Myositis 101

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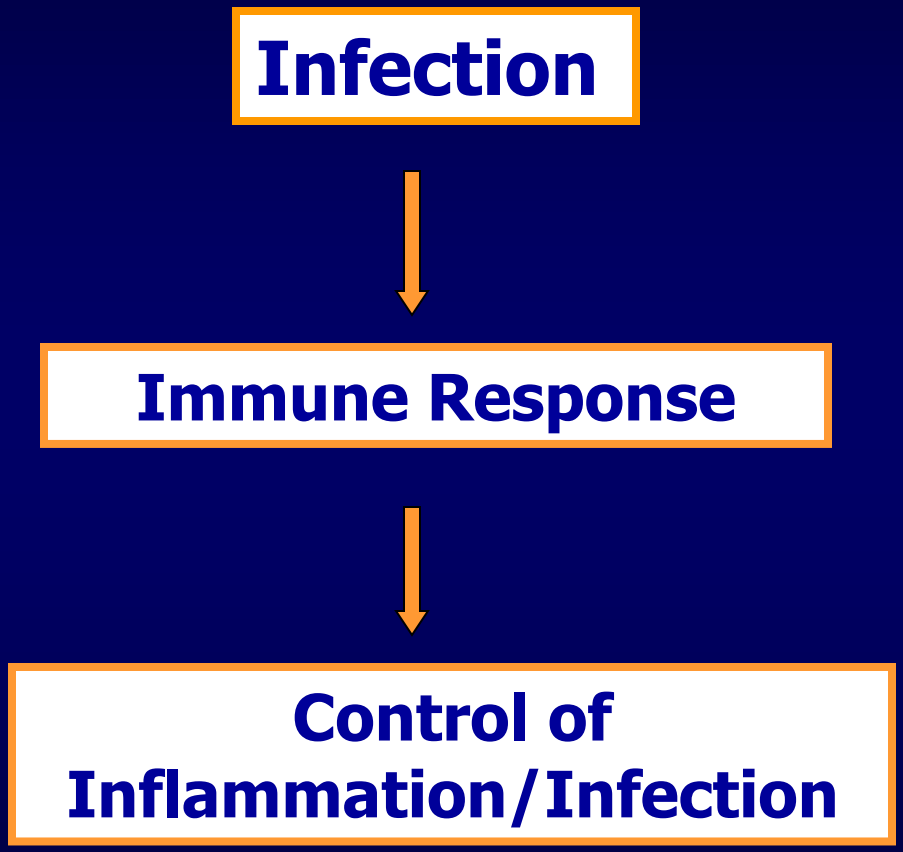
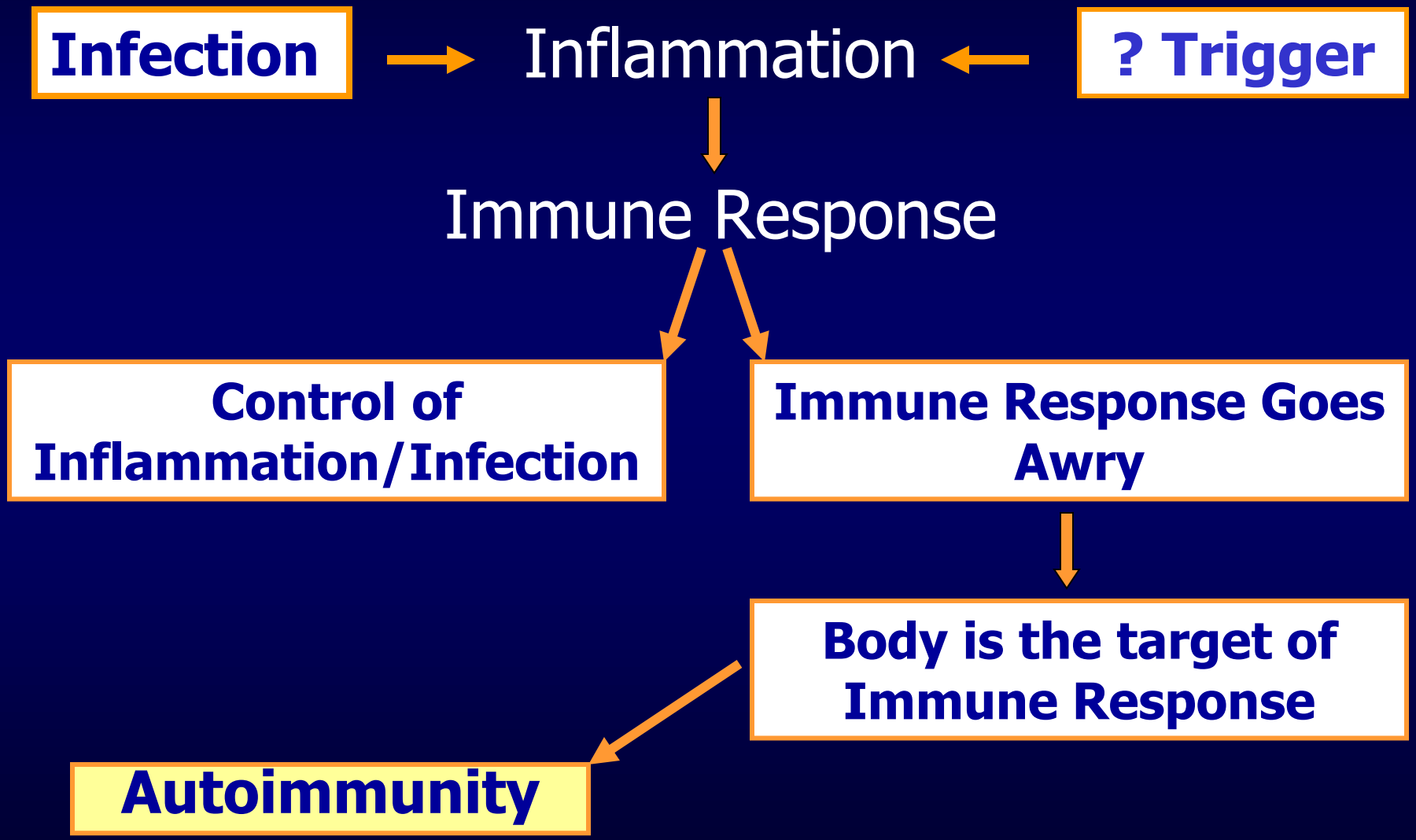
What is Myositis?

