

# Dermatomyositis Update

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### Cleveland, Ohio



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# Idiopathic Inflammatory Myopathies (IIM)

Heterogeneous group of autoimmune syndromes characterized by chronic muscle weakness and muscle inflammation, systemic complications and a cause that is unknown

# 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)
- Other uncommon forms

# IIM: Diagnostic Criteria

- Symmetric proximal muscle weakness
- Elevation of serum muscle enzymes: CK, aldolase, AST, ALT, LDH
- Abnormal electromyogram (EMG)
- Characteristic muscle pathology
  - degeneration (breakdown) and regeneration (healing)
  - inflammatory cells attacking muscle
- **Skin rash of DM:** Gottron's papules or sign, heliotrope rash

# Rashes of Dermatomyositis



Gottron's Papules





Prepared by IMOACSG, 2001

**Chronic Gottron's Papules**

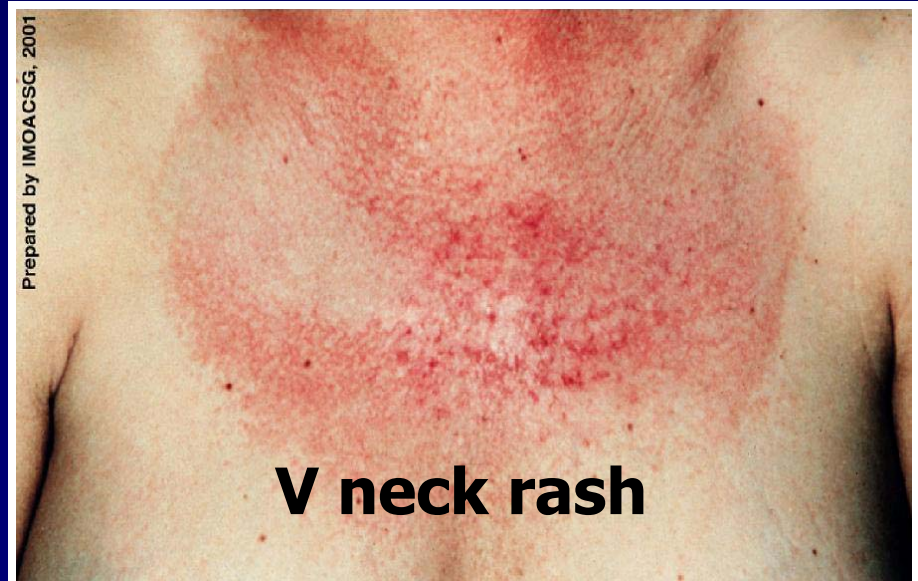
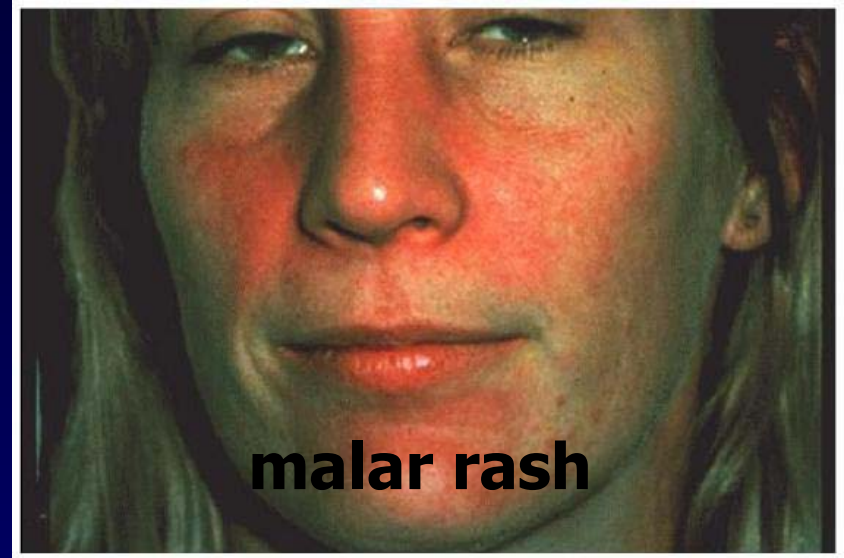


