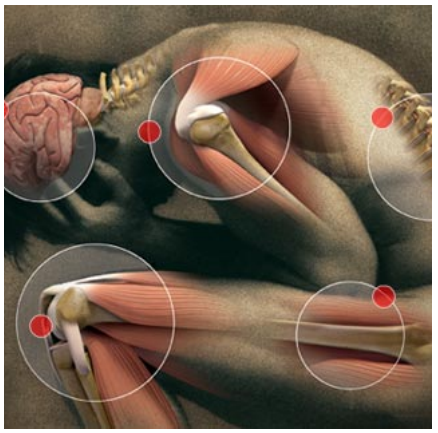
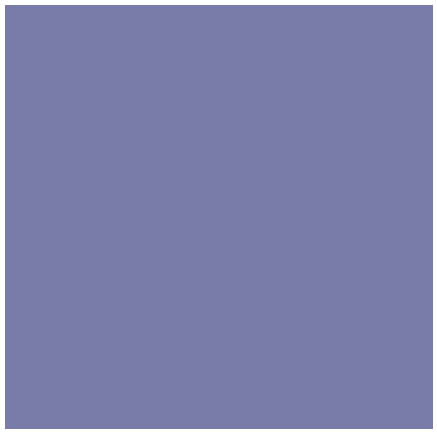
Myopathies





Myopathies

Slides & Step-Up

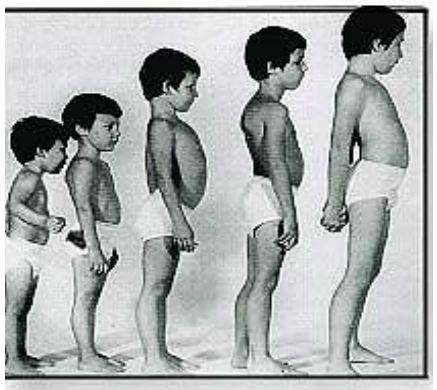
Congenital Myopathies

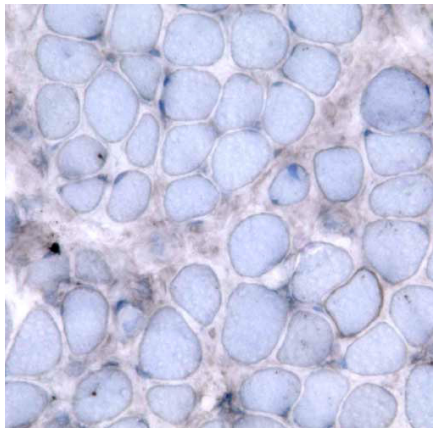
- Autosomal dominant, or recessive or sporadic
- Presents in early childhood or after birth
- Affects growth > deformities and contractures
- Could affect breathing
- Central core myopathy
  - When under anesthesia > malignant hyperthermia
- Dx:
  - Biopsy
  - +/- genetic testing
- Rx:
  - Prenatal screening
  - Genetic counseling
  - Medicine/surgery for complications

Hereditary Myopathies

X-Linked Hereditary Myopathies

- Cause: defective or absent dystrophin
  - Dystrophin gene: Xp.2.1
- Dystrophin:
  - Role in sarcolemmal stability
  - Loss > cascade = loss of other components of dystrophin associated glycoprotein complex > sarcolemmal breakdown > Ca++ influx > phospholipase activation > ROS > MYONECROSIS





1. Duchenne's Muscular Dystrophy

1/3 cases: w/FHx
2/3 cases: sporadic

- Males (1:3500 newborns)
- Age of onset: 3-5 years
  - First: delayed motor development
  - Initial symptom: **Gower's sign** = difficulty getting up
    - Weakness of limb girdle muscles and trunk erectors
  - Scoliosis
  - Contractures
  - Loss of ambulation (by 12 yrs)
  - Difficulty climbing stairs
  - Pseudohypertrophy, esp. calf muscles
  - Waddling gait
  - Clumsiness/frequent falls
  - Craniobulbar muscles are spared
  - Cardiomyopathy
- Death usually occurs in the 3rd decade; due to resp. failure
- Female carriers are usually asymptomatic

1. Duchenne's Muscular Dystrophy

Diagnosis

- Lab
  - CPK
  - EMG
  - **Biopsy**:
    - Lack of staining of dystrophin in muscle biopsy
  - **Genetic**: Demonstration of deletion in the dystrophin gene (limitation: small gene deletion in 30%)
- Prenatal: at 8 weeks

Treatment

- Supportive
  - Breathing: O2, ventilator, scoliosis correction, tracheotomy
  - Mobility: physical therapy, surgery on tight joints, wheelchair
- Steroids: delay deterioration
- Genetic counseling

2. Becker's

- Also autosomal recessive
- Males (1:35000 births)
- Onset: during first decade
- Small amount of dystrophin present
- Milder, more benign course

