INFLAMMATORY MUSCLE DISEASE
INCLUDES

- POLYMYOSITIS (PM)
- DERMATOMYOSITIS (DM)
- Body myositis
- Eosinophilic myositis
- Giant cell myositis
- Focal / localised myositis
- Myopathies caused by infections, drugs, toxins
POLYMYOSITIS
DERMATOMYOSITIS

Source: IMACS
TARGETS

- Definition
- Epidemiology
- Pathogenesis
- Clinical features
- Laboratory findings
- Diagnosis
- Treatment
- Prognosis
PM AND DM

- Are the most common of the inflammatory muscle diseases
- Cause nonsuppurative muscle inflammation
- The major clinical features are proximal muscle weakness and muscle fatigue with or without rash.
CLASSIFICATION OF PM AND DM

1. Adult polymyositis
2. Adult dermatomyositis
3. PM/DM associated with malignancy
4. Childhood DM (less often PM)
5. PM/DM associated with other connective tissue disorders
EPIDEMIOLOGY

- Prevalence: 2-10 cases/million
- Peak of age: bimodal distribution
  - 10-15 years
  - 45-55 years
- Female to male incidence ratio = 2.5:1
- This ratio is lower (nearly 1:1) in childhood disease and with malignancy, but is high (10:1) when there is a coexisting connective tissue disease.
- African, americans > whites = 3-4:1
Environmental factors:
- The most frequently reported: the infections.
- Rare cases: bacteria (mainly Staphylococcus aureus), parasites (trichinosis)
- Some viral infections (coxsackie, echo, parvo B19, influenza viruses) have been described to be associated with a self-limiting myositis mostly seen in children.
- Ultraviolet light
- Drugs- statins, fibrates, nicotinic acid.

Genetic factors:
- The exact contribution of the genetic component in these disorders is currently unknown.
- Certain HLA alleles- HLA HLA DRB1*0301 and the linked DQA1*0501 are the strongest known risk factors for all major forms of sporadic and familial forms of myositis in white adults and children.
- There are also genetic associations between myositis and non-HLA genes→TNF gene- the association was reported with a more severe disease in children with juvenile dermatomyositis.
There are specific **autoantibodies**, which target cytoplasmic molecules involved in protein synthesis associated with distinct clinical myositis subsets.

The major histopathologic findings of myositis:
- focal inflammation with T cells, macrophages and dendritic cells, often together with injury, death and repair myocytes
- expression of major histocompatibility complex (MHC) class I antigen on muscle fibers.

Differences in the immunopathology of **dermatomyositis** (perivascular CD4+ T cells, B-cells infiltration, deposition of late complement components and capillary loss) and **polymyositis** (endomysial infiltrates and activated CD8+ T cells and macrophages invasion of myocytes) may reflect different etiologies and molecular pathways.
Malignancies are more commonly associated with DM than PM

- Can occur 2 years prior to onset, to 2 years after onset of myositis
- Seems to be more common: ovarian, gastric, cervical, lung malignances, also pancreatic, stomach, colorectal cancer and non-Hodgkin lymphoma.
Complement, autoantibodies, cytokines, CD8 T cells, endothelial cell damage, MHC class I expression, hypoxia, ER stress, myofiber damage, Capillary loss, Loss of skeletal muscle fibers.

ER=endoplasmic reticulum
MHC=major histocompatibility complex
The clinical features of DM include all those described for PM plus a variety of cutaneous manifestations.

Constitutional features:
- fatigue may be proeminent
- weight loss due to anorexia and inflammatory burden
- morning stiffness.
• The most frequent symptom is **insidious, progressive and painless symmetric proximal muscle weakness** over the course of 3 to 6 months before the first visit to a physician.

• First usually appear the weakness of the proximal muscles of the legs → difficulty arising from a chair or climbing stairs.

• Weakness of the proximal arms muscles → difficulty raising the arms overhead, lifting heavy items or reaching up to shelves, even brushing the hair.

• Neck and axial muscles are commonly involved → the inability to raise the head from a pillow.
Muscle pain may occur and is more common in DM.
Pharyngeal muscle weakness may cause dysphonia or dysphagia (risk of aspiration pneumonia).
Ocular or facial muscle weakness is virtually never involved in PM/DM.

