Myositis 101
(or what we can discuss in a short time)

Mark Gourley, MD

THE MYOSITIS ASSOCIATION

What is Myositis?

- Myo = muscle
- itis = inflammation
- Therefore: an inflammatory muscle disease
- We don’t know the cause
- Problems = deterioration of the muscles and dysfunction of body tissues

Myositis – (aka) Idiopathic Inflammatory Myopathy (IIM)

- Autoimmune illness characterized by skeletal muscle inflammation
  - Typically associated with:
    - Weakness
    - Blood Laboratory changes
      - **CK**, AST, ALT, LDH, Aldolase, Serum myoglobin
    - Autoantibodies
      - Nonspecific and Disease Specific (Myositis Specific)
    - EMG and MRI changes
    - Muscle biopsy abnormalities (inflammation)
  - Typically respond to anti-inflammatory therapy

When is it Myositis?

The physician's task is to prove an idiopathic inflammatory myositis (IIM) is present

- Example of a noninflammatory disease
  - Adult onset
  - Proximal, symmetric muscle weakness
  - Elevation of CK, Aldolase and liver associated enzymes
  - Show degen/regen, inflammatory infiltrates and fibrosis on biopsy
  - EMG compatible with myopathy
  - MAY GET BETTER ON STEROIDS/DMARDS

Limb Girdle Muscular Dystropy = Dysferlinopathy

Does this mean you all have muscular dystrophy?

- NO!!

- But, we as health care providers need to be very sure about our diagnosis
  - Life changing – and NOT for the good!

What Brings The Patient To The Doctor?

- Most report fatigue/extremely tired
- Unable to do daily physical tasks
  - Typically patients say do to arthritis or something else
- May have breathing problems
- Some may have rash, arthritis, swallowing problems, weight loss
- Clue for the Doctor = history, exam and labs

Most Physicians Become Worried About IIM When The CK Rises

- CK is an enzyme released by damaged muscle
- Muscle (striated, smooth, cardiac types)
  - Exercise, Inflammation, dystrophies, metabolic, injections
- Drugs
  - antimalarials, colchicine, **statins**, penicillamine, zidovudine, **alcohol** and cocaine
- Infections – bacterial, viral, fungal, protozoal
- Neurologic – denervation, ALS, GBS
- Vascular – vasculitis, DMI
- Endocrine – thyroid, Ca, K
- Malignancies
- Trauma

Clues to the Diagnosis of IIM

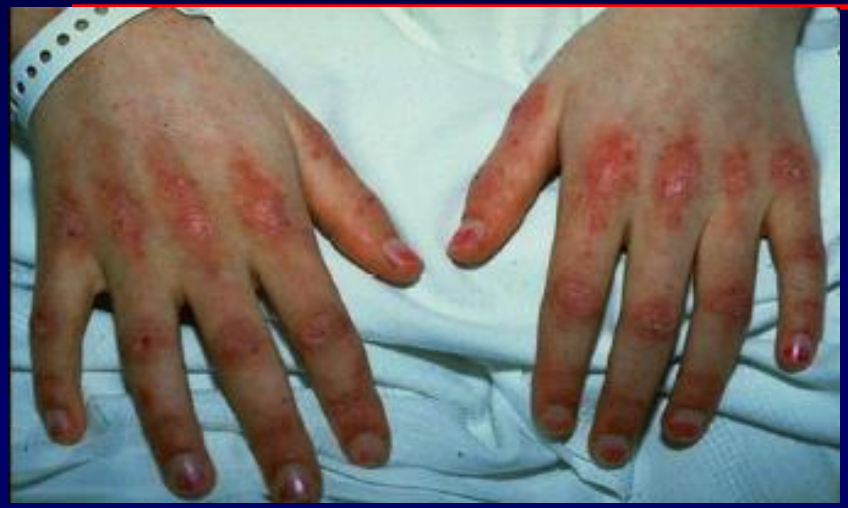
- ***Leading toward IIM***
  - FmHx of autoimmunity
  - Symmetric, chronic, prox. > distal weakness
  - No neuropathy, fasciculations, or cramping
  - Photosensitive rashes
  - Fever, arthritis, nailbed change, other CTD Sx
  - Enzymes 2-50X normal
  - Autoantibodies
  - Inflammatory STIR-MRI
- ***Leading away from IIM***
  - FmHx same syndrome
  - Weakness related to activity, fasting or of the face
  - Neuropathy, fasciculations or cramping
  - No rashes
  - No fever, arthritis, other CTD symptoms
  - Enzymes <2X or >100X nl.
  - No autoantibodies
  - MRI normal or only atrophic

We Classify IIM

- PM – no rash present
- DM – rash present
  - Gottren's, Heliotrope
- Cancer Associated
- Associated with CTD
- Inclusion body myositis
- Juvenile myositis

