Classifying Myositis

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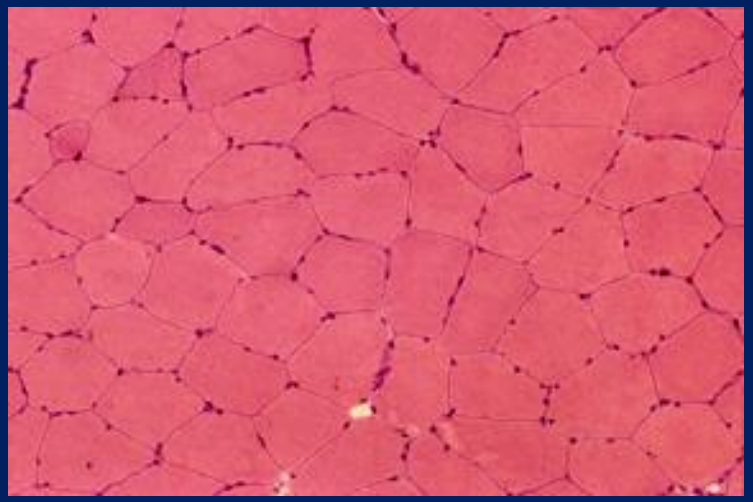
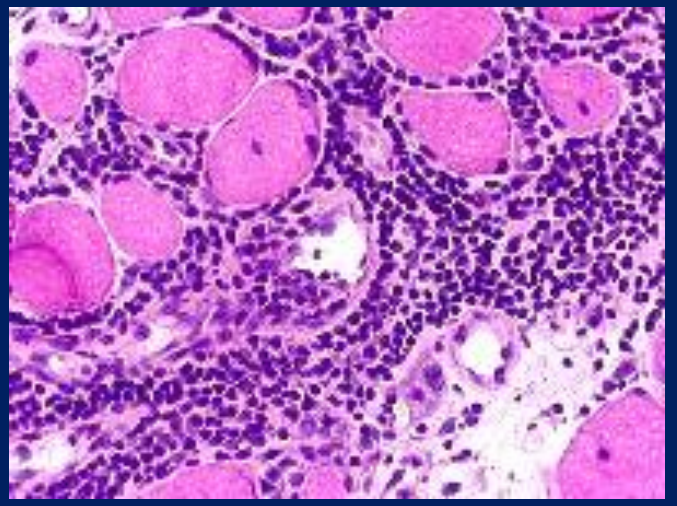
What is Myositis

- Inflammation of the muscle
  - Many causes for inflammation



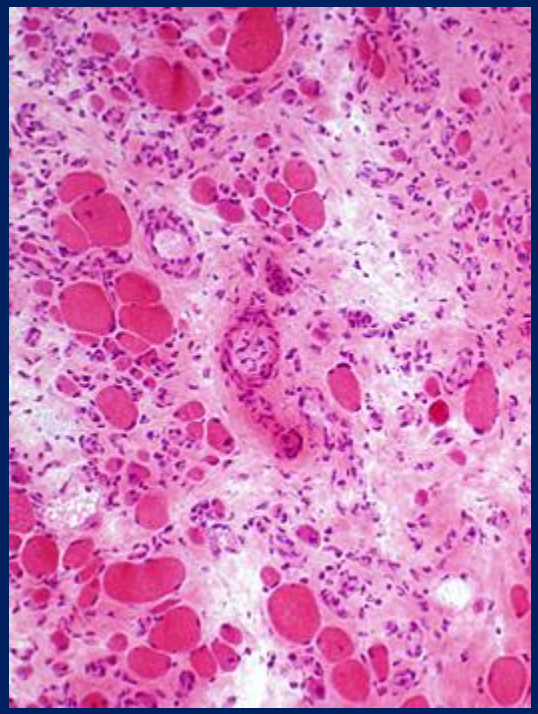
Normal



Inflammation

Is Inflammation Harmful?

- Inflammation heals with scarring
- Scaring leads to muscle damage
- Damage causes weakness



How is Myositis Defined?

