MYOPATHY

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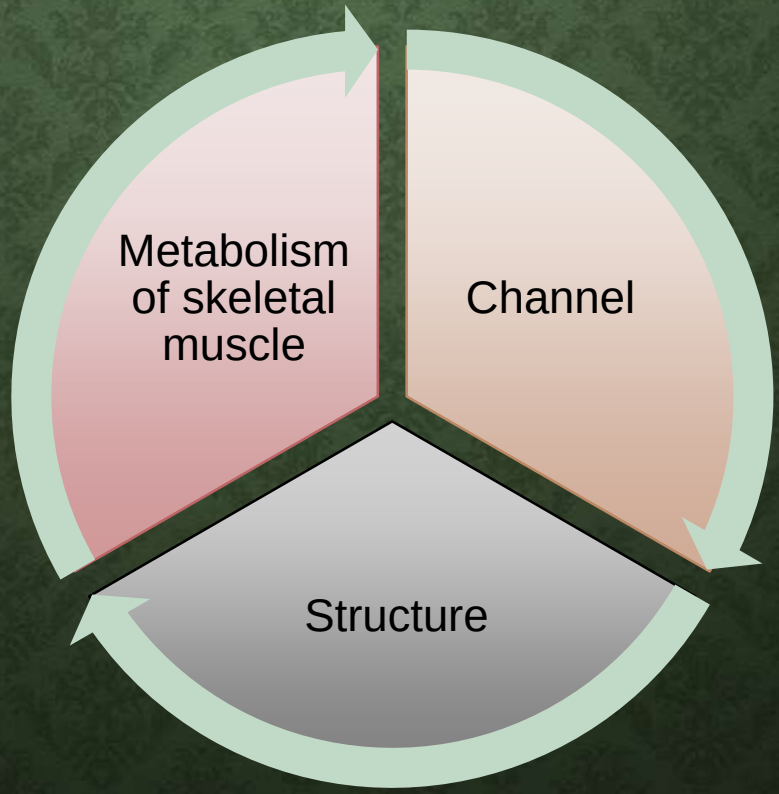
DEFINITION

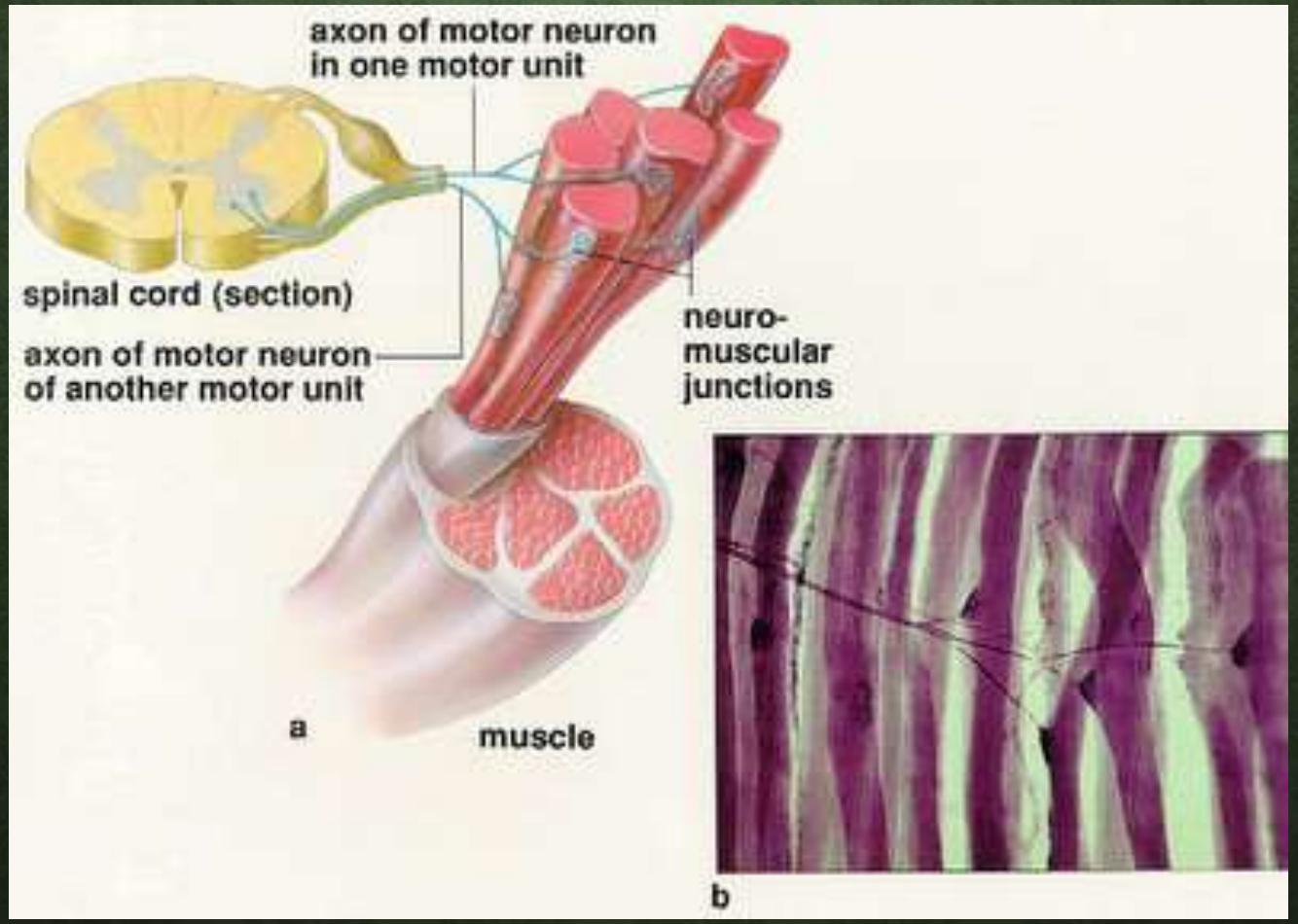
- Myopathy is a neuromuscular disorders in which the primary symptom is muscle weakness due to dysfunction of muscle fiber.
- Hetrogenous disorder
- Myopathies disorder affecting



EPIDEMIOLOGY

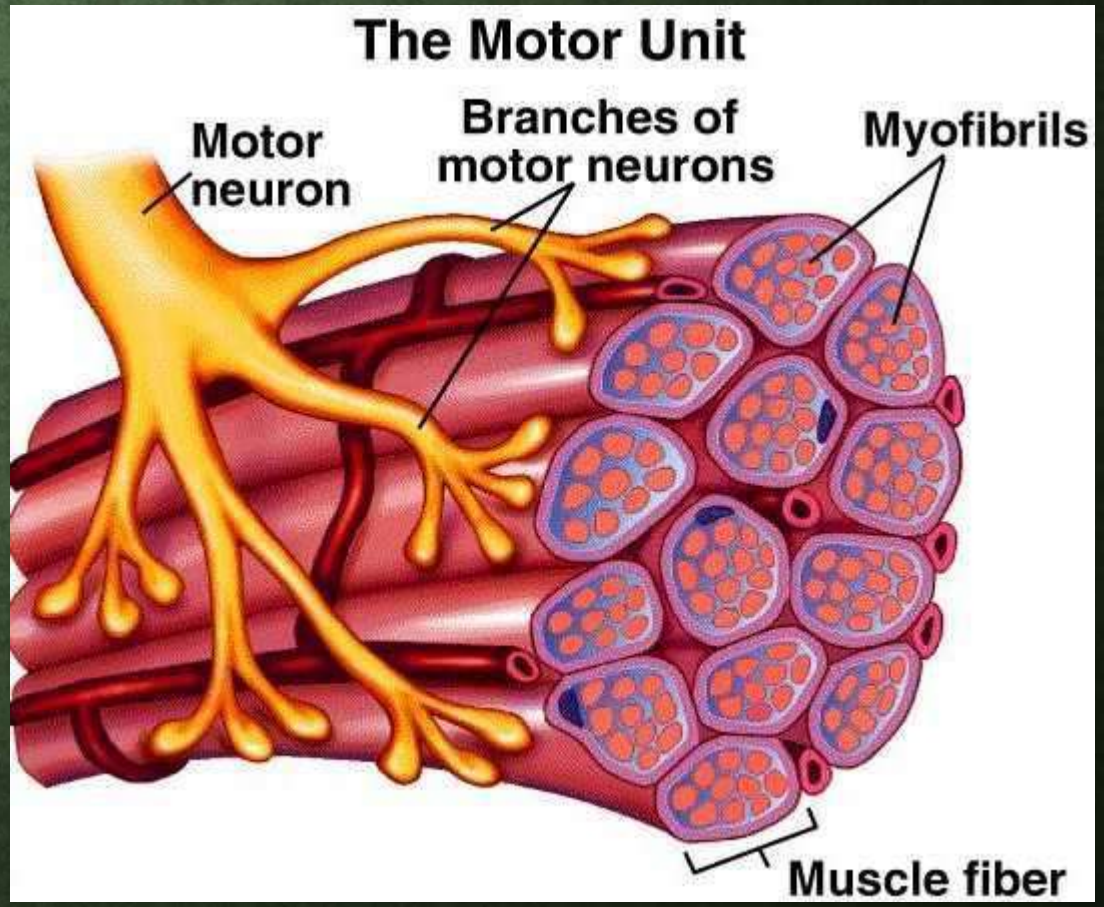
- Worldwide incidence of all inheritable myopathies is about 14%
- Overall incidence of muscular dystrophy is about 63 per 1 million.
- Worldwide incidence of inflammatory myopathies is about 5–10 per 100,000 people.
- More common in women
- Corticosteroid myopathy is the most common endocrine myopathy and endocrine disorders are more common in women
- Overall incidence of metabolic myopathies is unknown.

FUNCTION OF MUSCLE



MOTOR UNIT

- A motor unit is made up of a motor neuron and all the muscle cells it stimulates.
- vary in size
- Small motor units → for precise, small movements
- large motor units → for gross movements.
- The number of cells within a motor unit determines the degree of movement when the motor unit is stimulated.
- Muscle tone is maintained by asynchronous stimulation of random motor units.



