Dermatomyositis: Update 2009

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Conflict of Interest

Amgen – Speaker's Bureau/honoraria

Astellas – Speaker's Bureau/honoraria

Dermik/Sanofi Aventis – Speaker's Bureau/honoraria

Galderma – Advisory Board/honoraria

Stiefel – Advisory Board/honoraria

Warner Chilcott – Speaker's Bureau/honoraria

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Dermatomyositis: 2009
Why is this important for dermatologists?

- Serious, treatable, multisystem disease
- Prognosis and therapy different from lupus erythematosus
- Malignancy association in adults
- Diagnosis is commonly (maybe even usually) missed

Dermatomyositis: 2009

Reasons we dermatologists might miss the diagnosis

- Miss poikiloderma - diagnose as psoriasis - risk of phototherapy
- Note poikiloderma but miss photodistribution and nail fold changes - diagnose as cutaneous T-cell lymphoma
- Note poikiloderma and photodistribution - diagnose as lupus erythematosus - ANA and skin biopsy specimen may seem to support the misdiagnosis

BOHAN & PETER CRITERIA FOR DIAGNOSIS OF POLYMYOSITIS AND DERMATOMYOSITIS

Individual criteria

1. Symmetrical proximal muscle weakness
2. Muscle biopsy evidence of myositis
3. Increase in serum skeletal muscle enzymes
4. Characteristic electromyographic pattern
5. Typical rash of dermatomyositis

Diagnostic criteria

Polymyositis:

Definite: all of 1-4

Probable: any 3 of 1-4

Possible: any 2 of 1-4

Dermatomyositis:

Definite: 5 plus any 3 of 1-4

Probable: 5 plus any 2 of 1-4

Possible: 5 plus any 1 of 1-4

Modified from Bohan & Peter.[6]

Juvenile Dermatomyositis: 2009

- 8-22% of all DM/PM
- Higher incidence of vasculitis
- Early studies: 1/3 died, 1/3 crippled, 1/3 remission
- Recent studies: Low mortality (vasculitis with GI hemorrhage)
- Calcinosis cutis more common

Dermatomyositis: 2009
Malignancy Association

- No increase in incidence of neoplasia in children
- 5-11 fold increase in neoplasia in adults
  (PM: 2-3%; DM: 15-20%)
- Particularly lung, ovary, breast, stomach
- Usually DM antedates tumor by 1-2 years
- Drop off in malignancy after two years - Large Danish study
- "Directed" evaluation – repeated at intervals

Dermatomyositis: 2009
Clinical Features - Cutaneous

- **Heliotope sign**
- **Photodistributed poikiloderma-violaceous**
- Poikiloderma over extensor surfaces-violaceous
- Gottron's sign
- Cuticular dystrophy
- Nail fold telangiectasia
- Calcinosis cutis (complication: especially childhood)

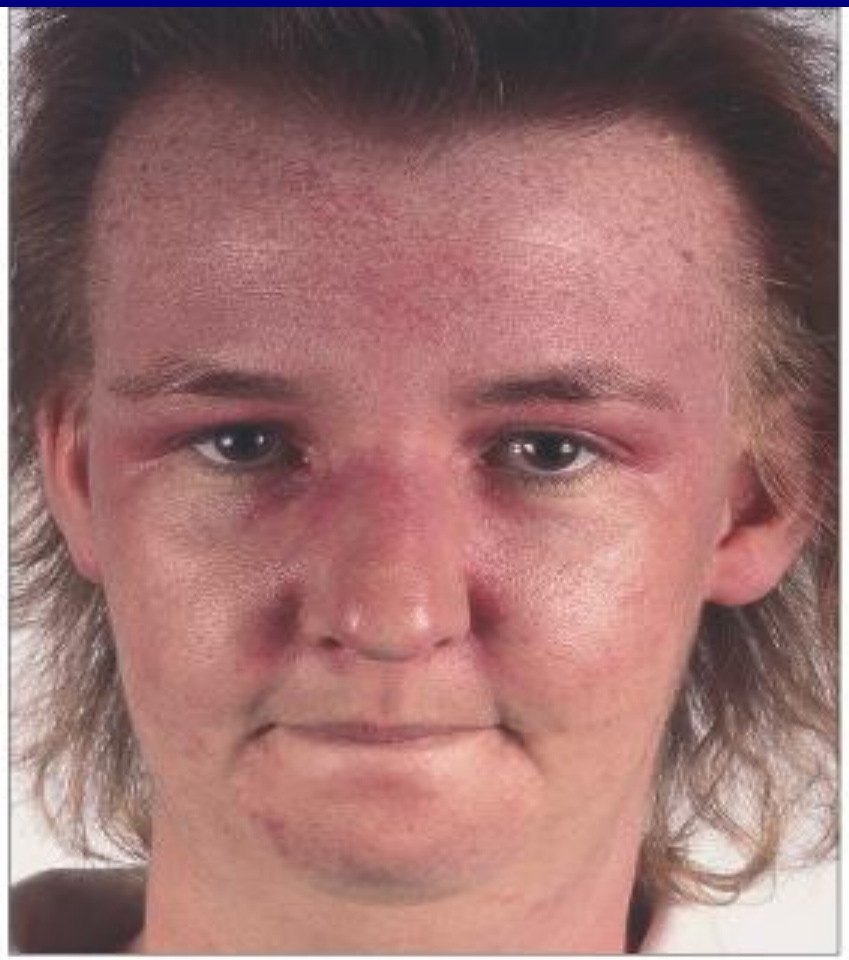

Fig. 43.1 Violaceous poikiloderma of the face.