- Inflammation of the muscle that causes weakness
  - Associated with
    - Elevation in serum muscle enzyme levels
    - Abnormal electromyography (EMG) testing
    - Characteristic muscle biopsy findings
    - Rashes (dermatomyositis)

- Bohan and Peter 1975

Classification Schemes

Clinical groups (Adult or Juvenile)

- Polymyositis
- Dermatomyositis
- Inclusion body
- Myositis with other CTD
- Cancer-associated
- Eosinophilic
- Granulomatous
- Focal / Nodular
- Ocular / Orbital

New Advances in Science

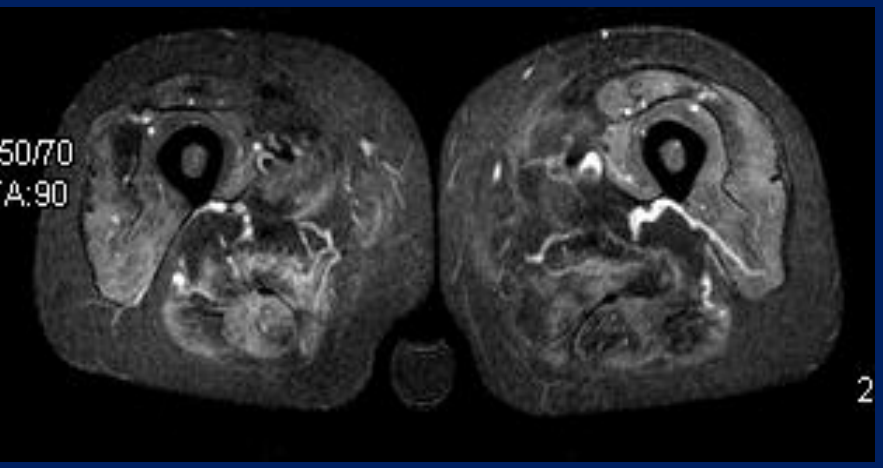
- Genetics
- Imaging Studies
  - MRI
- Laboratory Studies
  - Autoantibodies
  - Markers present in muscle on biopsy

Genetic Risk Factors

IIM Group	HLA-DRB1	HLA-DQA1	Comments (RR)
White IIM (PM, DM, IBM)	*0301	*0501	HVR1motif (~6)
JDM	*0301	*0501	IL1A1/A2 (~5)
Anti-Jo1	*0301	*0501	In Whites (~30)
Anti-SRP	*05	*0301	In Blacks (~8)
Anti-Mi-2	*07(B9-trp)	*0201	In Hispanics (~18)
D-penicillamine	*04	?	In Whites (~7)

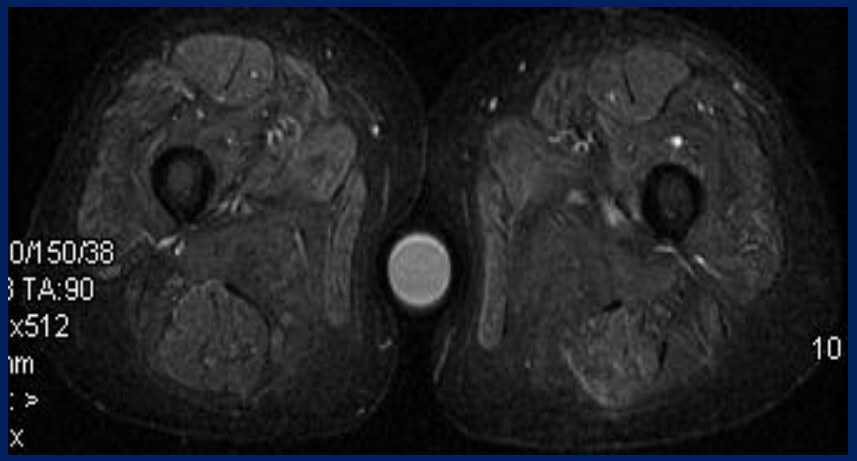
These markers may help define who is at risk for myositis