CLASSIFICATION OF MUSCLE FIBER TYPE

	Type I fibers	Type II a fibers	Type II x fibers	Type II b fibers
Contraction time	Slow	Moderately Fast	Fast	Very fast
Size of motor neuron	Small	Medium	Large	Very large
Resistance to fatigue	High	Fairly high	Intermediate	Low
Activity Used for	Aerobic	Long-term anaerobic	Short-term anaerobic	Short-term anaerobic
Maximum duration of use	Hours	<30 minutes	<5 minutes	<1 minute
Power produced	Low	Medium	High	Very high
Mitochondrial density	High	High	Medium	Low
Capillary density	High	Intermediate	Low	Low
Oxidative capacity	High	High	Intermediate	Low
Glycolytic capacity	Low	High	High	High
Major storage fuel	Triglycerides	Creatine phosphate, glycogen	Creatine phosphate, glycogen	Creatine phosphate, glycogen
Myosin heavy chain, human genes	MYH7	MYH2	MYH1	MYH4

CLINICAL EVALUATION

History

Muscle Weakness

- Proximal Muscles>distal muscles
- Fatigue
- Difficulty rising from a chair, floor, tub
- Difficulty with stairs
- Difficulty with overhead tasks
- Respiratory muscles
- Bulbar weakness- speech, swallowing, oculomotor, facial

Fatigue

Muscle pain, cramp, stiffness

Paresthesia and dysesthesias

PHYSICAL EXAMINATION

- Demonstration and quantification of weakness
- Muscle bulk
- Muscle palpation
- Fatigue
- Muscle tone
- Reflexes
- Sensation

CLASSIFICATION OF MYOPATHY

- Inherited
- Acquired

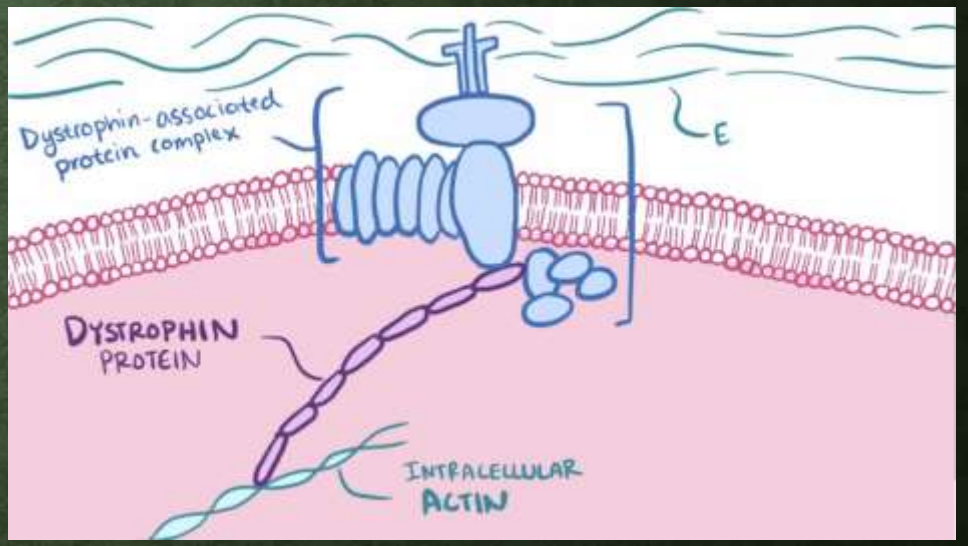
- **inflammatory myopathies**
  - polymyositis
  - dermatomyositis
  - inclusion body myositis
  - **viral**
- **muscular dystrophies**
  - X-linked
  - limb-girdle(ar/d)
  - congenital
  - fasioscapulohumeral (ad)
  - scapuloperoneal (ad)
  - distal (Welander) (ad/r)
- **myotonic syndromes**
  - myotonic dystrophy (ad)
  - inherited
  - Schwarz-Jampel
- **congenital myopathies**
  - central core disease
  - nemaline myopathy
  - myotubular
  - fiber-type disproportion
- **metabolic myopathies**
  - glycogenoses
  - mitochondrial
  - periodic paralysis
- **endocrine myopathies**
  - **thyroid**
  - parathyroid
  - adrenal / steroid
  - pituitary
- **drug-induced / toxic**

MUSCULAR DYSTROPHY

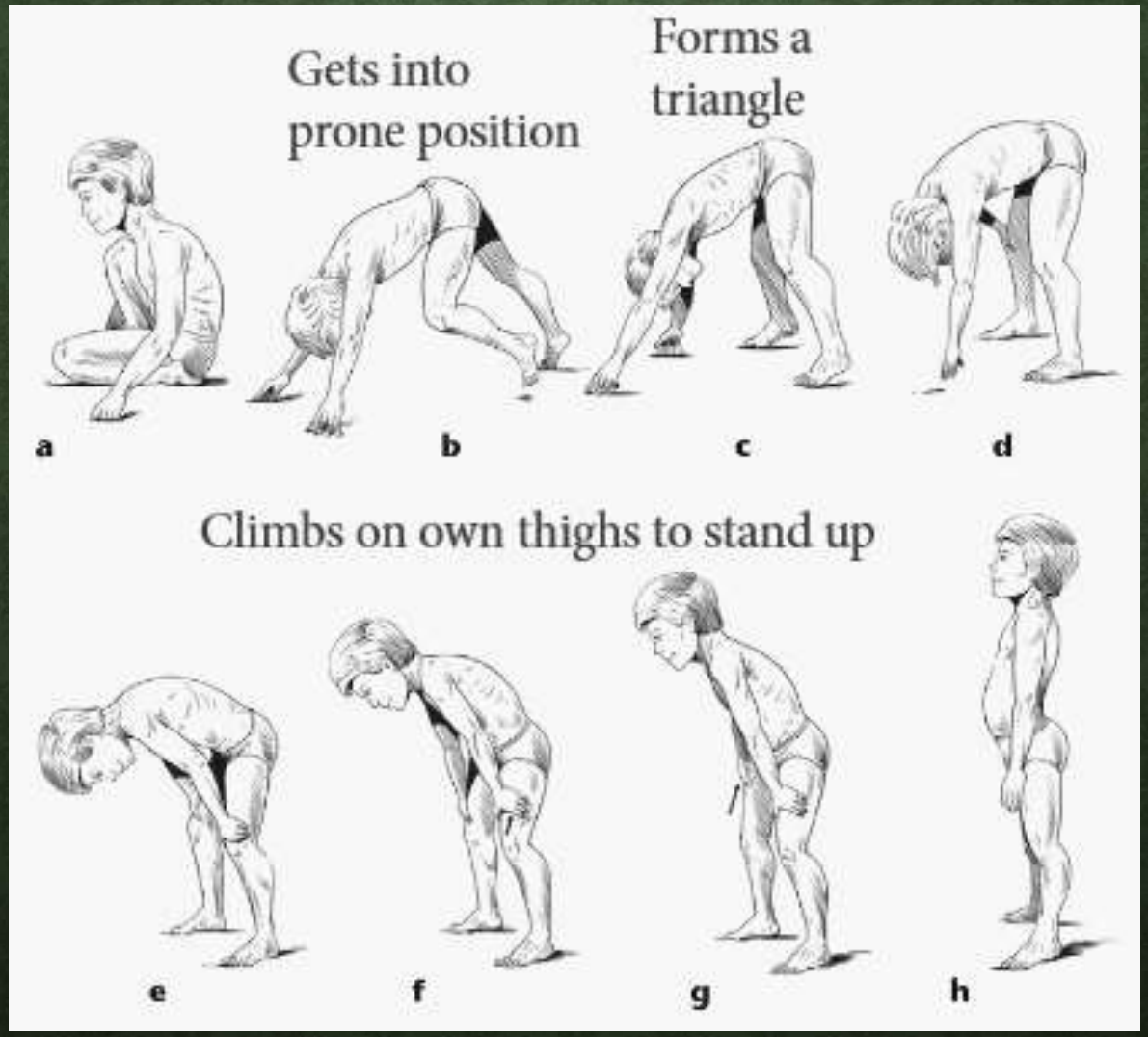
- Muscular dystrophy refers to a group of hereditary progressive diseases each with unique phenotypic and genetic features.
- Dystrophinopathies: Duchenne’s Muscular Dystrophy and Becker’s Muscular Dystrophy
- Facioscapulohumeral muscular dystrophy
- Emery-Dreifus muscular dystrophy
- Limb-girdle muscular dystrophy
- Myotonic dystrophy

DUCHENNE'S MUSCULAR DYSTROPHY

- Duchenne's muscular dystrophy (DMD) also called pseudo hypertrophic muscular dystrophy.
- It is an X linked recessive disorder.
- Dystrophin is deficient.
- The incidence of DMD is 1 in 3500 male births worldwide,
- DMD clinical feature:
  - It is present at birth but becomes evident at 3-5 years.
  - Gower's maneuver
  - Joint contractures, scoliosis, decreased pulmonary functions.
  - By 16 to 18 years patients die of severe pulmonary infections or aspiration pneumonia.
  - Respitatory failure in 2nd or 3rd decade.
  - IQ <~1 SD of the mean.



GOWER'S MANEUVER



Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Duchenne's muscular dystrophy (DMD)	XR Xp21 Dystrophin	• Onset: ages 2-6 yr • Delayed milestones • Progressive weakness of "girdle" muscles • Calf pseudohypertrophy • Inability to walk after age 12 yr • Joint contractures • Scoliosis	• Respiratory failure in 2nd to 3rd decade • Cardiomyopathy • Impaired intellectual function • Gastroparesis	• Clinical • Increased CK • DNA analysis • In some cases, EMG and muscle biopsy	• Pharmacological: steroids • Rehabilitative: PT/OT, ROM, contracture management, assistive devices, weight control, ambulation, seating, bracing • Pulmonary: assisted ventilation • Surgical: contracture release, spinal stabilization for scoliosis

BECKER'S MUSCULAR DYSTROPHY

- X linked recessive inheritance.
- Less severe form.
- Dystrophin muscle protein is deficient.
- The incidence of BMD is 5 in 100,000.

