Myopathies

Objectives:

- Understanding normal muscle histology and physiology.
- Understanding Myopathy definition.
- Understanding Approach to myopathy.
- Knowing the most common hereditary myopathies.
- Knowing the most common acquired myopathies.

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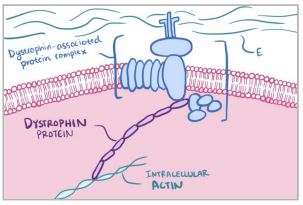
Resources: 435 team + Doctor's slides + Davidson + 500 best single answers in medicine.

- Editing file
- Feedback

Understanding normal muscle histology and physiology

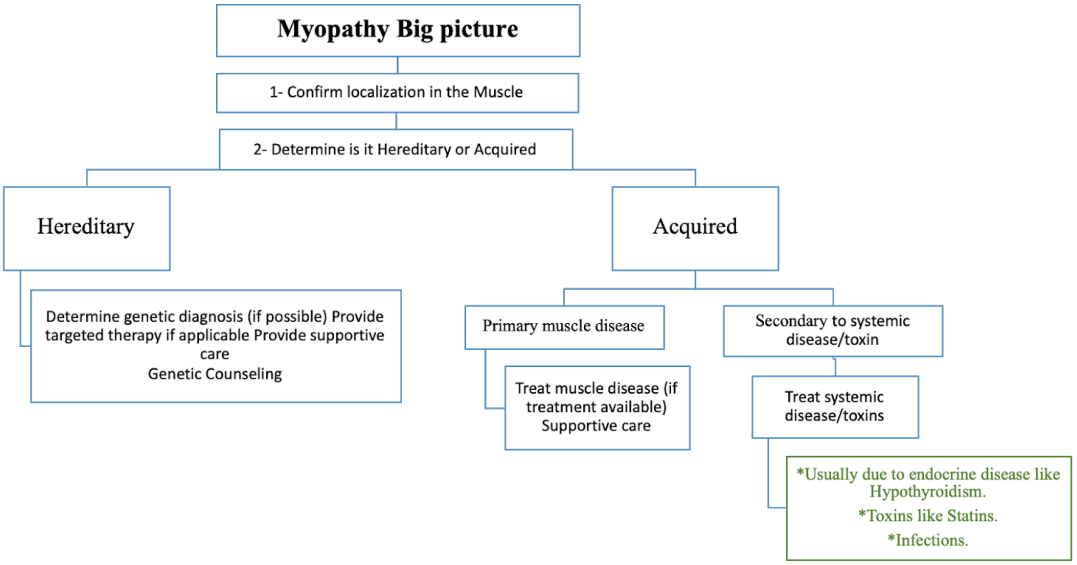
- Normal muscle physiology (click this link)
- Normal muscle Histology:
    - Dystrophin provides mechanical reinforcement to the sarcolemma and stabilizes the glycoprotein complex, its absence causes digestion of the glycoprotein complex. This initiates degeneration of the muscle fiber resulting in muscle weakness.



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 sub acute with fast progression. (See Myopathy big picture figure ↑)
6. Determine the management

[1] Neuromuscular junction
[2] Anterior horn cell

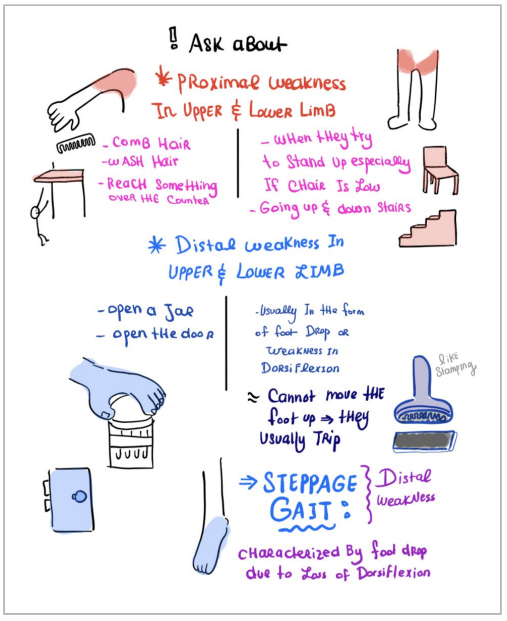
★ History Taking in Myopathy: What do we want to know when a person says they're weak?

