**Dermatomyositis: 2015**

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

**Conflict of Interest**

Advisory Boards/Honoraria
- Amgen
- Leo Pharmaceuticals

**Dermatomyositis Update: 2015 - Diagnosis**

Bohan and Peters, 1975
- Clinical signs and symptoms of proximal extensor muscle weakness
- Elevations of muscle enzymes (e.g. CPK, Aldolase)
- EMG changes of myositis
- Typical muscle histologic changes (infiltrate, necrosis, fibrosis, phagocytosis, regeneration)
- Typical cutaneous eruption
- New criteria are evolving
- Role of MRI debated

**Dermatomyositis: 2015**

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

**Juvenile Dermatomyositis: 2015**

- 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: 2015

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

Clinical Features - Cutaneous

Heliotope sign
Photodistributed poikiloderma-violaceous

Poikiloderm over extensor surfaces-violaceous
Gottron’s sign
Cuticular dystrophy
Nail fold telangiectasia
Calcinosis cutis (complication: especially childhood)
Dermatomyositis: 2015
Clinical Features - Cutaneous

- Heliotope sign
- Photodistributed poikiloderma-violaceous
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- Cuticular dystrophy
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- **Calcinosis cutis** (complication: especially childhood)

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)
GENETICS

- Monozygotic twins affected
- Associated human leukocyte antigens (HLA)
  - HLA-DR3 and B8 (juvenile dermatomyositis)
  - HLA-DR52 (patients with anti-Jo1 antibodies)
  - HLA DR7 and -DRw53 (patients with anti-Mi-2 antibodies)
  - HLA B14 and -B40 (adults with dermatomyositis overlap)
  - HLA DRB1*1502 (Japanese with juvenile dermatomyositis)
- TNF-α 308A allele polymorphism

CELLULAR IMMUNITY/APOPTOSIS

- Histopathologic findings in skin and muscle (CD8+ lymphocytes)
- Lymphocyte-mediated experimental myositis in mice
- Increased Ki-67 and p53 expression in keratinocytes after UVB irradiation
- Increased CD40 expression on muscle cells
- Decreased circulating CD54 (ICAM-1)-positive lymphocytes
- Fas ligand on T cells and Fas receptor on muscle cells
- MHC Class I overexpressed in affected muscle tissues
- Elevated expression of COX-1, COX-2, and 5-LOX mRNA in affected muscle tissues

HUMORAL IMMUNITY

- Association with autoimmune diseases (Hashimoto’s thyroiditis, Graves’ disease, myasthenia gravis, type I diabetes mellitus, primary biliary cirrhosis, dermatitis herpetiformis, vitiligo, and other autoimmune connective tissue diseases)
- Myositis-specific antibodies versus antibodies against aminoacyl-tRNA synthetases, non-synthetases, cytoplasmic antigens, and nuclear antigens. Examples include: antisynthetase, anti-Jo-1 (lung disease), and anti-Mi-2 (most specific for dermatomyositis)

INFECTIOUS PRECIPITANTS

- Seasonal variation
- Picornavirus substrate for aminoacyl-tRNA synthetases
- Escherichia coli, muscle protein and capsid protein of a picornavirus that induces mouse myositis all have some homology of amino acid sequences with Jo-1
- Echovirus infection in patients with hypogammaglobulinemia
- Coxsackievirus-9 myositis

DRUG AND VACCINE PRECIPITANTS

- Hydroxyurea, D-penicillamine, TNF-α inhibitors, nonsteroidal anti-inflammatory drugs, lipid-lowering drugs (statins >gemfibrozil), cyclophosphamide, BCG vaccine; single case reports of phenytoin, alfuzosin (α1-agonist for BPH), omeprazole, ipecac (repeated exposures), interferon-α-2b, tegafur, etoposide, articaine, sulfacetamide sodium ophthalmic drops

MALIGNANCY ASSOCIATION (ADULTS)

- Adenocarcinoma, breast cancer, lymphoma, uterine leiomyoma, melanoma, lung cancer, myeloproliferative disorders, myelodysplastic syndromes, and myeloma.
Dermatomyositis: 2015

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

Muscle Biopsy

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

Histopathologic Aspects

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

Electromyography

- Abnormal in about 90% of active cases
- Characteristic triad
- May support diagnosis and help exclude other conditions
**Dermatomyositis: 2015**

**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

**Classical 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)


**Therapeutic Ladder**

1. **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

2. **Methotrexate low dose weekly pulse (2)**

3. **Azathioprine 2-3 mg/kg/day (3)**

4. **IVIG (1)**

**Key**

- (1) - Double blind studies
- (2) - Clinical series
- (3) - Anecdotes

**Therapeutic Ladder for Dermatomyositis**

**SYSTEMIC THERAPY**

| Oral prednisone: 1 mg/kg/day tapered to 50% over 6 months and to zero over 2-3 years (1) |
| Option to use pulse, split-dose, or alternate-day (2) |
| Methotrexate: 5-20 mg weekly (2) |
| Azathioprine: 2-3 mg/kg/day (1) |
| Others: High-dose IVIg (2 g/kg/month) (1) |
| Pulse cyclophosphamide (0.5-1.0 g/m²/monthly) (2) |
| Chlorambucil (4 mg/day) (2) |
| Cyclosporine (3-5 mg/kg/day) (2) |
| Tacrolimus (0.12 mg/kg/day) (2) |
| Mycophenolate mofetil (1 g twice daily) (2) |
| Steroids (5 mg/kg/day x 2 weeks, 2 mg/kg/day x 2 weeks, then 1 mg/day) (3) |
| Infliximab (5-10 mg/kg every 2 weeks initially) (3) |
| Etanercept (3)† |
| Rituximab (375 mg/m²/infusion for 4 weekly infusions) (2) |
| Fludarabine (3) |
| Hematopoietic stem cell transplantation (3) |
| Plasmapheresis (3)† |

*†Double-blind trial showed no benefit*
# Therapeutic Ladder for Dermatomyositis

**CUTANEOUS LESIONS**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Notes</th>
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<tbody>
<tr>
<td>Sunscreens (high sun protection factor including protection against UVA)</td>
<td>(3)</td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>(3)</td>
</tr>
<tr>
<td>Topical tacrolimus</td>
<td>(3)</td>
</tr>
<tr>
<td>Hydroxychloroquine (200 mg twice daily; increased frequency of drug eruptions in patients with dermatomyositis)</td>
<td>(2)</td>
</tr>
<tr>
<td>Hydroxychloroquine (200 mg twice daily) plus quinacrine (100 mg/day)</td>
<td>(3)</td>
</tr>
<tr>
<td>Low-dose weekly methotrexate (5-15 mg weekly)</td>
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<td>Thalidomide</td>
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<td>Leflunomide</td>
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<td>Antiestrogens (e.g. Tamoxifen, anastrazole)</td>
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<tr>
<td>TNF-α inhibitors (e.g. Infliximab, etanercept)</td>
<td>(3)*</td>
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</tr>
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*Reported cause of drug-induced dermatomyositis.