Dermatomyositis: 2009
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Nail fold telangiectasia
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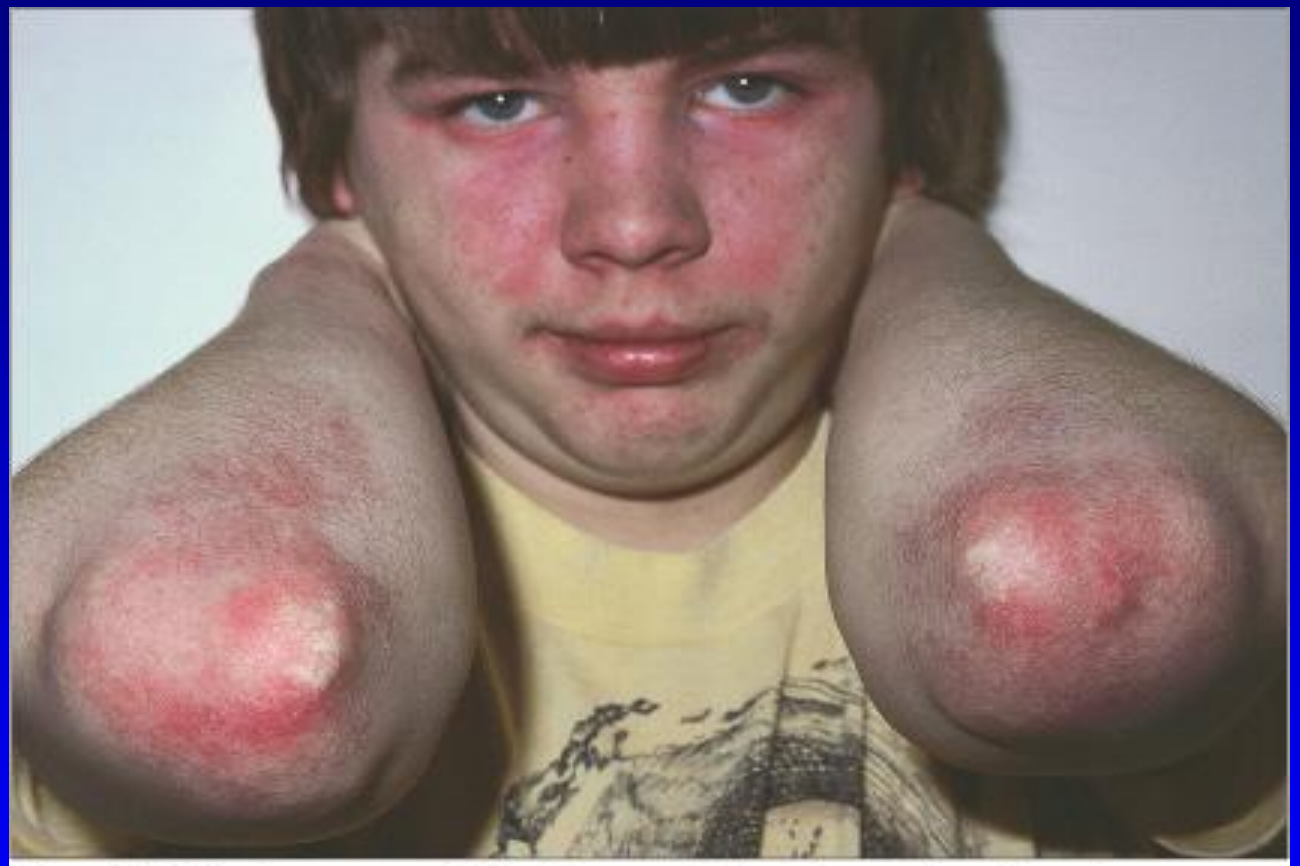

Fig. 43.2 Violaceous poikiloderma of the face, plus thin plaques on the elbows that are sometimes misdiagnosed as psoriasis.