- myo = muscle; -itis = inflammation
- "Idiopathic inflammatory myopathy" is most commonly used term (IIM)
- Heterogeneous group of autoimmune syndromes
- Muscle weakness due to inflammation in the muscle tissue
- Systemic complications (i.e. not just muscle)
- Unknown cause (idiopathic)

Understanding Autoimmunity



Understanding Autoimmunity



Autoimmunity

- Immune response against *self*
  - loss of tolerance
- Unknown cause
  - susceptibility factors (genetic)
  - environmental triggers
    - e.g. infection
- Multiple diseases and "syndromes"
  - which sometimes run in families

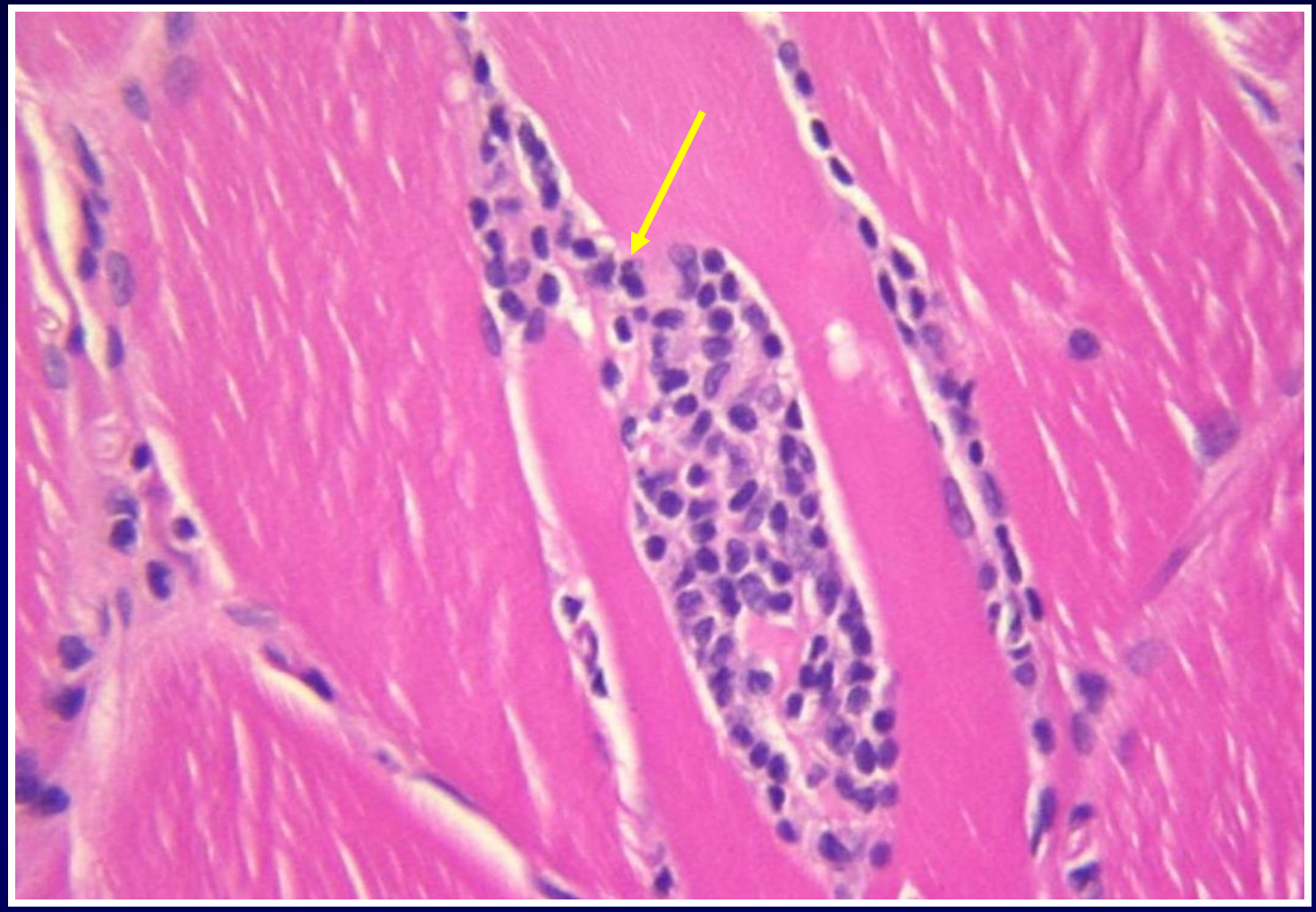
Autoimmune Diseases

Disease	Target
Rheumatoid Arthritis	Joints (synovium)
Systemic Lupus Erythematosus	Skin, joints, kidneys
Scleroderma	Skin
Multiple Sclerosis	Nervous system
Myositis	Muscle

Nearly every AI disease has **multiple** targets!

Autoimmunity (cont'd)

- Immune response against *self*
  - loss of tolerance
- Unknown cause
  - susceptibility factors (genetic)
  - environmental triggers
    - e.g. infection
- Multiple diseases and "syndromes"
  - which sometimes run in families
- Formation of autoantibodies
  - markers of autoimmunity
- Inflammatory in nature



Immune cells (lymphocytes) “attacking” normal muscle tissue in a patient with polymyositis