Imaging Studies - MRI

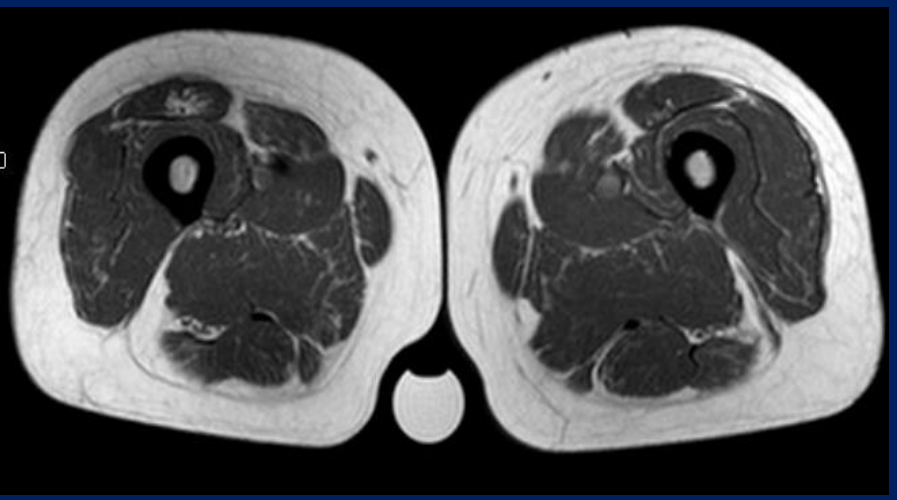


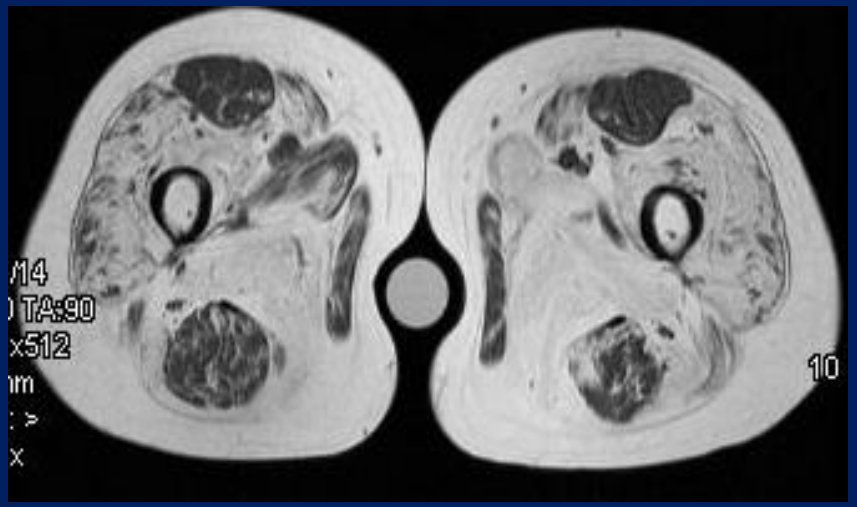
Patient 1

STIR MRI



Patient 2





T1 MRI

Laboratory Studies

- Tests for autoantibodies
  - Autoimmune diseases test positive for autoantibodies
    - Thyroid disease – anti-thyroid antibodies
    - Lupus – anti-nuclear antibodies
    - Rheumatoid Arthritis – antibody to an antibody (RF)
- Myositis Specific Autoantibodies (MSA)

Myositis Specific Autoantibodies

- Anti-Mi-2 Dermatomyositis
- Anti-SRP Myositis
- Anti-p155 Cancer associated myositis
- Anti-HMGCR Statin induced myositis
- Anti-synthetase Syndrome
  - A collection of autoantibodies associated with a syndrome of symptoms and myositis

