**Connective tissue disorders**

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**Idiopathic inflammatory myopathy (IM):**
A heterogeneous group of rare autoimmune muscle disorders

- Rare disease, annual incidence 5/100,000
- 3 peaks of onset: (1) 15-20 years, (2) 20-40 years, (3) 50-70 years
- Antecedent trigger: infection or vaccination
- Lack of exchangeable hint for diagnosis
- Brand & Warren phenomenon: temporal regression of symptom

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**Features of Myositis**

- Muscle weakness
- Fatigue
- Loss of strength
- Muscle atrophy
- Muscle tenderness
- Dry, cracked hands
- Insidious onset of proximal weakness

**Differential diagnosis of muscle weakness**

- Myasthenia gravis
- Lambert syndrome
- Myotonia dystrophia
- Myotonia congenita
- Myotonia nemaline
- Myotonia centronuclear
- Myotonia fascioscapulohumeral
- Lambert Eaton myasthenic syndrome
- Amyotrophic lateral sclerosis
- Dystrophinopathies
- Dystrophia muscularis congrena
- Schwartz-Jampel syndrome
- Congenital myopathies
- Rhabdomyolysis
- Pyomyositis
- Periodic paralyses
- Myoglobinuria
- Myositis

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**Many causes of raised CK!**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Cause</th>
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<tbody>
<tr>
<td>Myositis</td>
<td>Inflammation</td>
</tr>
<tr>
<td>Myoglobinuria</td>
<td>Myoglobin release</td>
</tr>
<tr>
<td>Rhabdomyolysis</td>
<td>Muscle trauma</td>
</tr>
<tr>
<td>Pyomyositis</td>
<td>Bacterial infection</td>
</tr>
<tr>
<td>Myotonia</td>
<td>Membrane permeability</td>
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</tbody>
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**Clues on bloods**

- Low creatinine
- High ferritin
- Raised Troponin T
- Negative ANA

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**How do patients' present with inflammatory myopathy?**

- Involuntary sense of muscle involvement
- Fatigue
- Weakness
- Myalgia
- Arthralgia/arthritis
- Skin abnormalities
- Dyspnoea
- Dysphagia
- Weight loss

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**Features of Myositis**

- C reactive protein
- Erythrocyte sedimentation rate
- Creatine phosphate
- Creatine
- ADP + H
- ATP
- Lactate
- Pyruvate
- Lactate dehydrogenase
- Alanine aminotransferase
- Aspartate aminotransferase
- Creatine phosphokinase
- Myoglobin
- Myoglobinuria
- Myoglobinuria

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**How do we classify myositis?**

1. Muscles
2. Myo: contractile protein
3. Dermatomyositis
4. Polymyositis
5. Inflammatory myopathy
6. Non-inflammatory myopathy
7. Congenital myopathies
8. Neuromuscular junction disorders
9. Myotonic syndromes
10. Dry/wet myopathies
11. Myofibrillar myopathies
12. Mitochondrial myopathies

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**What is myositis?**

- Inflammatory myopathy
- Autoimmune myopathy
- Myopathy
- Inflammatory autoimmunity muscle disease

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**How do we assess and treat myositis?**

- Case presentations
- Myositis disease spectrum antibodies
- How do we classify myositis?
what is myositis?
how do we classify myositis?
Myositis disease spectrum antibodies
case presentations
how do we assess and treat myositis?

Extra-muscular features of Inflammatory Myopathy

Gottron’s papules
Erythematous to violaceous papules and plaques over the extensor surfaces of MCP and IP joints & other large joints in a symmetric distribution

Nail changes

Bohan and Peter diagnostic criteria for polymyositis/dermatomyositis

- Symmetrical weakness of limb girdle muscles and anterior neck flexors
- Muscle biopsy evidence typical of myositis
- Elevation of serum skeletal muscle enzymes, particularly CK
- Typical EMG features of myositis
- Typical DM rash, including heliotrope and Gottron's papules

For the diagnosis of PM: For the diagnosis of DM:

- Definite
- Probable
- Possible

Item 5 plus 3 of items 1-4
Item 5 plus 2 of items 1-4
Item 5 plus 1 of items 1-4

Exclusion criteria: congenital muscular dystrophies, central or peripheral neurological disease, infectious myositis, metabolic/endocrine myopathies and myasthenia gravis.

Bohan A, Peter JB, N Eng J Med 1975

Myositis-Spectrum Disease Autoantibodies

- HLA
- Other genes
- Infections
- Uveitis
- Environmental factors

- Skin adapted from Dr Horvath

- Slide adapted from Dr Gunawardena

Always worth Checking ANA pattern for clues
What is myositis?

How do we classify myositis?

Myositis disease spectrum antibodies

Case presentations

How do we assess and treat myositis?

Myositis Spectrum Disease Antibodies & Clinical Associations in Adult Myositis

Betteridge Z, McHugh N.

Myositis - specific autoantibodies: an important tool to support diagnosis of myositis.


Anti-TIF1g: diagnostic utility in cancer associated myositis

Trallero-Aragues et al., Arthritis Rheum 2012;64:523–532

Pooled sensitivity for cancer-associated myositis

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
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<tr>
<td>0.78</td>
<td>0.89</td>
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Anti-HMG CoA reductase (HMGCR) positive patients (45/750, 6%)

- Features
  - Age: 52 ± 16 years
  - Female: 58%
  - Statin exposure: 30/45 (67%) (24/26, 92% >50 years)
  - CPK: 9,718 ± 7,383 IU/l
  - Proximal weakness: 96%
  - Necrosis on biopsy: 100%
  - Inflammation on biopsy: 20%

- Anti-HMGCR Ab not found in majority of statin treated subjects, including those with self-limited statin-associated myopathy

Statin-related myotoxicity phenotype classification

**Induction of remission (1)**

- 40-60mg prednisolone/day (≈0.75mg/kg) or if severe disease, initial methylprednisolone 250-500mg 2-3 doses alternate days.
- Continue dose until CK ≥2x ULN
- Then reduce by 10mg/week to 40mg, then 5mg/week to 35mg, then 5mg/week to 30mg daily, then further gradual reductions once established on a 2nd line agent

**Induction of remission (2)**

- If CK not improving after 4-5 weeks
  - Check diagnosis (+antibody, biopsy, EMG, 2nd opinion)
  - Add in methylprednisolone if not done so already
  - IV cyclophosphamide ± EULARUPUS or CYCLOPS (grade severity)
  - IVIG 2g/kg over 5 days
  - IV Rituximab

**Maintenance of remission:**

**Early introduction of disease modifying treatment**

- Methotrexate 10-20mg/week
- Azathioprine 2-5mg/kg (check TPMT levels)
- Mycophenolate mofetil 2g/day

**Disease resistance**

- Consider adding ciclosporin 3mg/kg x 1000mg
- Consider adding MTX/VA to MTX
- Tacrolimus 2-5mg/day
- Cyclophosphamide
- Rituximab
- TNF inhibitors

**Useful sites**

[Free resources](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4104537/)


[http://research.bmh.manchester.ac.uk/epidemiology/CIGMR/research/autoimmune/Autoimmunity/Myositis](http://research.bmh.manchester.ac.uk/epidemiology/CIGMR/research/autoimmune/Autoimmunity/Myositis)