Conventional Classification of Myositis

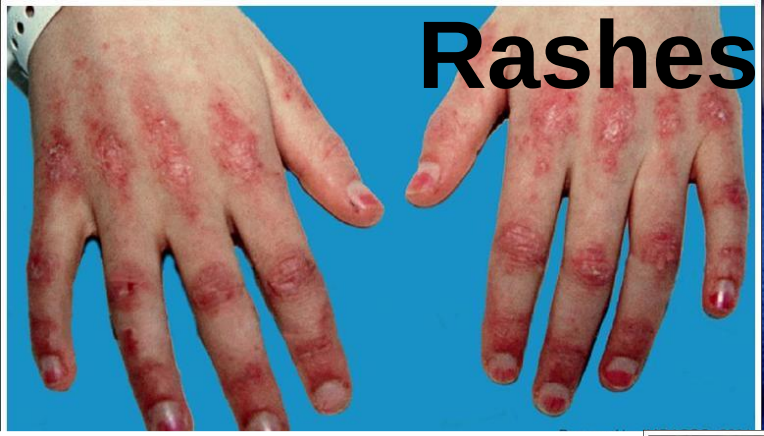
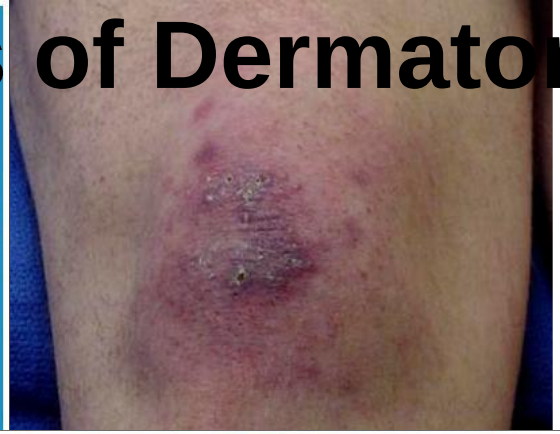
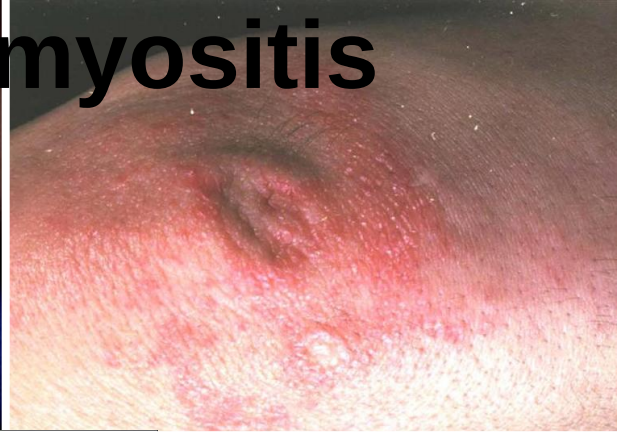
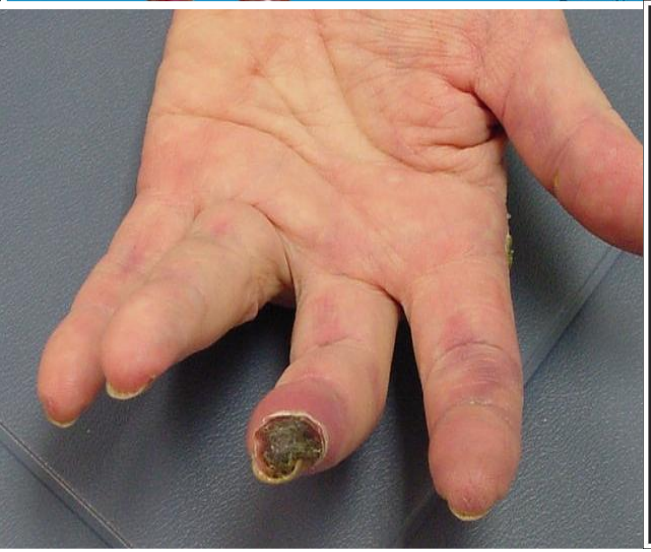
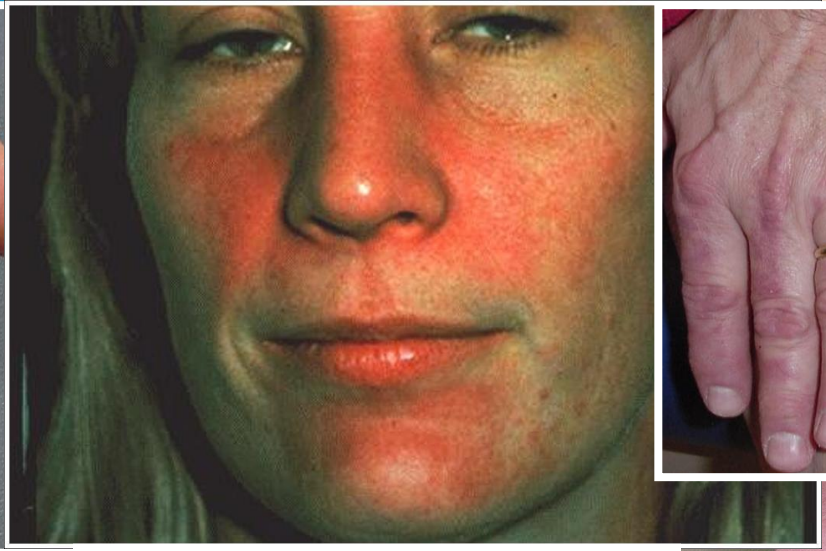
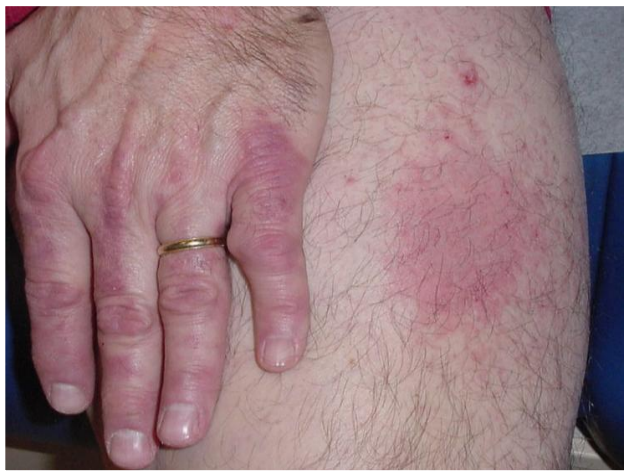
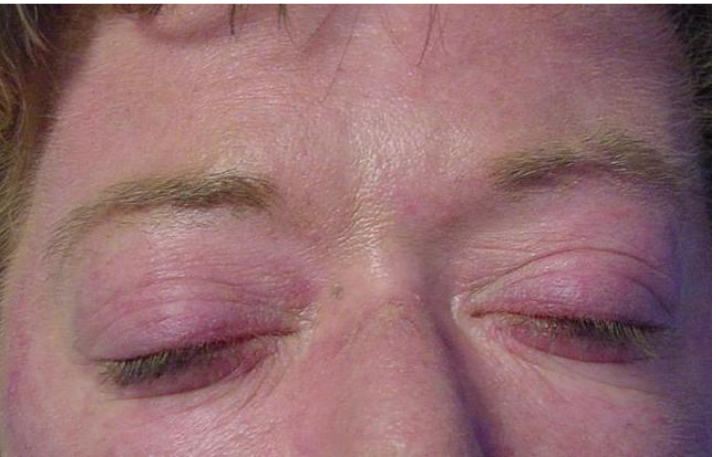
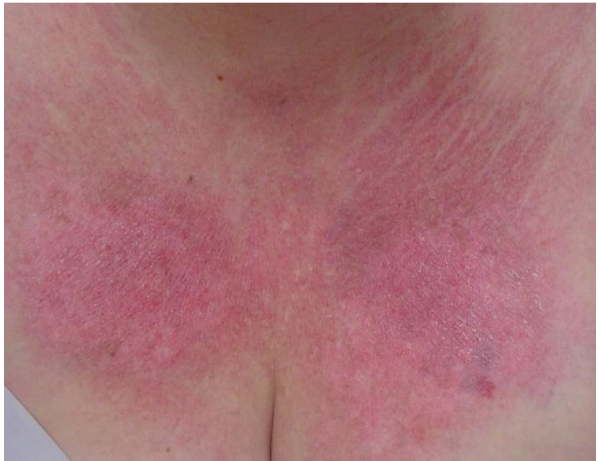
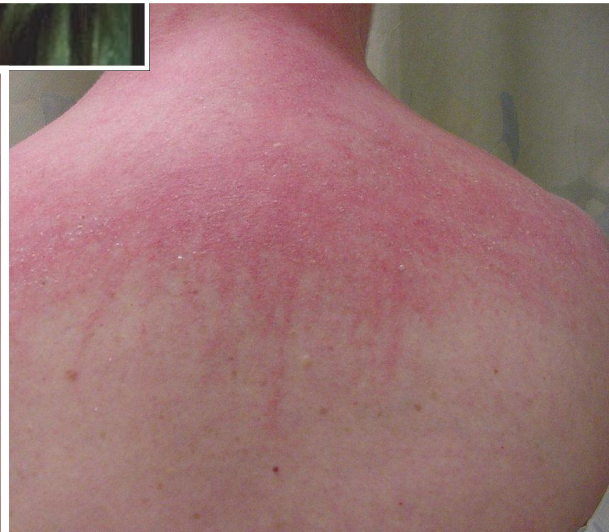
- Adult polymyositis (PM)
- Adult dermatomyositis (DM)
- Juvenile myositis (DM >> PM)
- Malignancy-associated myositis
- Myositis in overlap with another rheumatic disease
- Inclusion body myositis (IBM)

