Myopathies

435 medicine teamwork

[Important | Notes | Extra | Editing file]

Lecture objectives:

- Not given.

Dr. Hana's slides should be enough for exam purposes but For Further reading

★ check the summary

Done By: Aya Ghanim & Luluh Alzeghayer
Edited: Atheer Alnashwan
Revised By: Atheer Alnashwan & Ahmad Alyahya

References: Doctors' slides + notes + step-up + Kumar

Myopathy

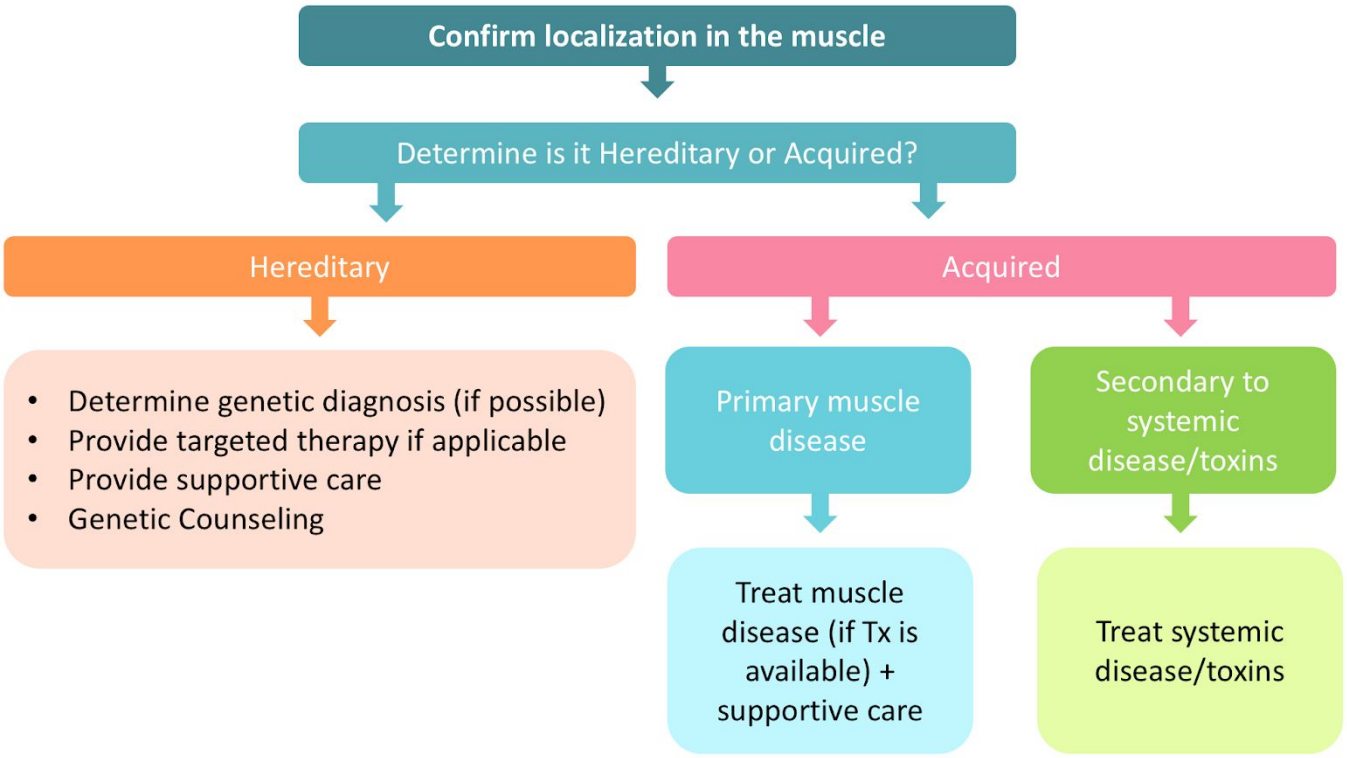
- MYO = muscle, pathos = suffering in Greek.
- Myopathies are disorders affecting the **channel, structure, or metabolism** of skeletal muscles:
  - **channel:** myotonia congenita is a disorder of stiff muscle caused by mutation in Cl- channel
  - **structure:** a lot of diseases are associated with impairment of structure, including duchenne in which there is deficiency of dystrophin-associated proteins in the sarcolemma.
  - **metabolism:** in pompe's disease, there is impairment of glycogen breakdown leading to lysosomes-mediated cell death. another example is the accumulation of fat.
- Important points:
  - **No** sensory symptoms, Reflexes are rarely absent (bc it doesn't affect the nerves, the main problem is within the muscle!)
  - Common presentation is **proximal** muscle weakness, can be distal but less common.

Approach to myopathy:

The evaluation of the patient presenting with a complaint of "weakness" involves 3 steps:

1. Distinguishing true muscle weakness from asthenia[1] or motor impairment not due to loss of muscle power e.g. SOB, joint pain, fatigue, poor exercise tolerance or paresthesia. This is the first step.
2. Localizing, within the neuromuscular system, the site of the lesion that is producing weakness
3. Determining the cause of the lesion

Here is the big picture and it's very high yield:



History in myopathy: | by Dr. Muhammad only

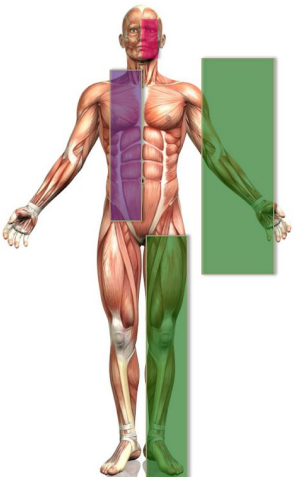
1- Does the patient have weakness? if yes:

A- Are they really describing weakness (people describe many things as weakness; fatigue, pain, numbness…etc) in case of fatigue, underlying cause of weakness might be **anemia**! but true myopathy can be specified to a certain group of muscle, thus ask open-ended questions to verify what type of activity is affected.