1. **Does the patient have weakness?** When a patient presents with weakness, it is important to **know:**
   - ❏ Onset, Course, Limbs involved, Muscle involved, Progression, and Presence of sensory/autonomic symptoms.

A. **Are they really describing weakness?** (people describe many things as weakness; fatigue, pain, numbness…etc)
(If the patient is describing twitching, cramping or stiffness then it's most likely not a myopathy)

B. **Verify weakness by hx:** Ask about how the weakness is affecting their activities of daily living, motor system is not upper and lower limbs only:

- Difficulty with using arms to wash hair/difficulty w combing hair/reaching above the head →Proximal upper limb weakness
- Difficulty with going up and down the stairs/ standing from sitting position →Proximal lower limb weakness
- Difficulty with opening door knobs, opening jars →Distal upper limb weakness
- Difficulty with walking due to tripping over toes, lifting their lower limb high and slapping it (Steppage gait) →Distal lower limb weakness.
- Occulo-facial-bulbar axis
- Axial: (neck/diaphragm/spine/abdo minal /scapular) axis
- Appendicular axis (upper and lower limbs)



C. **Distribution of weakness?**

- Proximal > distal weakness → Acquired/inherited (**Typical pattern** for acquired and inherited myopathies, also known as "limb girdle" pattern)
- Distal > proximal weakness (Unique atypical pattern) → Acquired (e.g. Inclusion Body Myositis) Inherited (e.g. myotonic dystrophy type1)
- Facial-Scapular-peroneal → Inherited (FSHD)
- Oculopharyngeal weakness → inherited (OPMD)
- Atrophy: Certain myopathies have a unique distribution; e.g. sIBM- usually starts in the quadriceps and then to deep flexors of the hand + foot dorsiflexors in asymmetric fashion and Periscapular in FSHD.
  - Scapular winging seen in:
    - ❖ FSHD, Pompe, Laminopathy, Calpain, SLONM[3]
- Hypertrophy → calf in dystrophin, sarcoglycan, fukutin, sarcoid, amyloid.
- Abnormal movements → (rippling)/myotonia

Be careful, sometimes the patient comes to you late when the weakness is diffused. Try to establish where the disease started.

D. **Positions in testing weakness:**

- Neck flexors: supine position
- Neck extensors: prone position
- Knee extension and hip flexion: tested in seated position
- Knee flexion: tested prone.
- Hip abduction: tested in the lateral decubitus position. (Patients present with waddling gait, the weakness is in the gluteus minimus)

[3] Sporadic late-onset nemaline myopathy

E. **Define pattern of weakness:**

F. **Symmetrical or Asymmetrical weakness?**
- FSHD → inherited asymmetrical.
- IBM → acquired asymmetrical.

G. **Temporal profile?**
- Onset:
  - Childhood: Duchenne
  - Adolescence or later: FSHD, LGMD
  - Adults: inflammatory, toxic, also genetic
  - After 50 yrs: IBM
- Chronic slowly progressive myopathy ± family hx ± consanguinity →Inherited myopathy
- Subacute onset in previously healthy person w/ fast progression →Acquired myopathy
- Episodic with normal strength interictal→Metabolic or PP[4]
- Acute or subacute progression →Inflammatory myopathies (DM[5] /PM[6]), Rhabdomyolysis.
- Chronic slow progression over years →Most muscular dystrophies
- Non-progressive weakness with little change over decades →Congenital myopathies

2. Positive and Negative symptoms of Myopathy[7]:
- Positive symptoms: Myalgia, Cramps, Contractures, Myoglobinuria (dark urine), Stiffness, Muscle hypertrophy.
- Negative symptoms:Weakness, Fatigue, Atrophy, Exercise intolerance.