There are many other types of myositis that are much more uncommon

Systemic Targets of Myositis

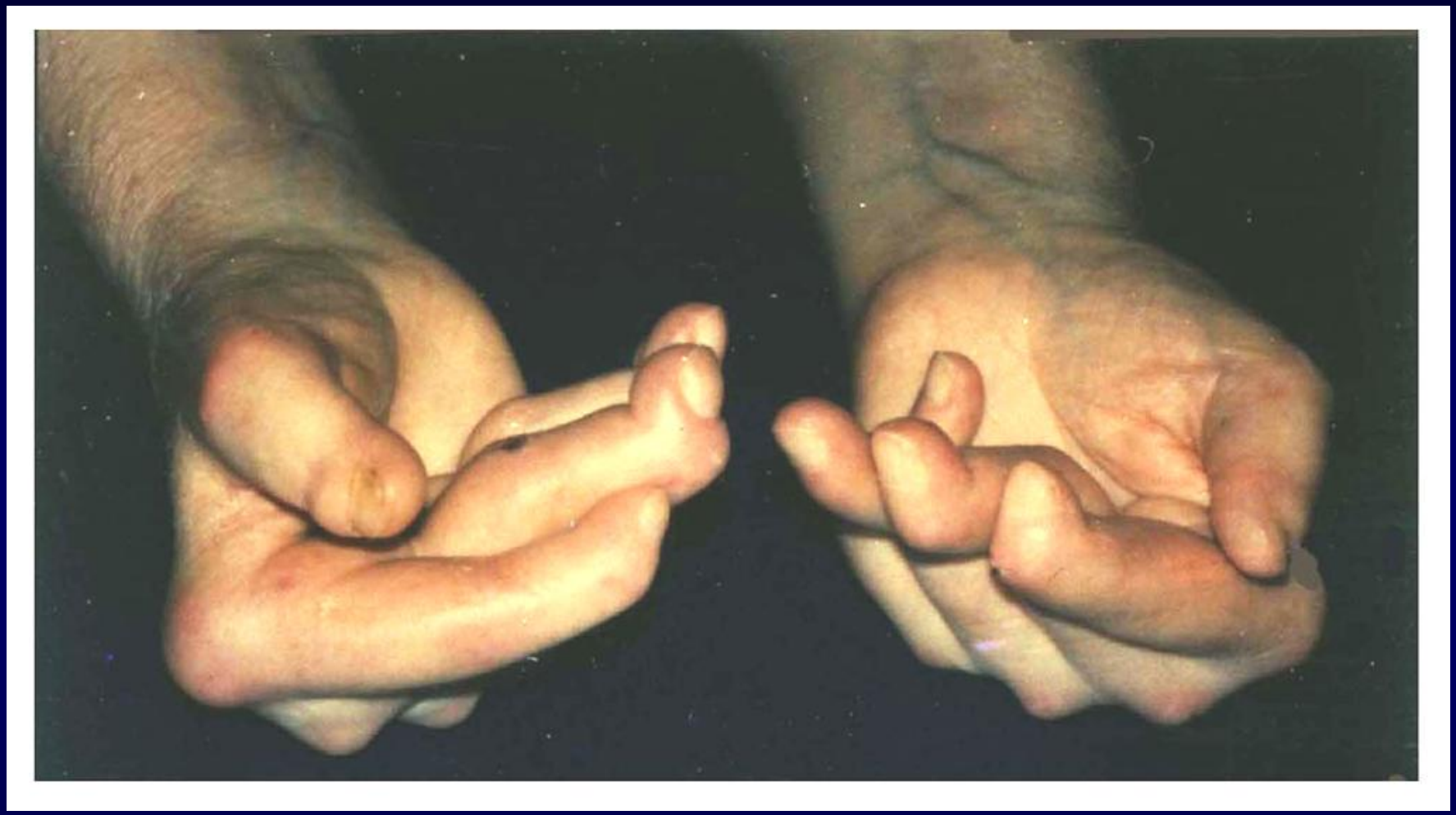
- Skin

Rashes of Dermatomyositis

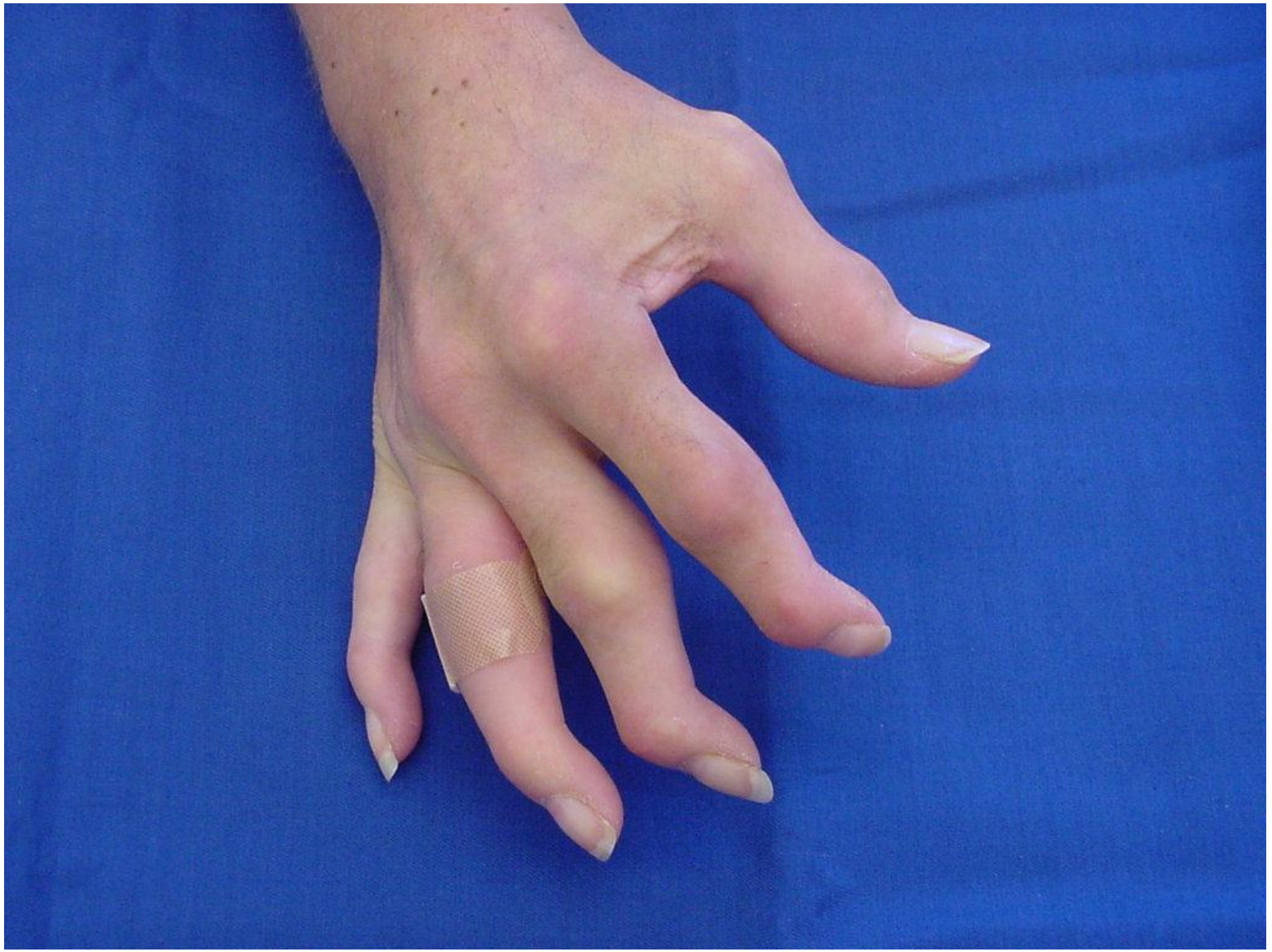
Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)



This patient looks like they have rheumatoid arthritis

… but they also have myositis



Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- GI tract: difficulty swallowing

Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- GI tract: difficulty swallowing
- Lung
  - Shortness of breath
  - Inflammation in lung tissue
  - Fibrosis (scar tissue)
  - Associated with markers in the blood called antibodies

Systemic Features of Myositis

Musculoskeletal

- Weakness
- Muscle pain/ tenderness
- Muscle atrophy
- Arthralgias
- Arthritis

Gastrointestinal

- Dysphagia
- Reflux
- Dysmotility

Cutaneous

- Rashes
- Calcification

Cardiac

- Arrhythmias
- Congestive failure

Pulmonary

- Atelectasis from muscle weakness
- Aspiration pneumonia
- ILD

General

- Fever
- Fatigue
- Weight loss
- Raynaud's

Slide, courtesy of Dr. Fred Miller

How Does Myositis Present ?

- In many different ways, developing slowly or quickly
- Weakness - difficulty walking/climbing, combing hair, lifting
- Rashes or skin sores
- Severe fatigue that limits normal activities
- Joint pain or joint swelling