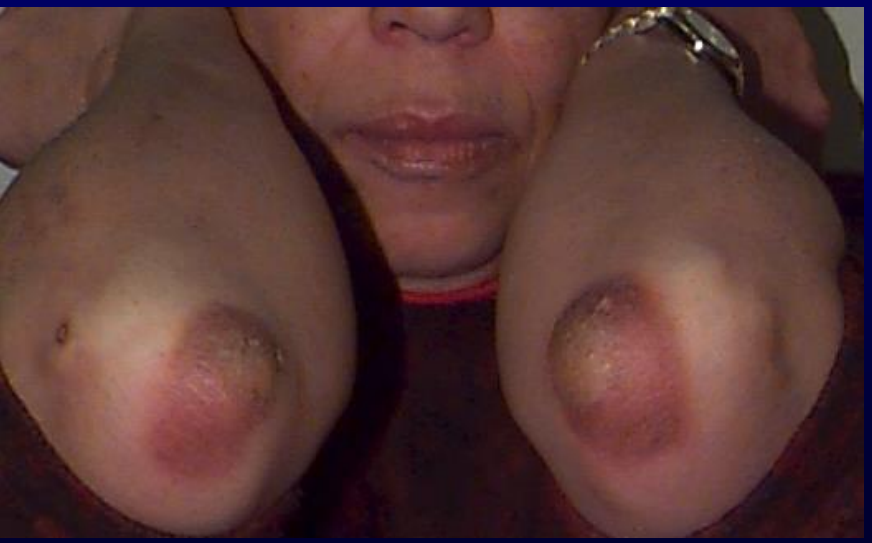
Helps providers think about the disease in terms of what to look for, how to treat and what be wary off.