3. Age of the patient when they first developed their symptoms?
- Some myopathies are unlikely to develop after a certain age limit. e.g. Duchenne muscular dystrophy does not start after childhood.
- Certain myopathies are unlikely to develop before a certain age e.g IBM[8] before 40 years of age

4. What was the onset of the myopathy? (chronic, likely inherited - acute/subacute, likely acquired)
(Ask if the patient was slower compared to other kids or if they weren't sure of the time of the onset, if yes then it's chronic)

5. Cardiac or Respiratory involvement?
- Cardiac:
  - Dystrophinopathy
  - DM1, DM2
  - LGMD: emery - dreifuss, sarcoglycanopathies, fukutin
- Respiratory:
  - DM
  - Acid maltase (adult pompe)
  - CNM, nemaline

6. Pharyngeal Muscle involvement?

7. Systemic symptoms?
- Fatty liver: CPT
- Cataracts, frontal balding: DM
- Rash: dermatomyositis
- Early contractures: laminopathy
- Systemic organ disease: amyloid, sarcoid, mitochondrial

8. Is patient coping with disease or not ? E.g. depression, anxiety.

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[4] Pompe disease
[5] Dermatomyositis
[6] Polymyositis
[7] Positive symptoms (things that normal muscle should do but is now absent), Negative symptoms (things that normal muscle should not do but now is present)
[8] Inclusion bodies Myopathy

9. **What is his limitations in terms of activities of daily living?** E.g. Can he feed himself, can he dress by himself…etc
10. **Is the patient coping with the disease or not?** E.g. depression, anxiety..
11. **What is his limitations in terms of activities of daily living?** E.g. Can he feed himself, can he dress by himself…etc
12. **Detailed family history:** (Click here for more :)
    - ✓ Use of canes or wheelchairs
    - ✓ Skeletal deformities
    - ✓ Functional limitations
    - ✓ Sudden deaths
    - ✓ Pacemakers
    - ✓ Early onset cataracts
    - ✓ Deaths/complications from anesthesia
    - ✓ Early onset dementia/Paget's disease of bone
13. **Are There Precipitating Factors That Trigger Episodic Weakness or Stiffness?**
    - Fever > CPT II deficiency
    - Carbohydrates followed by rest > Pompe's
    - Toxic
    - Immune mediated (checkpoint inhibitors, statin)
14. **Detailed medications/toxin history:** (Click here for more :)

    Medications that causes myopathies:
    chemotherapy, statins, chloroquine (SLE), colchicine, labetalol, recreational drugs(heroin and cocaine)

Symptoms

A. 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.

B. Myalgias:

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

C. Cramps:

- Specific type of muscle pain.
- May last from seconds to minutes.
- Usually localized to a particular muscle region, typically the calves.
- EMG: rapidly firing motor unit discharges.
- Typically benign, not related to an underlying disease process.
- Other causes:
  - ❖ Dehydration
  - ❖ Hyponatremia
  - ❖ Azotemia
  - ❖ Myxedema
  - ❖ Disorders of the nerve or motor neuron (ALS) They are most common in motor neuron disease and chronic neuropathies rather than myopathies, in which cramps are only common in metabolic.

D. Myotonia: Impaired relaxation after voluntary contractions.

Commonly involves intrinsic hand muscles (hand grip) and eyelids. seen in the hand grip examination.
Repetitive depolarization of muscle membrane & Impaired relaxation after voluntary contraction.
Worsens with cold.
Improves with repeated exercise.

E. 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)

F. Myoglobinuria: Excess release of myoglobin during periods of excessive muscle breakdown.

- Severe episodes: ATN → renal failure. If patient came with sudden onset of weakness and dark urine (cola like), immediately we consider renal failure and manage the situation with diuretic and IV fluid.
- Isolated episodes following strenuous unaccustomed exercise: commonly idiopathic
- **Causes:** (Click here for more :)
    - Idiopathic.
    - Prolonged, intensive exercise.
    - Drugs or toxin intake. especially statins
    - Infections.
    - Heat stroke.
    - Myopathies.
    - Malignant hyperthermia.