- Problems with swallowing or abdominal pain
- Shortness of breath or cough
- Fevers or weight loss

So … myositis can present in many ways affecting many parts of the body and, therefore, can mimic many other diseases and be difficult to diagnose

How Does a Doctor Diagnose Myositis ?

- Careful history and physical examination including tests for muscle weakness
- Blood tests for increased muscle enzymes: CK or CPK, aldolase, LDH, ALT/SGPT, or AST/SGOT
- EMG (electromyography): needle study of muscles
- Muscle biopsy: looking for characteristic pathologic changes in the muscle fibers and blood vessels
  - "immune cells" including lymphocytes
- Skin changes of dermatomyositis
- Other diagnostic approaches: autoantibody testing in blood; MRI; more specialized testing to rule out other diseases that might mimic myositis

Who Gets Myositis (Epidemiology) ?

- Rare disease with annual incidence of 5-10 cases/million; possibly increasing
- Prevalence of 50-90 cases/million
- "Bimodal" incidence peaks
  - childhood (5-15 years); adult mid-life (30-50 years)
- Females > Males (2-3:1)
- IIM subsets
  - overlap CTD: younger females
  - malignancy-associated: age>50, F=M

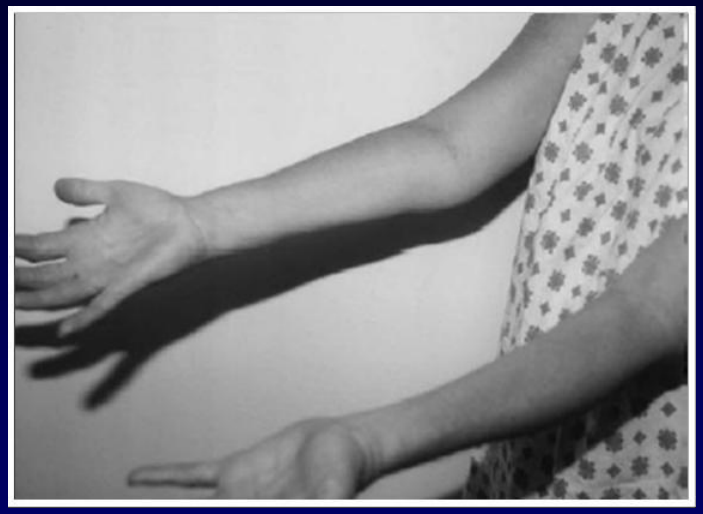
Inclusion Body Myositis

- Most common acquired muscle disease over the age of 50
- Affects men > women at 2-3:1
- Average time from symptom onset to diagnosis is ~ 6 years