The detection of muscle weakness on physical examination typically relieves on manual muscle strength testing (scale 0 to 5)
The clinical onset of DM is generally more rapid than that of PM.

DM has a characteristic skin rash that may precede, develop simultaneously with or follow muscle symptoms.

Gottron papules and the heliotrope rash are considered pathognomonic cutaneous features of DM.
**Gottron papules** = symmetric purpule to erythematous papules and plaques located over bony proeminences, particularly the metacarpophalangeal, proximal and distal interphalangeal joints of the hands.

**Gottron sign** = symmetric macular erythema that occurs in the same distribution and over other extensor areas such as the elbows, knees, and ankles.
MUCOCUTANEOUS (3)

- The **heliotrope rash** is purplish in color, may be edematous or scaling in nature and is located in the periorbital area, especially over the upper eyelids, malar region, forehead, nasolabial folds.

- Seen in less than 50% of patients with DM
Heliotrop rash
Involvement of the nasolabial area and forehead is an additional distinguishing feature of DM compared with SLE.
CUTANEOUS PHOTOSensitivity WITH FACIAL ERYThema OR A “SHawL SIGN” (MACULAR ERYTHEMA OF THE POSTERIOR SHOULdERS AND NECK) MAY ALSO BE SEEN IN DM.
macular erythema of the anterior neck and upper chest “V sign”
Cracking or fissuring of the lateral and palmar digital skin pads is termed **mechanic’s hands** and is most frequently seen in patients with PM who have anti-tRNA synthetase or anti-PM-Scl autoantibodies.
Capillary Loop Dilatation

Periungual Erythema
Vascular: Raynaud’s phenomenon (more common with the anti-synthetase syndrome)

Pulmonary and cardiac manifestations may precede the onset of muscle weakness or develop at any time during the course of disease

The most common: asymptomatic ecg abnormalities, but supraventricular tachycardia, cardiomyopathy and congestive heart failure may occur

Respiratory: interstitial fibrosis, aspiration pneumonia, respiratory muscle weakness
1. Nonspecific abnormalities

- The most sensitive indicator of skeletal damage: elevated creatine kinase (CK) serum level
- Normal CK may be found in: early disease, advanced cases with significant muscle atrophy or in myositis associated with a malignancy
- Aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), aldolase: elevated as released from muscle
- ESR: normal in 50%
2. **Myositis-associated antibodies:**

- **ANA:** (over 50% of cases) a high-titer ANA test may indicate the association of a connective tissue disease
- **Anti-RNP antibody** → MCTD and overlap syndromes
- **Anti-PM-Scl antibody** → PM+ Ssc
- **Anti-Ku antibody** → PM+ Ssc
3. **Myositis-specific autoantibodies:**

- **Antisynthetase** (anti-Jo1 is the most common 20-50%, anti PL 7, anti PL12, anti EJ, anti OJ)
- Anti-SRP <5% (in PM with very acute onset)
- Anti-Mi-2 5-10% (in DM with V or shawl sign)

Anti-Jo1 (PM>>DM) plus several extramuscular features (interstitial lung disease, arthritis, mecanic’s hans, Raynaud’s phenomenon) = *antisynthetase syndrome*
**EMG**: Electrical testing is a sensitive but non-specific method of evaluating muscle inflammation.

- **Pattern**: Polyphasic motor unit action potentials with short duration and low amplitude
- **Nerve conduction velocity** is normal in inflammatory myopathies (except the inclusion-body myositis with associated neurophatic disease)

**Muscle biopsy**: remains the **gold standard** for confirmation of the diagnosis of inflammatory myopathy.
Typical findings:

- **PM**: muscle fibers necrosis with degenerating and regenerating fibers scattered throughout the fascicles; increased cytotoxic CD 8+ T-cells invading muscle fibers, endomysial inflammation
DM: muscle fiber necrosis with degenerating and regenerating fibers in a perifascicular distribution, perimysial and perivascular inflammation with CD4+ T-cells in addition to B cells, complement deposition in blood vessels walls
MRI: short tau inversion recovery (STIR) images which show inflammation, edema, fibrosis and calcification of the muscle.
Individual criteria
1. Symmetric 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
Differential Diagnosis