Investigations

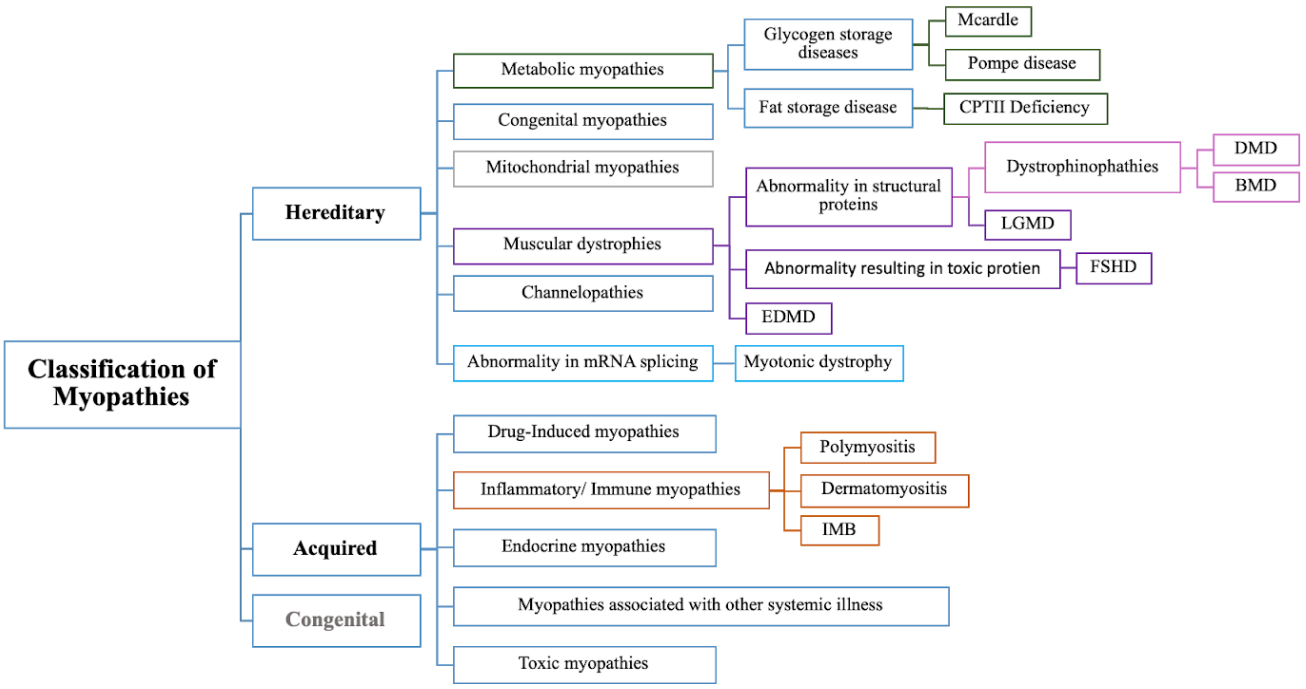
(Serum CK level significantly increases in acute conditions but not much in chronic conditions)

*For every patient with a myopathy we should order ECG, holter monitor & Echo (to rule out cardiomyopathy). Liver and kidney function tests (important for treatment).

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

- **Electromyography (EMG):** Small units with early recruitment, may see and hear myotonic discharges (Can differentiate between myopathy and neuropathy)
- **Genetic testing**

Myopathies



A. Hereditary Myopathy

★ Muscular dystrophy:

1. Abnormality in structural proteins:

- Dystrophinopathies: (Duchenne and Becker)
  - X linked recessive disorders.
  - Duchenne (early age) and becker (late age).
  - Caused by mutation in the dystrophin gene.
  - Carriers of dystrophinopathy **have to be** screened (EKG) for cardiac diseases because dystrophin is present in the cardiac muscles)

A. Duchenne Muscular Dystrophy (DMD):

1. Weakness:
   - Onset age: 2 to 5 yrs.
   - 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 hypertrophy:
   - Especially calf.
   - May be generalized.
   - Increases with age.
   - Most commonly due to: Muscle replacement by fat & connective tissue.
3. Scoliosis
4. Dilated cardiomyopathy: common after age 15
5. Cognitive impairment.
6. Death: 15-25 years.

Investigation:

- CK: very high, usual is 100 X ULN.
- Muscle biopsy: Absent dystrophin staining.
- Genetic testing is gold standard.