[1] abnormal physical weakness or lack of energy.

To verify weakness by hx: Ask about how the weakness affecting their **ACTIVITIES** OF DAILY LIVING:	
• Difficulty with using arms to wash hair • Difficulty combing hair/reaching above head	**Proximal** upper limb weakness
• Difficulty with going up and down the stairs • Difficulty in 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 "**high-steppage gait**" watch Due to weak dorsiflexion. You can hear **patient's footsteps** from distance	**Distal** lower limb weakness

B- Distribution of weakness: Motor system is not upper and lower limbs only!



- Occulo-facial-bulbar axis:

- Occulo-pharyngeal weakness (OPMD): inherited.

- Axial (neck/diaphragm/spine/abdominal/scapular) axis:

- Facial-Scapular-peroneal (FSHD): inherited

- Appendicular axis (upper and lower limbs):

- Proximal > distal weakness. Typical pattern for acquired and inherited myopathies, also known as "***limb girdle***" pattern, but exceptions exist:
  - Distal > proximal weakness
    - **Acquired:** e.g. **Inclusion Body Myositis** (IBM)
    - **Inherited:** e.g. myotonic dystrophy type 1 (DM1), Inherited Distal myopathies (e.g. Laing, Welander, miyoshi..), inherited IBM.
  - Certain myopathies have unique distribution; e.g. **IBM-** usually starts in quadriceps and then to deep hand flexors + foot dorsiflexors in an asymmetric fashion.
  - Both proximal and distal, in this case ask the patient which started first! Be careful sometime the patient comes to you late when the weakness is diffuse, try to establish where the disease started.

C- Symmetrical weakness or asymmetrical?

Myopathies are commonly **symmetrical**, but exceptions exist:

- **FSHD** (Facial-Scapular-peroneal): inherited **asymmetrical**
- **IBM**: acquired **asymmetrical**

Thus, symmetrical pattern is more helpful to guide us for a diagnosis because not many diseases cause it.

Note: **Double vision is NOT present** in symmetrical eye muscle weakness, because both are affected. If a muscle in one eye is weaker than the other, then the two eyes will not move smoothly together and can cause double vision.

2- Positive and Negative symptoms of Myopathy?

Dr. Muhammad: "it's confusing you can ignore it", while Dr. Hana explains some of them further next page.

-ve symptoms	Weakness, atrophy, exercise intolerance, periodic paralysis (channelopathy), fatigue.
+ve symptoms	Myalgia (muscle pain, Acquired > congenital), myotonia (sustained muscle contraction), cramps, contractures, myoglobinuria (change in urine color), muscle hypertrophy

3- Age of the patient when first developed symptoms?

- some myopathies are unlikely to develop after a certain age limit e.g. Duchenne muscular dystrophy does not start after childhood.
- certain myopathies unlikely to develop before a certain age e.g. IBM before 40 years of age

Q: A 30 y.o. patient with myopathy, is it Duchenne Muscular Dystrophy?

it's possible but unlikely. Duchenne usually present at 3-4 years of age and patients die by the age of 30.

4- What was the onset of the myopathy? (Temporal profile)

- **Chronic slowly progressive** myopathy +/- family hx +/- consanguinity: **INHERITED** MYOPATHY
  consanguinity هي صلة القرابة بين الوالدين especially in recessive inheritance.
- **Acute/Subacute** onset in previously healthy person with **fast progression**: **ACQUIRED** MYOPATHY

This is a general rule but exceptions exist! and onset isn't when the patient comes to you but when the disease started. some times onset isn't very clear but patient may say "when I was younger I was slower than the other kids and it has been slowly progressing".

5- Cardiac or Respiratory involvement?

Symptoms include: palpitation, syncope, **SOB when they lay down** (they sleep on 3-4 pillows because of diaphragm involvement, and it's better on setting due to gravity). May cause atelectasis and pneumonia (some take prednisolone > immunosuppression > pneumonia > ICU). It's very important to monitor and screen patients for cardiac and respiratory disease. e.g. **muscular dystrophies** affect not only skeletal muscle but also the diaphragm and cardiac muscle, thus may result in sudden death. But of course exceptions exist: Facial-Scapular-peroneal disease has low risk for cardiac disease.

6- Pharyngeal Muscle involvement?

Due to weakness of pharyngeal muscle they take a long time eating > thus they eat less > superimposed by the effect of muscle dystrophy > they lose weight.

7- Systemic symptoms?

suspect thyroid, cushing, or malignancy

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

= low energy makes them weaker.

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- Detailed family history

To determine pattern of inheritance, determine a genetic diagnosis, provide targeted therapy and supportive care such as tools to facilitate eating, canes to facilitate walking and so one. also to provide genetic counseling for their kids.

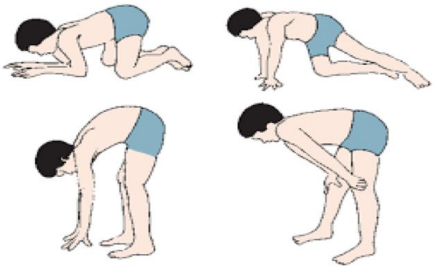
- **Autosomal dominant (AD):** Doesn't skip generations as there are no carriers, except in incomplete penetrance (mild phenotype) or novel mutation.
- **Autosomal recessive (AR):** It's more severe than autosomal dominant, because it affects both alleles. e.g. storage disease and diseases inherited in jews.