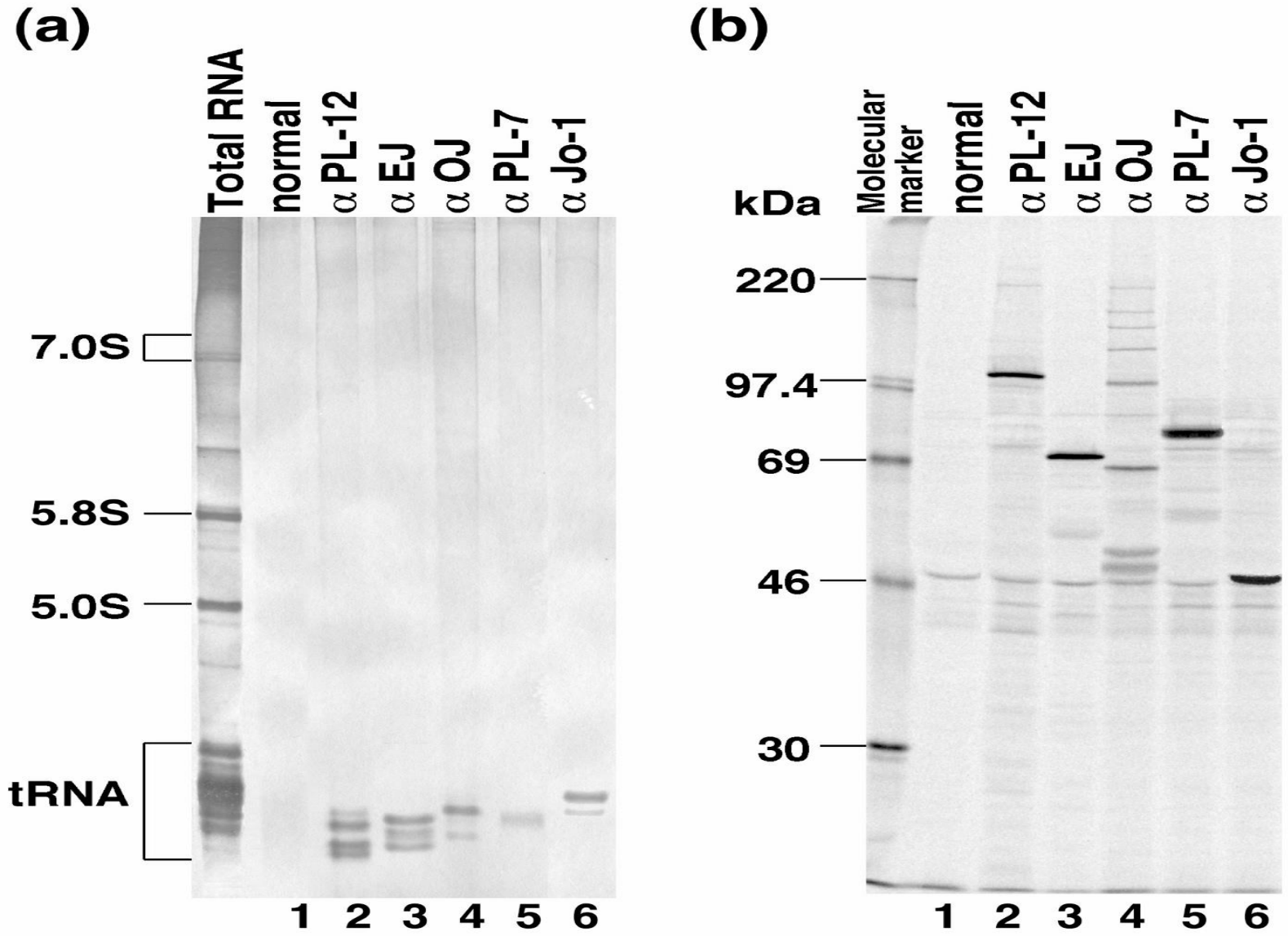
Anti-Synthetase Syndrome

- Characterized by
  - Fevers
  - Arthritis
  - Lung disease (interstitial pulmonary fibrosis)
    - severe
  - Hand rash (mechanic's hands)