B. Becker Dystrophy:

- Onset age: Usually > 7 yrs
- Weakness:
  - Proximal > Distal; Symmetric; Legs & Arms.
  - May be especially prominent in quadriceps or hamstrings.
  - Slowly progressive.
  - Severity & onset age correlate with muscle dystrophin levels.
- Calf pain on exercise.
- Muscle hypertrophy: Especially calves.
- Failure to walk 16 - 80 years
- Cardiomyopathy may occur before weakness

Investigation:

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

- Limb Girdle Muscular Dystrophy (LGMD)**:**
  - Inherited group of muscular dystrophy that share Limb-girdle pattern of weakness but have variable involvement of other muscle groups.
  - **Divided to 2 groups based on inheritance:**
    1. LGMD1 (AD) (Autosomal dominant) group
    2. LGMD2 (AR) (Autosomal recessive) group
  - LGMD2 is more common than LGMD1.
  - The most common LGMD2 in western world is LGMD2A (Calpainopathy).

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

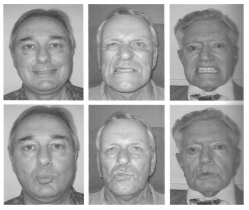
- Autosomal dominant or recessive.
- More than 7 subtypes with various genes.
- Age: Neonatal hypotonia to 3rd decade; Mean in teens.
- Function: Difficulty walking or climbing stairs
- Contractures before weakness.
- Weakness: Humeroperoneal
  - Bilateral
  - Symmetrical
  - Arms: Biceps & triceps; 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.

3. Abnormality resulting in toxic protein:

- Facioscapulohumeral dystrophy (FSHD): 3rd most common dystrophy in adults
  - 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[9].
  - Using straws (blowing up balloons)



Screen for:

✓ Hearing loss

✓ Retinal vascular disease

○ No screening for cardiac needed unless symptomatic

★ Abnormality in Mitochondria (Mitochondrial Cytopathies): (not important)

Mitochondria are intracellular organelles responsible for aerobic energy production (present in all mammalian cells). Mitochondrial cytopathies result from primary dysfunction of the mitochondrial respiratory chain. Some components in the respiratory chain encoded by nuclear DNA and some encoded by mitochondrial DNA.

Mitochondria cytopathies may result from either nuclear DNA or mitochondrial DNA mutation.

Mitochondrial cytopathies affect systems with high energy need:

- **CNS** (seizures, encephalopathy, stroke like, optic neuropathy, Depression, fatigue)
- **PNS** (myopathy, neuropathy)
- **Cardiac** (cardiomyopathy, conduction defects)
- **Endocrine** (Hypo-T/ParaT/Growth hormone, DM, Gonadal failure)
- **GI** (Dysmotility, hepatic failure)

There is a lot of distinct complex syndromes with combination of the above.

[9] Abnormal swallow and speech.

★ Abnormality in Glycogen/fat metabolism (Fat/glycogen storage diseases)

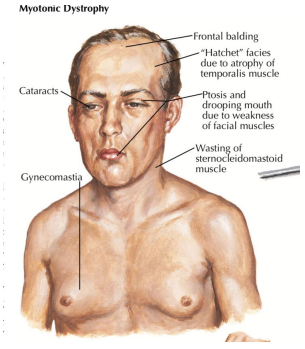
Hereditary myopathies caused by specific enzymatic defect in carbohydrate or fat metabolism.

Divided to 2 groups :

A. Episodic weakness group	B. Static Weakness group
Episodes of exercise intolerance with muscle contractures/stiffness and pain. In severe cases may result in Rhabdomyolysis. **2 diseases:** 1. **Mcardle** (glycogen metabolism defect): (triggered by exercising) ○ Enzyme defect (muscle glycogen phosphorylase) which normally breaks glycogen (Glycogenolysis). ○ Attacks happen in short term high intensity exercise. In the first minutes of exercise Mcardle patients have energy crisis due to blocked muscle glycogenolysis and low availability of extramuscular fuels. (cause muscle symptoms and tachycardia). In 6-8 minutes extramuscular fuels supplies become available and the patient feels less exertion and heart rate normalize (2nd wind phenomena) ○ **CK high** between attacks. ○ They have cramps. 2. **Carnitine Palmitoyltransferase II** (CPTII) **deficiency** (Fat metabolism defect): (triggered by fasting) ○ Enzyme defect- CPTII which normally transport long chain FA to mitochondrial matrix. ○ Attacks happen with prolonged exercise and fasting. ○ No cramps. ○ **CK** between attacks normal.	**Pompe disease** (AR)**:** (glycogen metabolism defect): ○ Enzyme defect **(Acid maltase)**, which leads to accumulation of glycogen in lysosomes of skeletal, cardiac and smooth muscles. ○ Adult onset phenotype: Weakness (onset 3rd or 4th decade) in truncal and proximal muscles (can present initially with respiratory insufficiency) ○ CK elevated. ○ Can measure Acid maltase enzymatic activity. ○ Muscle biopsy. ○ Treatment enzyme replacement Therapy.

