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

- Infection
  - Immune Response
    - Control of Inflammation/Infection
Understanding Autoimmunity

- Infection → Inflammation
- Immune Response
- Control of Inflammation/Infection
Understanding Autoimmunity

Infection \rightarrow \text{Inflammation} \rightarrow \text{Immune Response} \rightarrow \text{Control of Inflammation/Infection} \rightarrow \text{? Trigger}
Understanding Autoimmunity

Infection → Inflammation → ? Trigger

Control of Inflammation/Infection

Immune Response

Immune Response Goes Awry
Inflammation

Immune Response

Control of Inflammation/Infection

Immune Response Goes Awry

Body is the target of Immune Response

Understanding Autoimmunity

Infection ➔ Inflammation ➔ Immune Response ➔ ? Trigger

Body is the target of Immune Response
Understanding Autoimmunity

- Infection → Inflammation
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Immune Response

- Control of Inflammation/Infection
- Immune Response Goes Awry

Body is the target of Immune Response

Autoimmunity
Autoimmunity

- Immune response against *self*
  - loss of tolerance

- Unknown cause
  - susceptibility factors (genetic)
  - environmental triggers
    - e.g. infection (virus)

- Multiple diseases and “syndromes”
  - which sometimes run in families
## Autoimmune Diseases

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<thead>
<tr>
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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 (virus)

- Multiple diseases and “syndromes”
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- Formation of autoantibodies
  - markers of autoimmunity
Autoimmunity (cont’d)

• Immune response against *self*
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• Unknown cause
  ▪ susceptibility factors (genetic)
  ▪ environmental triggers
    ➢ e.g. infection (virus)

• 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
Subsets of Myositis

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

• Adult polymyositis (PM)
• Adult dermatomyositis (DM)
• Juvenile myositis (DM >> PM)
• Malignancy-associated myositis
• **Myositis in overlap with another rheumatic disease**
• Necrotizing myopathy
• Inclusion body myositis (IBM)
This patient looks like they have rheumatoid arthritis
This patient looks like they have rheumatoid arthritis
... but they have myositis in overlap with RA and scleroderma
Autoantibody Subsets in Myositis

[Image of a diagram showing various autoantibodies and their subsets, including Jo-1, U1RNP, PL-7, PL-12, PL-14, MDA-5, TIF-1γ, HMGCR, PM, SRP, PM-Scl, Mi-2, DM, MJ, SAE, and KS.]
# Univ. Pittsburgh Myositis Cohort

<table>
<thead>
<tr>
<th># Patients</th>
<th>PM</th>
<th>DM</th>
<th>Overlap</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>373</td>
<td>510</td>
<td>267</td>
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Anti-synthetetase Syndrome

- Defines a subset of myositis patients with several clinical features:
  - Fever
  - Myositis
  - Arthritis (misdiagnosed as RA)
  - Raynaud phenomenon
  - ‘Mechanic hands’
  - Interstitial Lung Disease
Clinical Features: Anti-synthetase Syndrome
General Concepts: Myositis Therapies

- Myositis is inflammatory and autoimmune

- Drugs will:
  - Decrease inflammation (e.g. steroids)
  - Suppress the immune system

- Borrowed from oncologists
  - Methotrexate, imuran, cytoxan and rituximab

- Borrowed from transplant surgeons
  - Cyclosporine, tacrolimus, MMF (CellCept)
Myositis is not a single disease!
Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
- Biologic agents
- Others
Medications After Prednisone

• Most physicians choose glucocorticoids as their initial treatment

• Most patients needs additional drugs
  – Steroids: side effects, intolerance, ineffective alone, flare ups on tapering

• Methotrexate is often given next or even concomitantly with steroids

• Azathioprine may be given using same rationale
<table>
<thead>
<tr>
<th>Drug</th>
<th>Level of evidence for use in myositis</th>
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<tbody>
<tr>
<td>Glucocorticoids</td>
<td>Retrospective studies</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Retrospective uncontrolled cohort studies</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Retrospective uncontrolled cohort studies</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>Retrospective uncontrolled studies</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Retrospective controlled studies</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>Retrospective controlled studies</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Prospective uncontrolled studies on myositis-ILD; case reports on myositis</td>
</tr>
</tbody>
</table>
Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
  - Difficulty swallowing
  - Severe rash
Main Features Requiring Treatment in Myositis

- Muscle (myositis)
- Skin
- GI tract: difficulty swallowing
- Joint pain (arthritis)
  - May get treated like you have rheumatoid arthritis (RA)
  - Multiple biologic agents approved for RA
Main Features Requiring Treatment in Myositis

- Muscle (myositis)
- Skin
- GI tract: difficulty swallowing
- Joint pain (arthritis)
- Lung (ILD)
  - Shortness of breath
  - Inflammation in lung tissue
  - Fibrosis (scar tissue)
How Do We Diagnose ILD?

- Think about it!
- Chest x-rays
- High resolution CT scans
- Lung biopsy
- Pulmonary Function Tests (PFTs)
- Blood tests
  - Antibody markers
Treatment of ILD in Myositis Patients

- Steroids (prednisone) still the initial treatment
- Cyclophosphamide and azathioprine used early or in steroid-resistant cases with variable results
- CellCept is being increasingly used
- Cyclosporin A and tacrolimus (medications used to prevent rejection of transplanted organs)
- Emerging use of biologic agents like rituximab
Monitoring Patients with ILD

- Frequent doctor visits
- Joint monitoring with a lung specialist (pulmonologist)
- Frequent pulmonary function tests (PFTs)
- High resolution CT (HRCT) scans with flare
- Pulmonary rehabilitation
- Echocardiograms
  - Assessing for pulmonary hypertension
Myositis Medications

- Glucocorticoids (steroids)
- Immunosuppressive Agents
- Combinations of drugs
- IVIg (gamma globulin)
- Biologic agents
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<th>Biologic Drugs</th>
<th>Level of evidence for use in inflammatory myopathy</th>
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<tr>
<td>Rituximab (RIM Trial)</td>
<td>Double-blind (improvement in 83% of PM, DM and JDM pts) and multiple case series</td>
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