Clinical features:

- Muscle wasting resembles Duchenne's.
- Proximal muscle weakness of lower extremities occur first.
- Onset 5-15 years or even 3rd to 4th decade.
- Patients may survive till 4th or 5th decade.

Laboratory findings are similar to that of Duchenne's muscular dystrophy.

Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Becker's muscular dystrophy (BMD)	XR Xp21 Dystrophin	• Onset: variable, but still ambulatory after age 15 yr • Progressive weakness of girdle muscles • Calf pseudohypertrophy • Respiratory failure after 4th decade	• Cardiomyopathy • Impaired intellectual function	• As in DMD	• As in DMD

Rehabilitation Approaches to the Treatment of Myopathies

Approach	Comments
Patient evaluation	
Initial assessment	Needed to assess impairments, stage of illness, and overall disease activity and damage and to gauge responses to therapy
Function	Needed to assess ability to perform physical tasks, interact psychosocially, and communicate to establish level of disability and to follow outcomes of treatment strategies
Quality of life	Needed to assess overall satisfaction with life activities and make treatment recommendations to improve it
Exercise	
Range of motion and stretching	Needed to preserve, maintain, and increase joint motion
Gentle toning exercises	May be used to maintain muscle strength Avoid overwork, high-resistance and eccentric exercises
Aerobic	Needed to maintain aerobic capacity and improve overall functional level
Recreational	Recommended to improve quality of life and provide socialization and informal exercise
Adaptive thinking	
Educational strategies	Instruction in energy conservation and compliance with exercise is essential
Assistive devices	Assistive devices can raise the individual's functional level from requiring the assistance of a person to independence with assistive devices
Heat and cold	Heat is used to increase collagen extensibility before tight joints are stretched Cold is useful for reducing pain and muscle spasm
Orthoses	Short leg bracing is used to compensate for quadriceps and ankle dorsiflexion weakness Long leg braces may be used to assist with ambulation in select patients

Adapted from Hicks JE: Role of rehabilitation in the management of myopathies, *Curr Opin Rheumatol* 10:551, 1998.

Prevention of Deformities in Duchenne's Muscular Dystrophy

Intervention	Timing	Comment
Achilles tendon stretching	As soon as possible	Typically already at diagnosis
Night splints	If loss of range of motion is ≥20°	Commonly a few years after diagnosis
Hip stretching	When contractures are detected	Common toward late phases of ambulation
Iliotibial band stretching	When contractures are detected	May occur during late phases of ambulation
Knee stretching	When contractures are detected	Rarely needed; may be found in children with asymmetrical ankle contractures

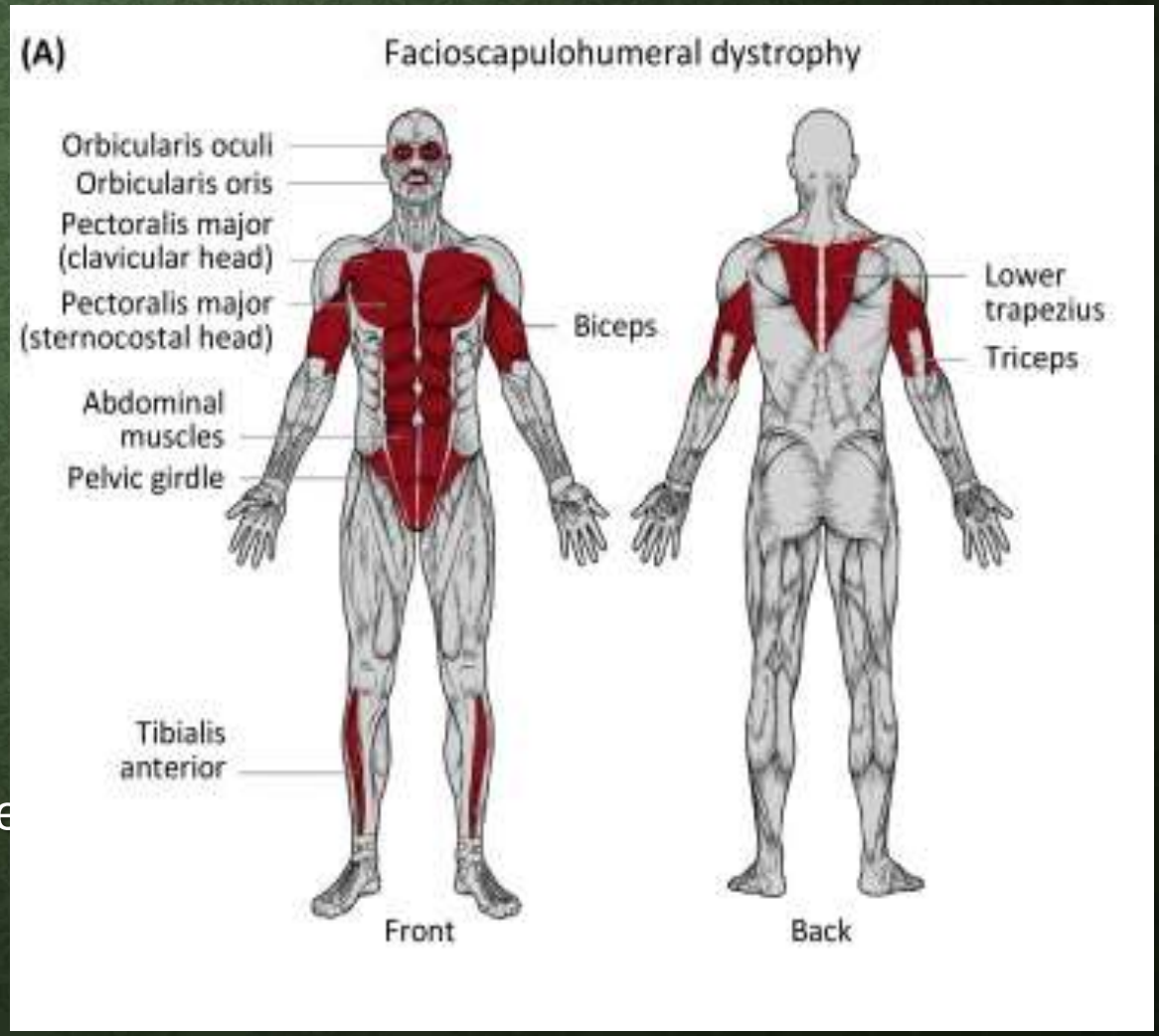
From Emery AEH, Muntoni F: *Duchenne muscular dystrophy*, ed 3, p 210, New York, 2003, Oxford University Press.

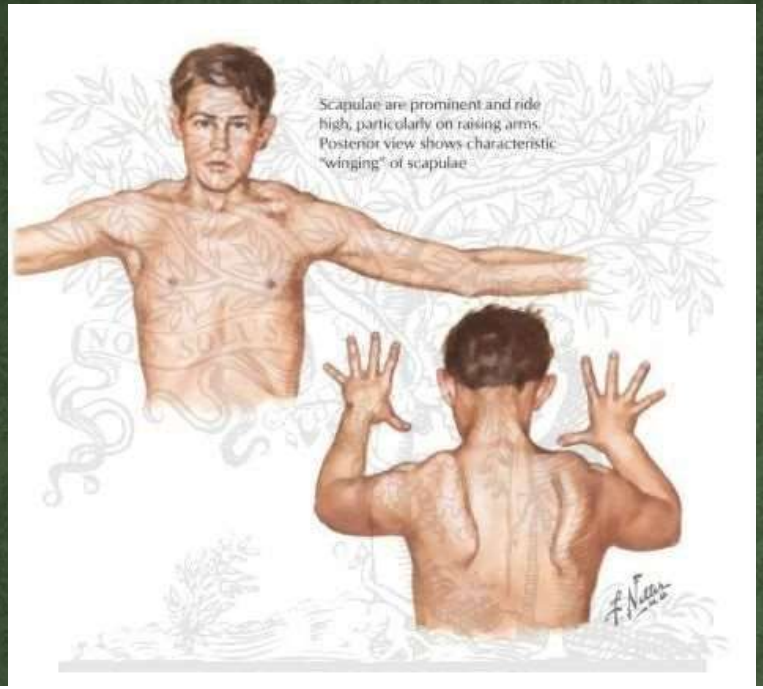
FACIOSCAPULOHUMERAL MUSCULAR DYSTROPHY

- Third most common after DMD and myotonic
- Onset of occurrence is childhood or young adulthood (age 3 to 44)
- Prevelence ranging from 1 in 20,000 to 1 in 455,000
- Autosomal dominant linked to chromosome 4q35

Clinical feature

- Onset is incidious
- Difficulty in overhead activity
- Humeral muscle affected with sparing of FA muscle give ‘popeye’ appereance
- Positive beevor sign





Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Facioscapulohumeral muscular dystrophy (FSHD)	AD 4q35	• Onset: 1st to 5th decade • Slowly progressive weakness of the face, shoulder girdle and scapular stabilizers, core and pelvic girdle muscles, tibialis anterior	• Pain in the neck, shoulders, posterior chest, lower back • Sensorineural hearing loss and retinal abnormalities in infantile-onset FSHD • Weakness of muscles of ventilation and cardiomyopathy possible in rare cases	• Clinical • CK: normal/ slightly elevated • EMG: myopathic • Muscle bx: myopathic changes • DNA analysis is gold standard for diagnosis	• Pharmacological: none • Rehabilitation: PT, OT, bracing, pain management • Surgical: scapular stabilization