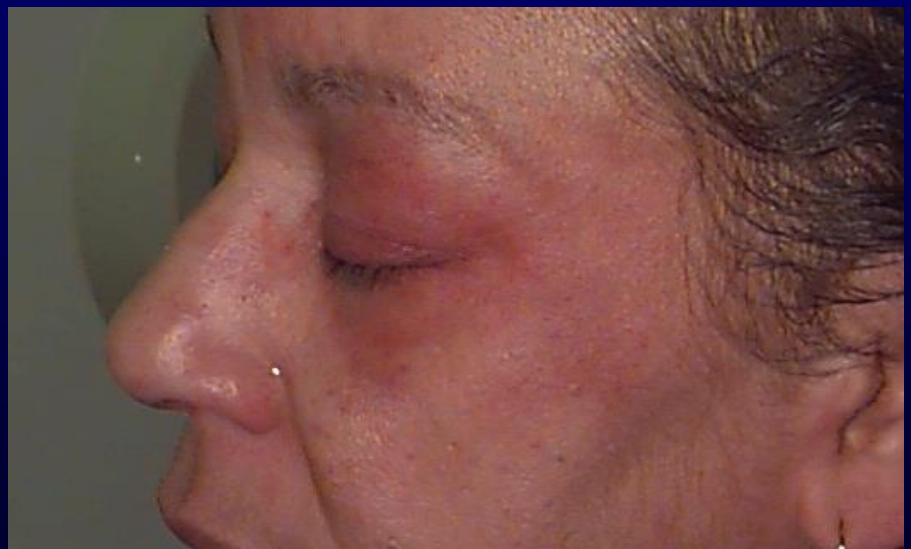
Rashes in DM



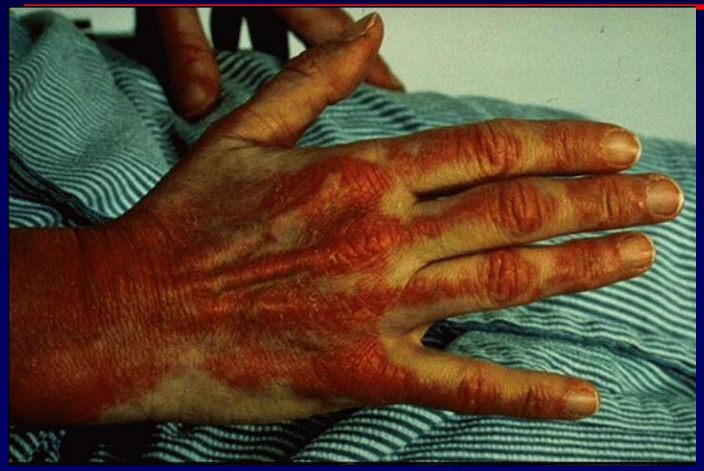
Gottren's

Heliotrope

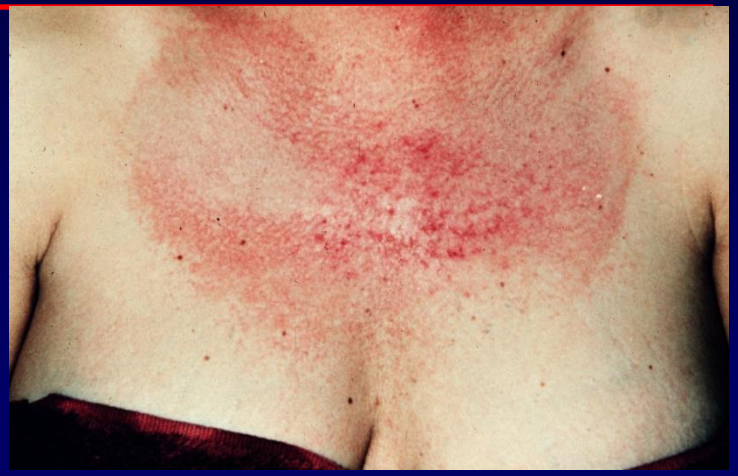




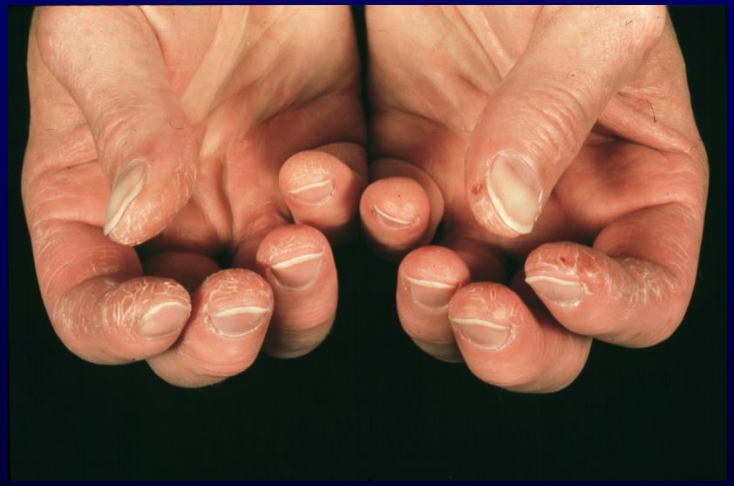
Rashes in DM



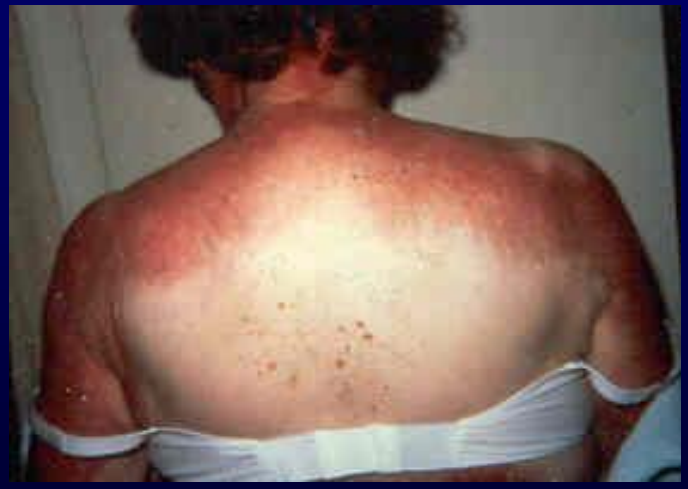
Linear Extensor Erythema



V - Sign



Mechanic's Hands



Shawl Sign

Cancers and Myositis

- Increased risk DM > PM
- Malignancy may occur several years after onset of myositis
- Types
  - PM
    - Lung, Bladder, Lymphoma (Non Hodgkins)
  - DM
    - Ovarian, Lung, Prostate, GI, Lymphoma
- Remember to screen carefully

Inclusion Body Myositis

- Most common form of IIM > age 50 years
- Insidious onset (years)
- Distal involvement (decreased grip, foot drop)
- History of falling
- Asymmetry and atrophy
- Diagnostic biopsy showing modest inflammation
- Mostly non-responsive to therapy

Connective Tissue (other autoimmune diseases) Associated Myositis

- Most common overlaps include:
  - Systemic sclerosis
  - Rheumatoid arthritis
  - SLE
  - Sjögren's syndrome

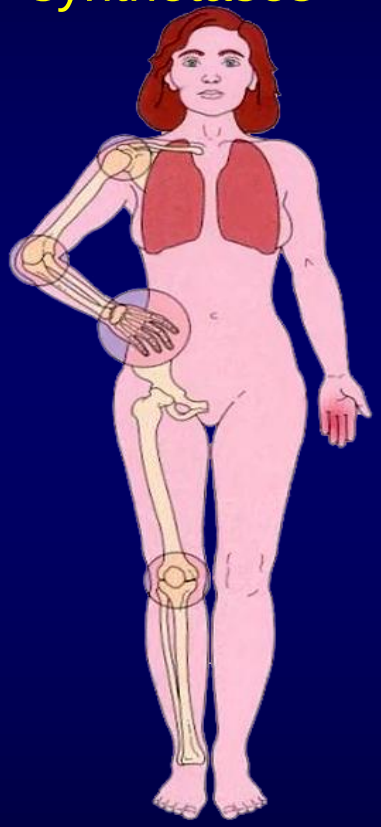
- Vancsa et al.
  - 130 primary IIM
  - 39 overlap myositis

