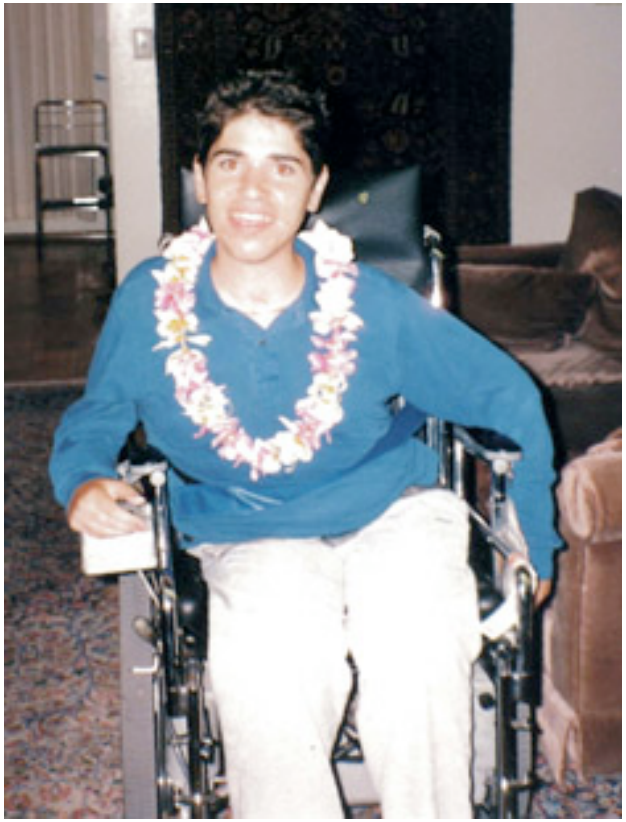
Duchenne Muscular Dystrophy



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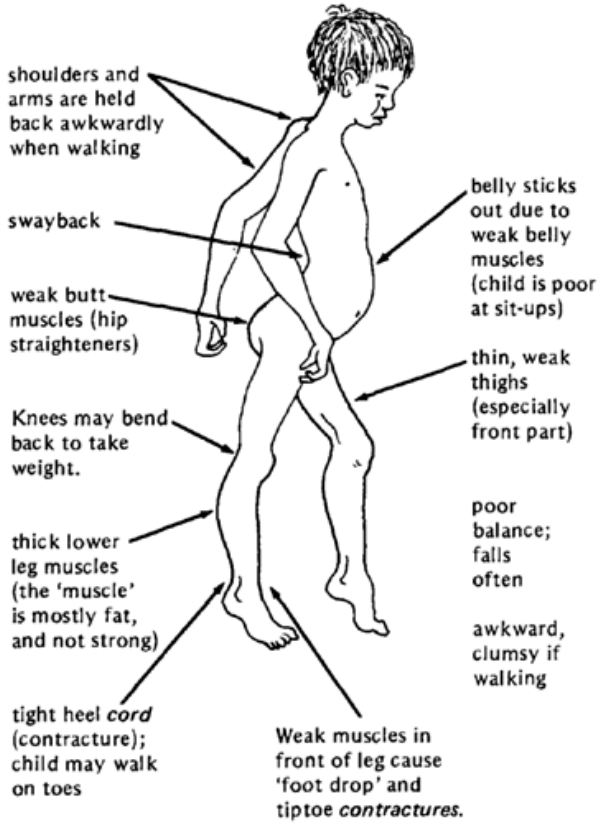
What is DMD?

- A prevalent type of muscular dystrophy
- Characterized by rapid progression of muscle degeneration
- Symptoms occur early in life
- X-linked and mainly affects males (1 in 3500 boys worldwide)
- Males with DMD do not reproduce
- Duchenne muscular dystrophy (DMD) vs. Becker muscular dystrophy (BMD)
- Heart failure from DCM is the most common cause of death

Diagnosis

- Delayed milestones in sitting and standing independently
- Clinical diagnosis is straightforward
  - Gait difficulty beginning at age three
  - progressive myopathic weakness
  - Pseudohypertrophy of calves
- Massive elevations of serum levels of creatine kinase permit diagnosis. Electromyography and muscle biopsy are confirmatory.

Noticeable Features



Treatment

- The management of DMD is **largely symptomatic** providing assisting devices for walking, prevention of scoliosis
- Prednisone to improve the strength and motor function in children with DMD unless side effects are severe
- Physical therapy to promote mobility
- Sunshine and a balanced diet rich in vitamin D and calcium to improve bone density and reduce the risk of fractures
- Frequent evaluations by a doctors

DMD Gene

- The ***DMD* gene** is the largest known human gene
- The protein product is **Dystrophin**, a membrane-associated protein present in muscle cells and neurons
- DMD is caused by partial deletions or duplications
- Mutations that lead to lack of dystrophin expression tend to cause DMD, whereas those that lead to abnormal quality or quantity of dystrophin lead to BMD

Novel Diagnostics

- **Molecular genetic testing** of *DMD* can establish the diagnosis of a dystrophinopathy
- Almost all males with DMD have identifiable *DMD* mutations
- A combination of clinical findings, family history, serum CK concentration, and muscle biopsy with dystrophin studies confirms the diagnosis.
- **Western Blot Testing** for dystrophin

Novel Therapy

- Application of the antisense rescue method
  - In each case of a nonsense mutation, the specific skipping of the targeted exon was induced, restoring dystrophin synthesis in over 75% of cells.
  - The protein was detectable 16 hours posttransfection, increased to significant levels at the membrane within 2 days, and was maintained for at least a week
- A study found that ventricular remodeling may occur in males with DMD and BMD with early diagnosis and treatment of cardiomyopathy

Novel Therapy

- **Aminoglycosides.** Suppression of stop codons; the treatment creates misreading of RNA and thereby allows alternative amino acids to be inserted at the site of the mutated stop codon.
- **PTC124** is a new, orally administered non-antibiotic drug that appears to promote ribosomal read-through of nonsense (stop) mutations.
- **Stem cell therapy** is under investigation but remains experimental

Reference Sources

- Image on Intro: http://www.tasteof2harbors.com/howardthomas.htm
- Noticeable Features Image: http://ahsanatomy.wikispaces.com/Muscular+Dystrophy
- OMIM – Muscular Dystrophy, Duchenne Type
- Gene Reviews: Dystrophinopathies
- Genes and Disease - NCBI