Anti-Synthetase Syndrome

Autoantibody	Immunoprecipitation Complex: Protein	Immunoprecipitation Complex: RNA	Antigenic Element
Antisynthetases			
• Anti-Jo-1	55 kD	tRNA-His	HisRS tRNA-His
• Anti-PL-7	80 kD	tRNA-Thr	ThrRS
• Anti-PL-12 (1) Anti-PL-12(2)	110 kD none	None tRNA-Ala	AlaRS tRNA-Ala
• Anti-OJ	> 130 kD	tRNA-Ile	IleRS
• Anti-EJ	75 kD	tRNA-Gly	GlyRS

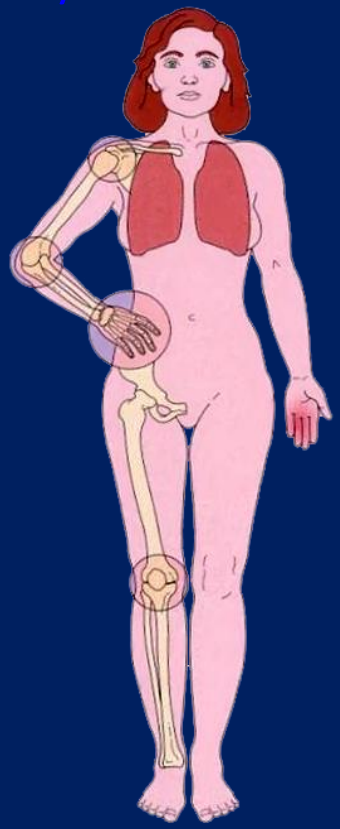
Antisynthetase Autoantibody Immunoprecipitation Patterns



ELISA testing

Myositis Autoantibody Phenotypes Differ in Clinical Presentation, Genetics and Prognosis