Classification by Myositis Specific Autoantibody (MSA)

- Look at my talk regarding MSAs
- Serologic groups
  - Myositis-specific
    - Anti-synthetases (Jo-1, Pl-7, Pl-12, OJ, EJ)
    - Anti-Mi-2
    - Anti-SRP (signal recognition particle)
    - MSA negative
  - Myositis-associated
    - Anti-PM/Scl
    - Anti-Ku
    - Anti-U1RNP
    - Anti-U2RNP
    - Anti-p155, Anti-MJ
    - MAA negative

MSA Subgroups

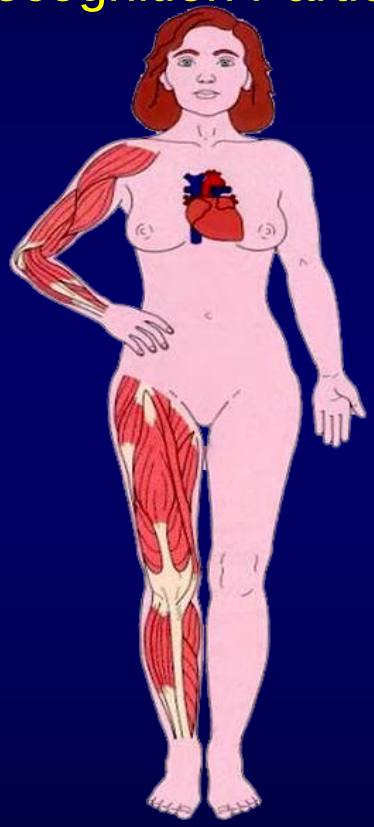
Anti-aminoacyl-tRNA synthetases



Interstitial lung disease, Arthritis, Fevers, Mechanic's hands

75% 5-year survival

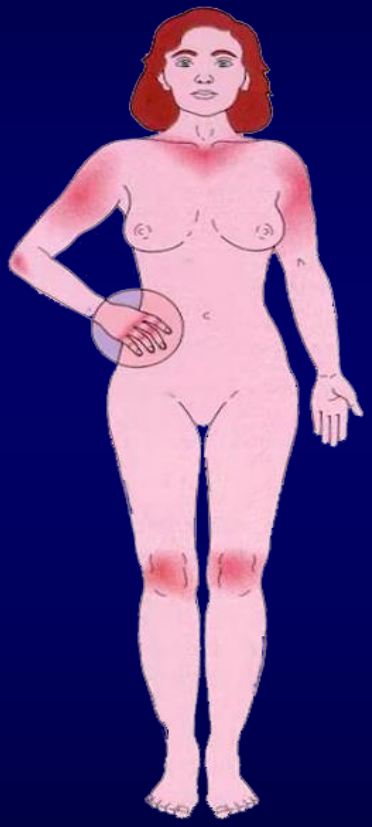
Anti-Signal Recognition Particle