11- Detailed medications/toxin history

Symptoms: | by dr. Hana only

Weakness

- ➔ Weakness is a cardinal symptom.
- ➔ The distribution of weakness is variable and **may change overtime "very imp".**
- ➔ Complaints such as difficulty rising from a chair or low toilet, difficulty climbing stairs, a waddling gait, difficulty lifting objects over the head, combing hair or brushing teeth.
- ➔ Distal weakness is less common.
- ➔ Patients with proximal leg weakness may rise from sitting on the floor by climbing up their legs with their hands. This is called "**Gower's Sign**". pic on the right
  It indicates severe proximal weakness.



- ➔ When a patient presents with weakness, it is important to know:
  - ◆ Onset
    - Rapid: necrotizing myopathy (it's acute, the patient will be aware of it),
    - Slow: congenital myopathy (it takes 4-5 years, the patient won't notice much)
  - ◆ Course (fixed course like in congenital, or progressive like dystrophies)
  - ◆ Limbs involved
  - ◆ Muscle involved (usually proximal)
  - ◆ Progression
  - ◆ Presence of sensory/autonomic symptoms. It's Atypical for myopathy to present with sensory involvement.
- ➔ Define pattern of weakness:
  - ◆ Proximal limb girdle
  - ◆ Distal distribution → like in inclusion body myositis.
  - ◆ Scapuloperoneal distribution
  - ◆ Distal arm and proximal lower limb
  - ◆ Associated symptoms: ptosis / ophthalmoplegia / cardiac / respiratory

Exercise Intolerance

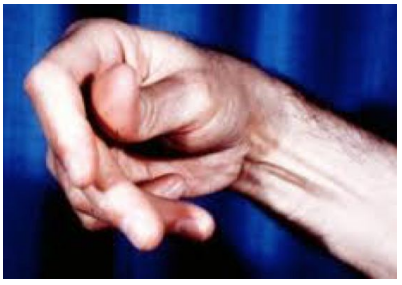
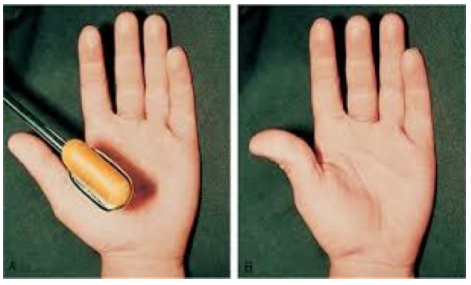
- ➔ **Less reliable negative symptom.** also present in patients with fatigue, malaise, depression, etc...
- ➔ Often reflects the general level of conditioning and health
- ➔ In patients without any objective weakness, **depression** should be considered
- ➔ Exclude certain metabolic myopathies e.g. Pompe disease or mitochondrial cytopathies
- ➔ Ask if it is elicited by brief or long term exercise (carbohydrates or lipid metabolism)

Myalgia

- ➔ Infrequent symptom. can be in necrotizing and inflammatory myopathies, but congenital is typically painless. Myalgia can be provoked or spontaneous.
- ➔ Orthopedic or rheumatologic conditions are more frequent causes e.g. Polymyalgia rheumatica (PMR)
- ➔ **Constant** proximal muscle pain often accompanies inflammatory myopathies.
- ➔ **Episodic** myalgias after exercise point to metabolic myopathies.
- ➔ In patients with waxing and waning diffuse myalgias, anxiety should be ruled out.

Cramps

- ➔ Involuntary painful contractions of muscle that last for seconds to minutes.
- ➔ Most are benign and occur predominantly in calves.
- ➔ **Risk factors** are old age, dehydration, prolonged sitting, use of diuretics, hypothyroidism and DM.
- ➔ They are most common in motor neuron disease and chronic neuropathies such as AML (characterized by cramps and fasciculations) rather than myopathies, in which cramps are **only common in metabolic** as in pompe disease (Glycogen storage disease type II)

	➔ Cramps aren't sufficient for myopathy, you have to look for other symptoms.
Myotonia	➔ Impaired relaxation after sustained voluntary contractions. ➔ A painless phenomenon. ➔ Commonly involves **intrinsic hand muscles and eyelids**. Atypical involvement of pharyngeal muscle can cause change in voice while mastication. ➔ It is due to repetitive depolarization of the muscle fibers. ➔ Can be spontaneous or provoked by: ◆ tapping the muscle (percussion myotonia) by examination, pt. isn't aware of it ◆ voluntary contractions of muscle groups (action myotonia). "مثلاً يقولون إذا مسكت شيء ما أقدر أفكه" ➔ It improves with repeated exercise. ➔ Typical tests are squeezing the hand of the examiner or forceful closure of the eye.  
Myoglobinuria	➔ Excess myoglobin in urine resulting in a **cola colored urine**. ➔ It is an uncommon finding. ➔ Severe and relatively acute muscle fiber damage. Necrotizing myopathy (drugs or autoimmune) ➔ Causes: ◆ Idiopathic. ◆ Strenuous exercise. ◆ Drugs or toxin intake. especially statins will be discussed later ◆ Infections. ◆ Heat stroke. ➔ In case of recurrent myoglobinuria, **glycogenoses** (glycogen storage disease)**, lipid storage myopathies or central core disease with malignant hyperthermia** should be ruled out.

Lab investigations: | by Dr. Hana only

➔ **Muscle enzymes**
- ◆ **CK** → levels increase significantly in acute condition, but aren't as high in chronic because muscle has already atrophied (No CK reserve). Polymyositis > IBM > inherited
- ◆ Aldolase
- ◆ LDH
- ◆ Aminotransferase (AST > ALT, markers of muscle as well as liver)

➔ ANA[2], ENA antibodies (anti Ro/SSA, anti La/SSB, anti Sm, and anti RNP) → done to detect inflammatory myopathies, associated with Sjogren's but can be present in overlap syndromes and SLE

➔ Myositis specific antibodies (anti-histidyl-t-RNA synthetase **anti Jo-1**) in dermatomyositis with interstitial lung disease (ILD).

➔ Genetic testing.