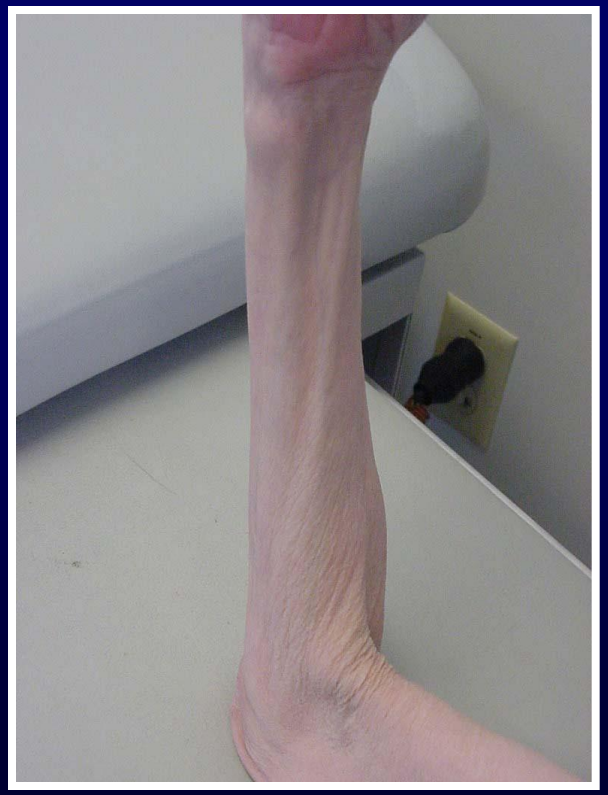
Clinical Features of IBM

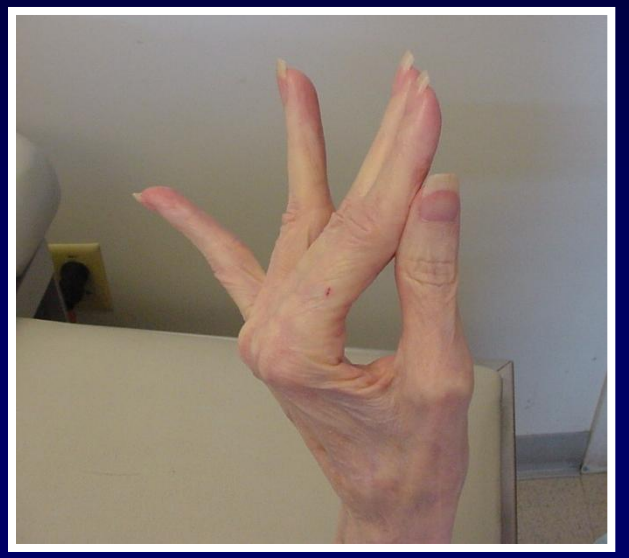
- Consider IBM when confronted with a PM patient who does not respond to treatment
- Insidious onset of painless muscle weakness with slow progression
- Tendency to distal (away from the trunk muscles) and asymmetric muscle involvement ("foot drop")
- Difficulty swallowing
- Characteristic pattern of muscle atrophy (forearm flexors, muscles of hands, thigh)

Inclusion Body Myositis



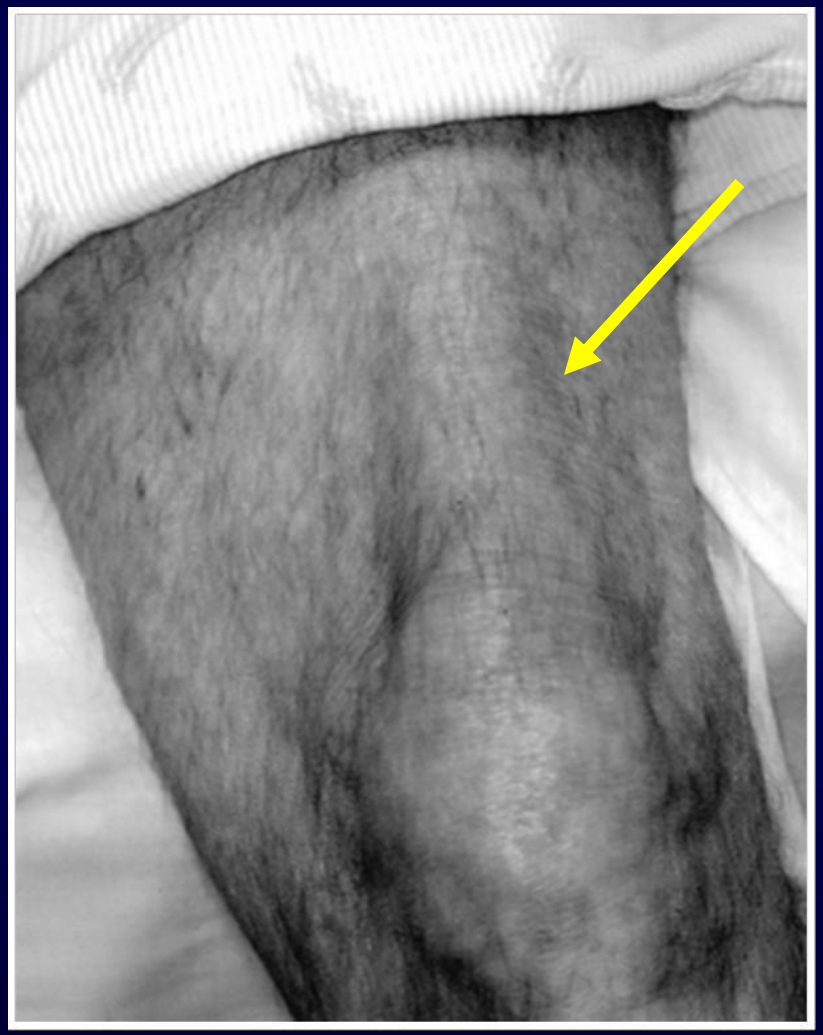
"scooped out" forearm





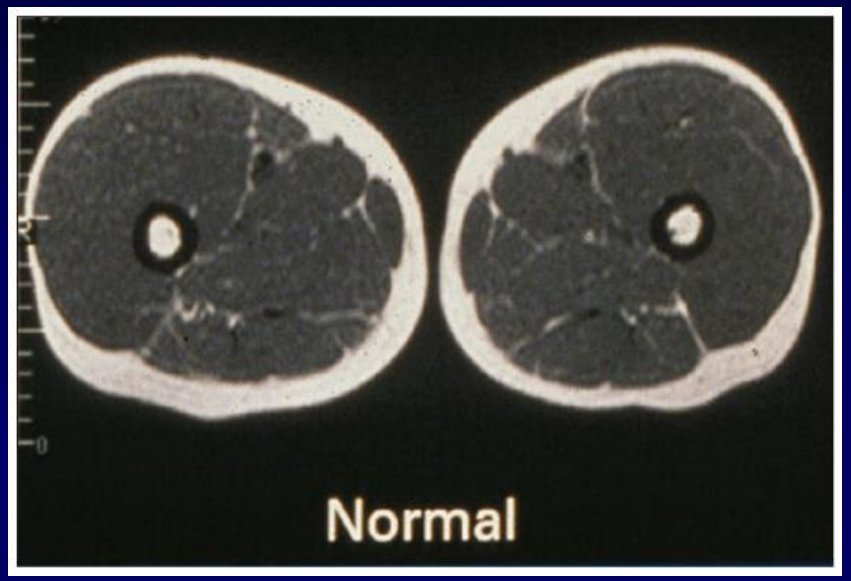
"teardrop sign"