Acute, severe muscle weakness, Myalgias, Cardiac involvement

25% 5-year survival

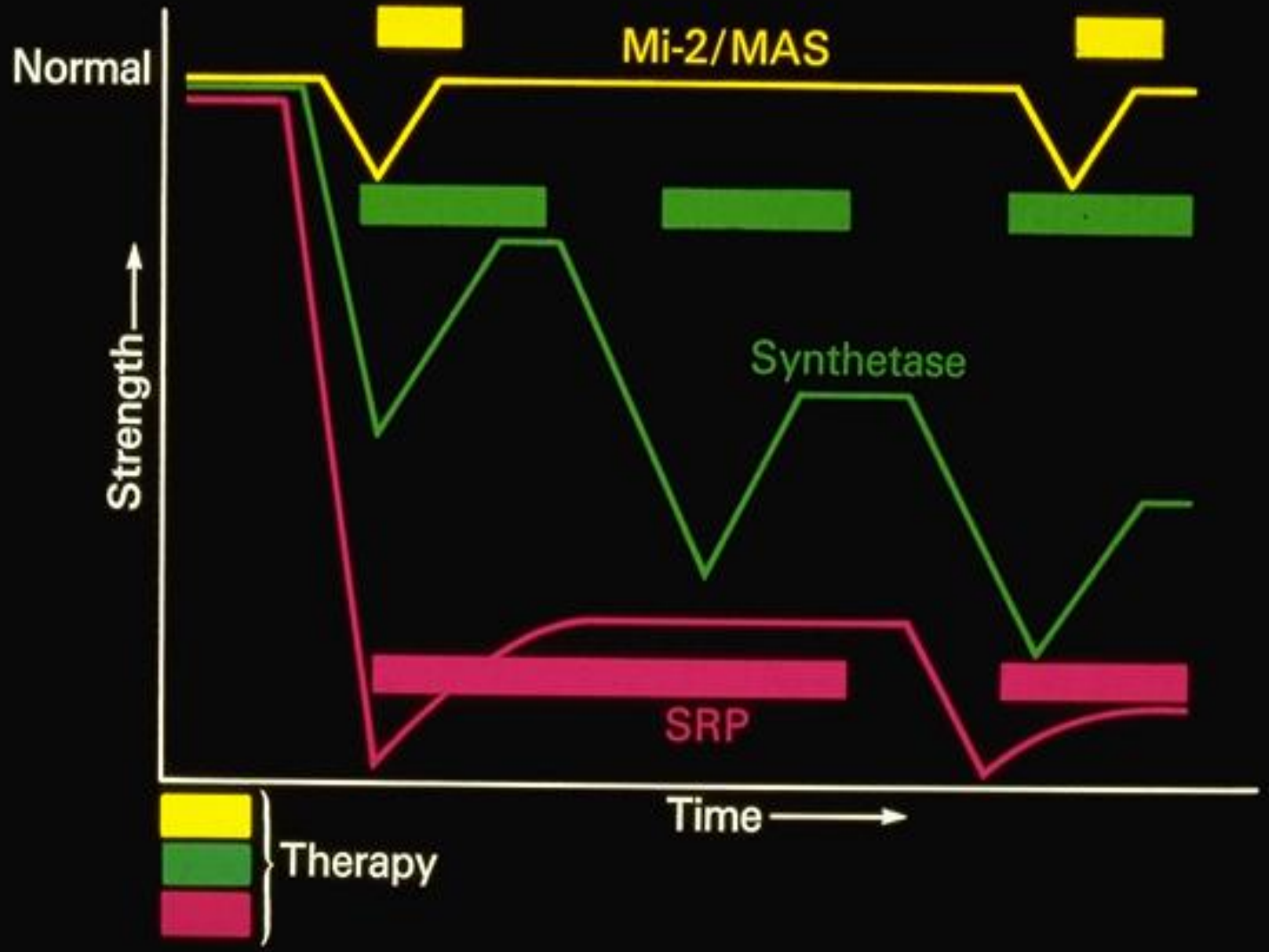
Anti-Mi-2: chromodomain helicase DNA binding protein 4



Classic dermatomyositis, V-sign & shawl rashes, Cuticular overgrowth

90% 5-year survival

IIM — SEROLOGIC GROUPS DIFFER IN DISEASE COURSE



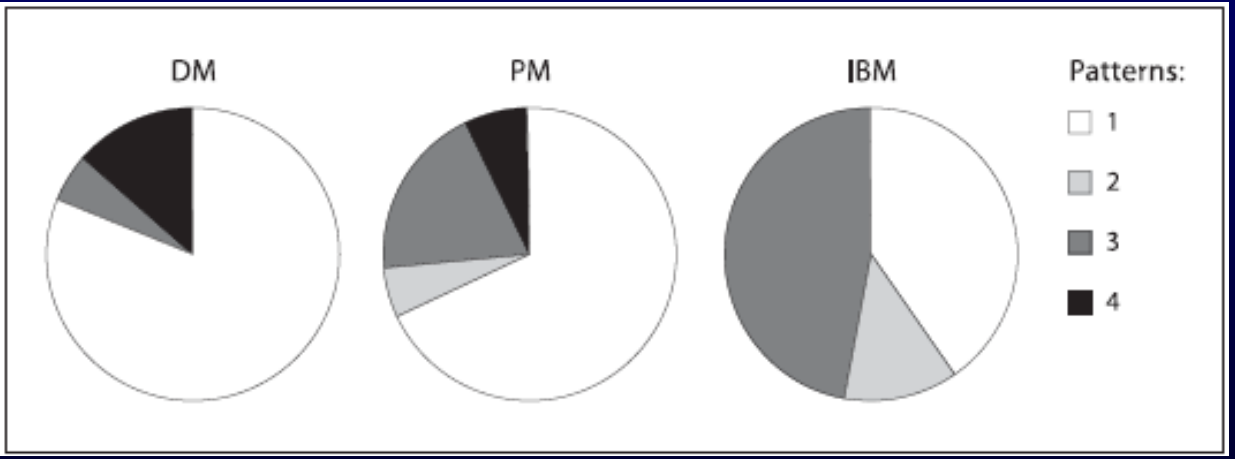
Statin-Induced Myositis

- Generally elderly
- Usually occurs within a few month of start of statin, usually goes away by stopping statin
- Aches, pains, weakness
- Recovery in 1 wk to >14 mo; mean of 2.3 months
- Recurrent in 57% if statin taken again
- Autoantibodies to the membrane receptor to which statins bind – HMGCoA reductase

