Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY

Myopathies

Objectives :

- Not Given

Done by :

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Resources :

- 437 slides | Not Same 436's slides
- Teamwork 436
- Doctor notes | Dr.Reem AlHammad & Dr.Salman AlJarallah

Normal Muscle Physiology & Histology

Histology slide

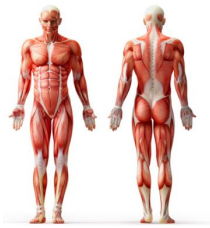
- ★ Dystrophin provides mechanical reinforcement to the sarcolemma and stabilizes the glycoprotein complex, its absence causes digestion of the glycoprotein complex. This initiates degeneration of the muscle fiber resulting in muscle weakness
- ★ Myopathies are disorders affecting the channel, structure, or metabolism of skeletal muscles.

Myopathy

Myo- Muscle

Pathos- Suffering

★ A disorder in which there is a primary functional or structural impairment of skeletal muscle.



Muscle Fibers

Type 1

Slow twitch, red:

- Aerobic
- Generating force over a more protracted interval.
- Fatigue slowly
- More dependent on a steady supply of oxygen
- ++++ myoglobin → redder Contain more lipid and mitochondria than fast-twitch fibers

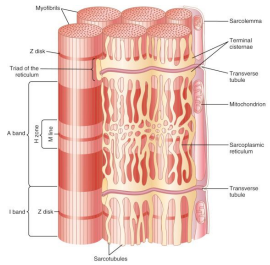
Basically less force longer time

Type 2

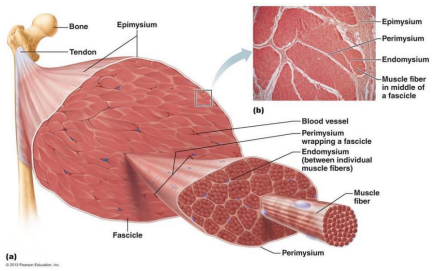
Type 2, Fast twitch, white:

- Anaerobic
- Generating large amounts of force quickly
- Contain more glycogen and myofibrillar ATPase
- Less myoglobin → white
- Fatigues easily

Basically more force shorter duration



The sarcoplasmic reticulum is where calcium is stored in the muscle.



Symptoms of Myopathies

Limb muscle weakness & atrophy

- ★ *Proximal muscle weakness* is the **cardinal symptom** of myopathy
- ★ E.g. difficulty combing hair, washing hair in shower, climbing stairs, squatting, waddling gait
- ★ Shoulder girdle → scapular winging
- ★ **Other muscles;**
  - Eye muscles → ophthalmoplegia, ptosis
  - Facial weakness → "myopathic facies", difficulty closing eyes, whistling, using straw,
  - Bulbar muscles → dysphagia, choking, nasal speech,
  - Respiratory muscles → dyspnea, orthopnea,
  - Cardiomyopathy → heart failure, arrhythmias

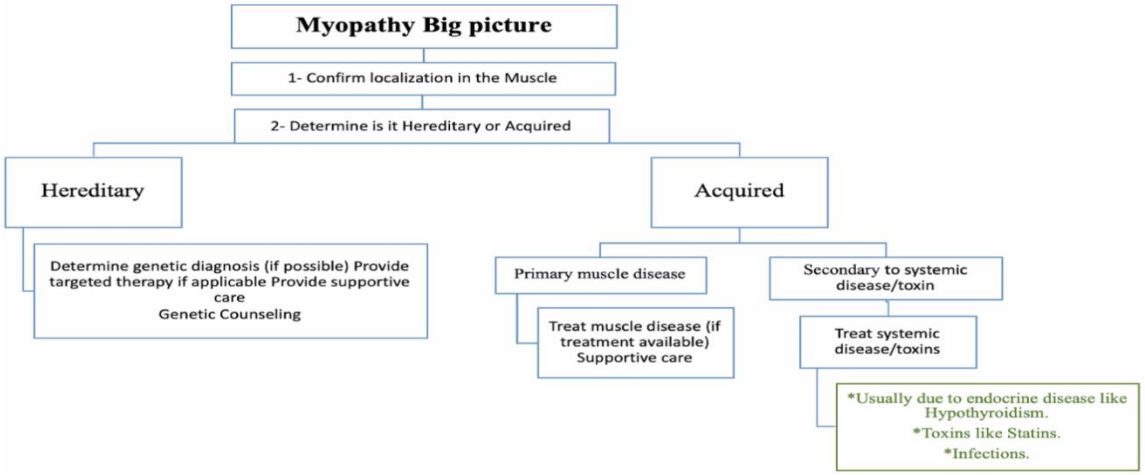
Lower limb weakness leads to what is called waddling gait or trendelenburg's gait

Most diseases including Myasthenia and Lambert Eaton start proximal, while neuropathies and INCLUSION BODY start distally.

Myopathy definition and Approach to Myopathy

MYO = muscle, pathos = suffering in Greek.

Myopathies are disorders affecting the channel, structure, or metabolism of skeletal muscles.