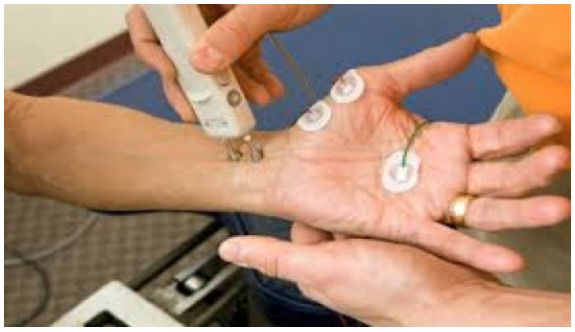
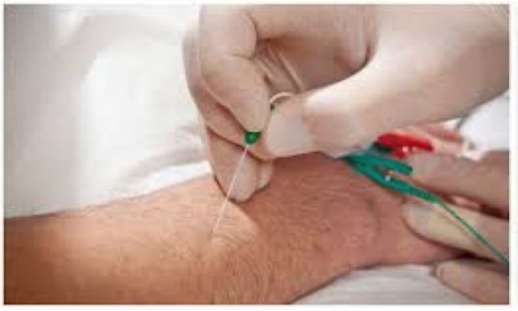
➔ ESR is elevated in acute acquired conditions

[2] Conditions in which ANAs are elevated: SLE, RA, Scleroderma, Sjögren's syndrome, Mixed connective tissue disease, Polymyositis and dermatomyositis, Drug-induced lupus

➔ **Electromyography (EMG):**

- Electrodiagnostic technique for evaluating and recording the electrical activity produced by skeletal muscles, the signals can be analyzed to detect abnormalities.
- can differentiate **between myopathy and neuropathy** (click here if interested), but doesn't tell if it's acute/chronic/acquired/congenital.
- Typical morphology of EMG in myopathy includes low amplitude wave and decrease duration. Insertional activity is increased in inflammatory myopathy.

➔ **Nerve conduction study (NCS):** (**NORMAL** in myopathy!) So u do NCS first, if -ve, go for EMG.

• **NCS:**	• **EMG:**
	

➔ MRI is becoming more involved in myopathy, it shows edema and fatty infiltration in chronic forms. It also helps to specify which muscles are involved in order to take a proper biopsy

➔ Muscle biopsy e.g. for pt. with acute presentation you may suspect necrotizing myositis, dermatitis, polymyositis. you have to take a biopsy to figure it out. Different findings for each disease, will be discussed later

Classification of myopathies:

- **The myopathies are subdivided into acquired and hereditary disorders:**

Congenital not important, just know them by name.	**Hereditary**	**Acquired**
• Central core disease (have risk of malignant hyperthermia after anesthesia) • Multicore (minicore) disease. • Nemaline myopathy. • Myotubular (centronuclear) myopathy. • Myofibrillar myopathy. • Congenital fiber type disproportion.	• Mitochondrial myopathies • Channelopathies • Metabolic myopathies • Muscular dystrophies • Myotonias	• Endocrine myopathies • Inflammatory/immune • Toxic /Drug-induced myopathies • Myopathies associated with other systemic illness

A- Congenital Myopathy

by dr. Hana only

- ➔ Clinical characteristics present from birth or prenatally.
  - Prenatal: decreased fetal movement.
  - Postnatal: hypotonia, poor respiratory effort, difficulty feeding, reduced muscle bulk, and weakness.
  - First year and beyond: hypotonia, weakness, delayed milestones, failure to thrive, recurrent respiratory infections, flaccid speech.
- ➔ **Slow or non progressive** course. may take 5-6 years without change in weakness
- ➔ **Management:**
  - Genetic counseling.
  - Detection and treatment of orthopedic complication e.g. contractures.
  - Follow up patient with ECG, echo. And prevent resp. infection
  - Prevention of complications (general anaesthesia) in central core disease.

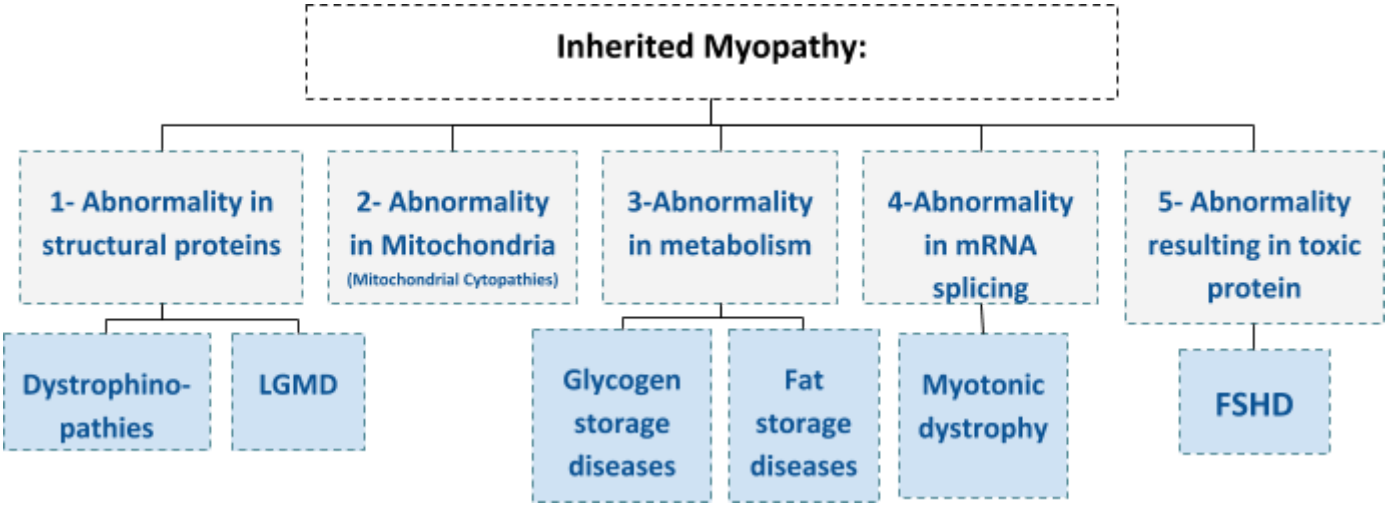
★ Malignant Hyperthermia (MH): video

- ➔ Hypermetabolic crisis.
- ➔ MH-susceptible individual is exposed to a volatile anaesthetic or **succinylcholine**.
- ➔ Genetic skeletal muscle receptor abnormalities allowing excessive calcium accumulation in the presence of certain anaesthetic triggering agents.