Dermatomyositis: 2009
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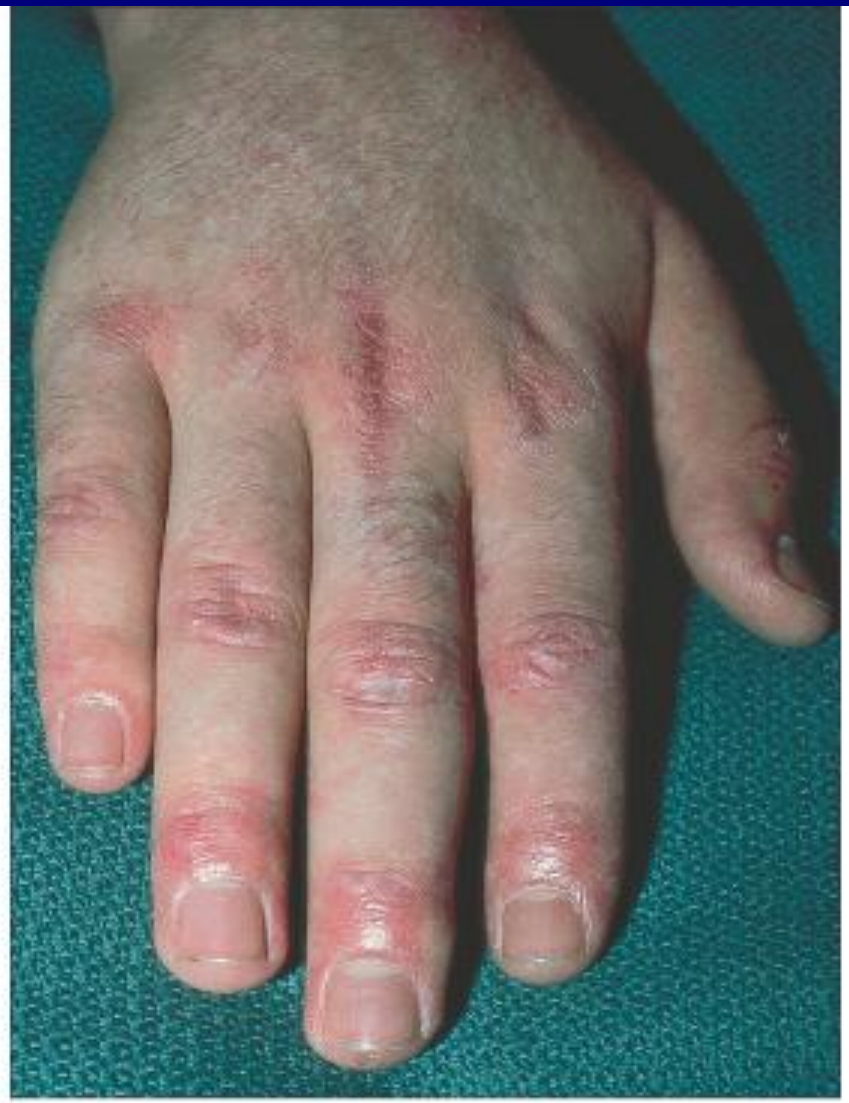

Fig. 43.4 Gottron's sign with violaceous poikiloderma over the knuckles.