The evaluation of the patient presenting with a complaint of "weakness" involves the following steps:

1. Distinguishing true muscle weakness from asthenia or motor impairment not due to loss of muscle power.
2. Localizing, within the neuromuscular system, the site of the lesion that is producing weakness: NMJ[1]?, AHC[2]?, roots?, motor nerves?
3. Identify whether the myopathy is caused by:
   - Defect in the muscle channel.
   - Abnormal muscle structure.
   - Dysfunction in muscle metabolism.
4. Most common clinical pattern of myopathy:
   - Usually no sensory loss or absent reflexes in myopathies.
   - Usually proximal more than distal, Symmetric
   - Elevation of serum CK
   - EMG, shows myopathy.
5. Identify whether its hereditary or acquired:
   - Heredity presents as Chronic and slowly progressive with Fam.Hx of myopathy, Acquired Presents as subacute with fast progression. (See Myopathy big picture figure ↑)
6. Determine the management

[1]Neuromuscular junction
[2]Anterior horn cell

Cramps

- Involuntary contractions of muscle for seconds to minutes.
- Most are benign
- Usually localized to a particular muscle region, typically the calves
- Not specific for muscle. Occur in motor neuron disease, chronic neuropathies, etc
- EMG: rapidly firing motor unit discharges.
- Risk factors: old age, dehydration, prolonged sitting, diuretics, low Mg, hypoT4, DM
- Other causes:
  - Dehydration
  - Hyponatremia
  - Azotemia
  - Myxedema
  - Disorders of the nerve or motor neuron (ALS)

Myalgia

- Muscle pain.
- Episodic → metabolic myopathies.
- Nearly constant → inflammatory myopathies.
- Vague aches and muscle discomfort + normal neuromuscular examination and laboratory studies → unlikely to be muscle in origin.

Exercise Intolerance

- Suggests a disorder of energy utilization.
- Short exercise (carb), long (lipid)

Myotonia

- Impaired relaxation after sustained voluntary contraction.
- Commonly involves intrinsic hand muscles and eyelids.
- Caused by repetitive depolarization of the muscle fibers. This is usually due to channelopathy like a problem in Ca / Na channels
- Myotonia can be tested clinically:
  - Tapping the muscle (percussion myotonia)
  - Voluntary contractions of muscle groups (action myotonia)
  - Squeezing on examiner's fingers or shaking his hand or forceful closure of eyes

Slow relaxing reflex is seen in myotonia and hypothyroidism

Fatigue

- Much less useful negative symptom! may be a result of patients' overall health, cardiopulmonary status, level of conditioning, sleeping habits, or emotional state.
- Define intensity and duration of exercise that provokes fatigue → metabolic and mitochondrial myopathies.

Muscle Contractures

- Uncommon but can superficially resemble a cramp.
- Typically provoked by exercise in patients with glycolytic enzyme defects.
- Last longer than cramps
- EMG: silent
- Do not confuse with fixed contractures of tendons. (Due to shortening of the tendon, ex: shortening of the achilles tendon leading to plantar flexion of the foot)

Myoglobinuria

- Excess release of myoglobin during periods of excessive muscle breakdown causing dark urine
- Severe episodes: ATN → renal failure
- Isolated episodes following strenuous unaccustomed exercise: commonly idiopathic
- Causes:

  - Idiopathic.
  - Prolonged, intensive exercise.
  - Drugs or toxin intake. especially statins
  - Infections.
  - Heat stroke.
  - Myopathies.
  - Malignant hyperthermia.

Physical Exam:

- General: wasting, myopathic facies, resp distress
- V/S: bradycardia, irregular heartbeat
- Memory abnormalities
- Specific pattern of weakness and atrophy (limb-girdle, scapuloperoneal, distal, facioscapulohumeral, ocular, etc)
- Cardiac; heart failure
- Respiratory: fibrosis

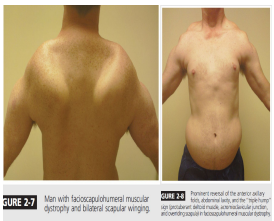
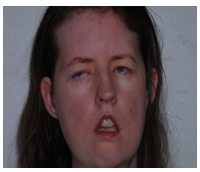


FIGURE 2-7 Man with facioscapulohumeral muscular dystrophy and bilateral scapular winging.

FIGURE 2-8 Prominent reversal of the anterior axillary folds, abdominal laxity, and the "triple-hump sign (pectoralis+ deltoid muscle, acromioclavicular junction) encountered in facioscapulohumeral muscular dystrophy.



Saggy face, tented mouth, bilateral ptosis, temporalis muscle atrophy

Lab Investigations

Muscle Enzymes:

- **CK**, aldolase (Aldolase B is specific), LDH and the aminotransferases
- ANA, ENA antibodies (anti-Ro/SSA, anti-La/SSB, anti-Sm, and anti-RNP)
- Myositis specific Ab (eg, anti-histidyl-t-RNA synthase [anti-Jo-1])
- Genetic testing for specific syndromes

CK

Serum Creatinine Kinase

- CK is an enzyme composed of muscle (M) and brain (B) monomers, resulting in MM, MB, and BB isoenzymes
- Serum CK reflects muscle membrane integrity and fluctuates with levels of activity
- Elevated creatine kinase may be seen with cardiac and skeletal muscle injury, including muscle, nerve, and motor neuron disorders affecting skeletal muscle.
- Strenuous exercise, intramuscular injections, or muscle trauma in the absence of generalized muscle disease