- Inflammatory myopathies
- Inflammatory myopathy secondary to malignancy
- Inclusion body myositis
- Drug-induced myositis: corticosteroids, HMG-CoA reductase inhibitors, alcohol, AZT, Plaquenil, Colchicine
- Endocrine: hypo/hyperthyroidism, Cushing, Addison’s disease
- Infectious myositis: HIV, Toxoplasma, Lyme disease
- Neuromuscular disorders: Myasthenia gravis, Eaton Lambert, ALS
- Metabolic myopathies
- Miscellaneous causes: sarcoidosis, Behcet disease, fibromyalgia
Predominantly affects white males over age 50.
Onset of weakness is slow and insidious.
Proximal muscles are involved, but distal muscles are also affected early in the disease course.
Weakness is usually bilateral, but asymmetry is common.
The legs, especially the anterior thigh, are typically affected more than arms, and muscle atrophy can be prominent.
CPK may be normal at presentation (20-30%), and if elevated is less than 600-800 mg/dl.
ANA can be present.
Anti myositis-specific Abs do not occurs.
Muscle biopsy: foci of chronic inflammatory cells (CD8+Tcells) without perifascicular atrophy. The characteristic findings: red-rimmed vacuoles containing beta-amiloid.
Poor response to immunosuppressive therapy.
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<tr>
<th><strong>Demographics</strong></th>
<th><strong>Inclusion body myositis</strong></th>
<th><strong>Polymiositis</strong></th>
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<tbody>
<tr>
<td>M &gt; F; age &gt; 50</td>
<td>F &gt; M; all ages</td>
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<tr>
<th><strong>Muscle involvement</strong></th>
<th><strong>Inclusion body myositis</strong></th>
<th><strong>Polymiositis</strong></th>
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<tbody>
<tr>
<td>Proximal and distal; asymmetric</td>
<td>Proximal symmetric</td>
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<tr>
<th><strong>Other organ involvement</strong></th>
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<th><strong>Polymiositis</strong></th>
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<tbody>
<tr>
<td>neuropathy</td>
<td>Interstitial lung disease, arthritis, heart involvement</td>
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<tr>
<th><strong>ANA</strong></th>
<th><strong>Inclusion body myositis</strong></th>
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<tbody>
<tr>
<td>sometimes</td>
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<tr>
<th><strong>Myositis specific Abs</strong></th>
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<th><strong>Polymiositis</strong></th>
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<tbody>
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<tr>
<th><strong>EMG</strong></th>
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<th><strong>Polymiositis</strong></th>
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<tbody>
<tr>
<td>Myopathic and neuropathic</td>
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<th><strong>Muscle biopsy</strong></th>
<th><strong>Inclusion body myositis</strong></th>
<th><strong>Polymiositis</strong></th>
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<tbody>
<tr>
<td>CD8+Tcells infiltrate Red rimmed vacuoles with beta amyloid</td>
<td>CD8+Tcells infiltrate</td>
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<th><strong>Response to immunosuppressives</strong></th>
<th><strong>Inclusion body myositis</strong></th>
<th><strong>Polymiositis</strong></th>
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<tr>
<td>no</td>
<td>frequent</td>
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**TREATMENT**

- **General**: education, avoidance of sunlight → DM, elevating the head of the bed → dysphonia, dysphagia

- **Physical therapy**: improve functional abilities by increasing muscle strength, endurance and aerobic capacity

- **Corticosteroids**: the standard first-line medication
  
  Prednison 1mg/kg/day

  If at 3 months the patient is not responding or requiring large doses of prednisone → a second agent should be introduced

  If the muscles are weak with normal enzymes → think about steroid myopathy

- **DMARDs**: may be used first-line in patients with poor prognostic features
  
  - Methotrexate 10-20 mg orally/15-50 mg sc
  
  - Azathioprine 2-3 mg/kg/d

- **Intravenous immune globulin**

- Cyclosporine

- Hydroxychloroquine

- Mycophenolate mofetil
Risk stratification for poor diagnosis
- Disease present >6 months prior to treatment
- Severe weakness
- Dysphagia
- Anti-SRP antibodies

Prognosis: overall 5-years survival with PM or DM is about 85%

Malignancy associated myositis has a worse prognosis
Last five minutes
Of exam

THANK YOU
THANK YOU