# Rashes of Dermatomyositis



Gottron's sign

# Other Rashes of Dermatomyositis



# Panniculitis



Prepared by IMOACSG, 2001

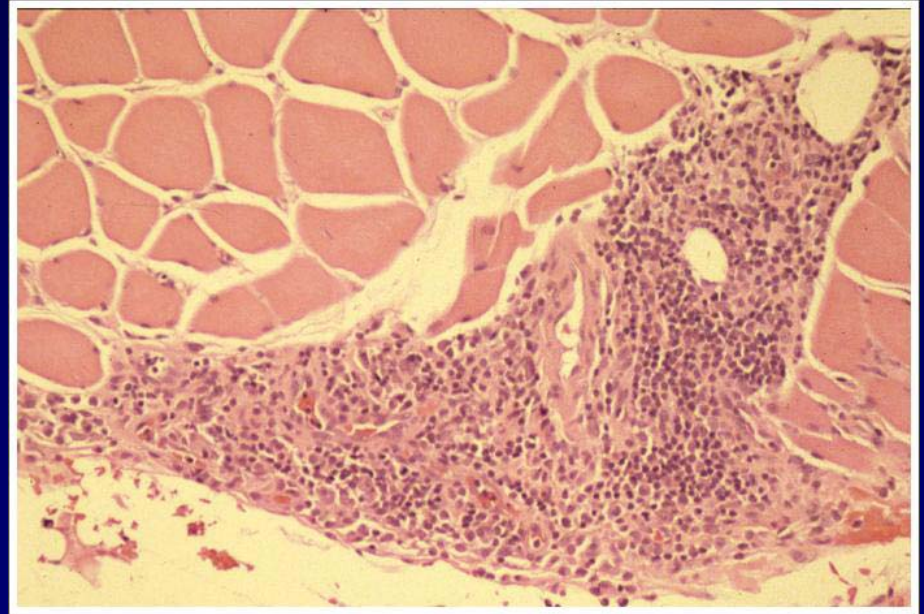
- Inflammation in the fatty tissue of the upper arm, which presented as swelling, redness and pain in a woman with DM

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# DM With Normal Muscle Enzymes

- Patient denied all symptoms including muscle weakness or pain
- **Physical Exam:**
  - faint heliotrope with Gottron's sign and periungual erythema
  - mild weakness of the neck flexors, shoulder and hip muscles
- **CK 47 IU/ml**
- EMG: mildly abnormal



More common in DM

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# Distinguishing Histologic Features

## Polymyositis

- inflammation within muscle tissue (fascicle)

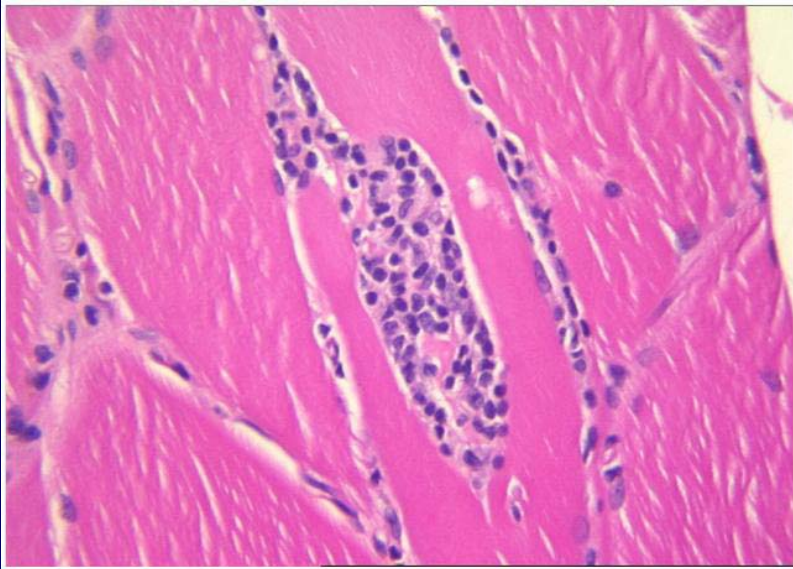
target = myofiber

## Dermatomyositis

- inflammation around fascicle
- perifascicular atrophy in 90% of children and >50% adults