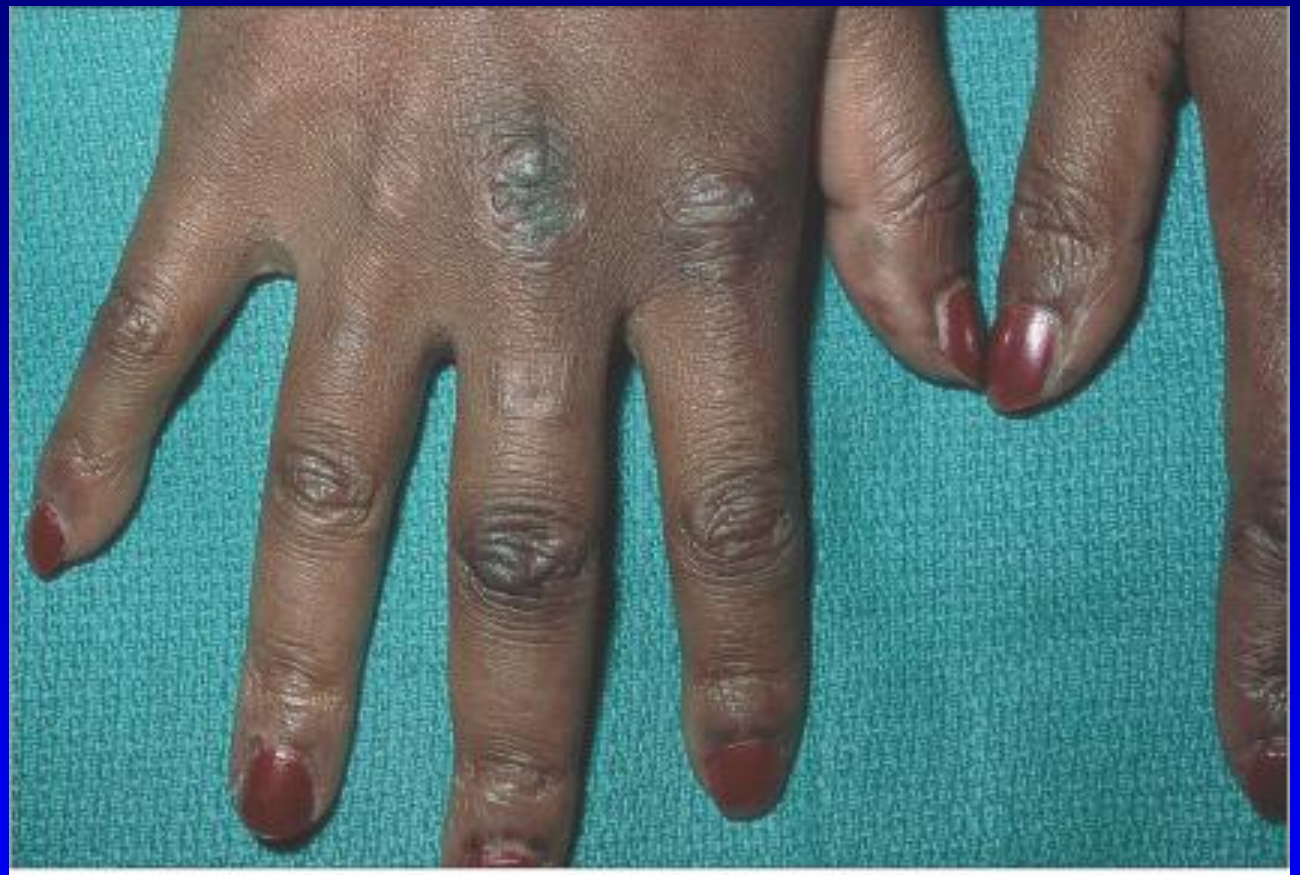

Fig. 43.5 Gottron's papules, with the knuckle lesions showing a papular lichenoid quality.

Dermatomyositis: 2009
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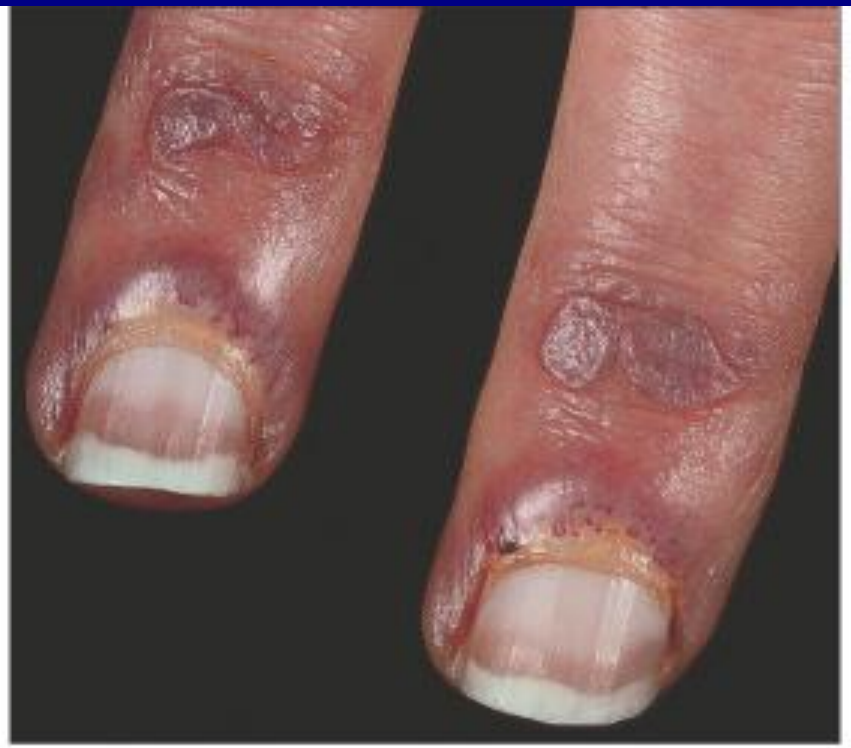

Fig. 43.6 Cuticular dystrophy and nailfold telangiectasias in a patient with dermatomyositis. Note the flat-topped (lichenoid) papules over the distal interphalangeal joints.

