Muscular Dystrophies

MUSCULAR DYSTROPHY

- **Heterogeneous** group
- **Inherited** disorders
- Often presenting in **childhood**
- Progressive **degeneration** of muscle fibers
- **Muscle** weakness and wasting

Muscular dystrophy (Types)

1. **X-linked muscular dystrophy**
    1. Duchenne muscular dystrophy
    2. Becker muscular dystrophy

2. **Autosomal muscular dystrophies**
    1. Limb girdle muscular dystrophies
    2. Facioscapular humeral muscular dystrophy
    3. Oculopharyngeal muscular dystrophy
3. **Myotonic dystrophy**

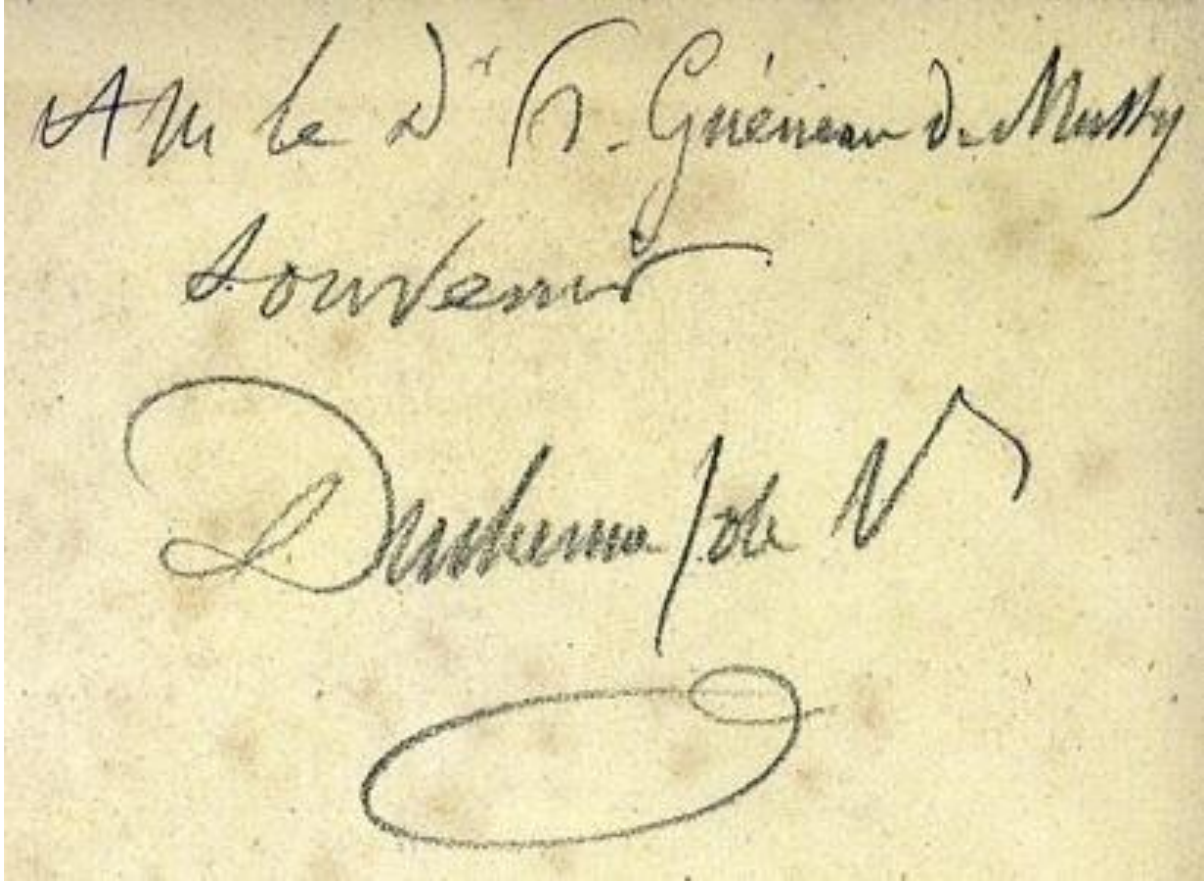
MUSCULAR DYSTROPHY

Two most common ones are:

X-linked muscular dystrophy:

- **Duchenne muscular dystrophy (DMD)**
- **Becker muscular dystrophy (BMD)**

Duchenne muscular dystrophy (DMD)



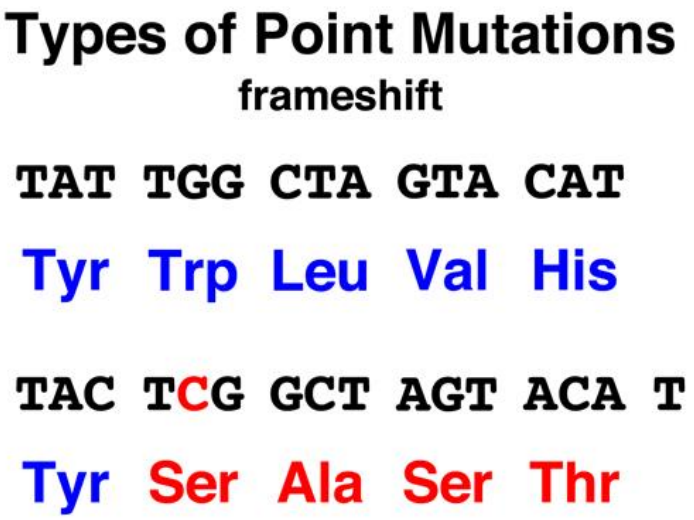
French neurologist Guillaume Benjamin Amand Duchenne

Duchenne muscular dystrophy

- **X-linked recessive**
- Absence of a structural protein termed **DYSTROPHIN**
- **Most common** and severe form of muscular dystrophy

Pathogenesis

- Absence of **dystrophin** due to **frameshift mutation** of the *dystrophin gene* on the X chromosome.



Pathogenesis

- **Dystrophin** protein is found in skeletal and cardiac muscle
- Dystrophin is a part of dystrophin-glycoprotein complex
- Dystrophin-glycoprotein complex damage results in **influx of ca++ ions**
- Increased cytosolic ca++ ions stimulates calpains
- Results in muscle proteolysis (**Necrosis**)

Pathogenesis

Results in :

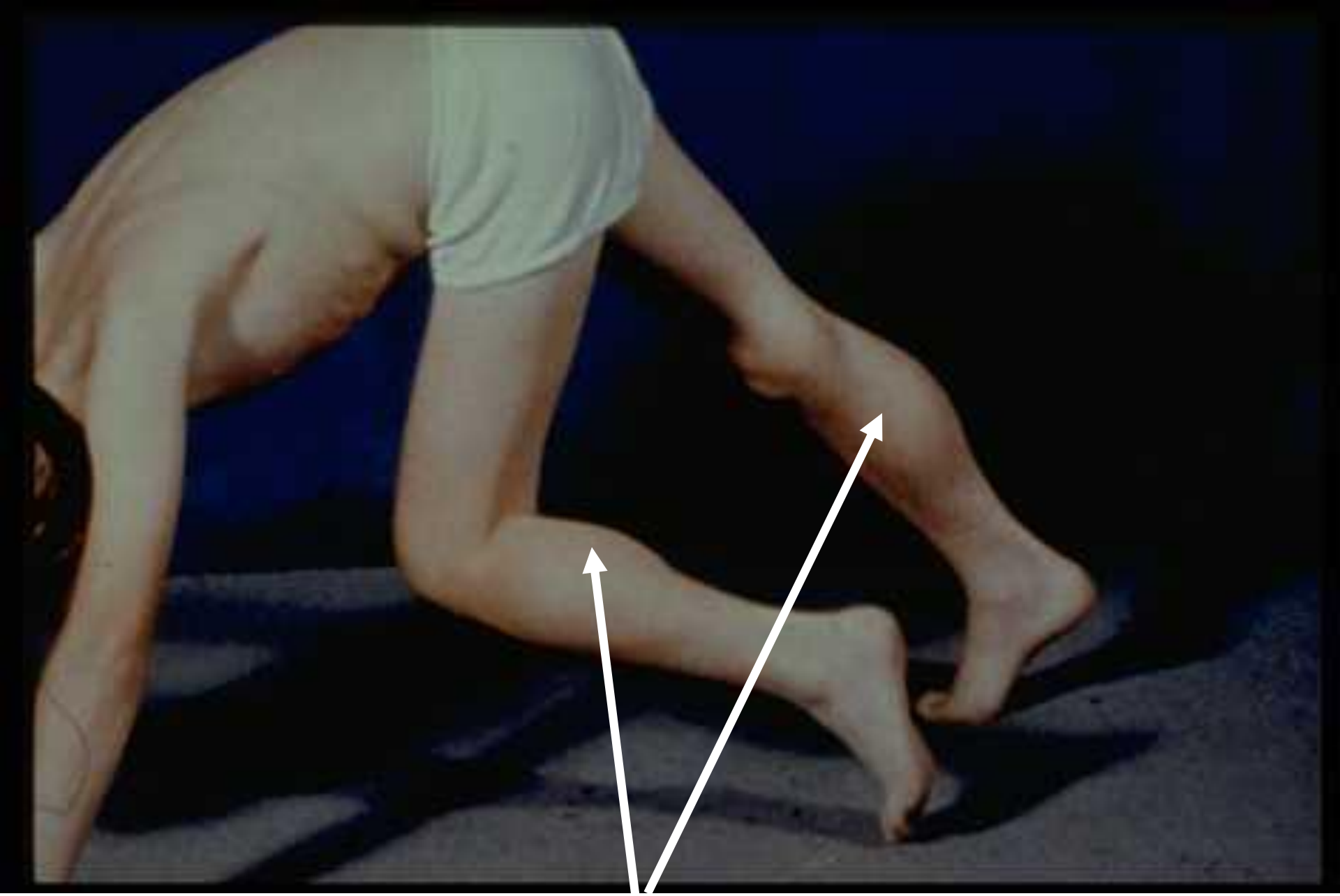
- Degeneration and Regeneration of muscle fibres.

Finally, leads to;

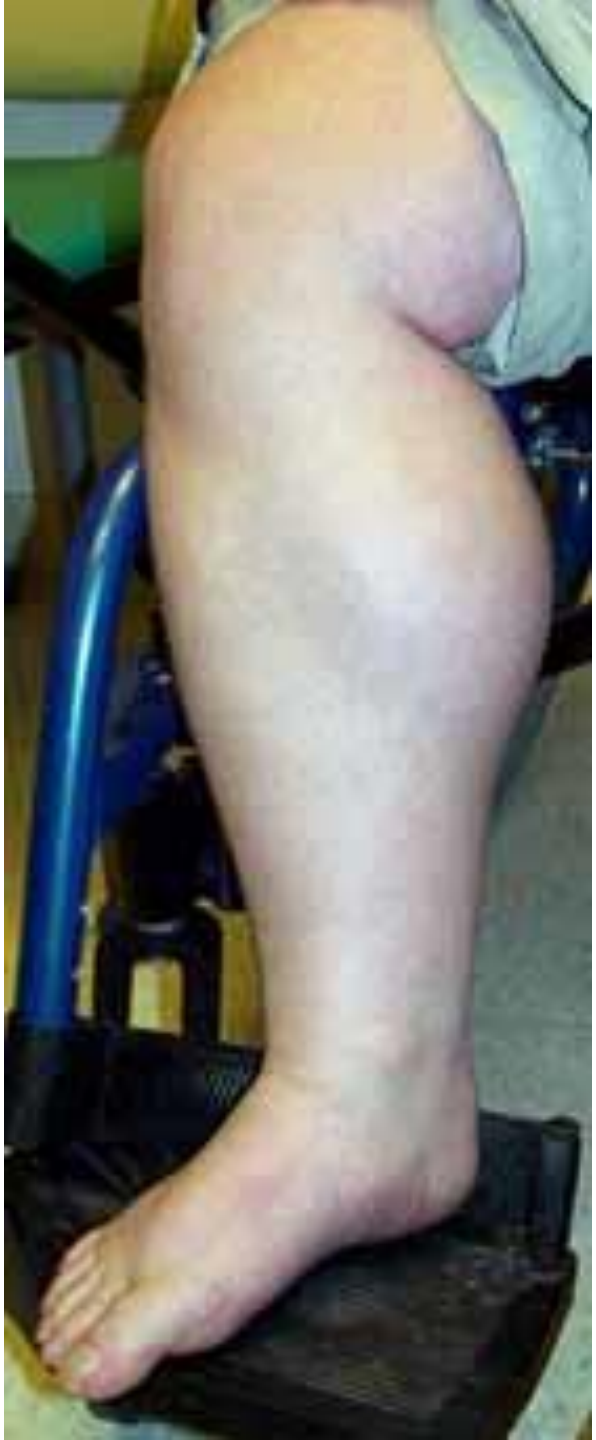
- Muscles fibres are **replaced** by **connective fibrous** tissue and **adipose tissue**

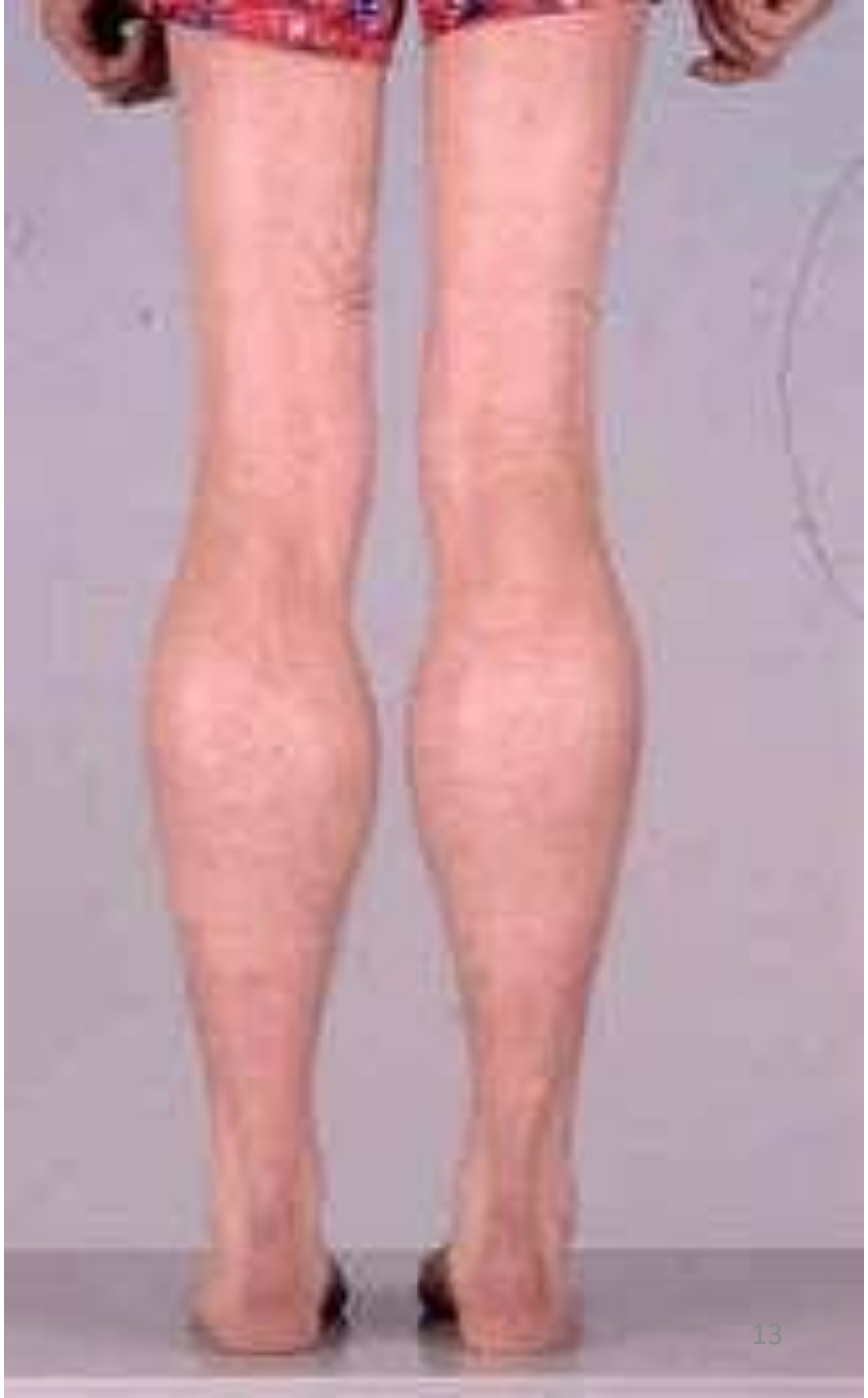
Clinical features

- Normal at birth, Onset of symptoms by age 5
- Waddling gait (Duck like)
- Wheelchair-bound by age 10
- Proximal weakness of shoulder and pelvic girdles
- Calf pseudo-hypertrophy (muscles replaced by fat and connective tissue)



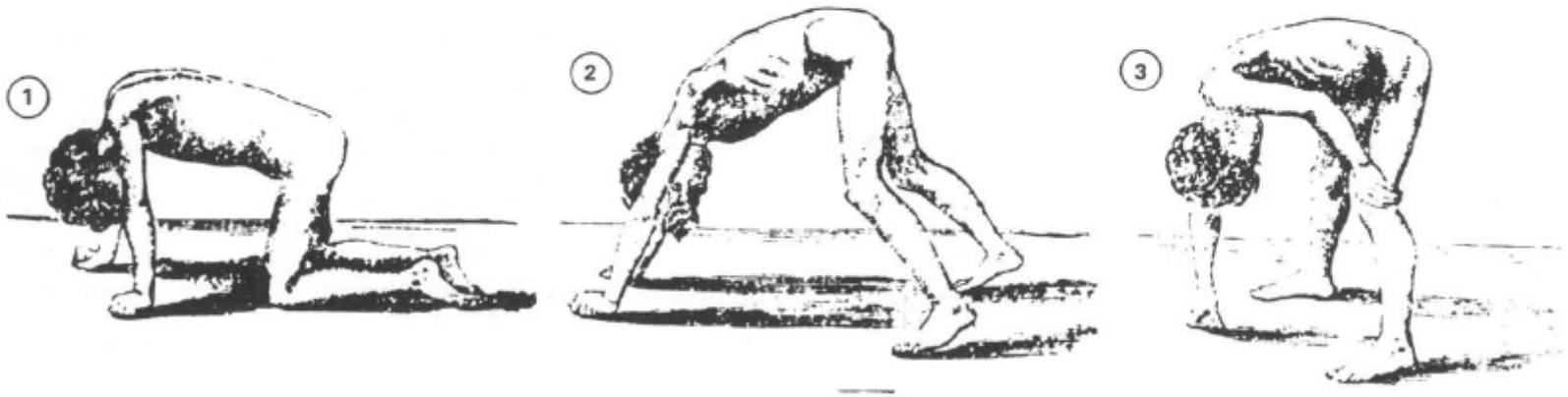
Calf pseudo-hypertrophy





Gowers Sign

- Patient uses his hands and arms to "walk" up his own body from a squatting position
  - due to lack of hip and thigh muscle strength



Gowers WR. Clinical lecture on pseudohypertrophic muscular paralysis. Lancet 1879;ii,73-5.

Waddling gait

Clinical features

- Heart failure and arrhythmias may occur
- Respiratory insufficiency and pulmonary infections
- Death due to respiratory failure by the second or third decade

Diagnosis

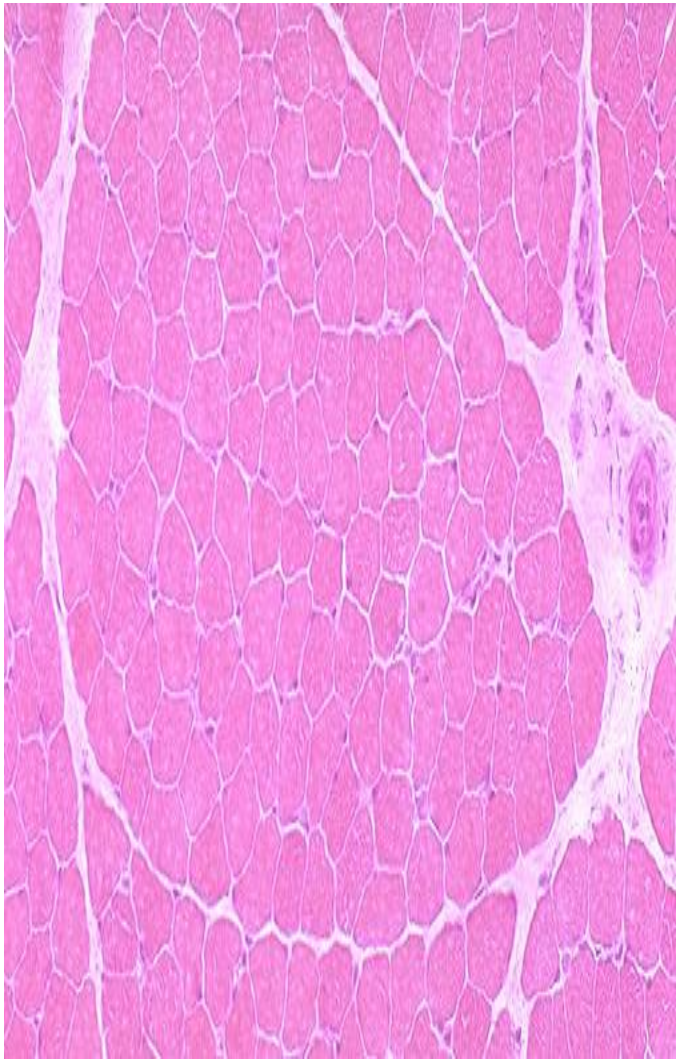
- Initially Elevated serum **Creatine kinase**
- Later, Decreased when the disease progresses.

Diagnosis

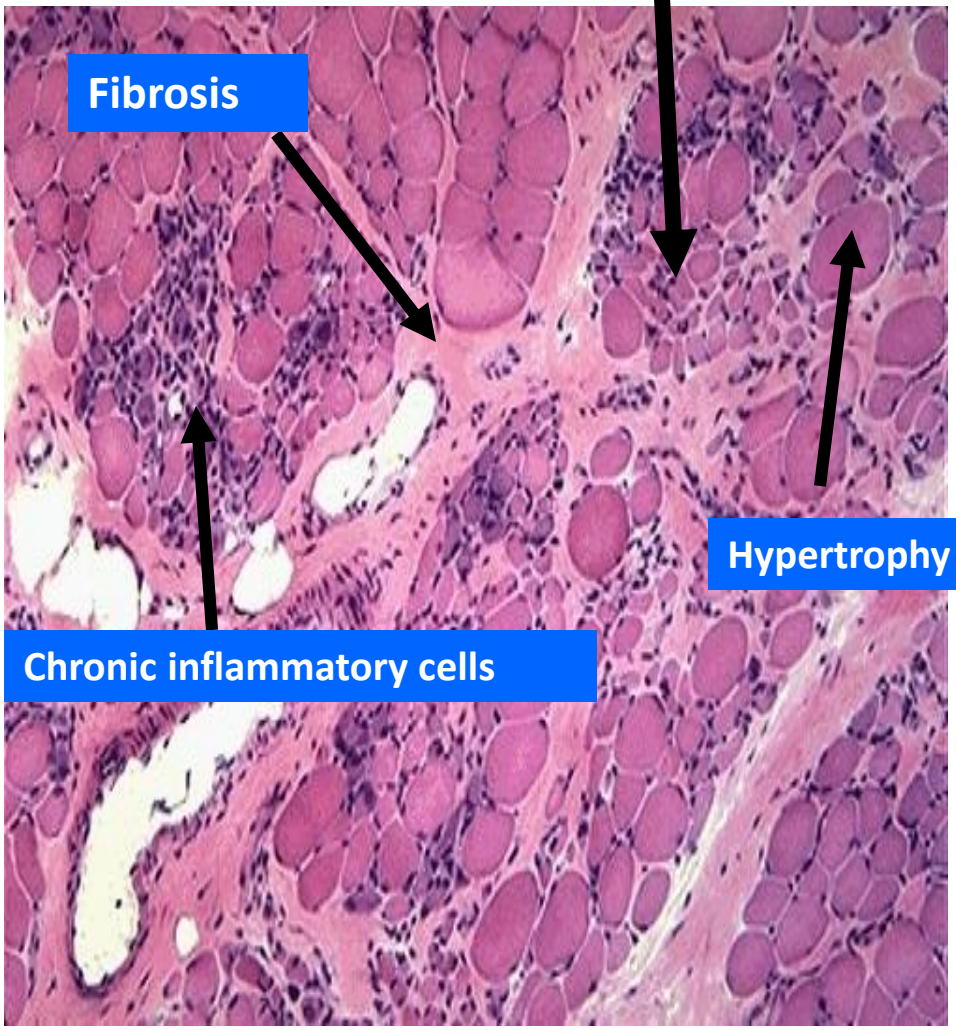
Morphology

- Muscle fibers of various sizes
- Necrosis, degeneration and regeneration of fibers
- Fibrosis
- Fatty infiltration

Normal Muscle



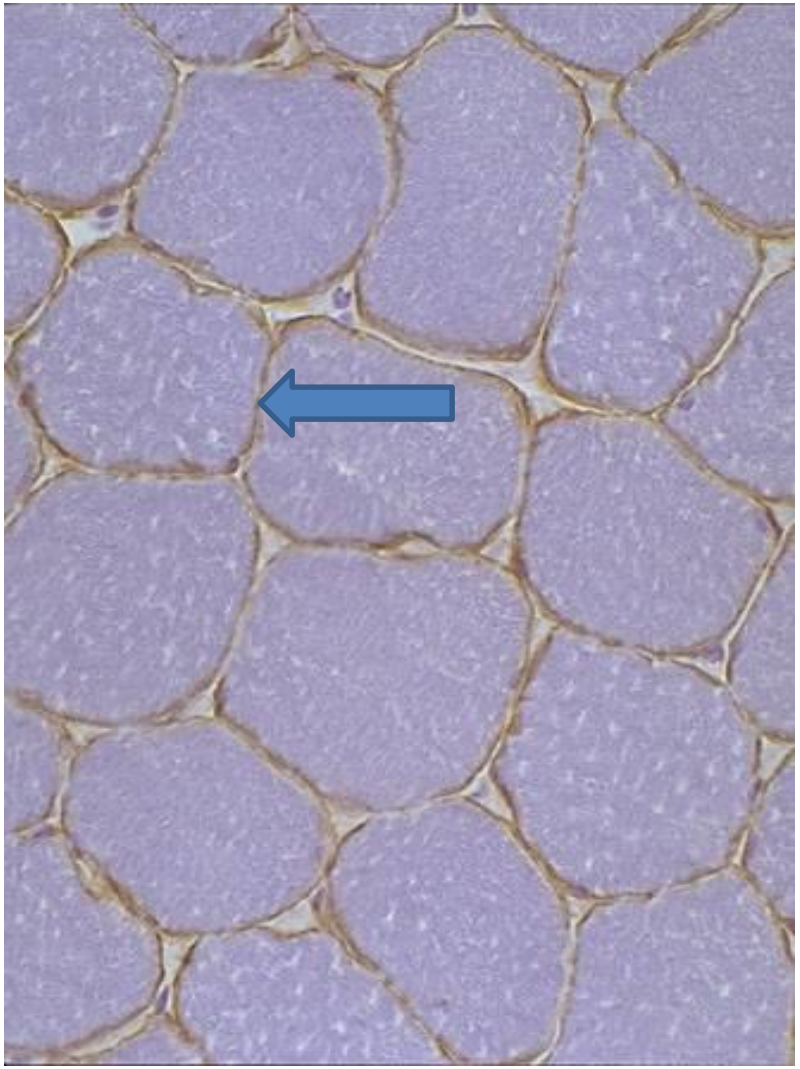
Duchenne muscular dystrophy (DMD)



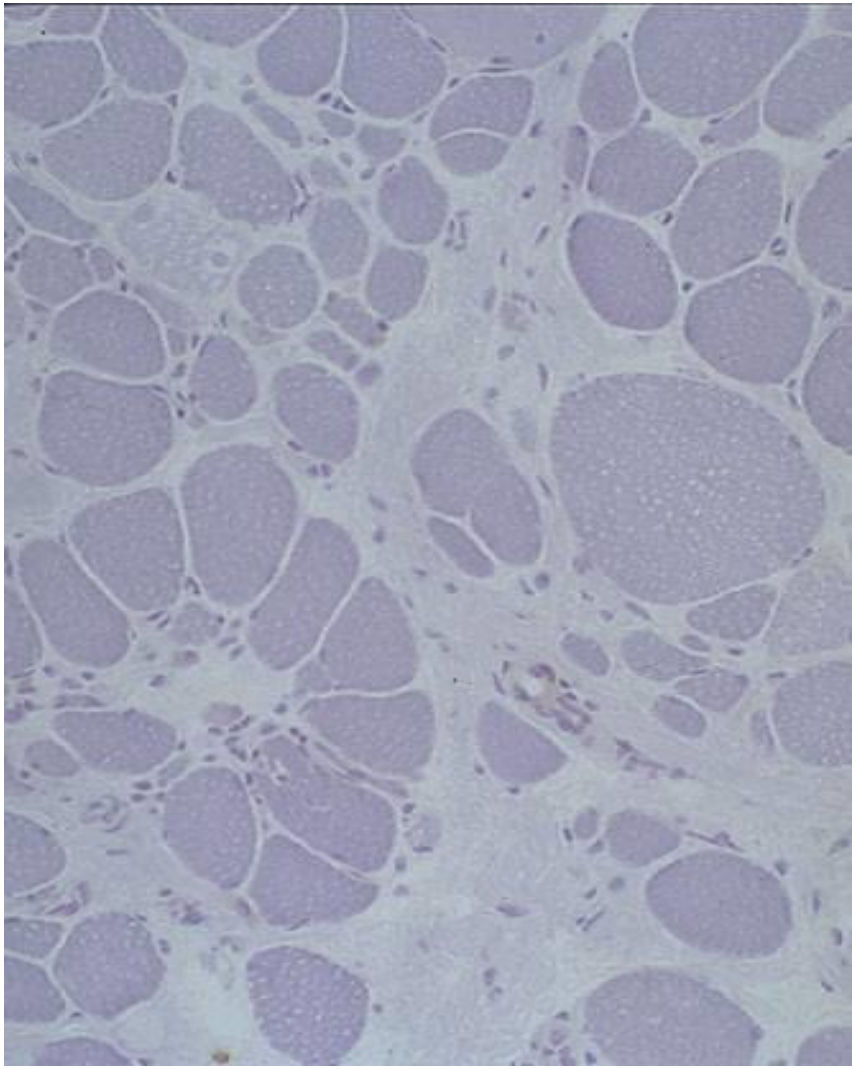
Diagnosis

- Immunostain: Decreased dystrophin protein
- PCR : DNA analysis

Immunoperoxidase stain revealing dystrophin in normal muscle



Immunoperoxidase stain – absence of dystrophin

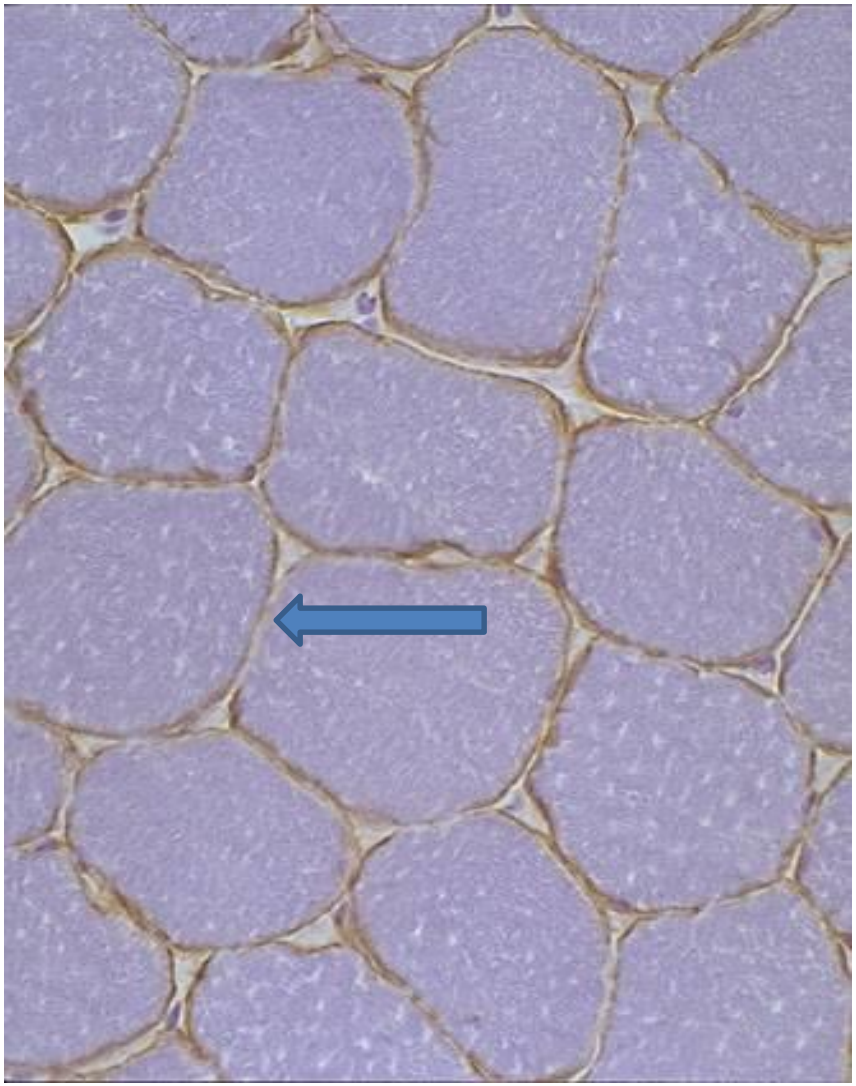


Gower maneuver

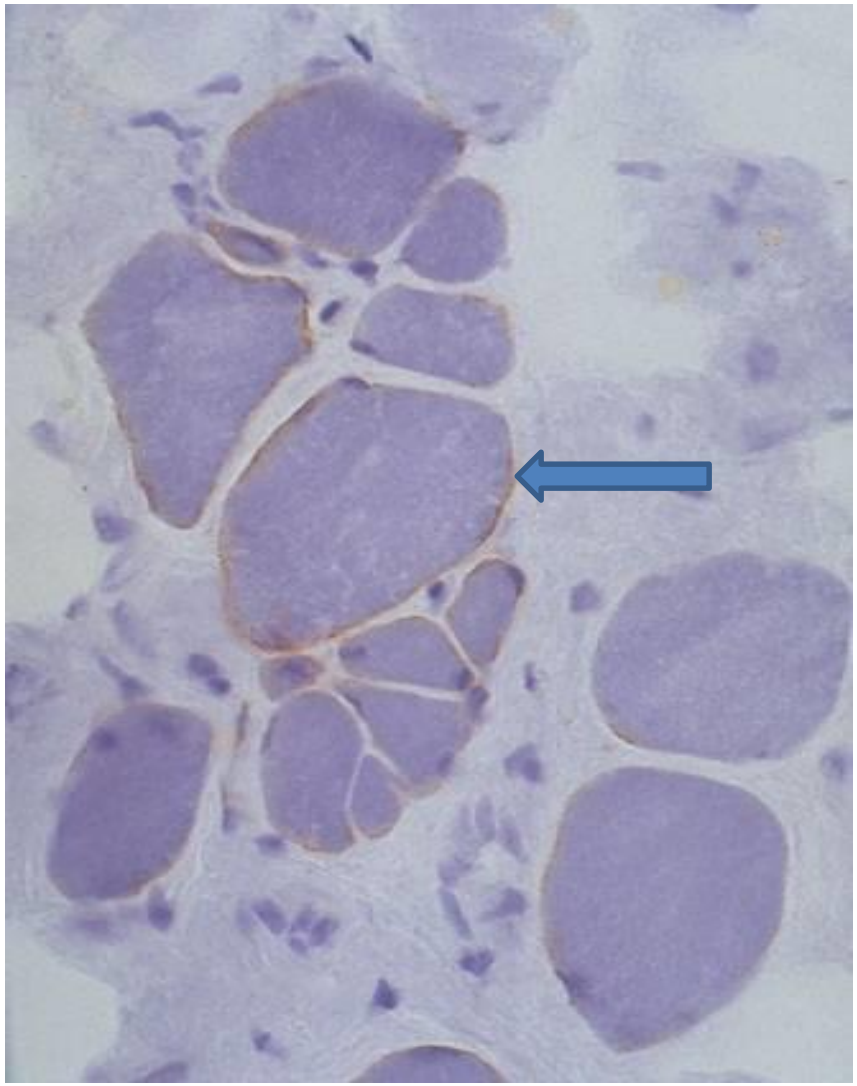
Becker’s muscular dystrophy (BMD)

- Less common and not as severe as Duchenne's.
- Mutation produces an altered dystrophin protein.
- Later onset with variable progression.
- Cardiac involvement is rare
- May have a relatively normal life span.

Immunoperoxidase stain revealing dystrophin in normal muscle



BMD : Dystrophin, present in small amounts



Management

Cardiac disease

- Cardiac surveillance beginning at 10 years and continuing on an annual basis.

- Early treatment of dilated cardiomyopathy with ACE inhibitors and beta blockers
  - improvement in LV function

Respiratory disease

- Baseline pulmonary function tests and respiratory evaluations beginning at age 8 to 9 years.

- Pneumococcal vaccine and annual flu vaccination

- Acute respiratory deteriorations due to infections require early management with antibiotics, chest physiotherapy and respiratory support.

- Nocturnal noninvasive intermittent positive pressure ventilation (NIPPV) for hypercapnia

Orthopedic problems

- Passive stretching
- Night splints
- Surveillance radiographs for scoliosis
- Maintenance of bone density
  - Monitoring of vitamin D levels and supplementing calcium and vitamin D

Corticosteroid Therapy

Prednisolone, prednisone and deflazacort have been the only drugs shown to be effective to date in DMD.

Gene Therapy