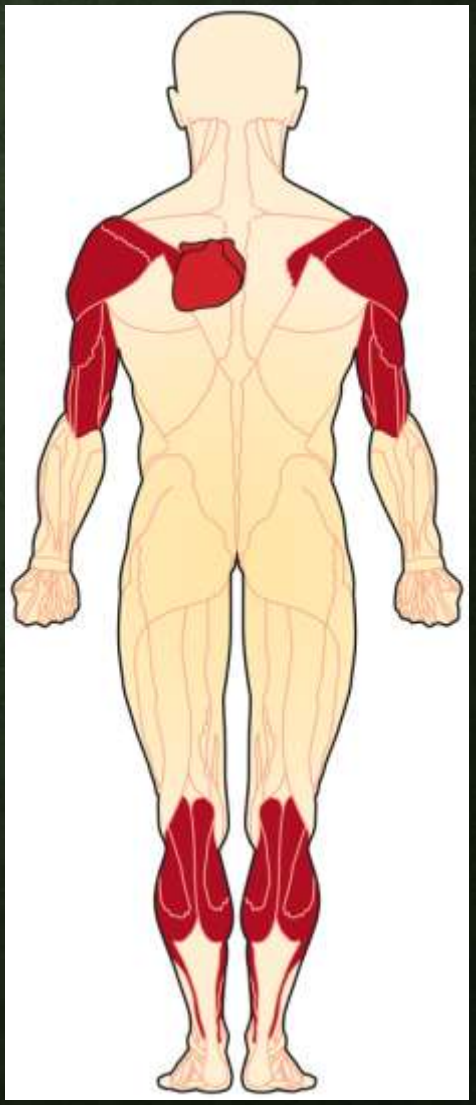
EMERY-DREIFUSS MUSCULAR DYSTROPHY

- Caused by mutation in STA gene which code for key nuclear protein or LMNA gene which code for lamins A and C.
- The X-linked form affects males, but females may present with isolated cardiomyopathy and therefore require cardiac evaluation.
- EDMD is characterized by a **triad** of clinical features:

  (1) early contractures in the elbows, Achilles tendon, and posterior cervical spinal muscles

  (2) slowly progressive muscle weakness, which begins in a humeroperoneal distribution;

  (3) cardiac abnormalities such as cardiomyopathy and conduction defects.



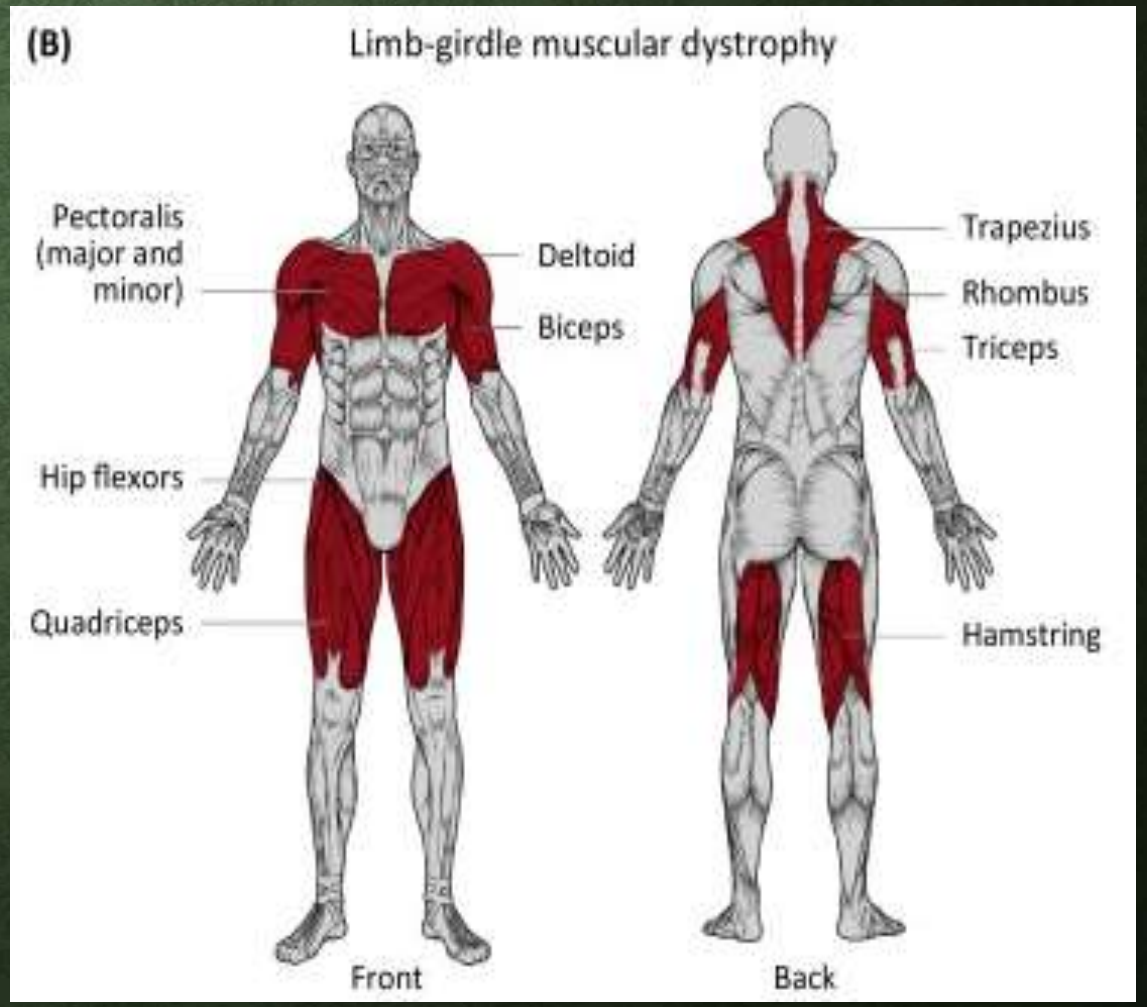
Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Emery-Dreifuss muscular dystrophy (EDMD)	XR Xq28 Emerin AD 1q11 Lamin A/C Mutations in other genes have been identified in selected individuals with an EDMD clinical phenotype	• Triad 1. Early contractures 2. Slowly progressive muscle weakness in humeroperoneal distribution 3. Cardiac abnormalities	• Sudden death from cardiac conduction defects • Gene mutations may manifest as isolated cardiomyopathy	• Clinical • CK: normal/ slightly increased • ECG: conduction abnormalities and arrhythmias • EDX: myopathic • DNA analysis	• Pharmacological: none • Cardiac evaluation, may require pacemaker and or implanted defibrillator • Rehabilitation: contracture management • Surgical: contracture release

LIMB-GIRDLE MUSCULAR DYSTROPHY

- Genetically heterogeneous group of disorders with an autosomal dominant (LGMD 1) or autosomal recessive (LGMD 2) mode of inheritance.
- The prevalence is approximately 8.1 in 1 million inhabitants.
- Underlying pathophysiology is unknown.

Clincal features;

- Lower limb and pelvic girdle weakness, later UL weakness and scapular winging
- Facial and extraocular muscle spared
- Diaphragmatic weakness
- Cardiac abnormality



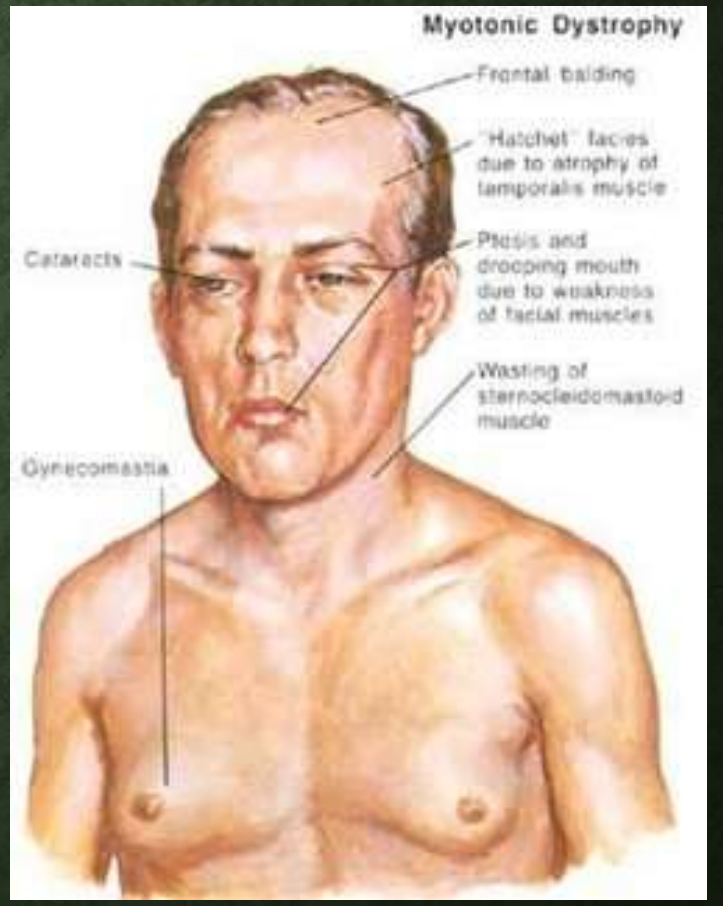
Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Limb-girdle muscular dystrophy	Multiple	• Onset: childhood to adulthood • Slowly progressive muscle weakness in pelvic girdle and shoulder girdle • Cardiac abnormalities (10%) • Onset: late childhood to adolescence	• Respiratory insufficiency	• Clinical, family history • CK: elevated • EDX: myopathic • Muscle bx: necrosis and regeneration, variable fiber size, increased connective tissue • DNA analysis	• Pharmacological: ?Creatine monohydrate • Cardiac monitoring • Rehabilitation: PT, OT to maintain mobility, minimize contractures, provide assistive devices • Ventilatory support

MYOTONIC DYSTROPHY

- Autosomal dominant mode of inheritance mapped to chromosome 19q13,53 which codes for the myotonic dystrophy protein kinase (DMPK).
- Incidence of myotonic dystrophy is approximately 13.5 in 100,000 live births, and the prevalence is 3 to 5 per 100,000.14.