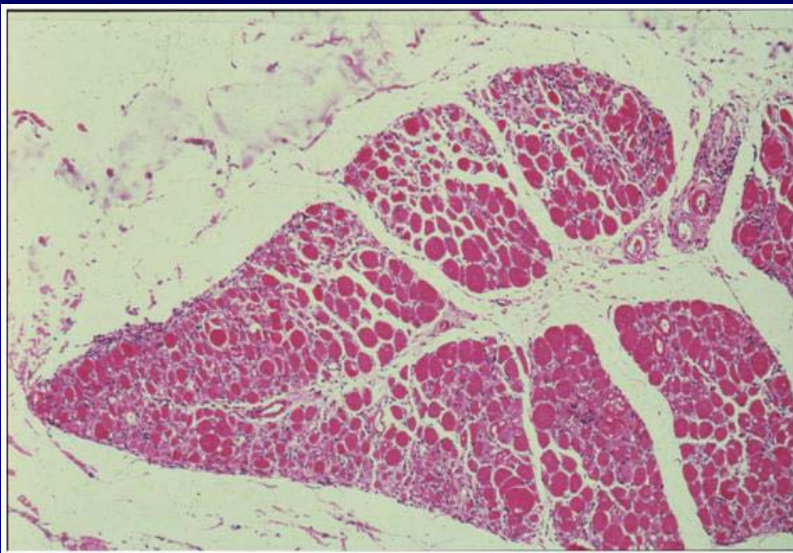
target = blood vessel

# Distinguishing Histologic Features



## Polymyositis

- lymphocytic (CD8+ T cell) invasion of non-necrotic (viable) myofiber
- CD4+ T cell



## Dermatomyositis

- perifascicular atrophy
- **B cells** and complement deposits
- endomysial CD8+ T cells
- CD4+ T cells

# Systemic Targets of Myositis

- Skin
- Joint pain (arthritis)
- Lung
  - shortness of breath
  - fibrosis (scar tissue)
- Gastrointestinal tract
  - difficulty swallowing (dysphagia)
  - ulcerations/bleeding (JDM)
- Cardiac

Dermatomyositis

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Polymyositis + Rash

# Different Classifications of Myositis

## Clinical groups (Adult or Juvenile)

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

## Serologic groups (Autoantibodies)

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

# Features of Anti-Mi-2 Subset

- Nearly exclusive association with **DM**
- “V-sign” and “**shawl-sign**” rashes  
(upper back and across upper arms  
in shawl distribution)



Shawl sign

# Features of Anti-Mi-2 Subset

- Nearly exclusive association with DM
- “V-sign” and “shawl-sign” rashes (upper back and across upper arms in shawl distribution)
- Good response to treatment and nearly 100% 5-year survival

# Treatment Options in Myositis

- Corticosteroids (prednisone)
- Immunosuppressive agents
  - methotrexate
  - azathioprine
  - fludarabine
  - leflunomide
  - mycophenolate mofetil
  - cyclosporine
  - cyclophosphamide
  - tacrolimus
  - chlorambucil
- IVIg
- Anti-TNF agents (etanercept, infliximab)
- “Biologic” response modifiers
- Other (stem cell transplant)
- Combination regimens

# Biologic Agents

- Anti-TNF (tumor necrosis factor) agents
  - anecdotal reports of etanercept and infliximab
  - larger study in progress (adult DM)
- Monoclonal anti-B cell agents
  - Rituximab directed against surface marker of B lymphocyte
  - pilot studies of efficacy in adult and pediatric DM
- Monoclonal anti-complement agents
  - Eculizumab (anti-C5) binds circulating C5 preventing downstream inflammation
  - pilot trial showed improvement in DM skin rash