Acute/subacute	chronic
CK	CK
TSH/PTH	TSH/PTH
EMG	EMG
HMGCR	Genetic versus muscle biopsy
Myositis panel	Acid alpha glucosidase
Cardiac and respiratory screen	Cardiac and respiratory screen
	ALP

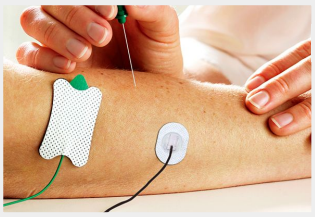
Other investigations:

★ MRI:
- Shows pattern of muscle involvement and features of inflammation
- Can't identify the exact etiology
- As a guide for the biopsy

★ Muscle biopsy:
- Essential for the diagnosis of inflammatory myopathies

★ Genetic testing: for specific syndromes

★ EMG:
- Small units with early recruitment.
- May see and hear myotonic discharges



EMG

NCS

NCS is usually normal in myopathies

Classification of Muscle Disorders

Acquired

Drug Induced	**statin**, penicillamine, **steroids**, chloroquine
Toxic	alcohol, cocaine, heroine
Infectious	parasite, virus
Endocrine	steroid, **hypothyroidism**, hypoparathyroidism
Inflammatory	**dermatomyositis**, **polymyositis**, inclusion body, Immune-mediated necrotizing myopathy

Hereditary

Muscular Dystrophies	Dystrophinopathies (Duchenne, Becker,), Limb-girdle muscular dystrophies, **Myotonic dystrophies**
Congenital Myopathies	born with it while duchenne & Limb girdle starts Later, commonly Associated with sensitivity to Anaesthesia Leading to Malignant hyperthermia due to Abnormality in Ca++ SR
Channelopathies	
Mitochondrial Myopathies	Maternal inheritance
Metabolic Storage Myopathies	

Inflammatory Myopathies

Polymyositis (PM) & Dermatomyositis (DM)

★ Epidemiology

The combined incidence is 2/100,000 annually, Female to male ratio of 2:1.

➢ Dermatomyositis affects children and adults. PM affects mainly adults.

➢ Can be part of an ***overlap syndrome***: DM or PM is associated with another well-defined connective tissue disorder such as scleroderma, mixed CTD, Sjögren, SLE, or RA.

★ IMMUNOPATHOGENESIS (SKIPPED SLIDE)

- In DM, capillaries and muscle fibers may be directly injured by type-1 IFNs secreted by nearby plasmacytoid dendritic cells.
- In PM, muscle fibers appear to be damaged by cytotoxic CD8 T cells.
- ?viral

Polymyositis

Bilateral proximal weakness, develops over days, No facial or extraocular involvement

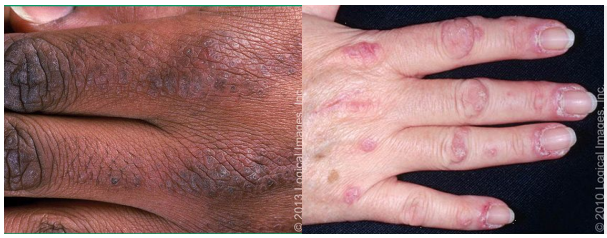
- Presents in adults (> 20 years), women > men
- Acute or insidious (weeks-months).
- Symmetrical weakness.
- Proximal >distal muscles.
- Mild pain and muscle tenderness.
- Can have malaise, fever, and anorexia.
- Dysphagia
- Extraocular and facial muscles spared.
- Deep tendon reflexes are normal unless weakness is severe
- Associated with malignancy (less than DM) (usually GI and Lung cancer)
- Cardiac myositis (arrythmia, heart failure)
- Polyarthritis in 45%, positive ANA in 40%

Dermatomyositis

- A form of small vessel vasculitis.
- Any age.
- Female > Male.
- Weakness: acutely (over several weeks) or insidiously (over months)
- Proximal >distal, legs>arms.
- Difficulties swallowing, chewing, and speaking occur (1/3).
- Signs & Symptoms:
  - Idiopathic inflammatory myopathy.
  - Characteristic cutaneous findings that occur in children and adults.
  - Systemic disorder most frequently affects the skin and muscles but may also affect the joints; the esophagus; the lungs; and, less commonly, the heart.
  - Eruption predominantly on photo-exposed surfaces.
  - Pruritus of skin lesions, sometimes intense enough to disturb sleep.

- Erythema of the mid-face.
- Eruption along the eyelid margins, with or without periorbital edema >
- Eruption on the dorsal hands, particularly over the knuckles >
- Changes in the nail folds of the fingers.
- Eruption of the upper outer thighs.
- Scaly scalp or diffuse hair loss.
- It could cause polyarthritis and Raynaud's Phenomenon.
- Complications:
  - Muscle fibrosis
  - Joint contracture

Dermatomyositis Physical Signs

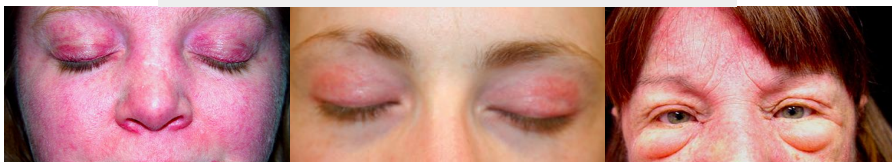


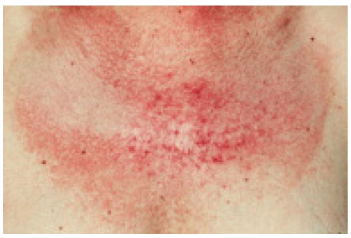
Gottron's Papule

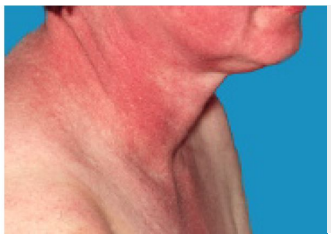
- Pathognomonic for dermatomyositis
- Violaceous scaly papules overlying the joints on the dorsal hand.