Accumulation of Ca → sustained muscle contraction → depletion of O2 → anaerobic metabolism → acidosis → Rhabdomyolysis.

- ➔ **Symptoms:**
  - **Masseter spasm immediately** following anaesthetic induction.
  - Hypercarbia.
  - Sinus tachycardia. arrhythmia developed due to hyper k
  - Generalized muscular rigidity.
  - Tachypnea.
  - Cyanosis.
  - Rapidly increasing temperature is a **later** sign of MH and is typically absent when the diagnosis is initially suspected.
  - Sweating
  - **Cola-colored urine**.
  - **Ventricular fibrillation**.

B- Hereditary Myopathy



Among inherited diseases, dystrophin is the most commonly mutated gene because it's a large gene, second most common is DM1 (dystrophia myotonica 1), not diabetes melitus (DM) nor dermatomyositis (DM) :)
MCQs may present a family tree in which only males are affected, this is an **x- linked recessive disease** e.g. duchenne and Becker's

1- Abnormality in structural proteins (Dystrophinopathies, LGMD)

★ Muscular dystrophies:

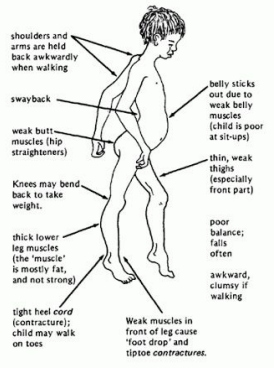
- ➔ Inherited myopathies.
- ➔ Variable age at onset.
- ➔ **Progressive degeneration** of the muscles with connective tissue replacing muscle fibers.
- ➔ **Types:**
  - ◆ **Dystrophinopathies (Duchenne and Becker)** → most common "will be discussed in the next page"
  - ◆ Emery- Dreifuss muscular dystrophy.
  - ◆ Autosomal dominant dystrophies:
    - Fascio-scapulo-humeral MD.
    - Oculopharyngeal MD.
    - Congenital and proximal myotonic dystrophy.
  - ◆ Limb Girdle Muscular Dystrophies (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: Autosomal dominant (AD)
      2- LGMD2: Autosomal recessive (AR) (more common). The most common LGMD2 in western world is LGMD2A (Calpainopathy).

Dystrophinopathies(Duchenne and Becker):

- ➔ **X linked recessive** disorders.
- ➔ Duchenne (early age) and becker (late age)
- ➔ Caused by mutation in the ***dystrophin gene***.[video(just watch it from 0.33 till 3:50 min)]
- ➔ 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.

Duchenne MD (DMD)

- Motor developmental delay.
- *Toe walking*, as a compensation for the progressive **weakness of the knee extensors.**
- Difficulty rising from sitting position.
- **Gower's sign** "proximal weakness"
- Lumbar lordosis, waddling gait, **pseudo-hypertrophy of the calves**. True muscle hypertrophy at first, followed by pseudohypertrophy as fat replaces muscle.
- 12 years: loss of ambulation, marked wasting of muscles, contractures, kypho-scoliosis, exaggerated lumbar lordosis.
- Death is usually due to respiratory complication between 15-30 years.



- Systemic involvement:
  - **Cardiomyopathy**: CHF and arrhythmias.
  - **Malignant hyperthermia** like reactions with rhabdomyolysis.
  - **Intestinal pseudo-obstruction**.
  - CNS involvement: mental retardation, learning disabilities
- Investigation:
  - CK is markedly elevated **early** in the disease. it decreases with chronicity because of muscle atrophy, not because it's improving.
  - Electromyography: myopathic potentials.
  - Muscle biopsy: necrosis, replacement with connective tissue and fibrosis, variation in muscle fiber size, **absent dystrophin**.
- Management:
  - **Early detection of systemic involvement:**
    - Assessing for evidence of cardiac dysfunction and treatment accordingly.
    - Screening for orthopedic complications to maintain function and prevent contractures.
    - Dietary calcium and vitamin D supplementation, and yearly DXA scanning.
    - Weight and growth monitoring.
    - Avoidance of anaesthesia and sedation if possible.
  - **Glucocorticoids are the mainstay** to decrease destruction.
    - Boys 5 years and older who are no longer gaining motor skills or whose motor skills are declining.
    - they increase strength, muscle and pulmonary functions thus prolong life.
    - Reduce cardiomyopathy and lower mortality.
    - Have an **anabolic action** in contrast to their catabolic action on normal skeletal muscle in unaffected people.
    - Stabilizes sarcolemma.
    - **ADRs of glucocorticoids:** Weight gain, Cushingoid facial appearance, acne, Short stature, compression fracture, Delayed puberty, Excessive hair growth, Gastrointestinal bleeding, Psychosis and behavioral changes, avascular necrosis of hips.

Becker Dystrophy

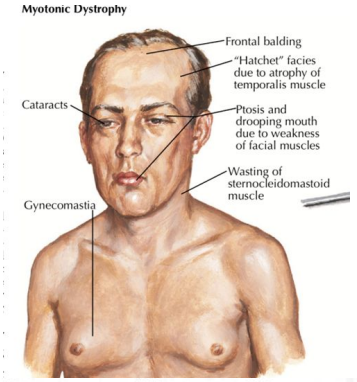
- Older age at onset.
- Less severe symptoms.
- Loss of ambulation is usually in the 4th decade.
- Muscle biopsy shows **decreased staining** patterns rather than complete absence of dystrophin.