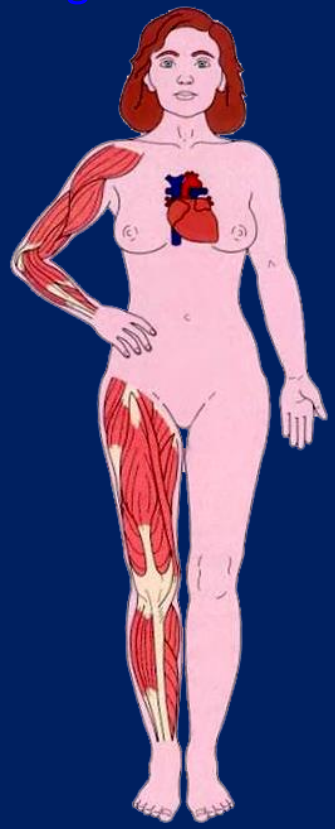
Anti-aminoacyl-tRNA synthetases



Interstitial lung disease, Arthritis, Fevers, Mechanic's hands; DR3

75% 5-year survival

Anti-Signal Recognition Particle



Acute-onset PM, Severe weakness, Myalgias, Myocarditis; DQA1*0104

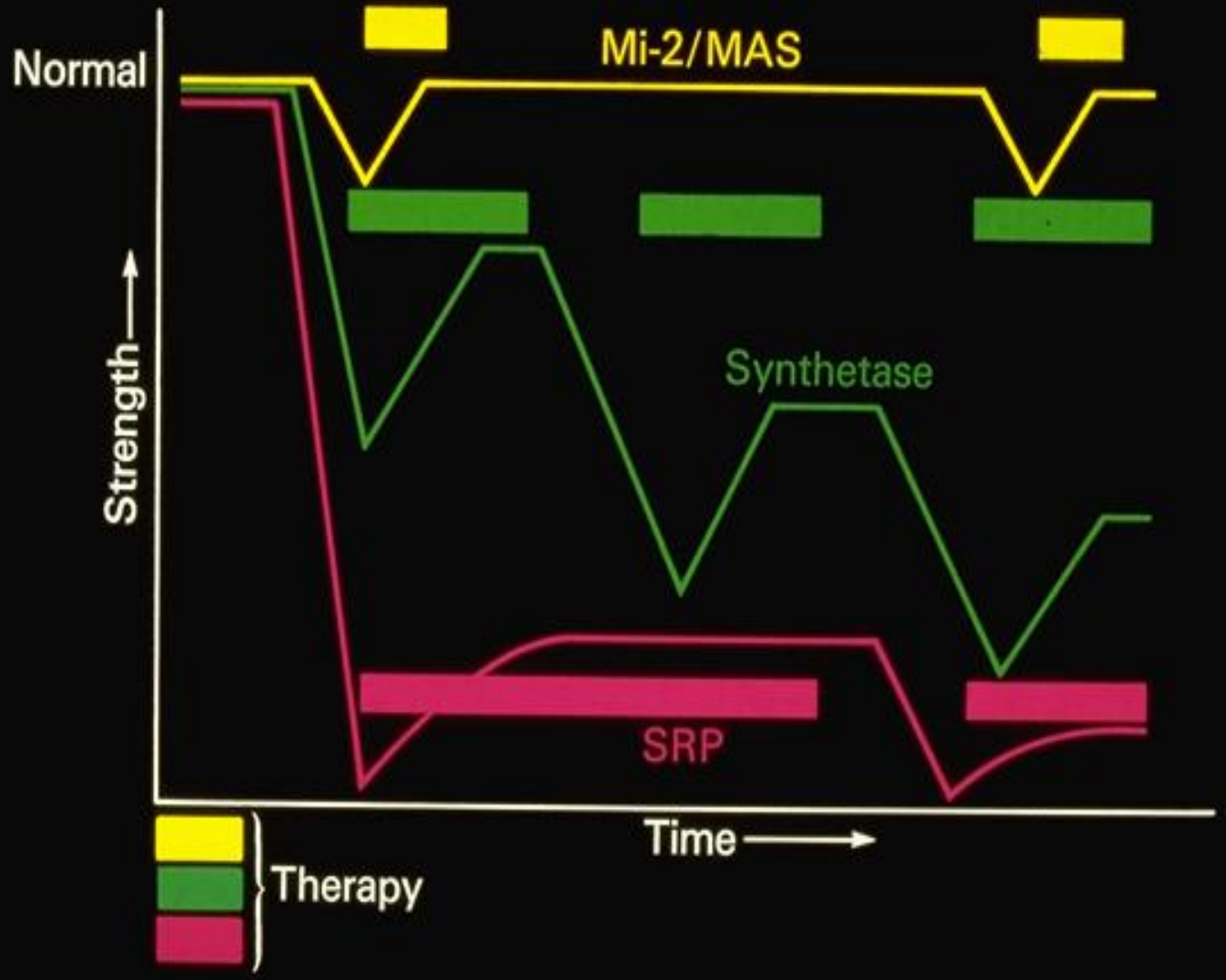
25% 5-year survival

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

Classic Dermatomyositis, V-sign & shawl rashes, Cuticular overgrowth; DR7

90% 5-year survival

IIM — SEROLOGIC GROUPS DIFFER IN DISEASE COURSE



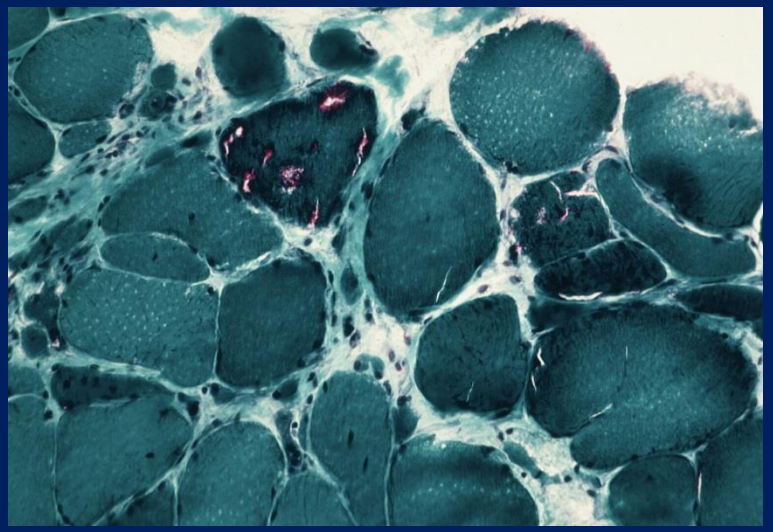
Other new laboratory tests

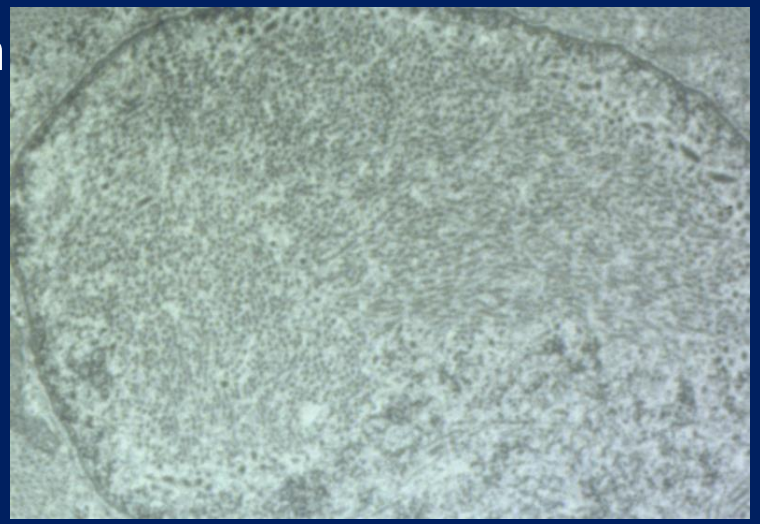
- Presence of a protein on the muscle cells where inflammation is occuring
  - HLA-1

Criterion	Polymyositis		Myopathic dermatomyositis		Amyopathic dermatomyositis
	Definite	Probable	Definite	Probable	Definite
Myopathic muscle weakness	Yes*	Yes*	Yes*	Yes*	No†
Electromyographic findings	Myopathic	Myopathic	Myopathic	Myopathic	Myopathic or non-specific
Muscle enzymes	High (up to 50 times normal)	High (up to 50 times normal)	High (up to 50 times normal) or normal	High	High (up to 10 times normal) or normal
Muscle-biopsy findings	Primary inflammation, with the CD8/MHC-1 complex and no vacuoles	Ubiquitous MHC-I expression, but no CD8-positive infiltrates or vacuoles‡	Perifascicular, perimysial or perivascular infiltrates; perifascicular atrophy	Perifascicular, perimysial or perivascular infiltrates; perifascicular atrophy	Non-specific or diagnostic for dermatomyositis (subclinical myopathy)