Helitrope Rash

- Pathognomonic for dermatomyositis
- Violaceous eruption on the upper eyelids, sometimes associated with periorbital edema







Shawl sign

-Erythematous rash covering the upper arms and shoulders or a V-shaped rash affecting sun-exposed surfaces on the upper chest.

Non-Skeletal Manifestations

- Cardiomyopathy.
- Dysphagia and delayed gastric emptying.
- Respiratory muscle weakness

Malignancy

- Increased risk of cancer in adults especially increases after the age of 50 (up to 40% of adults with).
- Type of screening depends on age and sex. For example Breast (mammogram) , ovarian, lung, pancreatic, NHL, stomach, colorectal or melanoma

Autoimmunity

- ANA can be positive
- Anti–synthetase antibodies (commonest anti-Jo-1, also anti-PL-7, anti-PL-12, etc).
- Myositis-specific antibodies: *Anti–Mi-2, anti-MDA5 (CADM-140), anti p155/140 or anti-MAS*

- **Interstitial lung disease (usually anti-Jo-1).**
- Raynaud's
- Polyarthritis

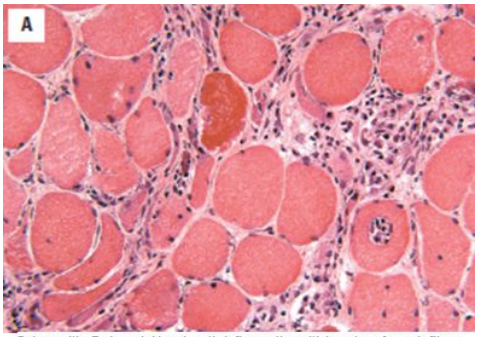
If you get a question about a patient with dermatomyositis and interstitial lung disease the antibody causing this is Anti-Jo-1

Diagnosis of PM & DM

Polymyositis

Diagnostic criteria:

- Subacute (weeks to months) symmetrical limb girdle weakness.
- Elevated serum CK (always elevated in PM, should be fivefold)
- EMG finding of irritable myopathy
- Muscle biopsy consistent with polymyositis
- Order Myositis antibody panel "Order anti-JO1 (ILD)"



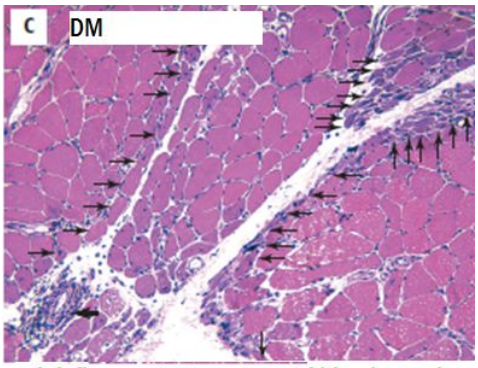
Polymyositis. Endomysial lymphocytic inflammation with invasion of muscle fibers

-Inflammatory cells (CD8+ T cells) invading non-necrotic, healthy muscle fibers.
-Invaded muscle fibers express MHC-1
-No perifascicular atrophy.
-No immunoglobulin deposition
-No complement deposition.

Dermatomyositis

Any case with proximal weakness and normal CK is probably DM

- Subacute (weeks to months) symmetrical limb girdle weakness.
- Skin changes consistent with dermatomyositis.
- Elevated or normal serum CK.
- EMG finding of irritable myopathy.
- Muscle biopsy consistent with Dermatomyositis.
- Increased risk of malignancy.
- Increased risk of interstitial lung disease (ILD).
- Order Myositis panel "Order anti-JO1 (ILD)"



1. Inflammation in perimysial blood vessels
2. Perifascicular atrophy

1-Perifascicular atrophy:

- Pathognomonic.
- Sublethal myofiber stress and ischemia at the interface of the muscle fascicle and the perimysium.

2-Inflammation:

- Perivascular in blood vessels in the perimysium
- CD4+ plasmacytoid dendritic cells.
- Complement activation (MAC) and deposition on capillaries.

Both

- Elevated levels of other enzymes such aldolase, AST, and ALT
- Autoantibodies, ANA (80%), anti-Jo1 (20%), anti SRP (5%), anti-Mi-2 (5-35%)
- Overlap antibodies : anti-PM/Scl, anti-Ro, anti-La, anti-U1 snRNP (SLE, systemic scleroderma, RA or mixed CTD), anti-U2 snRNP (scleroderma)
- Muscle MRI: edema, inflammation, fibrosis, calcification or fatty replacement of muscle tissue.