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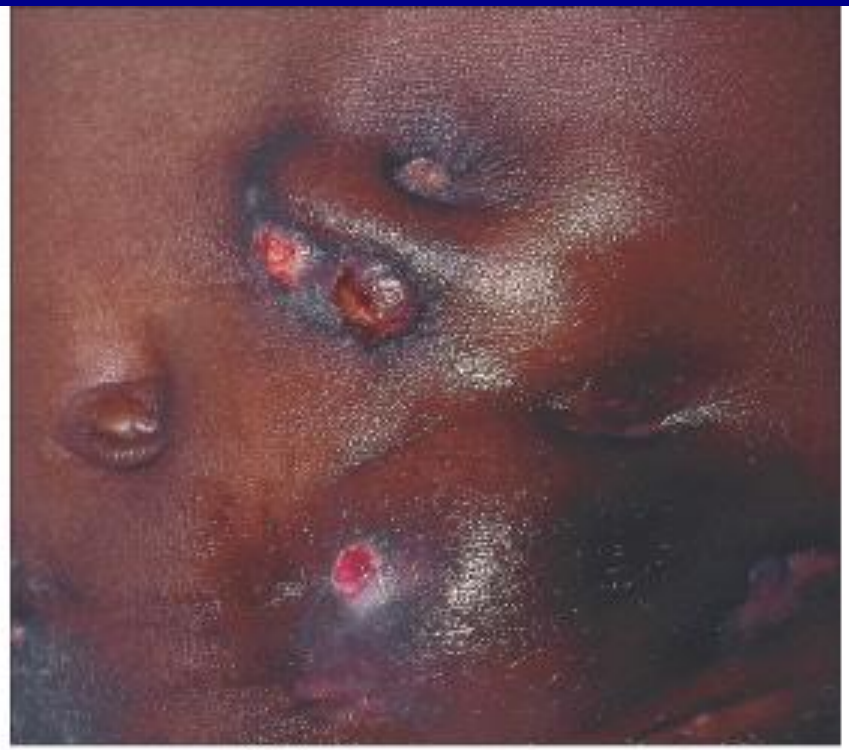


Fig. 43.7 Calcinosis cutis on the abdomen of a child with dermatomyositis.

Dermatomyositis: 2009
Selected Systemic Aspects

- Articular disease - if erosive, implies overlap
- Dysphagia - proximal is related to myositis true distal esophageal disease suggests overlap
- Lung disease - 15-30% diffuse interstitial fibrosis (Jo-1 antibody)

Dermatomyositis: 2009
Selected Systemic Aspects (cont.)

- Cardiac disease - myocarditis or pericarditis
  CK-MB band elevation alone does not prove cardiac disease
- Calcinosis - usually in childhood disease, may be reduced by early therapeutic intervention

IMMUNOLOGICAL ABNORMALITIES IN PATIENTS WITH INFLAMMATORY MYOPATHIES

Cellular abnormalities

T cell receptor restriction in inflamed muscle

Activated T and B lymphocytes expressing co-stimulatory molecules, CD86/CD80; CD28/CTLA4; CD40/CD40L in skeletal muscle

Increased peripheral mononuclear cell trafficking to muscle

Increased proportions of peripheral T and B lymphocytes bearing activation markers

Elevated serum IL-1 a, IL-2, soluble IL-2 receptors and soluble CD8 receptors

Decreased proliferative responses of peripheral mononuclear cells to T cell mitogens

Increased proliferative responses of peripheral mononuclear cells to autologous muscle

Increased expression of cytokines and chemokines in infiltrating mononuclear cells and muscle cells

Increased MHC class I (HLA-A,B,C), class II (HLA-DR) and ICAM-1 on skeletal muscle fibers

Humoral abnormalities

Immunoglobulin and complement deposition in muscle vascular endothelium

Myositis-specific autoantibodies

Myositis-associated autoantibodies (anti-U1RNP, anti-PM/Scl, anti-Ku)

Other autoantibodies (antithyroid, anti-Sm, anti-Ro, anti-La, etc.)

Hyper-, hypo- and agammaglobulinemiaMonoclonal gammopathy

Dermatomyositis: 2009
Laboratory Aspects

- Sedimentation rate only elevated in 50%
- Elevated: CPK, Aldolase, urine creatine, serum myoglobin, rarely urine myoglobin, other serum enzymes
- Positive ANA (90+%), anti-Jo-1 (25%), anti-Mi-1 and anti-Mi-2
- Negative anti-DNA

Dermatomyositis: 2009
Muscle Biopsy

- Can provide evidence supporting diagnosis
- Can definitively exclude certain other conditions in the differential
- Incisional vs needle biopsy
- Quadriceps, triceps

Dermatomyositis: 2009 Histopathologic Aspects

- Skin: Epidermal atrophy, interface change, vascular dilatation, occasional mucin deposition
- Muscle: Mixed/primarily lymphocytic infiltrate, necrosis of muscle fibers, fibrosis, phagocytosis, regeneration