Myotonia

- Autosomal dominant
- 1:8000 births
- Cause: trinucleotide (CTG) repeat expansion on chr. 19q13.3
- Onset: any age, usually 3rd decade
  - More repeats > younger age
- Hyperexcitability of muscle membrane → inability of quick muscle relaxation
- Dx:
  - Genetic testing
  - Screen for associated medical conditions like DM, cardiac,...
- Rx:
  - Counseling
  - Supportive
  - Prenatal Dx

- Muscle weakness can be mild
- Greater **distal** weakness
  - Hands are spared till late
- Clinical features
  - Signs:
    - Difficulty in releasing hand grip
  - Facial:
    - Weakness
    - Frontal balding
    - Wasting of muscles of mastication
    - Hollow temples
    - Wasting of neck and shoulder muscles
  - Cataracts
  - Arrhythmias; cardiac abnormalities
  - DM
  - Testicular atrophy
  - Mental retardation

Acquired Myopathies

Idiopathic Inflammatory Myopathies

Heterogeneous group of disorders characterized by: **Proximal** muscle weakness and **non-suppurative** inflammation of skeletal muscle with predominantly **lymphocytic infiltrates**

- 2-8 cases per million per year
- Female > male (2:1)
- May be associated with malignancy; common after age of 50
  - 35% with dermatomyositis (ovarian/ lung)
  - 15% polymyositis (lymphoma/lung)
- Mechanism:
  - **Cell mediated** in **polymyositis** and **IBM**
  - **Humoral** response with vasculitis in **dermatomyositis**
- **Common features**
  - Symmetrical proximal muscle weakness that develops subacutely
    - Neck flexors, shoulder girdle
  - Myalgia
  - Dysphagia

Polymyositis

- Adults
- Insidious onset (over 3-6 m)
- Shoulder and pelvic girdle muscles affected most severely
- Neck muscles (esp. flexors) involved in 50% of patients
- Dyspahgia (33%) and dysphonia
- Ocular and facial muscles almost never affected
- Distal muscles are spared in majority of pts

Systemic features

- Cardiac
  - CHF
  - Conduction abnormalities
  - Supraventricular arrhythmia
  - Asymptomatic ECG changes
- Respiratory
  - Interstitial fibrosis
  - Interstitial pneumonitis
- Other
  - Arthralgia (common)
  - Fever, malaise
  - Raynaud's

Dermatomyositis

- Features of Polymyositis as well as cutaneous manifestations
- The skin lesions may precede or follow the muscle syndrome
- Gottron's sign: apular, erythematous, scaly lesions over the knuckles
- Heliotrope rash: (butterfly)-around eyes, bridge of nose, cheeks
- Shawl sign: rash on shoulders and upper back, elbows, and knees
- *V* sign-rash on the face, neck, and anterior chest

- Vasculitis of the GI tract, kidneys, lungs, and eyes (more common in children)
- Increased incidence of malignancy
  - Dermatomyositis associated with malignancy often remits once the tumor is removed

Inclusion Body Myositis

Extramuscular manifestations are rare

- Usually affects **adults >50 yrs**
- Gradual **painless weakness** of **QUADRICEPS** and **fingers flexors**
  - Proximal and distal
  - Assymetrical
- Facial weakness in 1/3 pts
- Dysphagia in 1/2 pts
- Patients may have loss of deep tendon reflexes
- Dx: slightly high CK
- Poor response to therapy

Idiopathic Inflammatory Myopathies

Diagnosis

- Clinical presentation
- Elevation of CK (>10 times normal) - more at initial phase
- AST, ALT, aldolase and LDH are elevated in most cases
- ANA (50% of pts)
- Anti-synthetase antibodies > Raynaud's, ILD, abrupt onset of fever; poor response to Rx
- Anti-signal recognition particle
  - Cardiac manifestations (common)
  - Worst prognosis of all subsets
- Anti-Mi-2 antibodies-better prognosis
- Classic EMG findings for myositis
- Muscle biopsy = inflammation

Treatment

- Corticosteroids (prednisone) - less beneficial for IBM
- Immuno-suppresive agents e.g. azathioprine, methotrexate, mycophenylate mofetil
- Physical therapy
- IVIG (IV immunoglubulin) & Plasma exchange
- Early detection of malignancies!

Drug-Induced Myopathy

- Steroids
- Heroin
- ETOH
- Statins

Steroid-Induced Myopathy

- More in women
- Reported with inhaled steroids too
- **Mechanism:**
  - Decreased protein synthesis
  - Increased protein degradation
  - Alterations in carbohydrate metabolism
  - Mitochondrial alterations
  - Electrolyte disturbances
  - Decreased sarcolemmal excitability
- Tests:
  CK, EMG, and muscle biopsy are typically **NORMAL**
- Treatment:
  - Re-assess indication of steroid and consider dose reduction
  - Avoid excessive exercises
  - Pain control and other supportive measures