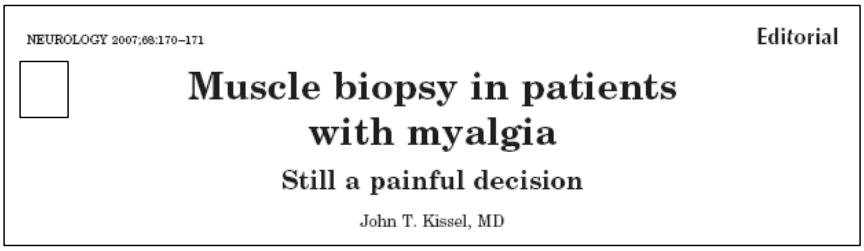
- Pain *only* symptom in many patients
  - No signs of disease (eg weakness)
  - Difficult to assess at bedside
- Myalgia may arise from many sources
  - Ortho, rheum, gen med, psych
  - May not be related to muscle disease
- Many patients are "undiagnosable" in the usual sense

Diagnoses in Myalgia Patients

Mills and Edwards, 1983

Diagnosis	*# Pts.*	*%*
Enzyme defects	16	15%
Inflammatory myopathy	8	7%
Neurogenic disorders	7	6%
Endocrine & metabolic	6	6%
No diagnosis	72	66%
Total	109	100%

Filosto et al, Neurology 2007



NEUROLOGY 2007;68:170–171 Editorial

Muscle biopsy in patients with myalgia

Still a painful decision

John T. Kissel, MD

- 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!

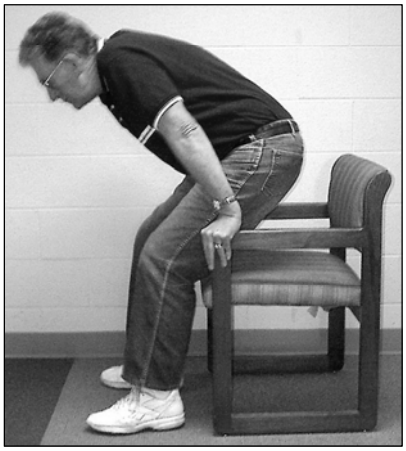
Approach to Patient with Myalgia
Objectives

- 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)

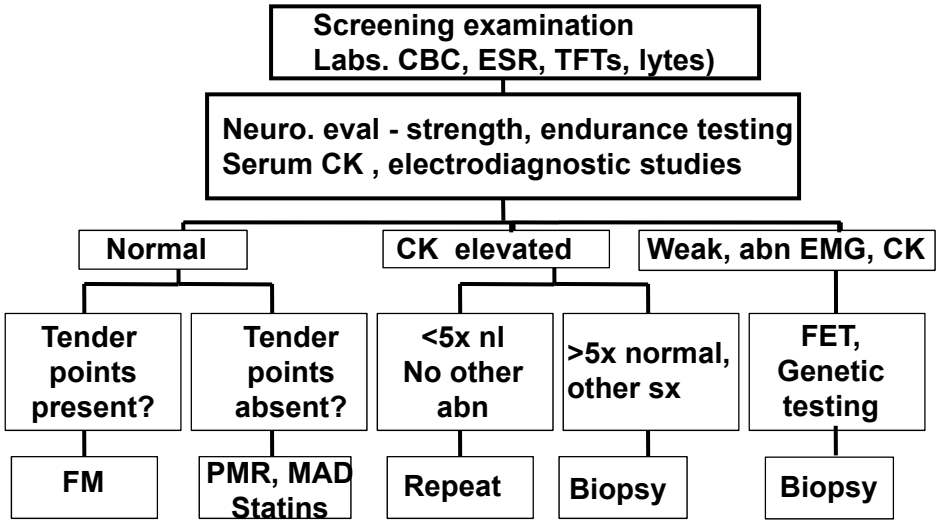
Patient with Myalgia
Case Presentation

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



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)