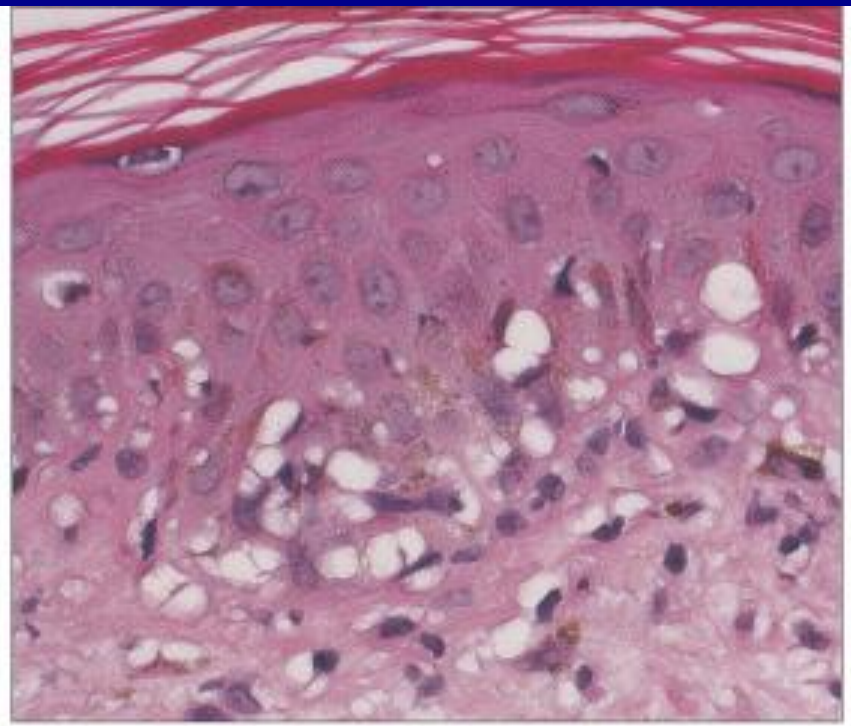
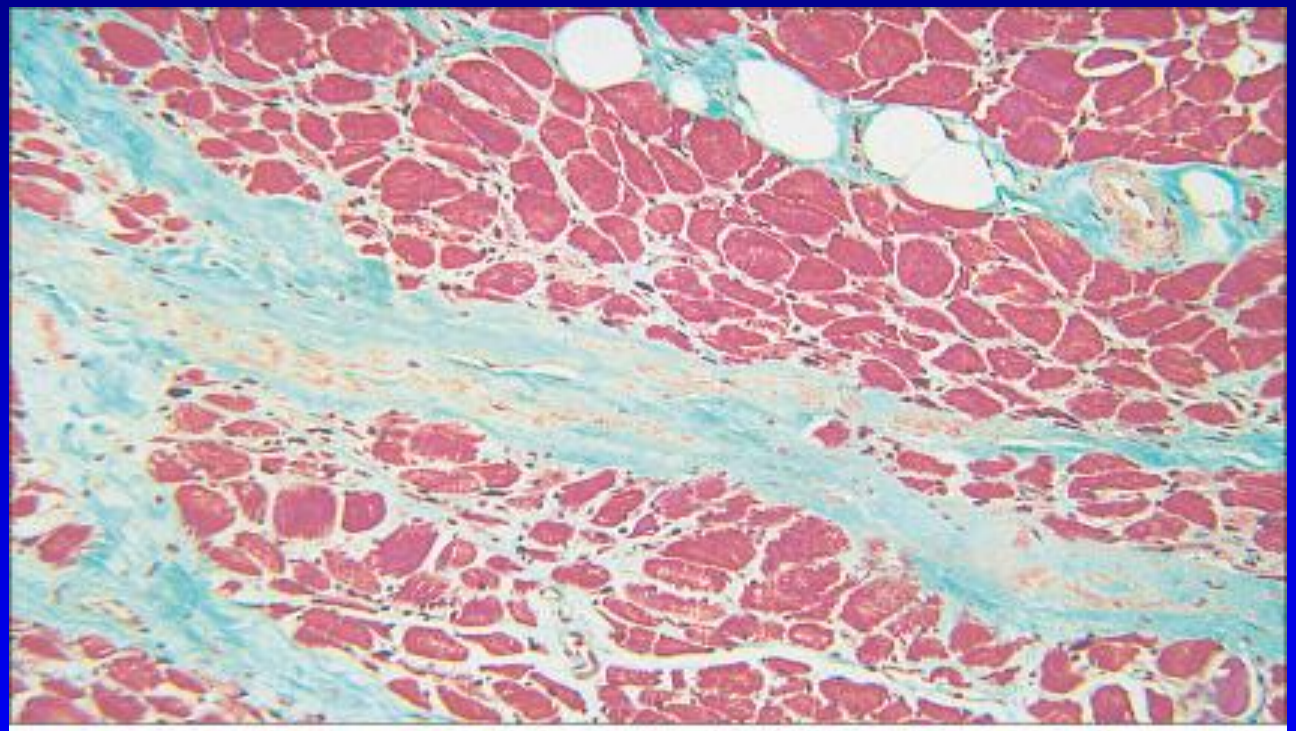


Fig. 43.9 Dermatomyositis. Higher-power view of vacuolar alteration of the basal layer.