Rash or calcinosis	Absent	Absent	Present	Not detected	Present

Inclusion Body Myositis Criteria *(Griggs et al. 1995)*

- Clinical features
  - Disease duration > 6 mos.
  - Age of onset > 30 years
  - Proximal and distal weakness involving quadriceps, finger flexors, and wrist flexor > wrist extensor weakness
- Laboratory features
  - Serum CK < 12 times normal
  - Muscle biopsy showing inflammation with MNC infiltrates, vacuolated myofibers, and either: 1) intracellular amyloid deposits or 2) 16-18 nm tubulofilaments by EM
  - EMG consistent with an inflammatory myopathy





IIM - Humoral Immunologic Abnormalities

- Hyper-, hypo-, or agammaglobulinemia
- Monoclonal gammopathy
- Circulating immune complexes
- Immunoglobulin and complement deposition in muscle vascular endothelium
- Autoantibodies also seen in other diseases - ANAs, anti-Ro, anti-La, anti-thyroid, etc.
- Myositis-associated autoantibodies - Anti-PM/Scl, -Ku, -U1RNP, -U2RNP
- Myositis-specific autoantibodies - Anti-synthetases, -SRP, -Mi-2

Classifying Myositis is Difficult

- Spectrum of disease
- Different causes
- Some are genetic, some are inflammatory

- Usefulness of classifying is mostly for research
- Goal is to provide better therapy