	Duchenne MD (DMD)	Becker Dystrophy
Severity	• **at 12 years:** loss of ambulation, marked wasting of muscles, contractures, kypho-scoliosis, exaggerated lumbar lordosis. • **Between 15-30 years:** Death due to respiratory complication	• Less severe symptoms. • Loss of ambulation is usually in the 4th decade. • They live longer.
Onset	• childhood onset (<10 y/o)	• Older age at onset: teens or adulthood (>10 y/o)
Muscle involvement	• calf pseudohypertrophy, contractures, initially Limb-girdle pattern (Gower's sign), later diffuse weakness, +/-respiratory system and cardiac muscle involvement	• limb girdle, calf pseudohypertrophy, +/-cardiac involvement +/- respiratory
CK	• very high CK (50-100 x normal)	• very high ck
Muscle biopsy	• Muscle biopsy: necrosis, replacement with connective tissue and fibrosis, variation in muscle fiber size, absent dystrophin.	• Muscle biopsy shows decreased staining patterns rather than complete absence of dystrophin unlike DMD.

Management: There is no curative treatment. Passive physiotherapy helps prevent contractures in the later stages. Portable respiratory support improves life expectancy. (Kumar)

2- Abnormality in mRNA splicing (Myotonic dystrophy) (DM):

- The most prevalent inherited neuromuscular disease in adults (Age of onset average is 29 years).
- **Autosomal dominant**.
- Myotonia. Myotonias are characterized by continued, involuntary muscle contraction after cessation of voluntary effort, i.e failure of muscle relaxation.
- Stiffness improves with exercise "the warm up phenomenon".
- Weakness of the forearms and peroneal muscles "DISTAL weakness", e.g. difficulty in opening door.
- Ptosis and weakness of other facial muscles (**temporal atrophy**).
- Frontal balding and long face.
- Mild axonal neuropathy "myopathy with co-existing neuropathy".
- Heart involvement.
- GIT dysmotility, constipation and diarrhea.
- Cataract.
- Endocrine abnormalities (gynecomastia due to gonadal atrophy).
- Low IQ.



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

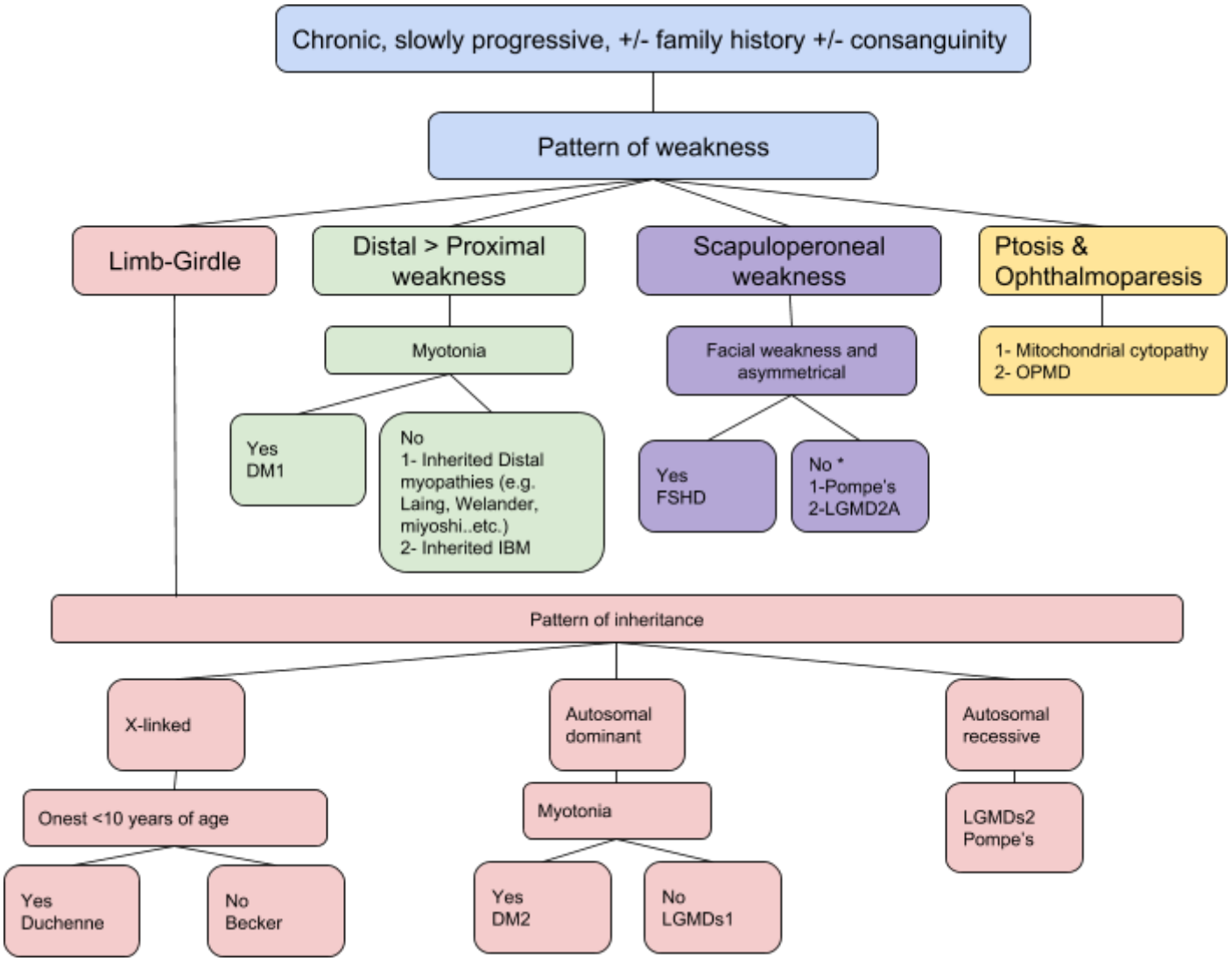
Myotonic Dystrophy 1 (DM1)	Myotonic Dystrophy 2 (less common)
• Distal • expansion of triplet repeat (CTG) on the myotonic dystrophy protein kinase (DMPK) gene.	• Proximal • expansion of triplet repeat (CCTG) on the Zinc Finger protein 9 (ZNF9) gene.

see the picture on the right to know the difference between DM1 and DM2

Videos from dr. slides: examining myotonia, EMG myotonia.