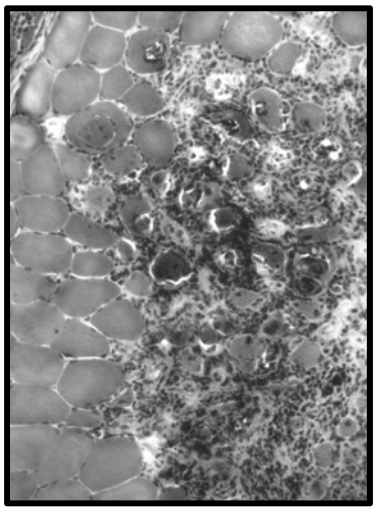
Muscle Pain Terminology
Types of Pain

- **"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**

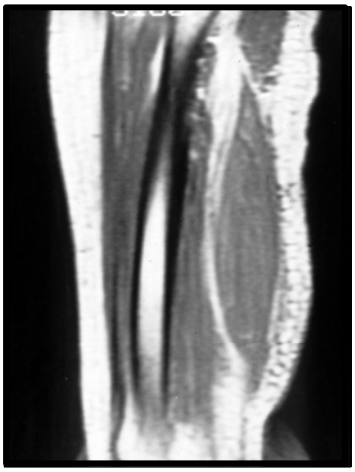
Deep Aching - Localized
Muscle Differential Diagnosis

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

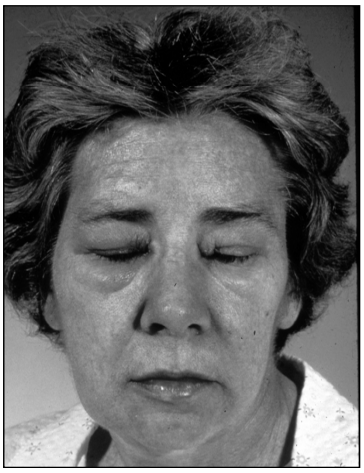


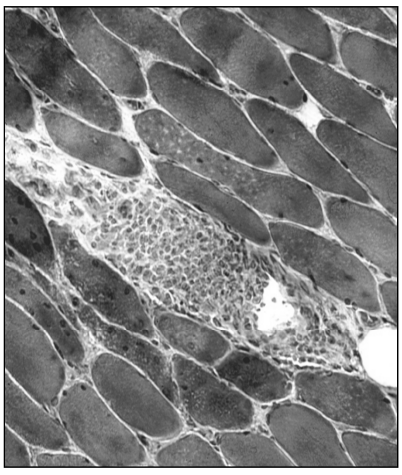
Sarcoid Myopathy



Diabetic Thigh Infarct

Diffuse Muscle Pain
*Inflammatory Muscle Disease**





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

Deep Aching - Generalized

Differential Diagnosis

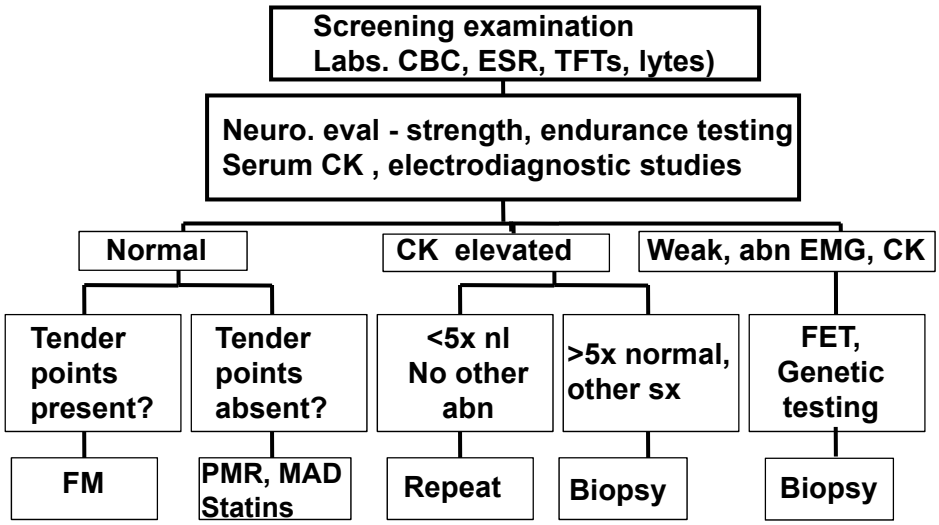
With weakness

- 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

Evaluation of Muscle Pain



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
Predisposing Factors

Patient Factors

- **Increased age**
- **Female sex**
- **Small stature**
- **Liver, kidney dysfunction**
- **Hypothyroidism**
- **Post-operative**
- **Diet (eg grapefruit juice)**
- **Genetic predisposition**
- **Underlying myopathy**

Cause still unknown!