Clinical features:

- Slow progressive weakness of face, jaw and distal limb
- Frontal baldness, ptosis, and atrophy in the temporalis and masseter muscles result in a characteristic “hatchet-faced” appearance.
- Dysarthria and dysphagia
- Myotonia
- Warm-up phenomenon



Systemic Involvement in Myotonic Dystrophy

System	Principal Involvement
Smooth muscle	Reduced gastrointestinal motility, constipation, pseudo-obstruction
Heart	Cardiomyopathy and conduction defects, such as heart block, atrial arrhythmias; sudden cardiac death may occur
Lungs	Hypoventilation from and diaphragmatic involvement; sleep apnea; aspiration pneumonia secondary to dysphagia
Brain	Behavioral and cognitive abnormalities common in DM1 and most severe in congenital DM1
Endocrine system	Testicular tubular atrophy; impotence; infertility; diabetes mellitus; hypothyroidism
Eye	Cataracts, ptosis
Skin	Premature balding

Modified from Engel AG, Franzini-Armstrong C, editors: *Myology,* ed 3, vol 2, p 1044, New York, 2004, McGraw-Hill.

Management of Myotonic Dystrophy

Problem	Management
Cardiopulmonary	
Arrhythmias and other heart conduction defects	Regular electrocardiograms and echocardiograms; drug management as appropriate for specific arrhythmia; pacemaker/implanted defibrillator if conduction defect severe or episodes of significant heart block; avoid aggravation by antimyotonic drugs
Hypoventilation	Consider assisted nocturnal ventilation (CPAP, BiPAP)
Central Nervous System	
Somnolence (sleepiness)	Exclude hypoventilation as cause; consider use of modafinil if severe
Depression and behavioral abnormalities	Pharmacological treatment
Gastrointestinal	
Swallowing difficulty	Dysphagia diet and compensatory strategies; feeding tubes may be considered
Constipation	Pharmacological treatment with stool softeners
Endocrine	
Diabetes mellitus type 2	Periodic monitoring of blood glucose and Hb A_{1c}
Other endocrine problems	Periodic monitoring of TSH; endocrine evaluation for infertility/impotence/testicular atrophy if clinically indicated
Ophthalmic	
Cataract	Periodic ophthalmological examination
Surgery and Anesthesia	
	Patients at higher risk for complications from general anesthesia and neuromuscular blocking agents

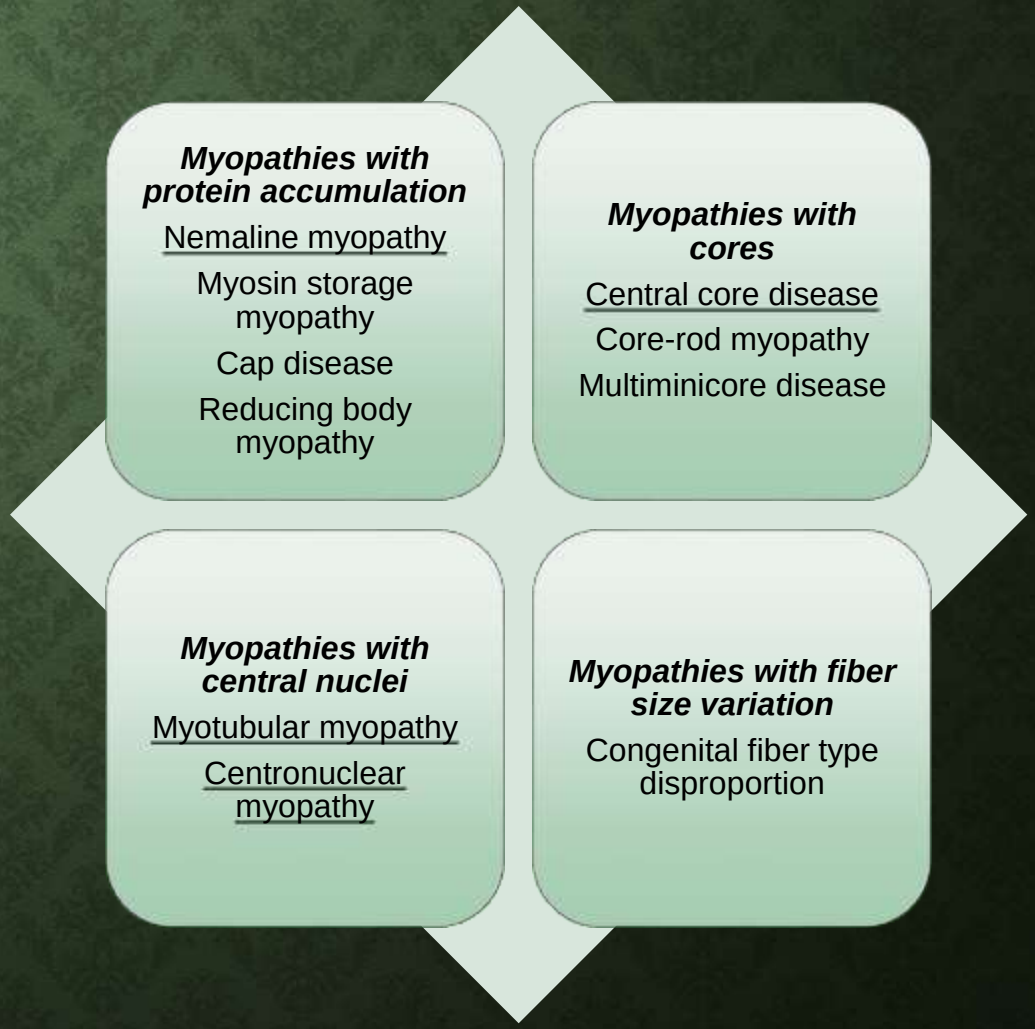
CPAP, Continuous positive airway pressure; *BiPAP,* bilevel positive airway pressure; *TSH,* thyroid-stimulating hormone; *Hb* A_{1c}, glycated hemoglobin.

Modified from Engel AG, Franzini-Armstrong C, editors: *Myology,* ed 3, vol 2, p 1070, New York, 2004, McGraw-Hill.

Type	Mode of Inheritance/ Gene Location/Gene Product	Clinical Presentation	Associated Features	Diagnosis	Treatment
Myotonic muscular dystrophy	AD 19q13 Myotonic dystrophy Protein kinase	• Onset: any age • Slowly progressive muscle weakness in face, distal limb • Percussion myotonia	• Cataracts, cardiac abnormalities, respiratory abnormalities, gastrointestinal abnormalities, CNS abnormalities, endocrine abnormalities	• Clinical • EDX: myotonic discharges • Muscle bx: myopathic • DNA analysis	• Pharmacological: medications for myotonia • Rehabilitation: PT, OT for contracture management, assistive devices, modification of ADLs

CONGENITAL MYOPATIES

• Heterogeneous group of nonprogressive or slowly progressive muscle disorders that usually present in the neonatal period.
• Not considered muscular dystrophies
• present with generalized weakness, hyporeflexia and hypotonia
•Delayed motor milestone and decreased muscle bulk
•A recent review article (North K., 2008) divided the congenital myopathies based on genetic and morphological features into 4 main groups:
• Affected both sexes equally
• laboratory finding: normal or minimally elevated CK level, emg finding can show polyphasic motor unit potential
• Management is multidisciplinary apporach



Management of Patients with Congenital Myopathies

Problem	Referral	Possible Interventions
Skeletal muscle involvement Hypotonia Weakness Contractures	Physical therapy and occupational therapy	Submaximum aerobic exercise program and gentle toning Active and passive stretching Standing frame Orthoses/splinting (upper and lower limbs) Enhance mobility (walking frames or wheelchair)
Respiratory muscle involvement Nocturnal hypoxia	Physical therapy Lung function tests Sleep study	Chest physiotherapy to clear secretions Nocturnal assisted ventilation
Bulbar involvement Feeding and swallowing difficulties Failure to thrive Excessive drooling	Speech pathologist Dietitian Gastroenterologist	Speech therapy Modified barium swallow Caloric supplementation/thickened feed Feeding tubes Anticholinergic medications
Developmental or psychosocial delay	Occupational therapy Physical therapy Speech pathology Psychologist Developmental physician	Advice about appropriate intervention/liaise with local services Developmental stimulation Home programs Reassessment if deterioration occurs
Scoliosis	Physiotherapy Orthopedic surgeon	Baseline assessment, including spinal radiographs Monitoring of degree of curve Bracing Corrective surgery
Foot deformities	Physical therapy Orthopedic surgeon	Splinting/serial casting Corrective surgery
Cardiac involvement; conduction defects; cardiomyopathy	Cardiologist	Electrocardiogram, Holter monitor, cardiac echocardiogram Medication if indicated

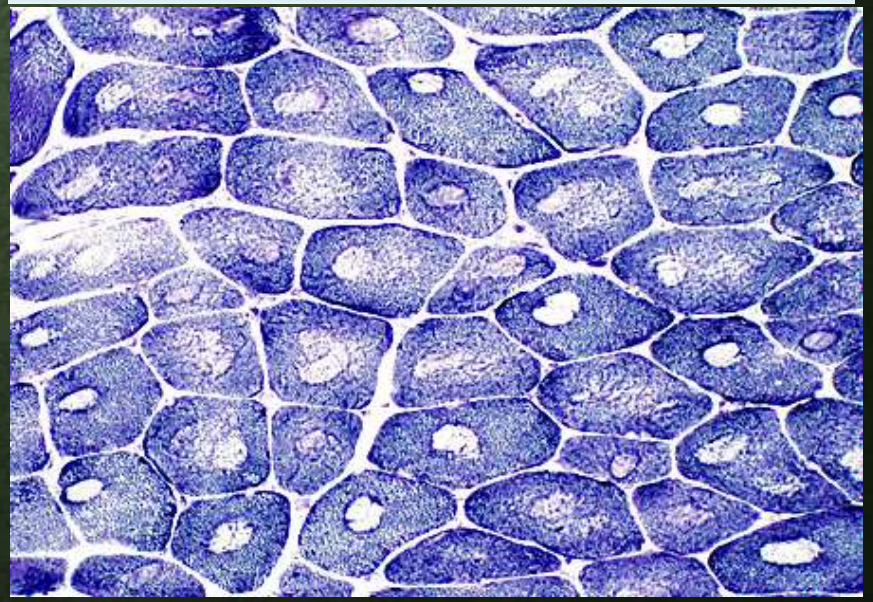
Management of Patients with Congenital Myopathies