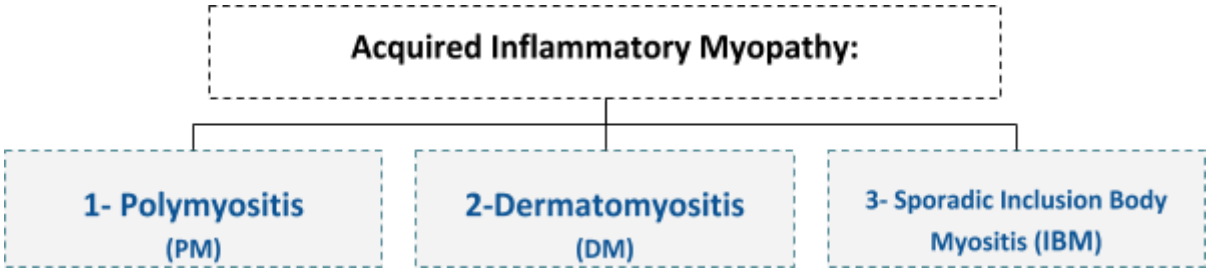
Approach to inherited myopathy: (aka summary)

Extremely important. by dr. Muhammad only



C- Acquired Myopathy

Inflammatory myopathies:



	PM	DM[3]	IBM
Epidemiology	The combined incidence is 2/ 100.000 annually. Female to male ratio of 2:1 (more in female) The peak incidence in adults occurs between the ages of 40-50.		More common in men. More common in whites.
	PM affects mainly adults.	children and adults.	Adults > 40
Onset	Subacute progressive (weeks to months)		Chronic slowly progressive (Insidious)
Mechanism	cell-mediated	humoral	cell-mediated
Clinical features	symmetrical **proximal** (limb girdle) weakness In advanced cases muscle wasting and hyporeflexia. **Multi-system disorders:** • **Interstitial lung disease** 10% (**anti-tRNA synthetase** or **Jo-1**). • Cardiac arrhythmias, bundle branch block and ST changes. Frank myocarditis may be the first presentation • Polyarteritis. • Raynaud phenomenon. • **Cutaneous manifestations in DM** that precede or accompany weakness: **Gottron's papules** and the **heliotrope eruption** are the hallmark and pathognomonic features. see the next page for pictures		Can be proximal and distal, asymmetrical weakness: • **Proximal lower extremity** weakness (usually the first sign). • Distal in upper limbs (weak fingers flexion is a strong sign, if you see it in elderly think of IBM)
Myalgia	Mild myalgias and muscle tenderness.		Myalgia in 40%.
Muscles involved	**Neck flexors** are commonly involved. **Facial muscles are usually spared** (may be, but not typically, involved) **Dysphagia** due to pharyngeal and upper esophageal muscles involvement (30%). **Respiratory** muscles weakness.		**Wrist and finger flexors**, hip flexors, **quadriceps** and ankle dorsiflexion Mild facial weakness in 60 % Esophageal dysmotility and **dysphagia** in 60%.
Diagnosis	**Elevated levels of muscle enzymes** (CK, LDH, aldolase, AST, ALT) **Autoantibodies (ANA[4])** in up to 80% of patients. **Antibodies associated with primary myositis syndromes: anti-Jo1** in ILD (20%) **Antibodies associated overlap syndrome:** anti-PM/Scl, anti-Ro, anti-La, anti U1 snRNP (SLE, systemic scleroderma, RA or mixed CTD), anti U2 snRNP (scleroderma). **Elevated levels of serum and urine myoglobin.** **MRI:** inflammation, edema with active myosotis, fibrosis, and calcification.		**Muscle enzymes** are typically normal or mildly elevated, CK is less than 10 times normal (while in PM and DM it's significantly elevated). **Myositis-specific antibodies are typically absent.** **EMG** **MRI** **Biopsy**
EMG	EMG finding of irritable myopathy (not specific)		
Muscle biopsy	• **Endomysial**, perimysial and perivascular inflammatory infiltrates. • Muscle destruction and regeneration, muscle fiber size variation.	• Perifascicular atrophy. • **Microvascular injury** and deposition of membrane attack complex, endothelial microtubular inclusions and	• **Endomysial inflammation** 90%. • **Basophilic rimmed vacuoles** 70%. • **Eosinophilic inclusions** adjacent to the basophilic-rimmed vacuoles 50%

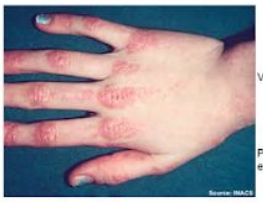
[3] The term dermatomyositis is used when polymyositis is associated with a characteristic skin rash.