★ Abnormality in mRNA splicing:

- **Myotonic dystrophy:**
  - Most prevalent dystrophy in adults.
  - Characterized by progressive muscle wasting and weakness.
  - Prolonged muscle contractions (myotonia) and are not able to relax certain muscles after use.
  - Difficulty releasing hand grip on a doorknob or handle.
  - Slurred speech or temporary locking of their jaw.
  - Cataracts.
  - Diabetes and other endocrine.
  - Cardiac conduction defects.
  - Anticipation.
  - Gynecomastia.



Lab:

- CK.
- EMG: myopathic plus myotonic discharges.
- ECG and echo.

- **Genetic testing; type 1 and type 2.**

Divided to 2 types: gene. (carriers need to be screened for cardiac disease)

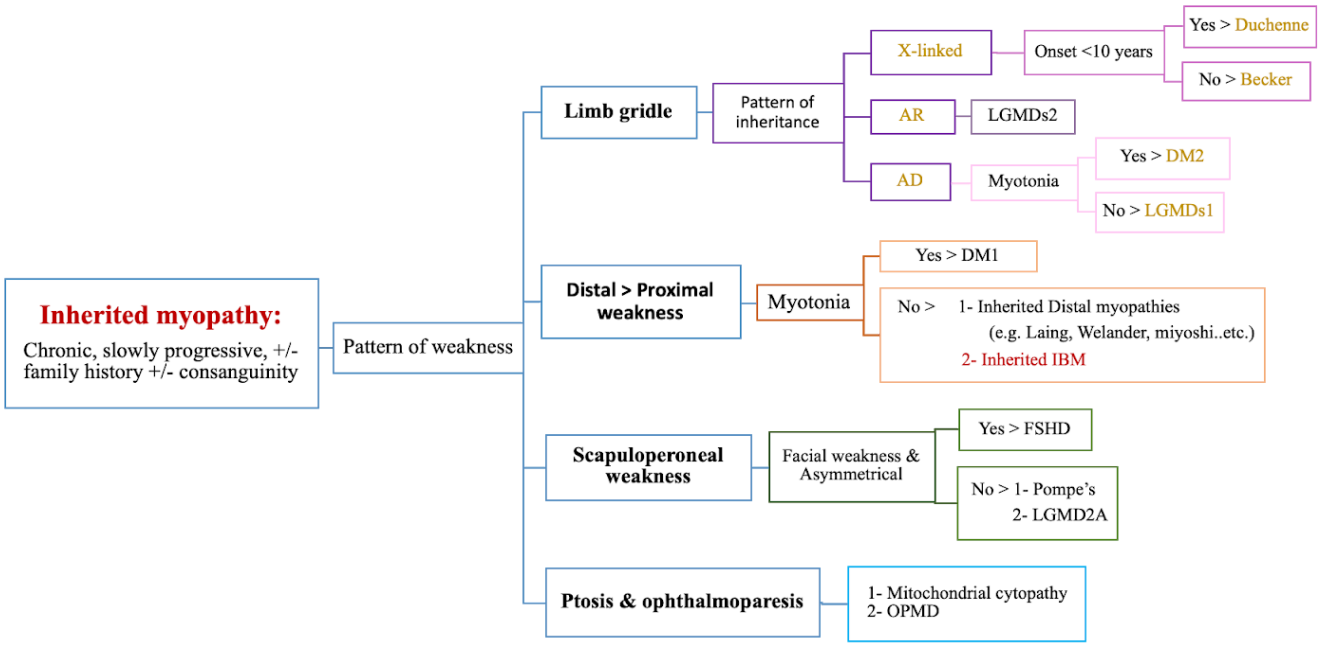
- **Myotonic Dystrophy 1**(DM1): AD from expansion of triplet repeat (CTG) on the myotonic dystrophy protein kinase (DMPK) gene.
- **Myotonic Dystrophy 2**(DM2): AD from expansion of triplet repeat (CCTG) on the Zinc Finger protein 9(ZNF9) gene.