Dermatomyositis: 2009
Electromyography

- Abnormal in about 90% of active cases
- Characteristic triad
- May support diagnosis and help exclude other conditions

Dermatomyositis: 2009
Prognosis

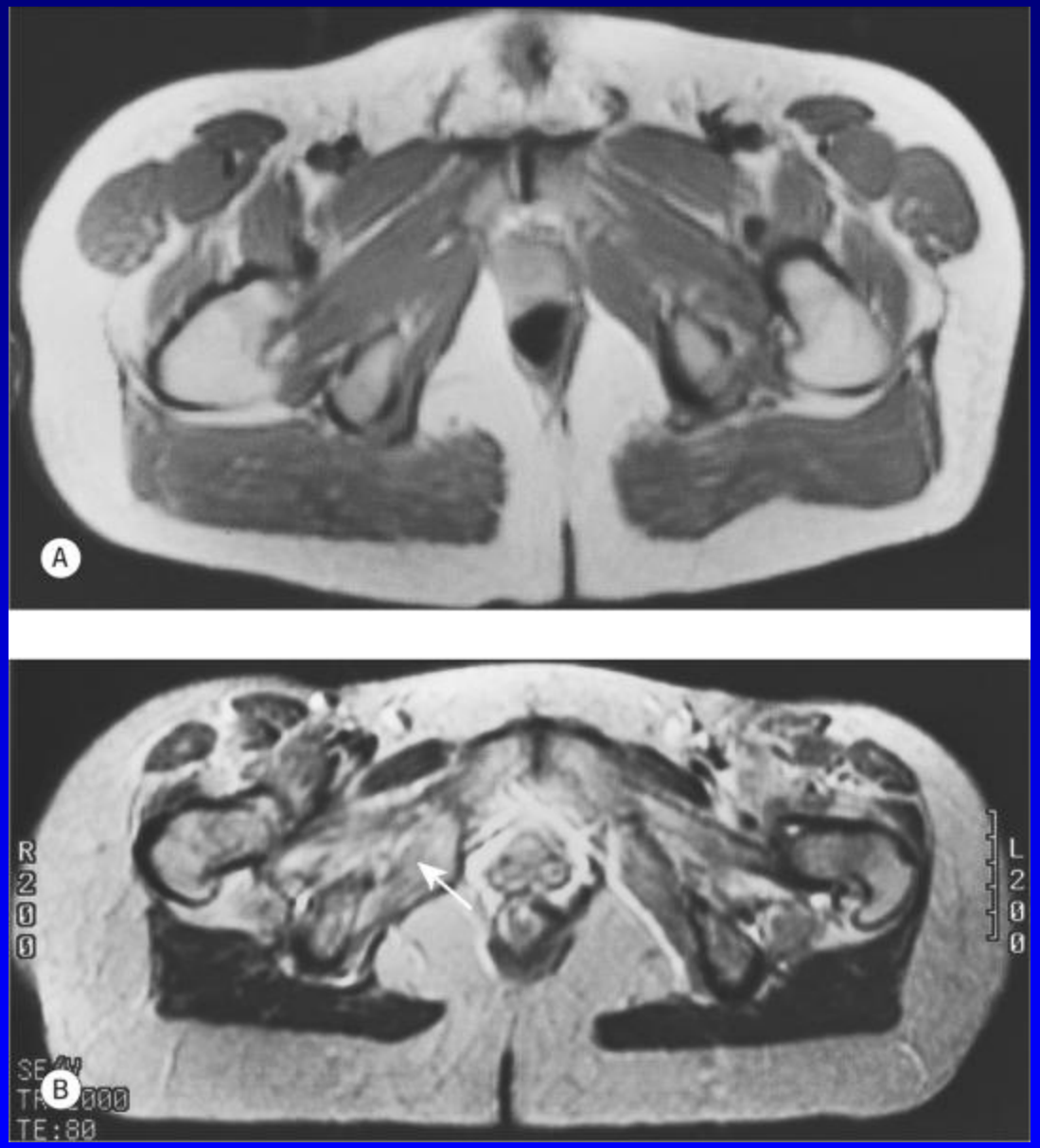
- Precorticosteroid era: 50-60% mortality
- Newcastle series: Childhood mortality 5%, Overall mortality 28% (6 years)
- Johns Hopkins survey: Similar to Newcastle overall mortality 27% (8 years)
- Variable morbidity data in childhood PM/DM from 1/3 with severe impairment versus mean of no objective impairment
- Our data on 20 children after 2-20 years

Dermatomyositis: 2009

Classic clinicopathologic disease in patients with normal muscle enzymes

- Group 1: Cutaneous changes only: 5 patients (1-10 years)
- Group 2: Cutaneous changes only at baseline with subsequent evolution of myositis: 2 patients (1/2-2 1/2 years)
- Group 3: Cutaneous changes with normal muscle enzymes but invasive tests revealed myositis: 4 patients (4 positive EMG, 2 positive biopsy)