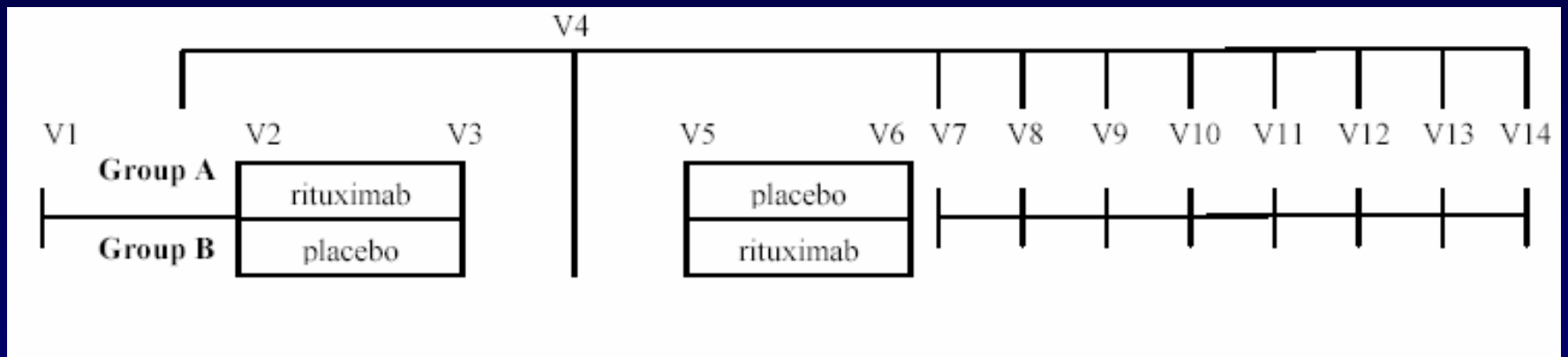
# Rituximab in Autoimmune Diseases

- Autoimmune blood disorders (**peds**/adult)
- Systemic lupus erythematosus (SLE)
- Rheumatoid arthritis (RA)
- Neuropathies associated with autoantibodies
- Myasthenia gravis
- Wegener's granulomatosis
- **Dermatomyositis** (Levine, A&R, 2005)
- Autoimmune multiorgan **pediatric** syndromes

# Summary: Rituximab in Myositis

- To date 13 of 14 patients have had an excellent response
  - 7 responses as early as 3-4 weeks but some patients have later responses
- No serious infectious complications
  - 1 case of shingles (herpes zoster)
  - 1 pediatric case with low white blood cell count but patient also treated with methotrexate - reversed following discontinuation

# Study Schematic



# Rituximab Trial

- **Primary Aim:** To assess the efficacy of rituximab in a multi-center, double-blind, placebo-controlled trial of refractory PM and DM in adults and DM in children
- **Secondary Aim:** To assess the determinants of treatment response and disease pathogenesis in patients receiving rituximab
  - collect immunologic data
  - autoantibodies
  - selected pts with pre and post treatment muscle biopsies

# Participating Centers

## Adult Sites

- Alabama (Fessler)
- Boston (Rutkove)
- Czechoslovakia (Vencovsky)
- Dallas (Olsen)
- Duke (St. Clair)
- Kansas City (Barohn/Latinis)
- Kentucky (Crofford)
- London (Isenberg)
- Mayo Clinic (Ytterberg)
- Miami (Bradley)
- Michigan (Seibold)
- Milwaukee (Cronin)
- New York (Marder)
- NIH (Miller)
- Oklahoma (Targoff)
- Philadelphia (Eisenberg/Kolasinski)
- Phoenix (Levine)
- Pittsburgh (Oddis/Ascherman)
- Sweden (Lundberg)

## Pediatric Sites

- Boston (Sundel)
- Chicago (Pachman)
- Cincinnati (Lovell)
- Dallas (Punaro)
- Duke (Schanberg/Rabinovich)
- London (Pilkington)
- Mayo Clinic (Reed)
- Miami (Rivas-Chacon)
- Michigan (Adams)
- Nebraska (Jung)
- New York (Ilowite)
- NIH (Rider)
- Nova Scotia (Huber)
- Philadelphia (Sherry)
- Pittsburgh (Kietz)
- Stanford (Sandborg/Lee)
- Toronto (Feldman)