Rhabdomyolysis *Only in Dr. Reem's slides

- 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.



B. Acquired Myopathy

★ Inflammatory Myopathy:

1. Polymyositis: *Not mentioned by Dr.Reem.

Diagnostic criteria:

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

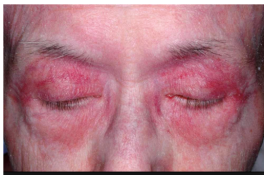
Treatment: Immunosuppression, screen for malignancy (3-5years) & monitor for ILD

2. Dermatomyositis:

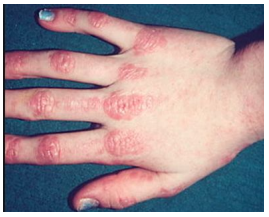
Feature	DM1	DM2
Epidemiology	Widespread	Regionally selective
Age of onset	Any	Adulthood
Anticipation	Yes	No/mild
Congenital form	Yes	No
Muscle		
Weak face/neck/swallow	Common	Uncommon
Weak limbs—proximal	Late	Early
Weak limbs—distal	Early	Late
Myotonia	Mild to moderate	Mild to moderate
Myalgia	Mild to moderate	Mild to severe
Systemic		
Cataracts	Very common/early	Common
Frontal balding	Very common	Uncommon
Cardiac arrhythmias	Very common/early	Common/late
Respiratory failure	Very common/late	Uncommon/late
Cognitive disorder	Common/mild to severe	Uncommon/mild
Gonadal failure	Common	Uncommon
Excessive daytime sleepiness	Very common and early	Common and late
Hyperhidrosis	Mild	Mild to severe
Laboratory		
Hyperinsulinaemia	Common/mild	Common/moderate
Electromyography: myotonia	Very common	Common
Chromosome	19q13.3	3q.21
Gene	*DMPK*	*ZNF9*
Mutation type	CTG repeat	CCTG repeat
Repeat size	50–4000	Mean in 1000s

Signs and 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. (Rash in sun exposed area).
- 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.

Lab tests:

- CK, LFT, RFT (to start treatment)
- Myositis-specific antibodies
- Antinuclear antibody levels
- Pulmonary function studies with diffusion capacity
- Electrocardiography
- Esophageal manometry
- CT CAP or PET scan and Colonoscopy to screen for underlying malignancy.
  - ➢ CA-125 and CA-19-9 for malignancy screening

Diagnosis criteria:

- Subacute (weeks to months) symmetrical limb girdle weakness.
- Skin changes consistent with dermatomyositis.
- Elevated 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)"

Treatment: Immunosuppression, screen for malignancy & ILD.

3. Inclusion Body Myositis (IBM): Important!

Signs and symptoms:

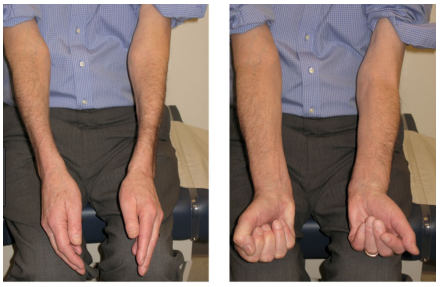
- Progressive slow-onset inflammatory/degenerative myopathy.
- Common after age 50 (prevalence:35-71/1000000), M:F → 2:1
- Unique clinical and pathological features
- Relentless progression, lacks effective therapies

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.
- 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

Summary

Myopathies:

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

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

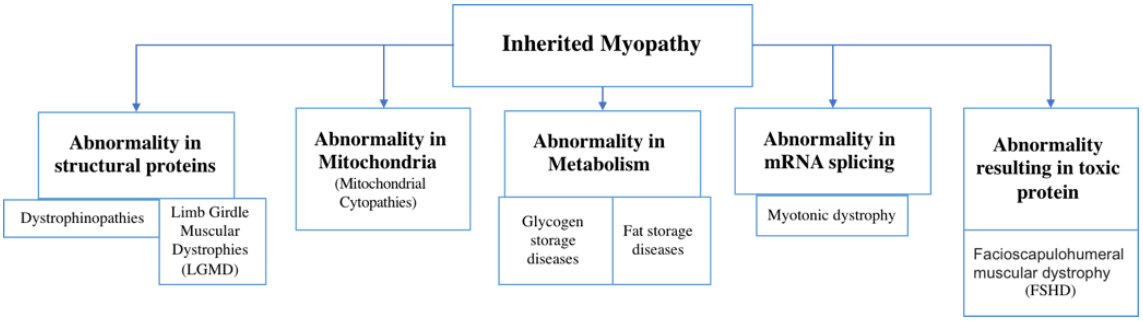
B) DM

Idiopathic, systemic disorder, pruritus of skin lesions, erythema of midface, eruption along eyelid margins & over knuckles, anti-JO1 (ILD), screen for malignancy.

C) IBM

Degenerative, after the age of 50, dropped head syndrome, dysphagia.

D) Toxic myopathies < Statin induced



Questions

1. 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.

2. 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

3. 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

5- Everyone with dystrophic myopathies should be screened for cardiomyopathy?

A. True
B. False

6- Any patient with asymptomatic FSHD should do EKG, Echo and PFT ?

A. True
B. False

7- Inherited myopathies are always symmetrical.

A. True
B. False

8- We need to screen asymptomatic Myotonic dystrophy patients for cardiac disease.

A. True
B. False

9- Myotonia commonly involves which muscles ?

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

10- 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

11- What is the immediate management of rhabdomyolysis?

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

Answers:

1. C /2. D /3. A /4. A / 5. A / 6. B / 7. B / 8. A / 9. C / 10. B /11. B

Patterns: only in Dr.Reema's slides

Pattern 1:Proximal limb girdle:

- Most common.
- Frequent involvement of neck flexor/extensor.
- Least specific.

Pattern 2: Distal Weakness:

- Involves the distal muscles of the upper or lower extremities
- (anterior or posterior compartment muscle groups)
- Usually symmetric.
- Asymmetric posterior compartment : ANO-5, dysferlinopathy
- Anterior compartment with sparing of quadriceps: GNE
- Finger flexor: IBM
- Finger extensor: TIA1 (Welander)
- Rule out neuropathy!!!!

Pattern 3: Proximal Arm/Distal Leg Weakness (Scapuloperoneal)

- Can be very asymmetric.
- When associated with facial weakness: FSHD.
- Laminopathies (emery dreifuss) frequently associated with cardiac arrhythmias , VCP, calpain.

*Usually present with contracture preceding weakness

Pattern 4: Distal Arm/Proximal Leg Weakness

- Distal forearm muscles (wrist and finger flexors) + proximal leg
- (quadriceps)
- Facial muscles typically spared
- Asymmetric: IBM
- Symmetric: IBM, myotonic dystrophies

Pattern 5: Ptosis with or Without Ophthalmoparesis

- Ocular involvement: ptosis and ophthalmoparesis
- Usually (not always), occurs without diplopia
- Facial weakness: not uncommon
- Extremity weakness : variable, depending on the diagnosis.
- Ptosis, ophthalmoparesis without diplopia, and dysphagia !OPMD
- Ptosis + ophthalmoparesis without prominent pharyngeal involvement ! mitochondrial myopathies

*Unilateral ptosis usually caused by NMJ, unlike myopathy which affect both sides.

Pattern 6: Prominent Neck Extensor Weakness

- Severe weakness of the neck extensor muscles
- Dropped head syndrome
- Limb and neck flexor involvement : variable
- Rule out ALS or MG

Pattern 7: Bulbar Weakness

- Tongue and pharyngeal weakness.
- Acquired: sarcoid, pompe, NAM, inflammatory
- Hereditary: OPMD, myotilin

Pattern 8: Episodic Pain, Weakness, and Myoglobinuria

- Episodic pain, weakness, +/- myoglobinuria
- May be related to a variety of conditions (non muscle)
- Triggered by exercise ! metabolic myopathy likely

Pattern 9: Episodic Weakness Delayed or Unrelated to Exercise

- PP: genetic AD and secondary (thyrotoxicosis)
- Rule out NMJ

Pattern 10: Stiffness and Decreased Ability to Relax

Dystrophic and non-dystrophic myotonias