Management

- Cancer screening (CT CAP or PET scan and Colonoscopy to screen for underlying malignancy. CA-125 and CA-19-9 for malignancy screening)
- Evaluate coexisting autoimmune disorders (ANA) + LFT, RFT to begin treatment
- Exclude cardiac and pulmonary involvement (Pulmonary function studies with diffusion capacity,electrocardiography, esophageal manometry)
- Corticosteroids:
    - Some require high dose for long time.
    - Risk of opportunistic infections (PCP), osteoporosis, cataract, weight gait, etc
    - Monitor blood glucose, serum potassium levels, BP, and eyes
    - Steroid-sparing therapy: Methotrexate, azathioprine, mycophenonlate, etc
    - Physical therapy & Occupational therapy

Steroid sparing medications need time to work so usually the best management is by starting both steroid and steroid sparing medications together and gradually start lowering steroids until the 6-7 month the patient is only left on steroid sparing meds for lesser side effects

Inclusion Body Myositis (IBM)

- Progressive **slow-onset** inflammatory/degenerative myopathy, adult men> 50 y.
- Proximal lower extremity weakness is usually the first sign
- Chronic slowly progressive symmetric myopathy
- Mild facial weakness
- Esophageal dysmotility and dysphagia
- Anti-cN1A (NT5C1A) antibodies
- Poor response to immunotherapy

Clinical presentation

- Quadriceps femoris ± long finger flexors (Asymmetric)
- Biceps, foot dorsiflexors
- Paraspinal muscles: Camptocormia or dropped head syndrome
- Oropharyngeal dysphagia : 40–86% (upper esophageal sphincter dysfunction)
- Heart muscle: usually unaffected.

Diagnosis criteria:

- Insidious onset of proximal and distal initially asymmetrical weakness (wrist and finger flexors, quadriceps and ankle dorsiflexion), severe dysphagia develops.
- EMG: irritable myopathy.
- Biopsy suggestive of IBM: **Endomysial inflammation** and **rimmed vacuoles.**Definitive diagnostic feature is **filamentous inclusions** and vacuoles 90%
- Severe dysphagia develops.

Treatment: Supportive.

Female doctor at the end of the lecture focused on:

★ Scapuloperoneal weakness (emery dreifuss and its manifestation > need cardiac screening)

★ Rhabdomyolysis (IV hydration)

★ Scapular winging

Steroid Myopathy

- Chronic exposure to high-dose oral steroids .
- May occur after just a few weeks of treatment.
- Unknown mechanism.
- ?diminished protein synthesis, increased protein degradation, alterations in carbohydrate metabolism, mitochondrial alterations, and reduced sarcolemmal excitability
- Women > men.
- Progressive proximal muscle weakness (worse in LE) .
- Normal CK levels.
- EMG: normal or myopathic.
- Biopsy: type 2 fiber atrophy and lipid accumulation in type 1 fibers.

Statin Induced Myopathy

Statins inhibit HMG-CoA reductase, rate-limiting enzyme of cholesterol biosynthesis. Can cause:

- Mild statin-associated myalgia or cramps (20%)
- Myopathic weakness (up to 11%)
- Severe myotoxicity or rhabdomyolysis, rare
- Rarely, statins can cause an ***Immune-Mediated Necrotizing Myopathy*** *with* ***very high CK*** *and* ***antibodies to*** **Anti-HMG CoA-reductase**

In most cases, both mild and severe side effects are self-limiting

Discontinuation of the statin → resolution of symptom

Risk factors:

1. Dose of statin.
2. Preexisting liver disease → reduce metabolism of statin
3. Liver enzyme inhibitors → increase levels of statins
4. Genetic susceptibility: SLCO1B1 gene
5. Older age
6. Hypothyroidism
7. Obesity
8. Type of statin: Fluvastatin and Pravastatin are more myotoxic than to rosuvastatin

Mechanism (not imp.)

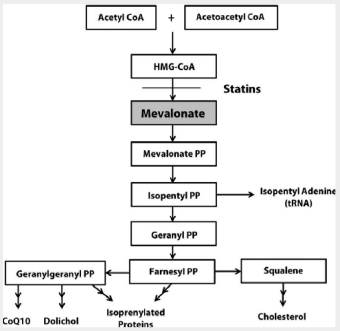
↓Mevalonate = ↓ farnesyl pyrophosphate and geranylgeranyl pyrophosphate → ↓ protein prenylation

Reduced prenylation of proteins causes:

1-impaired ubiquinone synthesis= mitochondrial dysfunction.

2-Impairment GTPases that promote cell survival= cell death.