Medication Factors

- **High statin dose**
- **Agent (eg lovastatin)**
- **Polypharmacy**
  - **Colchicine**
  - **Erythromycin**
  - **Cyclosporine**
  - **Niacin**
  - **Calcium channel blockers**
  - **Nefaxodone**
  - **Anti-fungals**
  - **Fibric acids (gemfibrozil)**

Statin Myopathy Characteristics
Franc et al, 2003

Table 4. *Time to onset of muscle pain*

Time to onset of muscle pain	Total
1–2 days	4.5% ($n = 6$)
<1 month	24.8% ($n = 33$)
1–3 months	9.8% ($n = 13$)
3–12 months	12% ($n = 16$)
>12 months	24.8% ($n = 33$)

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

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!**

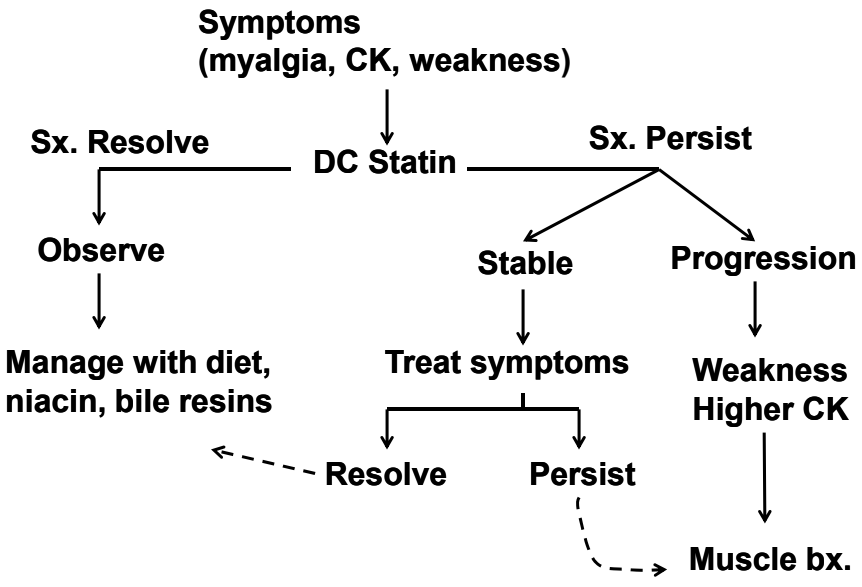
Grable-Esposito et al
Muscle & Nerve 2010

IMMUNE-MEDIATED NECROTIZING MYOPATHY ASSOCIATED WITH STATINS

PHYLLIS GRABLE-ESPOSITO, MD,[1] HANS D. KATZBERG, MD,[2] STEVEN A. GREENBERG, MD,[1] JAYASHRI SRINIVASAN, MD, PhD,[3,4] JONATHAN KATZ, MD,[5] and ANTHONY A. AMATO, MD[1]

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

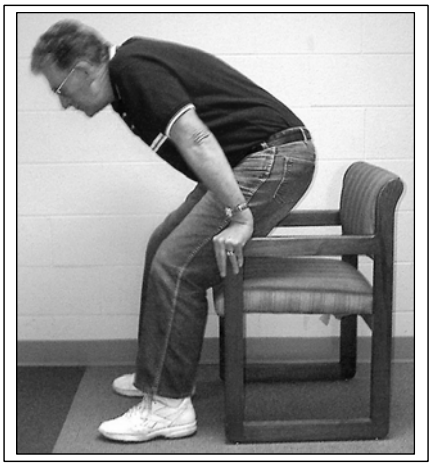
Statin Myopathy Management



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**



The Patient with Myalgia
Case Presentation

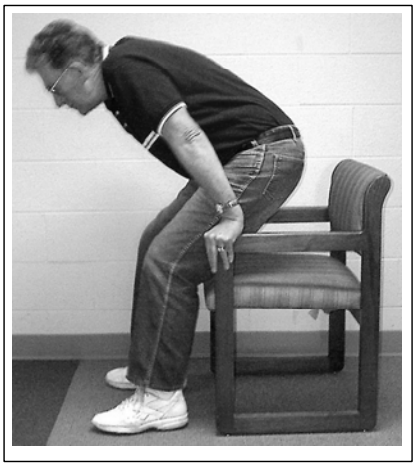
- **Examination NORMAL, including strength**
- **Screening blood work normal**
  - **Including CK, aldolase**
- **EMG - completely normal (but painful)**
- **Muscle biopsy deferred**
- **ESR = 80 mm/hour; diagnosis of PMR**
- **Prednisone 40 mgs/day**
  - **Complete resolution in 2 days**