Stonecipher MR, Jorizzo JL, White WL et al. J Am Acad Dermatol 1993;28:951-956.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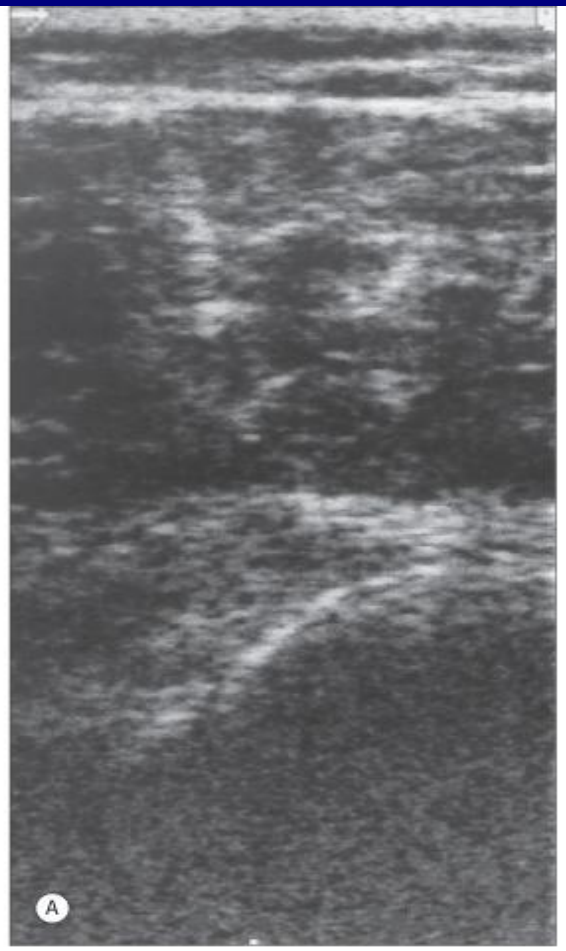

Fig. 43.14A Ultrasound images of the triceps muscle. A Cross-sectional ultrasound image from normal (control) triceps muscle. **B** Ultrasound image from affected triceps muscle in a patient with dermatomyositis. An increase in interstitial echoes is seen *(arrows)*.

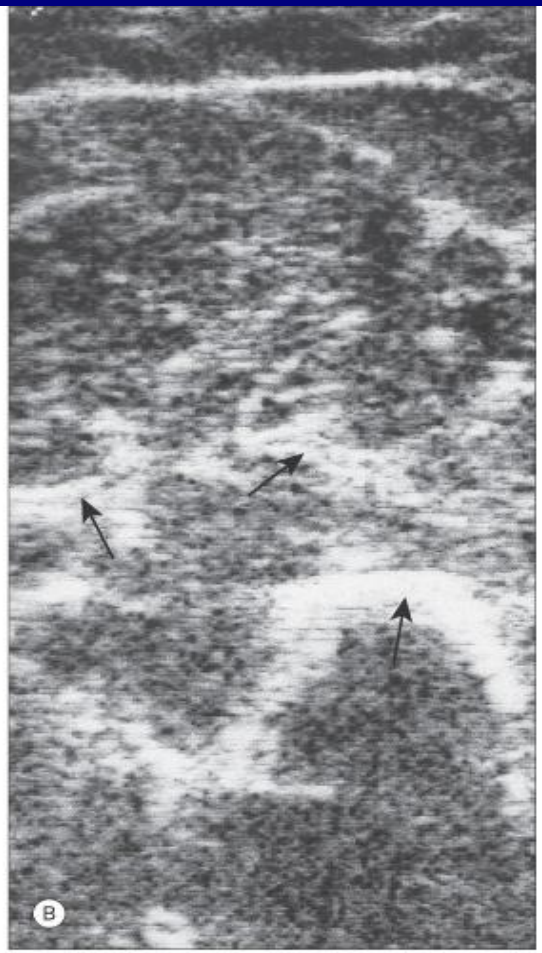

Fig. 43.14B Ultrasound images of the triceps muscle. A Cross-sectional ultrasound image from normal (control) triceps muscle. **B** Ultrasound image from affected triceps muscle in a patient with dermatomyositis. An increase in interstitial echoes is seen *(arrows)*.

Dermatomyositis
Update: 2009
Therapeutic Ladder

- Systemic Corticosteroids (2)
  - Prednisone 1mg/kg/day taper to 1/2 over 6 months
  - Then attempt to reach qod dosing
  - Usually required for 2 years
  - Pulse and split dose options
- Methotrexate low dose weekly pulse (2)
- Azathioprine 2-3 mg/kg/day(3)
- IVIG(1)

Key

(1) - Double blind studies

(2) - Clinical series

(3) - Anecdotes

Dermatomyositis:
Update 2009
Therapeutic ladder - Other treatments

- Mycophenolate mofetil (2)
- Pulse cyclophosphamide (3)
- Chlorambucil (3)
- Cyclosporine (2)
- Plasmapheresis (probably not effective)
- Monthly Fludarabine (2)
- Infliximab (2)
- Etanercept (2)
- Rituximab (2)
- Oral tacrolimus (3)
- Rapamycin (3)
- Other future biological therapies

Dermatomyositis
Update: 2009
Therapeutic Ladder: Cutaneous lesions

- Sunscreens with high SPF plus UVA protection (3)
- Mild topical corticosteroids +/- pramoxone (3)
- Topical tacrolimus (2)
- Antimalarials, including combinations (2)
- Methotrexate (2)
- Dapsone (3)
- Retinoids (3)
- Thalidomide (3)
- Mycophenolate mofetil (2)
- Diltiazem for calcinosis cutis (2)
- Others