Problem	Referral	Possible Interventions
Inability to perform activities of daily living (ADLs); inability to achieve independence with bathing, toileting, dressing, feeding; difficulties with access; handwriting difficulties	Occupational therapy Community nurse	Aids for individual ADLs Wheelchair assessment Home nursing assistance Home visit and modifications School visit and modifications Typing and computer programs Car modifications Liaise with local services
Family support	Social work Muscular Dystrophy Association Government assistance agencies	Disability allowance/pension Caregivers' allowance Support groups Financial assistance with equipment and home modifications Transport and travel assistance
Planning future pregnancies	Genetic counselor	Genetic counseling
Planning surgery	Consult with anesthetist Respiratory physician	Malignant hyperthermia precautions Lung function tests and physiotherapy before surgery
Planning future employment	Vocational counseling service Occupational therapy	Planning school studies Vocational planning Work experience Training, work placement and support
Coordination of care	Pediatrician or subspecialist with an interest Neurologist, geneticist, or rehabilitation specialist	Contact with general practitioner by telephone Liaise with local services Copy of all correspondence to key personnel Arrange case conferences when necessary Determine timing of respiratory, orthopedic, and palliative interventions

Modified from Engel AG, Franzini-Armstrong C, editors: *Myology*, ed 3, vol 2, pp 1521-1522, New York, 2004, McGraw-Hill.

CENTRAL CORE MYOPATHY

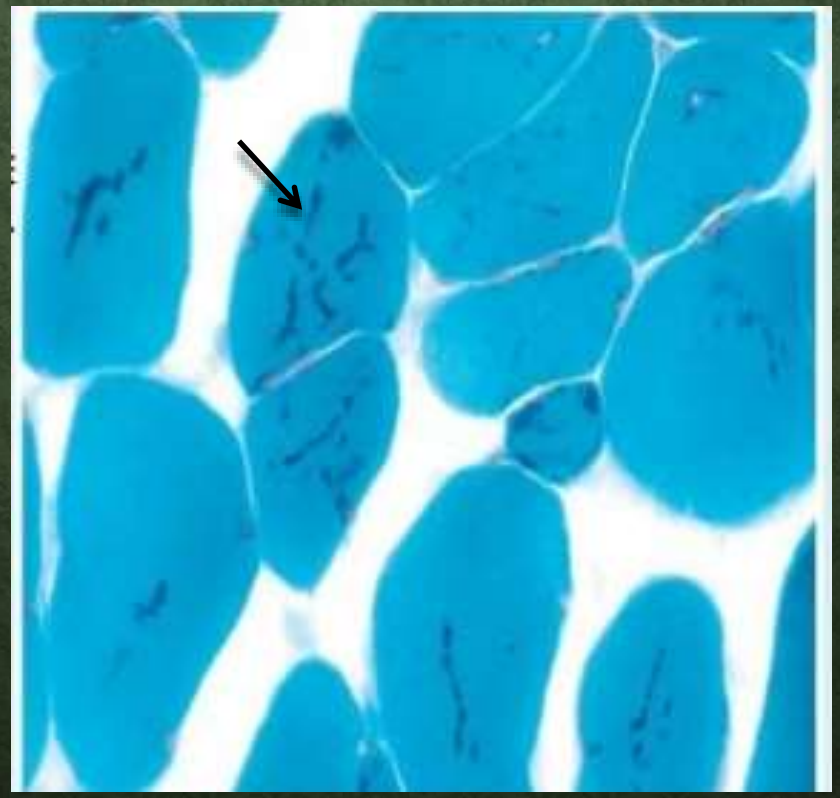
- Autosomal dominant
- Mutation in ryanodine receptor gene *(RYR1)*
- Higher risk for malignant hyperthermia
- Presentation: hypotonia, decreased muscle bulk, slender frame, and symmetrical weakness.
- Weakness can varies and predominantly affect proximal muscle of lower limb
- Motor milrstone delayed but able to walk by age 3 to 4.
- No CNS abnormality
- Muscle biopsy shows characteristic structural alterations within the center of type 1 muscle fibers known as cores. These cores are single, centrally located, and circular.



NEMALINE MYOPATHY

- Nema in Greek means thread.
- An autosomal dominant, recessive, or sporadic mode of inheritance
- Caused by mutations in genes that code for proteins that are responsible for the development and function of the Z-disks, including actin, troponin, nebulin, and tropomyosin.
- The disease may present as three phenotypes and the most severe phenotype is the infantile onset, common phenotype is childhood onset.
- Neonates present with hypotonia, feeding and respiratory difficulty, children can have delayed milestones
- The long, narrow facies, higharched palate, and openmouthed appearance due to a prognathous jaw. Pectus excavatum, kyphoscoliosis, pes cavus, and clubfoot deformities.

- Muscle biopsy reveals characteristic threadlike structures (rods) that consist of Z-disk protein material
- No specific pharmacological treatment is available. Rehabilitation should focus on maintaining function and preventing deconditioning through mild exercise and physical therapy.



MYOTUBULAR/ CENTRONUCLEAR MYOPATHY

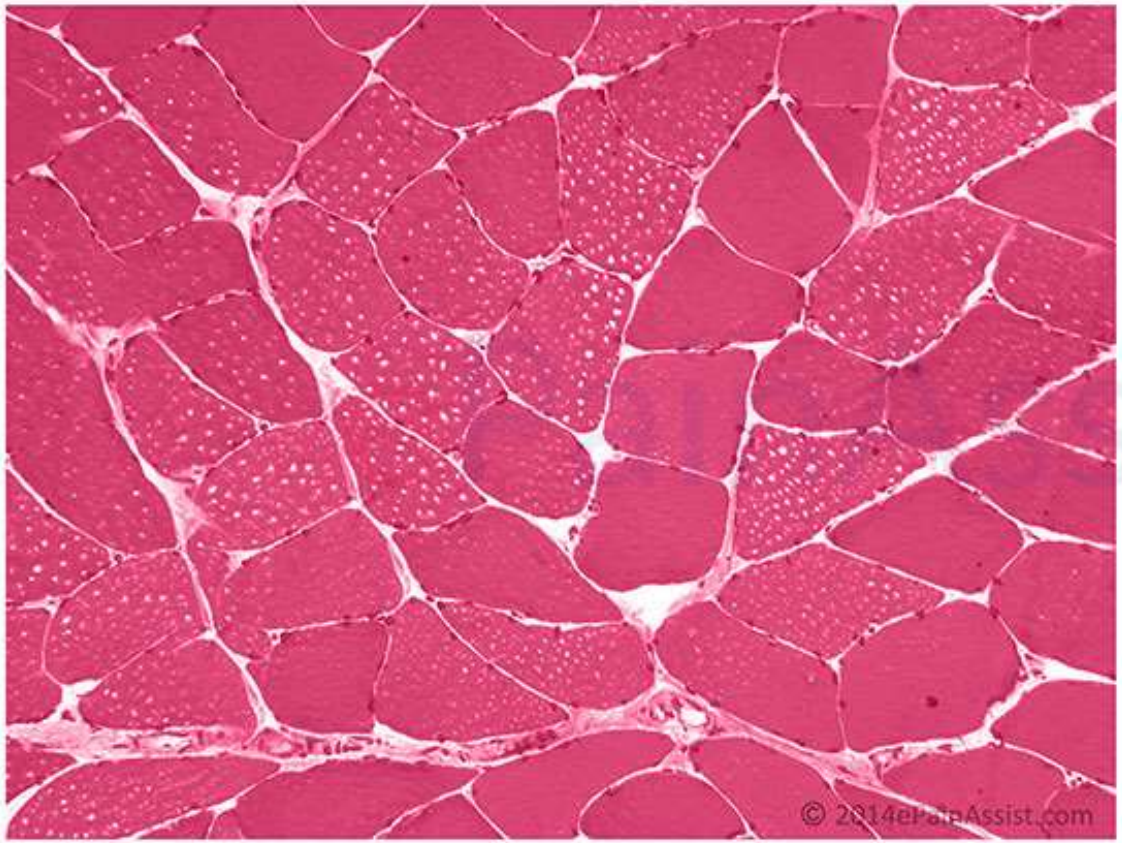
- The disease can be X-linked, mapped to chromosome Xq28 at a locus coding for myotubularin.
- It can have an autosomal dominant or recessive mode of inheritance

Three variants:

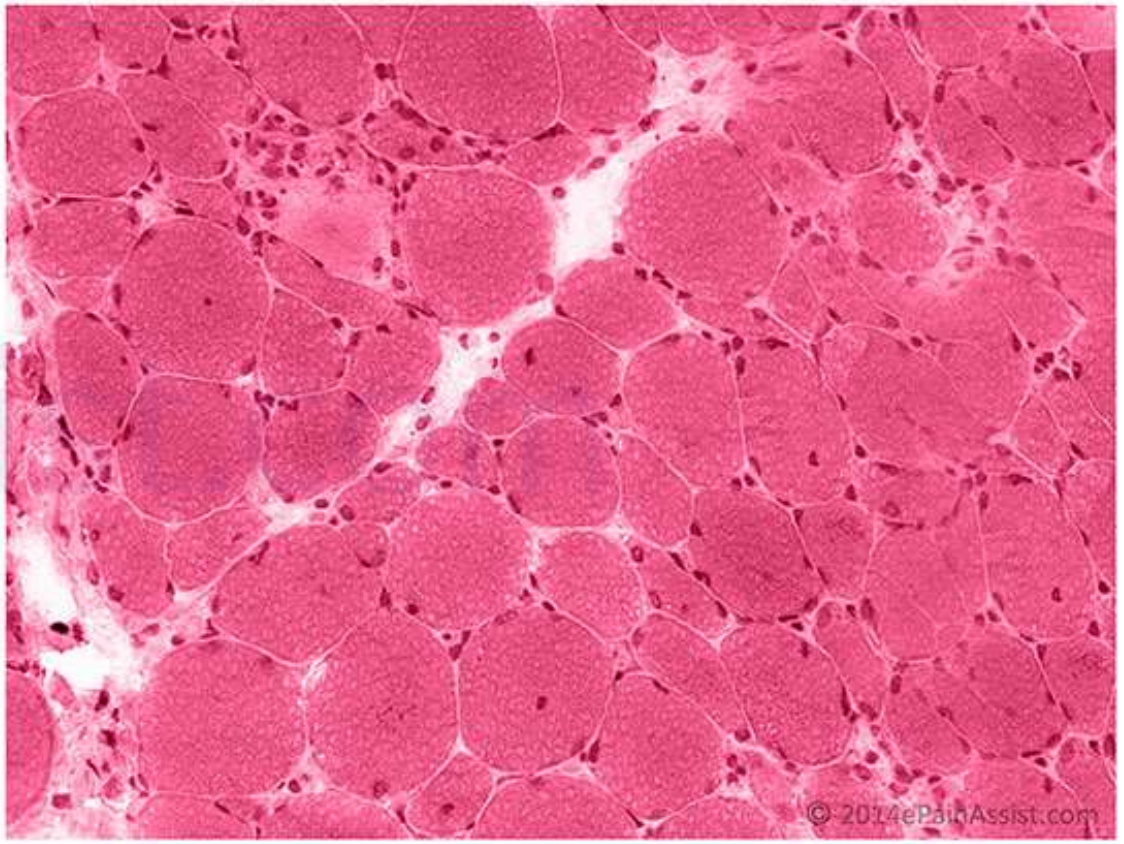
  - A neonatal form presents with severe hypotonia and weakness at birth.
  - The late infancy–early childhood form presents with delayed motor milestones.
  - Later, difficulty with running an stair climbing

- A marfanoid, slender body habitus, long narrow face, and high-arched palate are typical.
- Presentation at birth: hypotonia, feeding difficulty, respiratory distress, bilateral ptosis, limited eye movements, and absent tendon reflexes.
- Early childhood: Gait is waddling and hyperlordotic
- Facial dysmorphic features are often present
- Muscle biopsy shows myonuclei in the center of the muscle fibers
- Treatment: multidisciplinary approach

Centronuclear Myopathy (CNM)



Normal Muscle

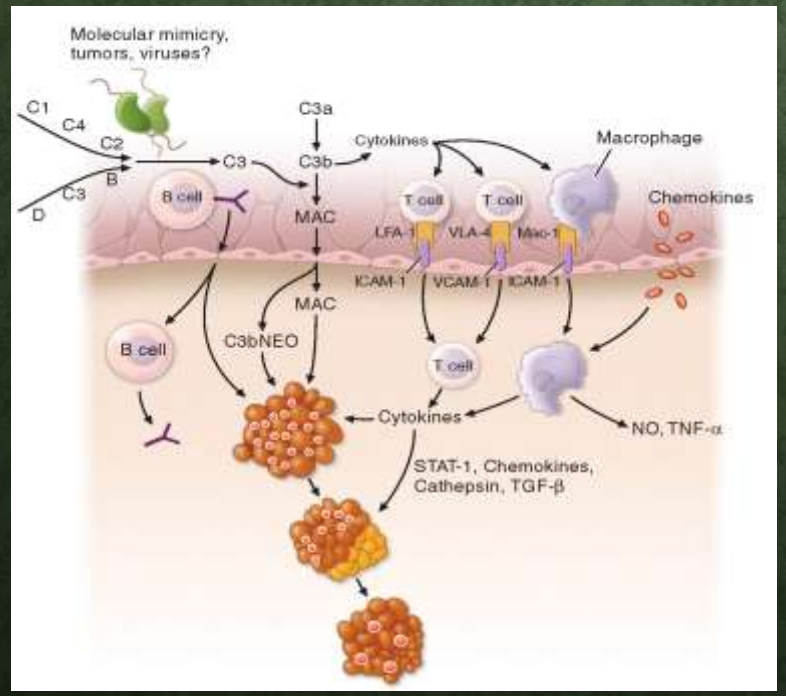


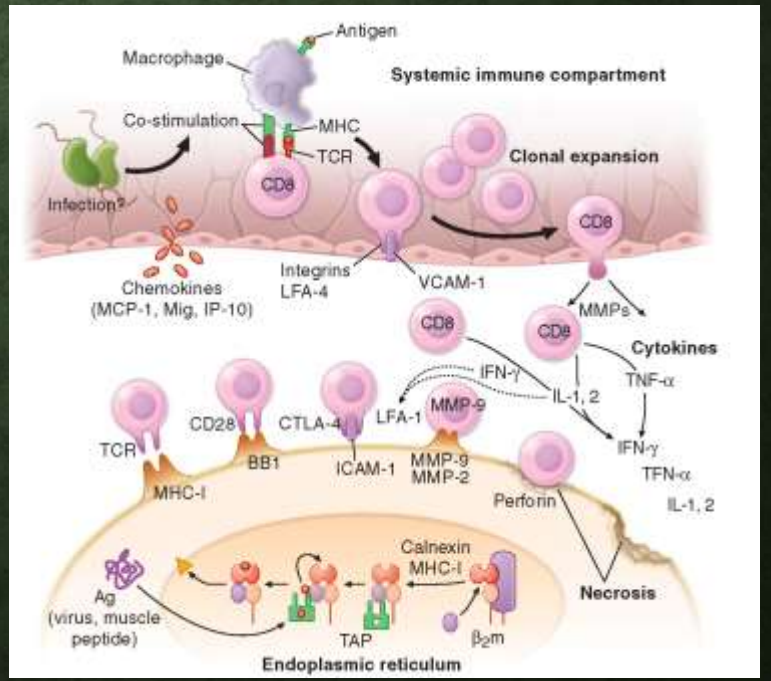
Centronuclear Myopathy

Abundance of centrally located nuclei including majority muscle fibre (mostly in type 1 fibres)

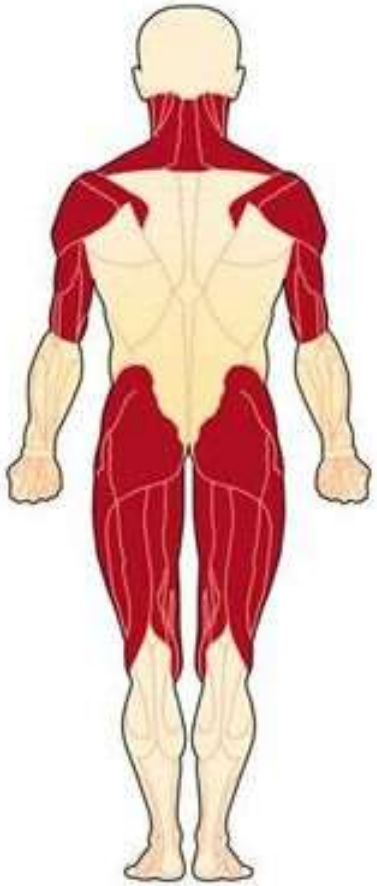
INFLAMMATORY MYOPATHIES: POLYMYOSITIS AND DERMATOMYOSITIS

- Idiopathic inflammatory disorders.
- Usually presents in those older than age 20.
- Female-to-male ratio is approximately 2:1.
- Pathogenesis:



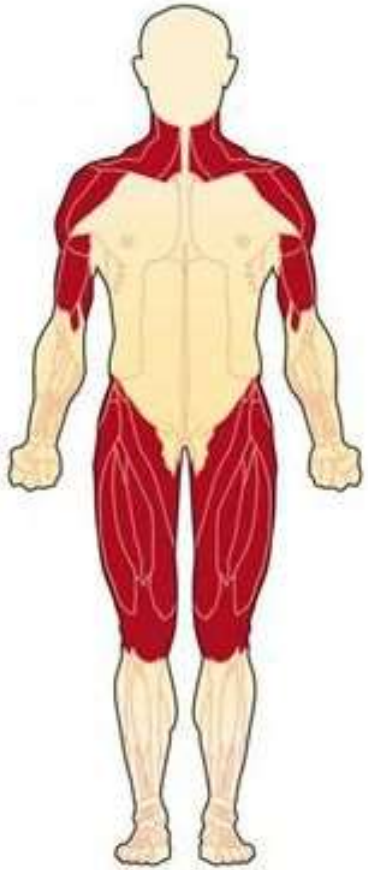


What is polymyositis (PM)?



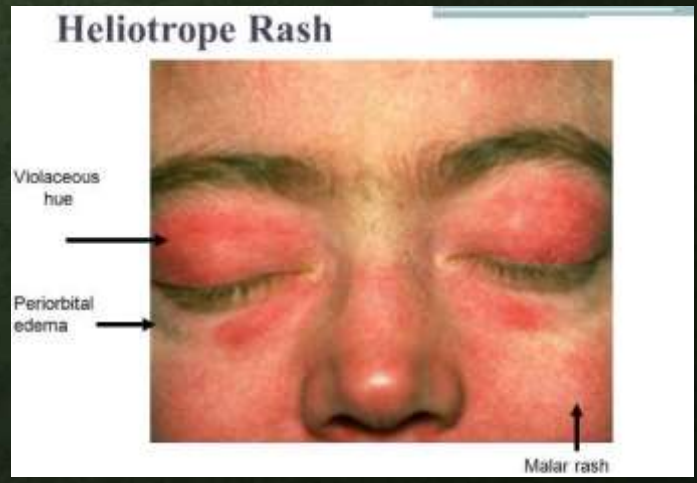
Polymyositis is one of the inflammatory myopathies, a group of muscle diseases that involves inflammation of the muscles or associated tissues, such as the blood vessels that supply the muscles. A myopathy is a muscle disease, and inflammation is response to cell damage.