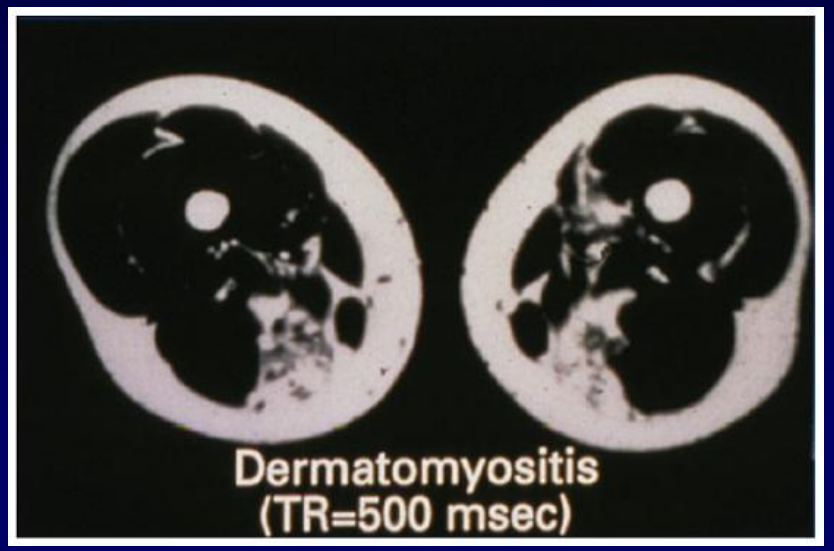
IBM: Quadriceps Atrophy

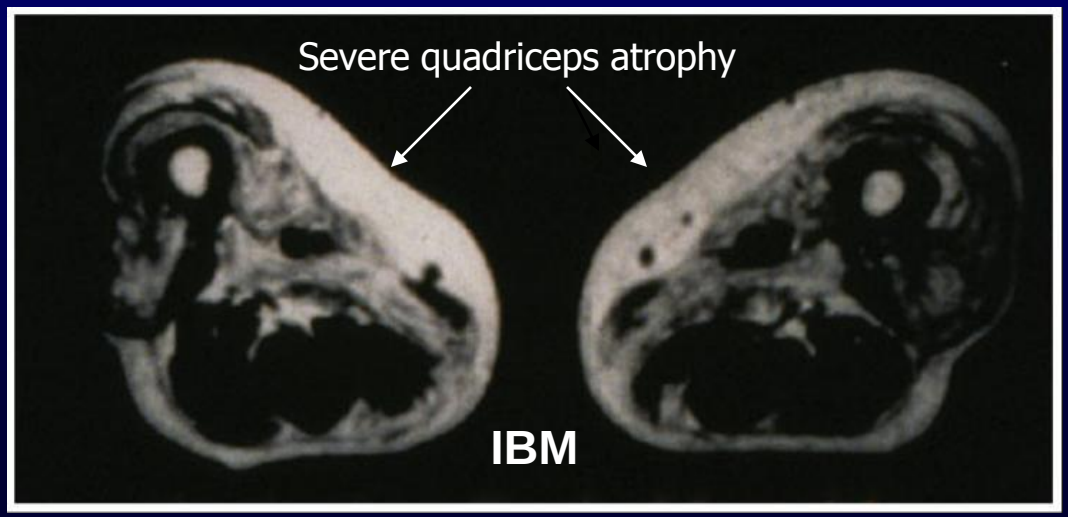


Felice, Medicine, 2001

MRI of Muscle

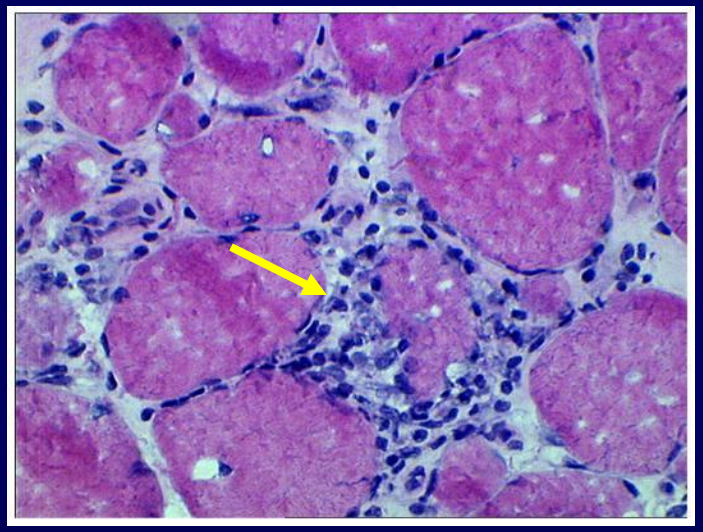


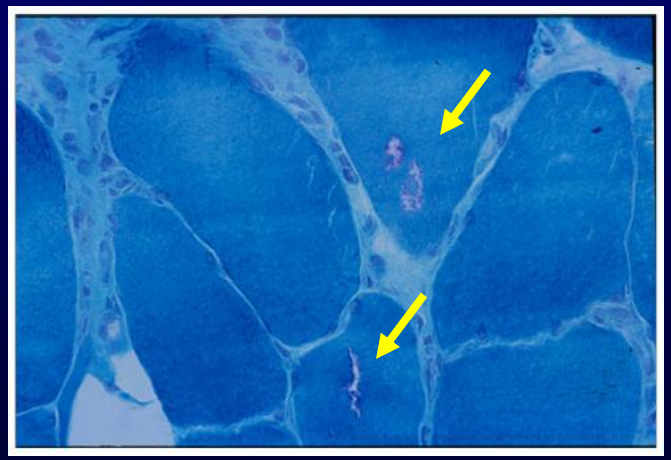




Inclusion Body Myositis: Muscle Pathology

- Distinctive histology:
  - inflammation
  - rimmed vacuoles/red "inclusions"





