Duchenne Muscular Dystrophy

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Biochemistry 118

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Duchenne Muscular Dystrophy

- One of the most prevalent types of muscular dystrophy
  - MD: diseases that cause progressive muscle weakness
- Rapid muscle degeneration occurs early in life
  - Wheelchair bound by 12 years
  - Cardiomyopathy after 18 years
  - Few live beyond third decade
- Affects 1 in 3500 boys worldwide

Symptoms

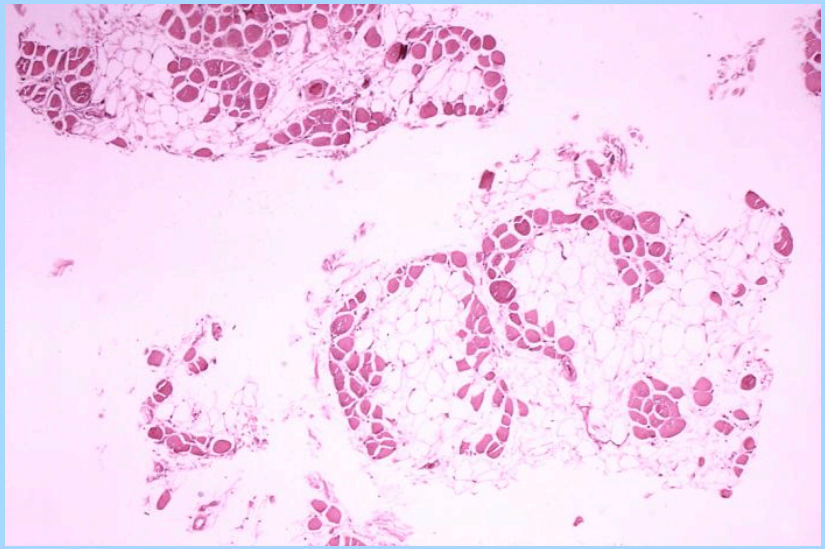
- Pseudohypertrophy
- Onset before age 3
- Awkward gait
- delayed motor skills
- Affects shoulder and upper arm muscles, muscles in hips and thighs first
- Mild retardation

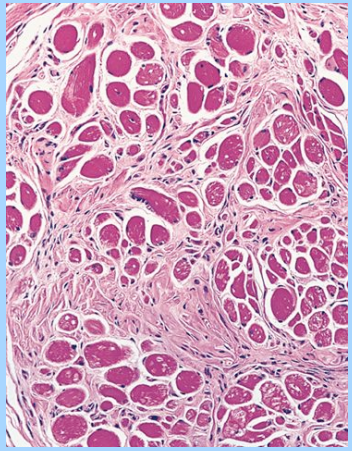
Classical Diagnoses

- Early childhood with delayed milestones, such as delays in sitting, standing, walking, learning
- Symptoms before 5 yr.
- Positive Gower's sign
- Creatine phosphokinase test (CPK)

Classical Diagnosis

- Muscle Biopsy
  - Pseudohypertrophy



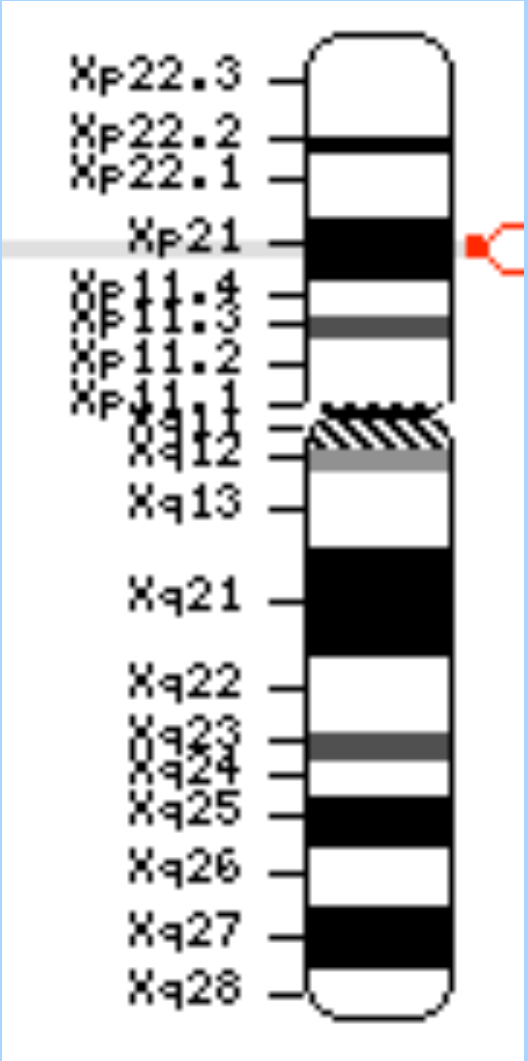


Classical Treatment

- Aims to control symptoms and maximize quality of life
- Anti-congestive medicines to preserve myocardial function and prevent cardiomyopathy
- Cardiac transplantation in severe cases
- Physical therapy to promote mobility
- Weight control
- Corticosteroids: Prednisone and Deflazacort

Genetic Information

- Found on the DMD gene
- Codes for dystrophin
  - anchors cytoskeleton with membrane proteins
  - Without it, EC components enter cell
- Recessive, x-linked
- Location: Xp21.2
- Mutations: frameshift (deletion) and nonsense mutations
  - Premature stop codon

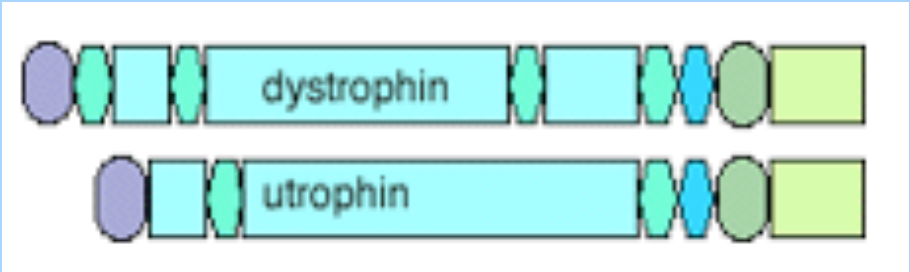


Genetic Diagnosis

- Muscle biopsy for presence/lack of dystrophin
- Molecular genetic testing
  - Deletion/duplication
  - Mutation scanning
- DNA testing confirms in most cases
- Prenatal testing

Therapies under Investigation

- Aminoglycoside treatment: suppresses stop codons
- PTC124:reads through nonsense mutations
- Gene therapy: adeno-associated viral vectors to insert DMD gene (Gregorevic)
- Utrophin Alternative
- oligonucleotide vectors to modify DNA



Similar size and architecture

Work Cited

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