[4] Conditions in which ANAs are elevated: SLE, RA, Scleroderma, Sjögren's syndrome, Mixed connective tissue disease, Polymyositis and dermatomyositis, Drug-induced lupus

	• No perifascicular atrophy, microvascular injury, endothelial hyperplasia and inclusions.	hyperplasia. • Perimysial inflammatory cells.	• The definitive diagnostic feature is filamentous inclusions and vacuoles 90%.
Malignancy	Risk is 15% (non-hodgkin's lymphoma and lung). (mnemon.: PNL)	Risk in DM is 30-40 % (ovarian and lung). (mnemon.: DOL)	-
Treatment:	• Immunosuppression: Prednisone at 1mg/kg/day to be tapered slowly over 12 months. • Vitamin D and calcium supplements to prevent complications • Glucocorticoids sparing agents: azathioprine and methotrexate (AVOID it in anti-Jo1, may predispose to ILD). • screen for malignancy & ILD • Physiotherapy and occupational therapy. • Prevention of aspiration: swallowing assessment, elevation of the head of the bed, nasopharyngeal or gastric tube, semi thick diets. • Sun protection.		The response to therapy is generally poor. • Supportive • Steroids and steroids sparing agents but no response. • IVIG for dysphagia. • Physiotherapy and occupational therapy.

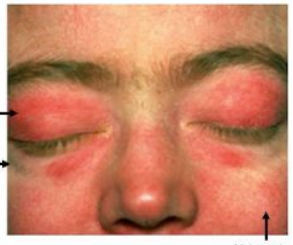
Cutaneous manifestations in DM:

Gottron's papules

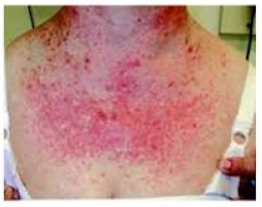


papular, erythematous, scaly lesions over the knuckles

Heliotrope eruption

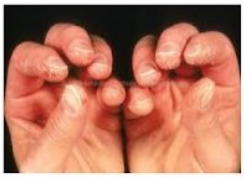


V sign



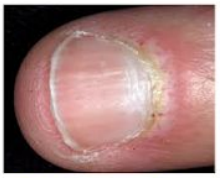
V shaped rash on anterior chest

Mechanic's hands



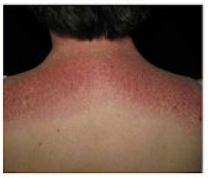
Dry scaly hand

Calcinosis cutis

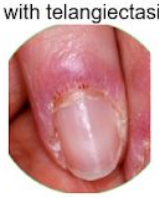


Subcutaneous nodules (Ca deposition)

Shawl sign

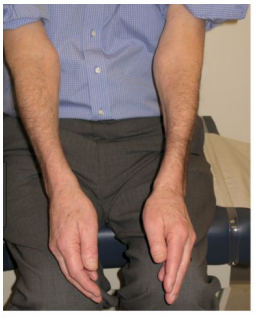


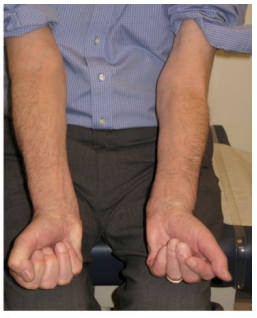
Periungual erythema with telangiectasia



Others:
- Generalized erythroderma.
- Psoriasiform changes in scalp.

Inclusion body myopathy:
- scalloping of the forearm and severe muscle wasting
- Can't make a fist (weak finger flexion)
- Difficulty gripping
- Quadriceps weakness
- Foot drop





Toxic myopathies:

Alcohol, cocaine, Steroids, Antimalarials (chloroquine), antiretroviral, Antipsychotic, Chemotherapy, Lipid lowering agents and most importantly STATINS.

Statin induced myopathy:
- The mechanism is not well understood.
- Myalgia, Myopathic weakness, Myositis, Myonecrosis, Rhabdomyolysis
- PREVENTION:
  - Pravastatin and fluvastatin → less likely to cause myopathy.
  - A baseline CK level prior to starting statin.
  - Patients should be alerted to report the new onset of myalgia and weakness.
  - Caution in patients with renal failure, hypothyroidism and liver failure.

MCQs

1) A 55 years old female presented with sensory loss and incoordination in both upper and lower limbs for 5 months. Her neurological examination showed normal muscle power and absent reflexes. She had sensory loss to pinprick, vibration and position in both upper and lower limbs.
Which one of the following localization describe pattern is associated with?
A. Anterior horn cell
B. Diffuse Peripheral Nerves
C. Dorsal root ganglia
D. Neuromuscular Junction

2) What is the mode of inheritance in Duchenne muscular dystrophy?
a. Autosomal dominant
b. Autosomal recessive
c. X-linked dominant
d. X-linked recessive

3) A 45 year old lady presented to the clinic with 4 month history of fatigue, muscle pain, progressive increase in her weight and tendency to sleep longer time she also noticed occasionally abdominal pain and constipation . She was found to be obese, dry skin and peripheral muscle weakness .
what is the appropriate next step to reach diagnosis ?
A. calcium level
B. thyroid function test
C. colonoscopy
D. ultrasound abdomen

4) True or false:
Inherited myopathies are always symmetrical
False, not always, exceptions include **FSHD**

5) True or False:
Myopathy is always proximal more than distal weakness
False, although this is the most common phenotype, exceptions exist

6) True or false
We need to screen asymptomatic Dystrophinopathy patients for cardiac disease
True, Holter monitor, ECG and echo due to high risk of cardiac complications

7) True or false
We need to screen asymptomatic Myotonic dystrophy patients for cardiac disease
True, high risk for conduction problem

8) True or False:
Myotonia on EMG only happen in Myotonic Dystrophy
False, it's not specific e.g. Pompe's

9) True or false
We need to screen asymptomatic FSHD patients for cardiac disease
False, very low risk for cardiac complications

Answer key:

1 (c) | 2 (d) | 3 (b) | 4 (F) | 5 (F) | 6 (T)| 7(T)| 8 (F)| 9 (F)|

Extra summary: