NOTES
CONGENITAL MYOPATHIES

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Inherited, progressive myopathic disorders caused by genetic dystrophin gene mutation (dystrophinopathies)
- Duchenne and Becker's muscular dystrophy (most common types)
  - X-linked recessive inheritance pattern
- Dystrophin protein
  - Normally links intracellular actin, dystrophin-associated protein complex to extracellular matrix to stabilize sarcolemma
- Genetic defect → misshapen/absent dystrophin protein → weak sarcolemma, cell damage → creatine kinase escapes from/calcium enters damaged cell → cell death → muscle degeneration → progressive weakness

SIGNS & SYMPTOMS

- Motor development milestone delays (e.g. walking)
- Progressive limb, girdle weakness
- Gowers' sign
  - Weak hips, upper legs → using arms to help stand
- Waddling gait
- Musculoskeletal abnormalities (e.g. calf pseudohypertrophy, scoliosis, contracture)
- Progressive mobility impairment

DIAGNOSIS

- See individual myopathies

TREATMENT

- See individual myopathies

BECKER'S MUSCULAR DYSTROPHY

osms.it/beckers-dystrophy

PATHOLOGY & CAUSES

- Caused by misshapen dystrophin gene due to missense mutation
  - See mnemonic: BMD

MNEMONIC: BMD

Cause of Becker's Muscular Dystrophy

Badly

Made

Dystrophin (truncated protein)

COMPLICATIONS

- Rapidly progressive heart failure, arrhythmia

SIGNS & SYMPTOMS

- Milder form, later onset than Duchenne muscular dystrophy
- Symptoms appear 10–20 years old
- Intellectual disability, contractures not as common/severe as Duchenne muscular dystrophy
- Cardiac fibrosis may be predominant presentation feature
  - Starting with right ventricular involvement, left ventricular dysfunction later

DIAGNOSIS

LAB RESULTS

- ↑ serum creatine kinase
- Mutations in dystrophin by DNA test/ Western blot
- Muscle biopsy
  - Stain for dystrophin

TREATMENT

- No cure

MEDICATIONS

- Glucocorticoids to slow muscle degeneration

OTHER INTERVENTIONS

- Vitamin D, calcium supplements support bone health
- Physical therapy, conditioning
- Complication management

DUCHENNE MUSCULAR DYSTROPHY

osms.it/duchenne_muscular_dystrophy

PATHOLOGY & CAUSES

- Caused by absent dystrophin gene due to nonsense/frameshift mutation
  - See mnemonic: DMD

MNEMONIC: DMD

Cause of Duchenne Muscular Dystrophy

Doesn't
Make
Dystrophin

COMPLICATIONS

- Wheelchair needed for mobility → scoliosis
  - Scoliosis → poor pulmonary function
- Weak diaphragm → respiratory failure (may develop)
- Fibrosis progression in dilated cardiomyopathy → mitral regurgitation (may develop)
- Dilated cardiomyopathy (late stages) → heart failure, arrhythmias (may develop)
- Falling → arm, leg fractures
  - Vertebral compression fractures with glucocorticoid therapy
- Respiratory insufficiency/cardiomyopathy → death (late teens, early twenties)

SIGNS & SYMPTOMS

- More severe dystrophinopathy form
- Symptoms appear by five years old; weakness usually occurs 2–3 years old
- Walking begins later in childhood; may have slow, ungainly run; difficulty jumping, walking up steps
- Proximal-limb muscle weakness before distal, lower extremities before upper
- Gowers' sign
- Waddling gait, calf pseudohypertrophy
- Decreased mobility
  - May lead to independent ambulation impairment, wheelchair-use by 12 years old (usually)
- Primary dilated cardiomyopathy, conduction abnormalities

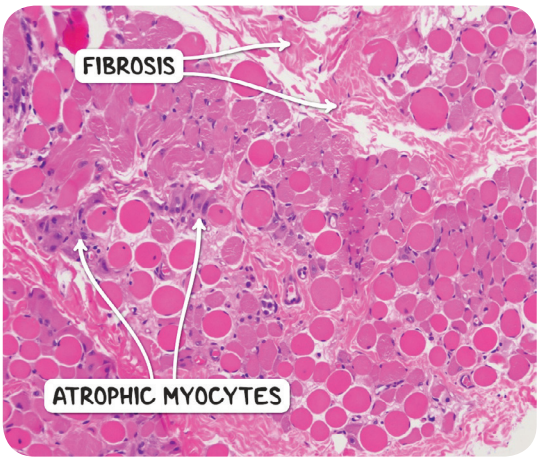

Figure 69.2 A muscle biopsy from an individual in the early stages of Duchenne muscular dystrophy. There is variation in myocyte size with small atrophic myocytes juxtaposed with large, rounded hypertrophic myocytes. There is intervening fibrosis.

DIAGNOSIS

LAB RESULTS

- ↑ serum creatine kinase
- Mutations in dystrophin by DNA test/ Western blot
- Muscle biopsy
  - Stain for dystrophin

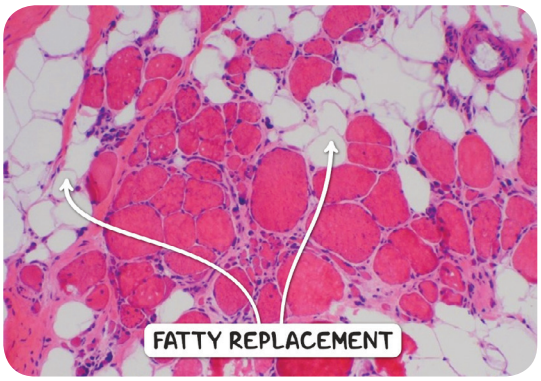

Figure 69.1 A muscle biopsy from an individual in the later stages of Duchenne muscular dystrophy. The myocyte hypertrophy is even more pronounced and there is marked fatty replacement of the muscle.

TREATMENT

- No cure

MEDICATIONS

- Glucocorticoids to slow muscle degeneration

OTHER INTERVENTIONS

- Vitamin D, calcium supplements support bone health
- Physical therapy, conditioning
- Complication management

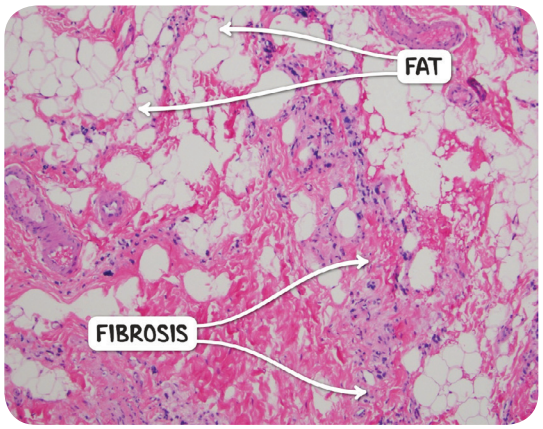

Figure 69.3 A histological section of muscle showing complete fibrofatty replacement in end stage Duchenne muscular dystrophy.