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

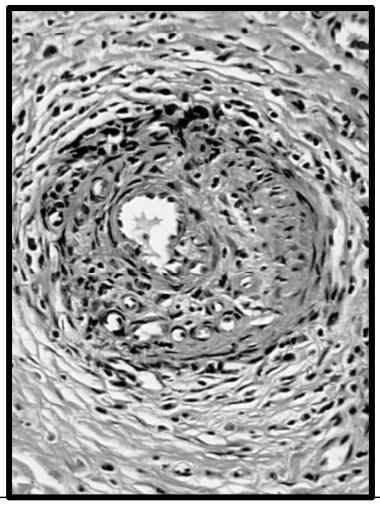
Polymyalgia Rheumatica
Symptoms

- 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)



Polymyalgia Rheumatica
Laboratory

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

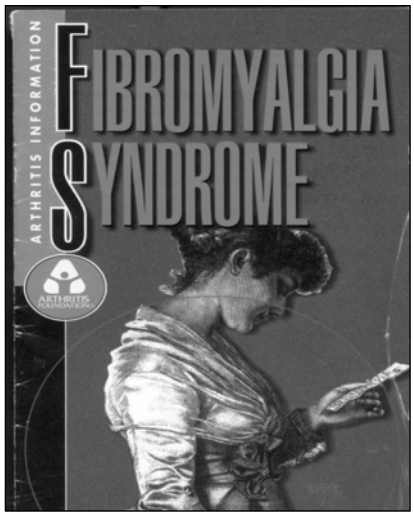


Polymyalgia Rheumatica
Treatment

- 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 sxs. 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 diagnose 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."

Fibromyalgia
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

The American College of Rheumatology Preliminary Diagnostic Criteria for Fibromyalgia and Measurement of Symptom Severity

FREDERICK WOLFE,[1] DANIEL J. CLAUW,[2] MARY-ANN FITZCHARLES,[3] DON L. GOLDENBERG,[4] ROBERT S. KATZ,[5] PHILIP MEASE,[6] ANTHONY S. RUSSELL,[7] I. JON RUSSELL,[8] JOHN B. WINFIELD,[9] AND MUHAMMAD B. YUNUS[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
Treatment

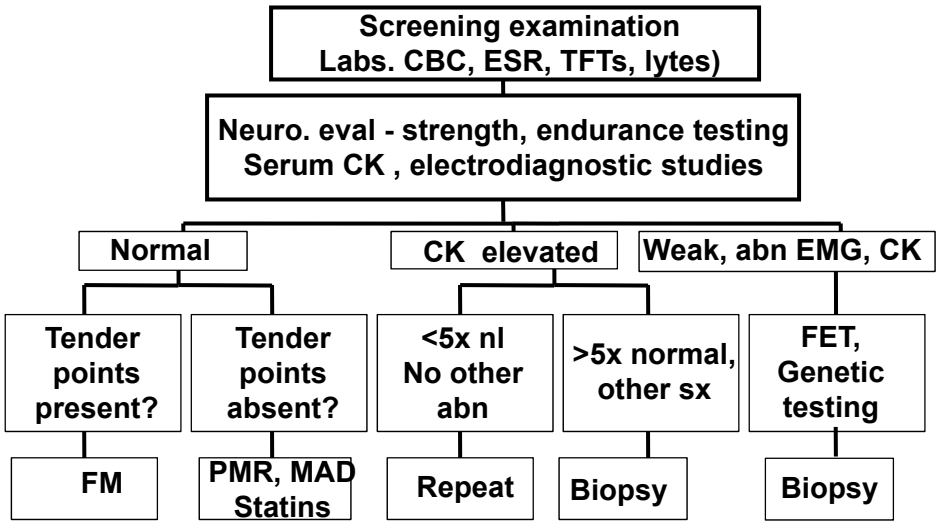
Beneficial	Possibly Beneficial
Pregabalin	Imipramine
Duloxetine	Fenfluramine
Milnacipran	Fluoxetine
Exercise	NSAIDs (used alone)
BCT	Zolpidem
Amitriptyline	Cyclobenzaprine
Clomipramine	Alprazolam

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**

Evaluation of Muscle Pain



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 NH_3 (on ice!)
- Do not do ischemmically
- Squeeze ball MAXIMALLY for 1 minute
  - Cuff deflated
- Lactate, NH_3 at 1, 2, 4, 6, & 10 min
- Do NOT do ischemically (contracture)!