Another word for inflammatory myopathy is myositis. The *myo* root means muscle, and the *itis* root means inflammation; so a myositis is an inflammatory muscle disease.



CLINICAL PRESENTATION

- Present with a progressive, symmetrical, proximal (i.e., more than distal) pattern of muscle weakness.
- Muscle pain and tenderness
- Later neck, swallowing, and respiratory muscles may become affected
- Arthralgia (50% patient)
- DM present with erythmatous skin lesion, **Heliotrope rash**, **Gottron's rash is a violaceous,** raised, scaly rash over the knuckles.
- PM and DM are associated with abnormalities in the cardiac and pulmonary systems.
- Patients with PM or DM may have a connective tissue disease, such as rheumatoid arthritis, systemic lupus erythematous, scleroderma, or Sjögren's syndrome.



Overview of Polymyositis and Dermatomyositis

Disorder	Clinical Presentation	Associated Features	Diagnosis	Treatment
Polymyositis	Symmetrical proximal muscle weakness Muscle pain, tenderness Arthralgias	Interstitial lung disease Cardiac abnormalities Gastrointestinal abnormalities Collagen vascular disease Certain malignancies	Increased creatine kinase EMG Muscle biopsy	Corticosteroids and/or other immunomodulatory agents Range of motion, stretching
Dermatomyositis	As for polymyositis plus rash	Interstitial lung disease Cardiac abnormalities Gastrointestinal abnormalities Collagen vascular disease Certain malignancies	Increased creatine kinase EMG Muscle biopsy	As for polymyositis

EMG, Electromyography.

METABOLIC MYOPATHIES

- Heterogeneous group of disorders caused by genetic defects that compromise muscle energy production.
- Enzyme dysfunction can result in an inadequate supply of ATP.
- At least 14 enzyme defects that affect glycogen synthesis, glycogenolysis, and glycolysis have been described.
- Other metabolic myopathies affect lipid metabolism.
- the more common metabolic disorders that result in myopathies, including myophosphorylase deficiency, phosphofructokinase (PFK) deficiency, debrancher enzyme deficiency, and acid maltase deficiency

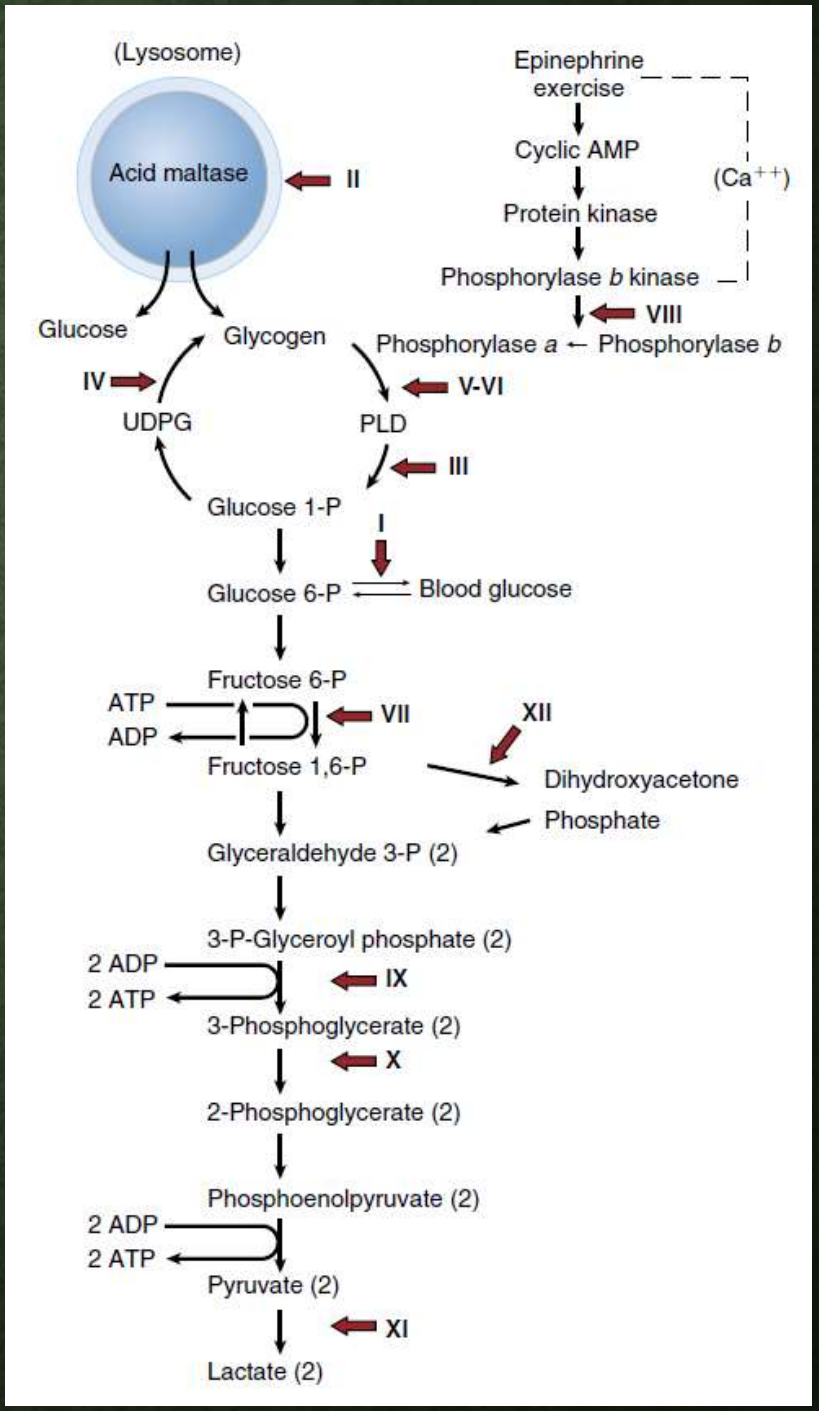


TABLE **32-11**

Metabolic Myopathies Associated with Carbohydrate Metabolism

Glycogenosis/Pattern of Inheritance	Abnormal Enzyme	Clinical Presentation	Diagnosis	Forearm Exercise Test	Treatment
Type V McArdle's disease	Myophosphorylase	Childhood onset Exercise intolerance Myalgias Myoglobinuria (15%)	Increased CK Muscle biopsy DNA analysis	Abnormal	Leverage "second wind" phenomenon Avoid high-intensity exercise
Type VII Tarui's disease	Phosphofructokinase	Exercise intolerance Myalgias Hemolytic anemia arthralgias	Increased CK Muscle biopsy DNA analysis	Abnormal	No specific treatment
Type III Cori-Forbes disease	Debranching enzyme	Exercise intolerance Muscle weakness Cardiomyopathy Hepatomegaly	Increased CK	Abnormal	? High-protein diet
Type II Pompe's disease	α-Glucosidase	Muscle weakness Three variants with different severity: infantile-, childhood-, adult-onset	Increased CK Muscle biopsy Abnormal EMG Dried blood test, followed by DNA confirmation if screening test is positive	Normal	Enzyme replacement

CK, Creatine kinase; *DNA*, deoxyribonucleic acid; *EMG*, electromyography.

ENDOCRINE MYOPATHIES

- Frequently manifest with muscular impairment.
- The features of endocrine myopathies most amenable to rehabilitation intervention include muscle weakness and atrophy.
- Exercises, orthoses, or assistive devices may be necessary, depending on the severity of the deficits.

Endocrine myopathy	Features	Clinical presentation	Diagnosis	Treatment
Steroid myopathy	•Most common •incidence is 2.4% to 21% •Women at risk	•Insidious onset •proximal muscle weakness and atrophy •greater involvement of the lower limbs	•Normal CK. •Muscle biopsy shows atrophy of type II fibers	•Stoping and reduce the dose •Strenth training to overcome weakness
Hyperthyroidism	•82% affected •Female more than male •Pathogenesis: enhanced muscle protein catabolism with ↑ muscle amino acid by the elevated thyroxine	•Weakness •Muscle atrophy •Fatigue, myalgia, and exercise intolerance. •Respiratory muscle involvement •Dysphagia and dysphonia. •Tendon reflexes:normal or brisk.	•elevated T3 and T4 and a low TSH •Needle EMG is usually normal, fasciculations may be present.	•Active exercises
Hypothyroidism	•Proximal muscle weakness, stiffness, fatigue, and slowed movements	•myoedema	•CK usually is elevated •T3 and T4 are depressed, TSH is elevated.	•Treatment of the underlying thyroid dysfunction

TOXIC MYOPATHIES

Toxic Myopathies Secondary to Medications or Toxins

Myopathy	Medication/Toxin	Clinical Features	Laboratory Findings
Necrotizing	Statins, clofibrate, gemfibrozil Alcohol abuse	Painful proximal myopathy	Increased creatine kinase EMG with muscle membrane irritability Possible myoglobinuria
Hypokalemic	Diuretics Laxatives Alcohol abuse Amphotericin B	Acute-onset weakness Myalgias	Increased creatine kinase Possible myoglobinuria Hypokalemia
Inflammatory	D-Penicillamine Interferon-α	Proximal muscle pain and weakness	Increased creatine kinase EMG with muscle membrane irritability Possible myoglobinuria
Mitochondrial	Zidovudine	Proximal muscle pain and weakness	Normal or increased creatine kinase EMG may be normal or show myopathic units
Focal	Heroin Diazepam Lidocaine	Local pain, swelling Contracture of affected muscle	Normal or increased creatine kinase
Antimicrotubular	Colchicine Vincristine	Proximal muscle weakness Mild peripheral neuropathy	Increased creatine kinase