3-Impairment of the process of N-glycosylation → defective proteins → muscle cells damage



Dystrophinopathies

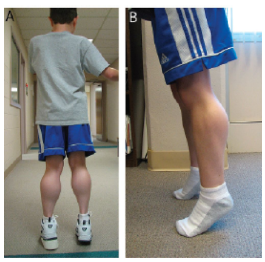
- X linked recessive disorders (manifest in males)
- Duchenne & Becker (DMD, BMD). Duchenne (early age) and becker (late age).
- Mutation in the **dystrophin gene** → absent (in duchenne) or reduced (in becker) Dystrophin protein → loss of mechanical reinforcement to the sarcolemma and instability of the glycoprotein complex
- Degeneration of muscle fibers, resulting in muscle weakness.
- Carriers of dystrophinopathy have to be screened (EKG) for cardiac diseases because dystrophin is present in the cardiac muscles)

Duchenne Muscular Dystrophy (DMD)

- Boys.
- Absence of dystrophin

1) Weakness:

- Onset age: 2 to 5 yrs. 5-6 y can't jump or climb then wheelchair 10 years of age
- Distribution: Proximal > Distal, Symmetric, Legs & Arms.
- Course:
  - Reduced motor function by 2 to 3 years.
  - Steady decline in strength: After 6 to 11 years.
- Gowers sign: Standing up with the aid of hands pushing on knees
- Loss of Ambulation:
- Age: 9 - 13 years.
- Later with: Steroid treatment.



2) Muscle (Pseudo) hypertrophy:

- Especially calf. May be generalized.
- Increases with age.
- Most commonly due to: Muscle replacement by fat & connective tissue. (that's why it is called pseudo)
- Death at 15-30 years.
- Complications: contractures, kypho-scoliosis, exaggerated lumbar lordosis

Systemic Involvement

1. Cardiomyopathy: dilated cardiomyopathy and arrhythmias
2. Malignant Hyperthermia like reactions with rhabdomyolysis
3. Intestinal pseudo-obstruction
4. CNS involvement: Mental retardation, learning disabilities

Investigations

1. CK is markedly elevated early in the disease
2. Electromyography: myopathic potentials
3. Muscle biopsy: necrosis, replacement with connective tissue and fibrosis, variation in muscle fiber size, absent dystrophin
4. **Genetic testing is gold standard. (most imp.)**

Management

- ★ Screening and treatment of cardiac, respiratory, gastrointestinal, and orthopedic complications.
- ★ Screening for osteoporosis plus calcium and vitamin D supplementation.
- ★ Physical therapy, occupational therapy and bracing
- ★ Avoidance of anesthesia and sedation if possible
- ★ **Glucocorticoids**: (slows the disease but they will eventually die)
  - Mainstay of treatment
  - Stabilizes sarcolemma
  - Increases strength, muscle, and pulmonary functions
  - Reduces cardiomyopathy and lowers mortality
  - Has an anabolic action in contrast to its catabolic action on normal skeletal muscle in unaffected people

Becker's Muscular Dystrophy

- Onset age: Usually > 7 yrs (Older age at onset)
- Less severe symptoms, loss of ambulation is usually in the 4th decade

Weakness:

- Proximal > Distal; Symmetric; Legs & Arms.
- May be especially prominent in quadriceps or hamstrings.
- Slowly progressive.
- Severity & onset age correlate with muscle dystrophin levels.

severity of the disease depends on how much is left of the enzyme

- Calf pain on exercise.
- Muscle hypertrophy: Especially calves.
- Failure to walk 16 - 80 years
- Cardiomyopathy may occur before weakness
- Muscle biopsy shows decreased staining patterns rather than complete absence of dystrophin

	Clinical Phenotype			Gene Information		
Condition	Typical Onset	Progression	Creatine Kinase Level	Allelism	Gene	Protein
Duchenne muscular dystrophy	Early childhood	Slow to moderate	100–200X	Becker muscular dystrophy	*DMD*	Dystrophin
Becker muscular dystrophy	Late childhood	Slow	10–15X	Duchenne muscular dystrophy	*DMD*	Dystrophin

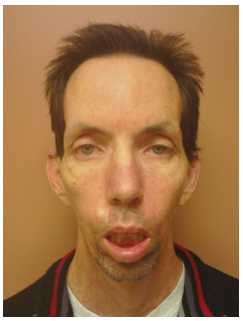
Investigation:

- CK high: 2000 to 20,000
- Partial loss of dystrophin staining
- Genetic testing

Emery – dreifuss muscular dystrophy *Only in Dr. Reem's slides

- Autosomal dominant or recessive.
- More than 7 subtypes with various genes.
- Age: Neonatal hypotonia to 3rd decade; Mean in teens.
- Function: Difficulty walking or climbing stairs
- Contractures before weakness.
- Weakness: Humeroperoneal
    - Bilateral
    - Symmetrical
    - Arms: Biceps & triceps; Deltoids spared.
    - Scapular winging
    - Legs: Late
    - Face: Mild weakness or normal
- Contractures, often more limiting to function than weakness in elbow. -Spine:
    - Posterior neck (extension)
    - Lower back: Usually later onset, but may present with rigid spine syndrome.
- Testing: CK, EMG, **Cardiac screening for arrhythmia and cardiomyopathy**