Diagnostic Evaluations

- Manual Muscle Examination
- Laboratory
  - CK, Aldolase, AST, ALT, LDH, serum myoglobin, MB fraction
- Electromyography - increased membrane irritability in the form of a classic triad:
  - Increased insertional activity and spontaneous fibrillations
  - Abnormal myopathic low amplitude, short–duration polyphasic motor potentials
  - Complex repetitive discharges

Fig. 1. EMG patterns at low to maximum voluntary contraction in patients with myositis. Distribution of pattern 1 (short-duration MUPs with low-amplitude IP envelope), pattern 2 (long-duration MUPs with high-amplitude IP envelope), pattern 3 (mixture of pattern 1 and 2 characteristics), and pattern 4 (normal MUPs and normal IPs).



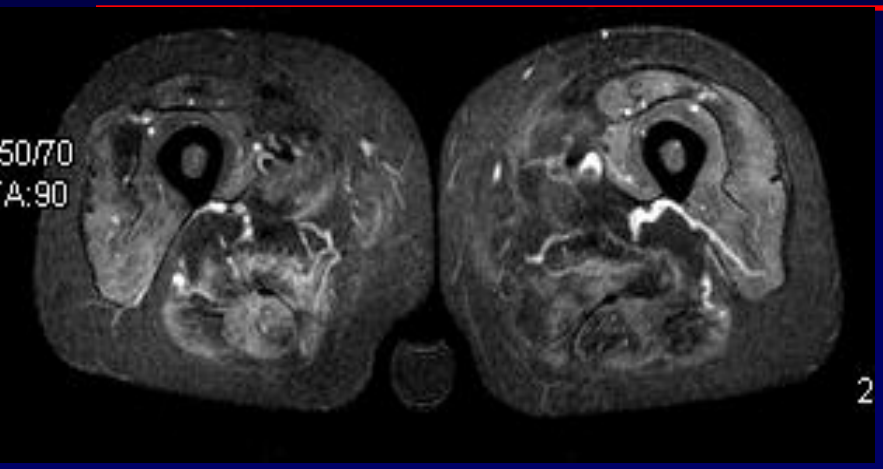
Blijham, et al. Eur Neurol, 2006

EMG

Diagnostic Evaluation

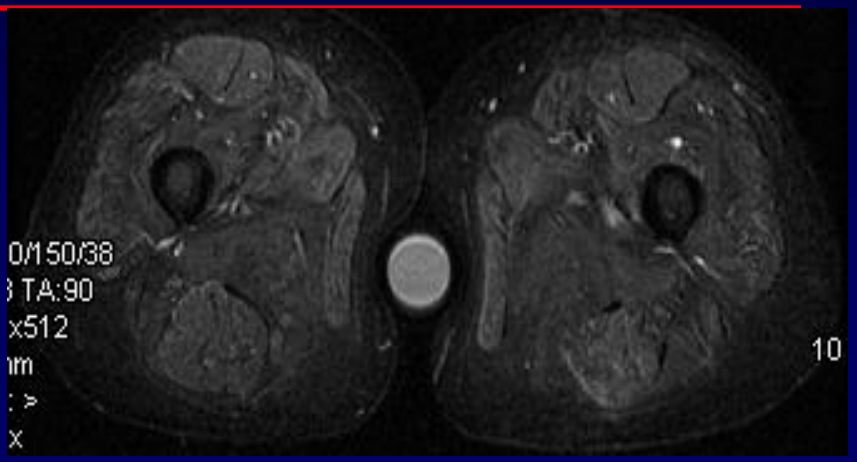
- MRI
  - Sensitive detection for activity and damage
    - Activity = spotty bright areas
    - Damage = fatty replacement