Different Classifications of Myositis

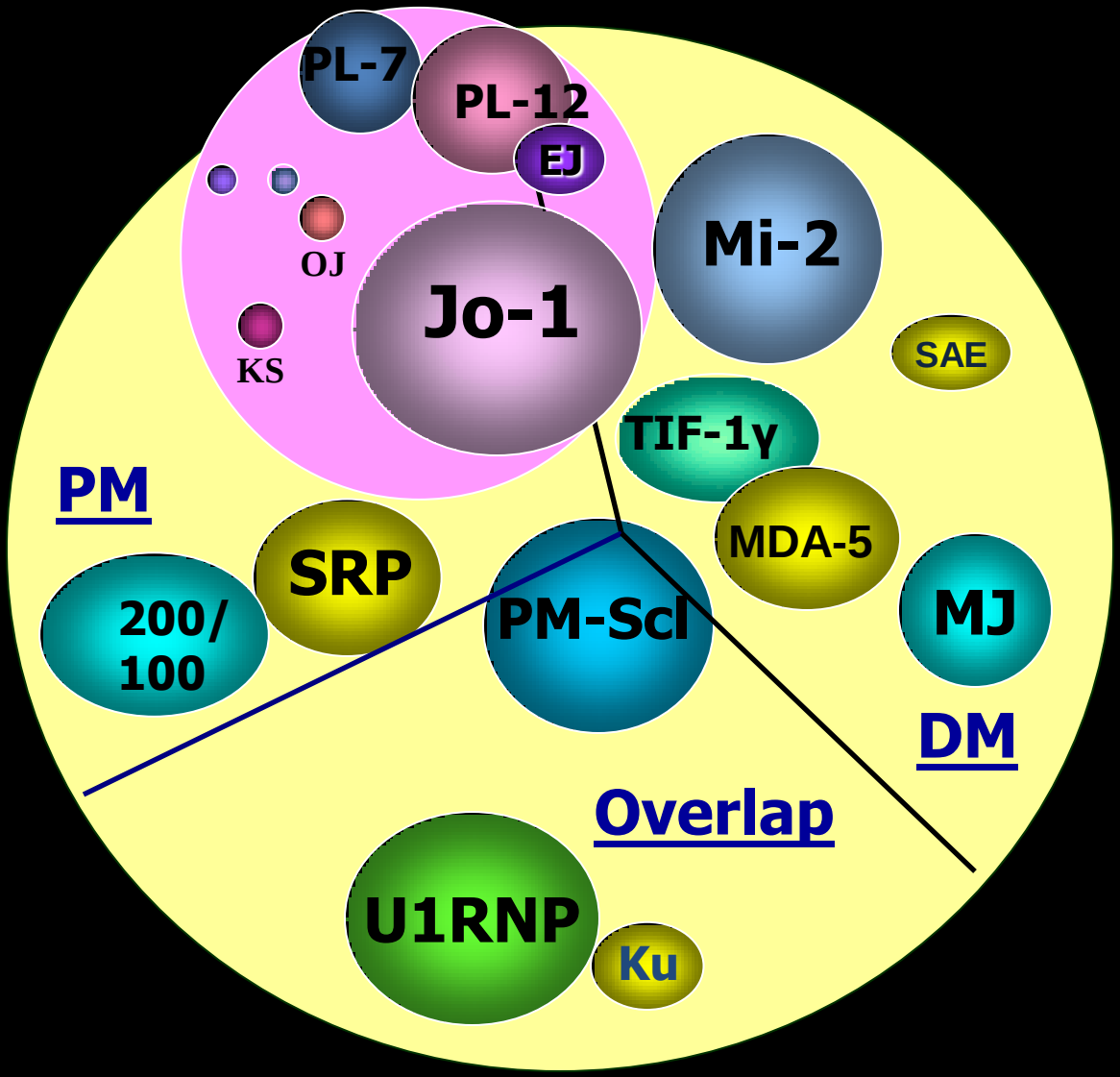
Clinical groups (Adult or Juvenile)

- Polymyositis
- Dermatomyositis
- Inclusion body
- Myositis with other rheumatic syndromes
- Cancer-associated

Serologic groups (Autoantibodies)

- Myositis-specific
  - Anti-Jo-1 & others (lung)
  - Anti-Mi-2
  - Anti-SRP
- Myositis-associated
  - Anti-PM/Scl (scleroderma)
  - Anti-Ku
  - Anti-U1RNP (mixed CTD)
  - Anti-MJ (JDM)

Autoantibody Subsets in Myositis



Pharmacologic Therapy of IIM

- Corticosteroids
- Immunosuppressive Agents
- Combination regimens
- IVIg
- Biologic agents

Drug	Dose	Common side effects	Level of evidence for use in myositis	Special comments
Corticosteroids	Starting at 1 mg/kg or 60–80 mg/d in 2 or 3 divided doses	Osteoporosis, steroid myopathy, glaucoma, cataract, risk of infection	Case series	Usual initial therapy with or without additional immunosuppression
Methotrexate	Starting at 10–15 mg/wk (orally or subcutaneously) with an increase to 25 mg/wk	Hepatic toxicity, bone marrow suppression, risk of infection	Uncontrolled cohort studies	First-line immunosuppression unless contraindicated
Azathioprine	Starting at 50 mg/d and increased by 50 mg every 2 wk up to 2–3 mg/kg/d	Gastrointestinal symptoms, bone marrow suppression, hepatic toxicity, pancreatitis, risk of infection	Uncontrolled cohort studies	First-line immunosuppression unless contraindicated
Cyclosporine	Starting at 50 mg twice daily and increasing to final dose of 100–150 mg twice daily	Nephrotoxicity, neurotoxicity, abnormal glucose metabolism, hyperkalemia, headache, tremor, hypertension, risk of infection	Case series	Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease
Tacrolimus	Starting at 1 mg twice daily and slowly increasing for trough level of 8–12	Similar to cyclosporine	Case series	Second-line immunosuppression; some evidence of efficacy in myositis-associated lung disease
Immunoglobulins	Starting at 2 g/kg/mo given over 2–5 d	Hypertension, volume overload, renal toxicity, headaches	One double-blind, placebo-controlled trial	Second-line immunosuppression for refractory myositis patients; some evidence of efficacy in dysphagia and refractory skin disease; can be used in patients with infection
Mycophenolate	Starting at 500 mg twice daily, slowly increasing to 2–3 g/d	Bone marrow suppression, gastrointestinal intolerance, risk of infection	Case series	For refractory cases; some efficacy in refractory skin disease and possibly in interstitial lung disease
Cyclophosphamide	Oral: 2-mg/kg/d dose	Malignancy, bone marrow suppression, hepatotoxicity	Case reports	Limited to very refractory cases with interstitial lung disease
Rituximab	2 doses of 1,000-mg intravenous infusion 2 wk apart	Risk of infection	Case series	For refractory cases; possible use in interstitial lung disease

Aggarwal/Oddis, Curr Rheum Rep, 2011