Myotonic Dystrophy



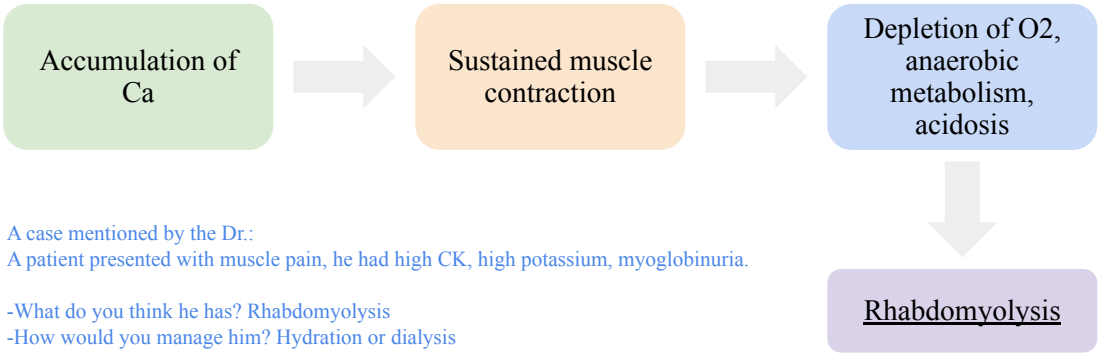
- A multisystem disorder
- The most prevalent inherited neuromuscular disease in adults
- Autosomal dominant
- **Tandem repeats at DMPK gene (Anticipation phenomenon)**
- Age of onset average is 29 years
- Myotonia
- Characterized by progressive muscle wasting and weakness.
- Prolonged muscle contractions (myotonia) and are not able to relax certain muscles after use (eg, Difficulty releasing hand grip on a doorknob or handle)
- Slurred speech or temporary locking of their jaw
- Gynecomastia
- Weakness of the forearms and peroneal muscles
- Ptosis and weakness of other facial muscles
- Frontal balding
- Cardiac: arrhythmias, heart failure, sudden death
- Respiratory weakness: orthopnea,
- GIT dysmotility, constipation and diarrhea
- Cataract
- Endocrine abnormalities: NIDDM, hypothyroidism, male hypogonadism
- Low IQ, cognitive impairment
- Lab:
    - CK.
    - EMG: myopathic plus myotonic discharges.
    - ECG and echo
    - Genetic testing; type 1 and type 2.
- Myotonic Dystrophy 1(DM1): AD from expansion of triplet repeat (CTG) on the myotonic dystrophy protein kinase (DMPK) gene.
- Myotonic Dystrophy 2(DM2): AD from expansion of triplet repeat (CCTG) on the Zinc Finger protein 9(ZNF9) gene.

Congenital Myopathies

- Prenatally, decreased fetal movements
- Postnatally: Hypotonia, poor respiratory effort, difficulty feeding, reduced muscle bulk and weakness
- First year and beyond: delayed milestones, failure to thrive, recurrent respiratory infections and flaccid speech
- Include (not imp.): *Central core disease, Multicore (minicore) disease, Nemaline myopathy, Myotubular (centronuclear) myopathy, Myofibrillar (desmin related), Congenital fiber type disproportion*
- Some are associated with **malignant hyperthermia**
- Slow or non progressive course
- No treatment

Malignant Hyperthermia (MH)

- Hypermetabolic reaction to volatile anesthetics and depolarizing neuromuscular blocking agents.
- Tachypnea, tachycardia, **rigidity**, **acidosis, hyperkalemia**, rhabdomyolysis, **high CK**, and **hyperthermia**.
- Associated with genetic muscle abnormalities causing calcium accumulation
- Associated with mutations of the ryanodine receptor (RYR1 gene), Na or Ca channels.
- Can be fatal
- Treatment:
    - **Remove** anesthetic agent.
    - Core **cooling**
    - **Dantrolene sodium**, an inhibitor of calcium release from the sarcoplasmic reticulum.

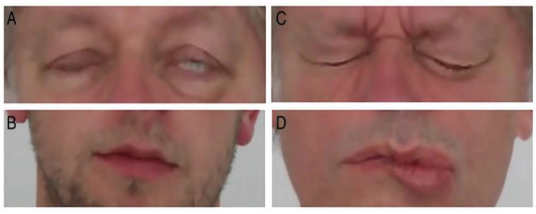


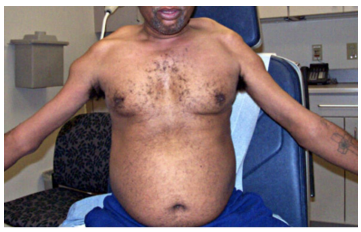
A case mentioned by the Dr.:
A patient presented with muscle pain, he had high CK, high potassium, myoglobinuria.

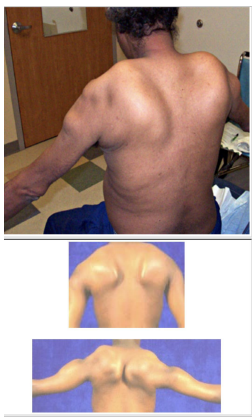
-What do you think he has? Rhabdomyolysis
-How would you manage him? Hydration or dialysis

Facioscapulohumeral dystrophy

- 3rd most common dystrophy in adult
- Autosomal dominant
- Face: Initial manifestation: Frequency: 95% at age 30 with examination
- Asymmetry
- Eyes: Often early in disease course Lid closure: Incomplete
- Sleeping: With eyes open
- Bulbar dysfunction
- Using straws -blowing up balloons
- Screen for hearing loss
- Screen for retinal vascular disease
- No screening for cardiac needed unless symptomatic







Rhabdomyolysis

- ★ Definition & General features:
  - Acute syndrome due to extensive injury of skeletal muscle
  - Weakness: Proximal > Distal
  - Pain+swelling
  - Cola or tea color urine
  - May have fever, leukocytosis
  - Serum CK: > 10,000, Usually > 30,000
- ★ Most common causes: Exercise, Drugs & Alcohol
- ★ More likely hereditary etiology:
  - Rhabdomyolysis on minimal exertion or fasting
  - Family history
  - Multiple episodes
- ★ Common etiologies
  - Metabolic myopathy: glycogen, lipid, mitochondrial • Statins
  - Muscular dystrophy: baseline ck high
  - Malignant hyperthermia!!!!!
- ★ Management:
  - IV hydration to avoid acute tubular necrosis and renal failure!!!
  - Other treatment according to underlying etiology.