Disease Activity vs. Damage

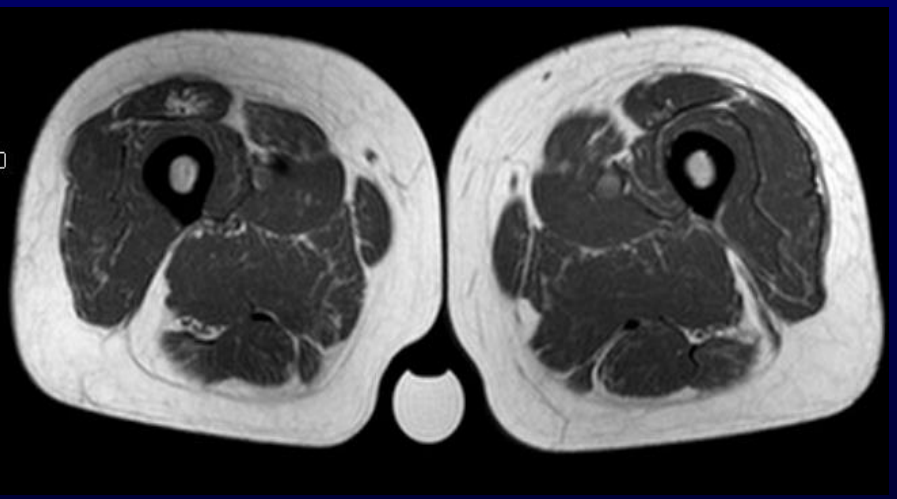


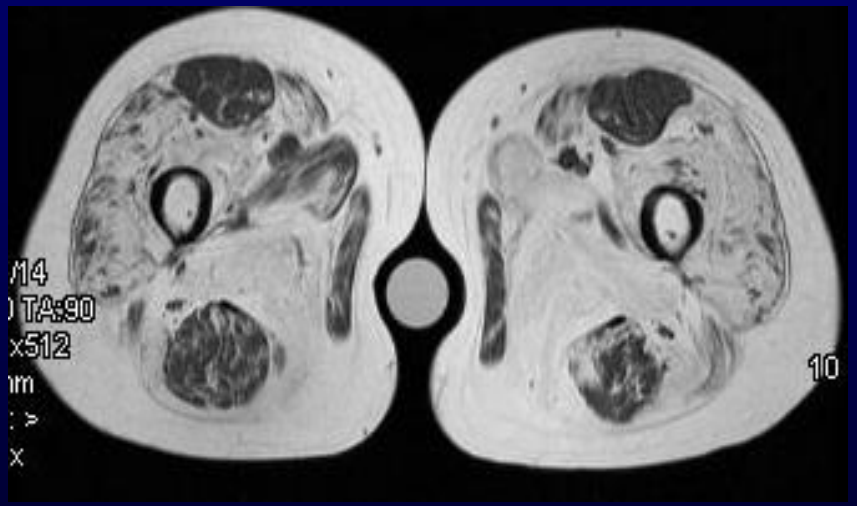
Patient 1

STIR MRI



Patient 2



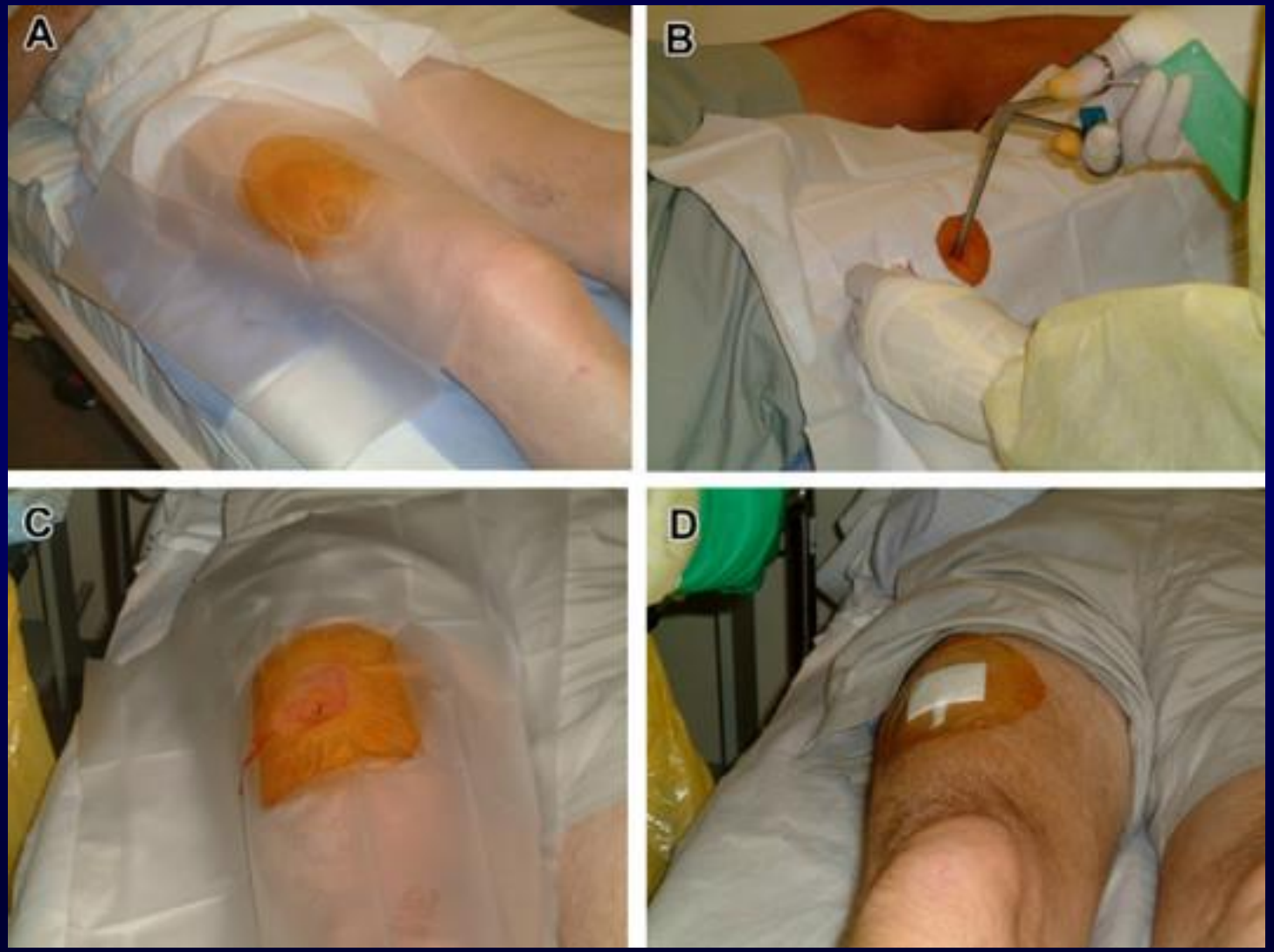


T1 MRI

Muscle Biopsy

- Helpful, not always diagnostic
- Use MRI imaging to guide site of biopsy
- Send sample to reliable pathologist
- Complete histological examination
  - Standard stains
  - Enzymatic (metabolic)
  - MHC
  - Immunohistochemical (cell types)

Muscle Biopsy



Therapy

- Knowledge
  - Talk to your health care providers
  - Get involved in a support group
    - In person, on the web, etc
  - Read
  - Join TMA and other organizations

  - Never, Never, Never give up HOPE!!!!!

Modify Your Space

- Adjust to make your life easier
  - Reaching, getting around, eating, sitting, bathroom, car, sleeping, etc.
- Help with stairs
- Avoid loose rugs, carpet (don't fall)
  - Careful of stuff on the floor
  - Wear good shoes
- Care when eating – don't aspirate

Modify Your Lifestyle

- Know your abilities
- Be careful in the sun
  - Sun block, protective clothing
- Be knowledgeable about your health insurance
- Recognize the difficulties of family members and care providers

Keep Strong

- Physical therapy
  - Exercise is more important now than ever
  - Exercise won’t hurt the muscles
- Occupational therapy
  - Use adaptive devices to help
- Eat well
  - Nutritious diet, watch your weight

Follow Health Care Instructions

- Take your meds
  - If you don't, let your care provider know
  - Meds are there to help but may hurt
  - Remember meds to prevent complications