Summary

Classification of Muscle Disorders

1- Congenital Clinical characteristics present Prenatal & Postnatal. Malignant hyperthermia

2- Hereditary

A) Muscular dystrophies	●Dystrophinopathies (mutation in the dystrophin gene. X linked recessive) Proximal > Distal, Symmetric & hypertrophy of the calves & Cardiomyopathy, require Genetic testing. 1. Duchenne (DMD) age <10 , Gowers sign, Cognitive impairment. CK: very high, biopsy: Absent dystrophin staining. 2. Becker (BMD) age >10 , Prominent in quadriceps or hamstrings, Calf pain on exercise. CK: high & Partial loss of dystrophin staining. ● LGMD Limb-girdle pattern of weakness, LGMD2 is more common than LGMD1. ● Emery- Dreifuss. Difficulty walking or climbing stairs, Contractures before weakness, Weakness: Humeroperoneal, Scapular winging, Cardiac screening.
B) Mitochondrial Cytopathies	Maternal inheritance
C) Fat/glycogen storage diseases	A. Episodic weakness group (Mcardle & CPTII deficiency) B. Static Weakness group (Pompe disease)
D) Myotonic dystrophy	(Most common in adults) <Abnormality in mRNA splicing Progressive muscle wasting, Prolonged muscle contractions, slurred speech, gynecomastia.
E)Facioscapulohumeral dystrophy (FSHD	< Abnormality resulting in toxic protein

3- Acquired:

A) PM	Subacute (weeks to months) symmetrical limb girdle weakness. Elevated serum CK , anti-JO1
B) DM	Idiopathic, systemic disorder, pruritus of skin lesions, erythema of midface, eruption along eyelid margins & over knuckles, anti-JO1 (ILD), screen for malignancy.

Questions

1- Over the past 6 weeks a 35-year-old nurse has developed progressive difficulty getting out of chairs and climbing stairs. She can no longer get in and out of the bathtub. She has no muscle pain and takes no regular medications. She does not use alcohol and does not smoke cigarettes. On examination she has a purplish rash that involves both eyelids. There is weakness of the proximal leg muscles. Neurological examination is normal. What is the best next diagnostic test?

a. Vitamin B12 level
b. HLA B27
c. MRI scan of the lumbar spine
d. CK

2- A 45-year-old woman presents to her physician with a 6-week history of gradually increasing limb weakness. She first noticed difficulty climbing stairs, then problems rising from a chair, and, finally, lifting her arms above shoulder level. Aside from some difficulty swallowing, she has no ocular, bulbar, or sphincter problems and no sensory complaints. Family history is negative for neurological disease. Examination reveals significant proximal limb and neck muscle weakness with minimal atrophy, normal sensory findings, and normal deep tendon reflexes. Affected muscles are slightly tender; there is no skin rash. What is the likely pathogenesis of her condition?

a. B- and T-cell mediated attack against muscle autoantigens
b. Anterior horn cell degeneration in the spinal cord
c. Antibodies to the acetylcholine receptor at the neuromuscular junction
d. Vasculitis with focal nerve and muscle necrosis
e. Abnormal trinucleotide repeat in the DMPK gene

3. A kid found himself to be clumsy, as he has just turned 5. His mother decided to bring him to a clinic and explained how her son couldn't keep up with his peers which made her worry. Which of the following could be the disease ?

A. Becker muscle dystrophy.
B. Inclusion Body Myositis.
C. Duchenne muscle dystrophy.
D. Myotonic dystrophy.

4. Which of the following do we need to screen for cardiac diseases?

A. Dystrophinopathy carriers.
B. FSHD carriers.
C. Myotonic dystrophy carriers.
D. A and C

Questions

5. A patient complains of a history of generalized muscle weakness. On examination, his facial muscles show marked atrophy, and when you ask him to shake your hand, he appears to be unable to relax his grip for an extended period. What is the likely diagnosis?

A. Myotonic Dystrophy.
B. Becker's dystrophy.
C. Inclusion body myositis.
D. Myasthenia Gravis

6. Myotonia commonly involves which muscles ?

A. Quadriceps
B. Biceps
C. Eyelid muscle
D. Calf muscle

7. - 50 year old female known case of SLE came to the ER with sudden onset of weakness and dark urine. Which of the following do you expect the patient to develop ?

A. Rhabdomyolysis
B. Renal failure
C. Sepsis
D. Paralysis

8- What is the immediate management of rhabdomyolysis?

A. Analgesics
B. IV hydration
C. Antibiotics
D. Reassure and discharge

1. D
2. A
3. C
4. D
5. A
6. C
7. B
8. B