    - Calcium, vitamin D, folic acid, etc.
  - Careful about supplementations
    - Let your physician know what your taking
- Do your therapy

How Does Your Doctor Choose Medications?

- Based on best practices, evidence and experience
- There is no standard therapy
- Severity of illness
- Type of myositis

Therapeutic Decisions

- No FDA approved drugs for IIM
- Steroids are mainstay
  - The most effective and prevalent therapy for IIM
  - Timing, dose and route of administration should be based on disease severity
- Factors important in achieving responses are:
  - Adequacy of the initial dose (>1 mg/kg/d)
  - Maintenance of high dose therapy until or after CK normalization
  - A slow taper (averaging ~ 10 mg/month)
- Improvement in strength may lag behind CK improvement by weeks to months
- An important cause of secondary myopathy and other adverse events

IIM Systemic Therapies Overview

Agent	*Dose*	*Comments*
Corticosteroids	>1 mg/kg/ qd - 1 g IV bolus qm	Taper to 0.25 mg/kg/qd or qod over months
Methotrexate	5-25 mg po/wk	SQ, IV routes also useful
Azathioprine	50-200 mg po qd	GI intolerance often
Hydroxychloroquine	200-400 mg po qd	For systemic symptoms
IVIG	0.5-1g/kg/dX2d/m	Taper by time or dose
Cytoxan	0.5-1g/m2 IV qm	Or 50 – 150 mg po qd
Mycophenolate	1 – 1.5 gm po BID	GI intolerance
Cyclosporin	2-4 mg/kg/d	Follow levels and Cr
Tacrolimus	3-6 mg po BID	Renal toxicity
Rituximab	1 gm x 2, 14 days apart	Infusion rxn, B cell depletion
Anti-TNF	Varies	A hint of help
Combinations		Very helpful in some

DON’T

- Fall
- Aspirate
- Give up HOPE!