Pathology

teamwork 437

Lecture three (3) : An introduction to myopathies and muscular dystrophy.

Color Index :-

- **VERY IMPORTANT**
- **Extra explanation**
- **Examples**
- **Diseases names: Underlined**
- **Definitions**

تمت المراجعة
غيداء آل مصمع
&
عبدالرحمن الحيسوني

نَستهِّينُ كل غالٍ كي نُحقِقَ الحُلم ..إن سَمِّنا لا نُبالي بل نسِّير للأمام ..إنّ قِمةَ الجِبالِ تسَّتحِقُ لا جَرم

OBJECTIVES:

- Understand the structure of the various types of muscle fibers.
- Acquire a basic knowledge of the classification of myopathies and give examples of these disorders.
- Understand the meaning of the term muscular dystrophy and have a basic knowledge of the incidence and clinicopathological manifestations of Duchenne's and Becker's muscular dystrophies.
- Know the pattern of inheritance of myotonic dystrophy and its clinicopathological presentations.

RECALL : MOTOR UNIT

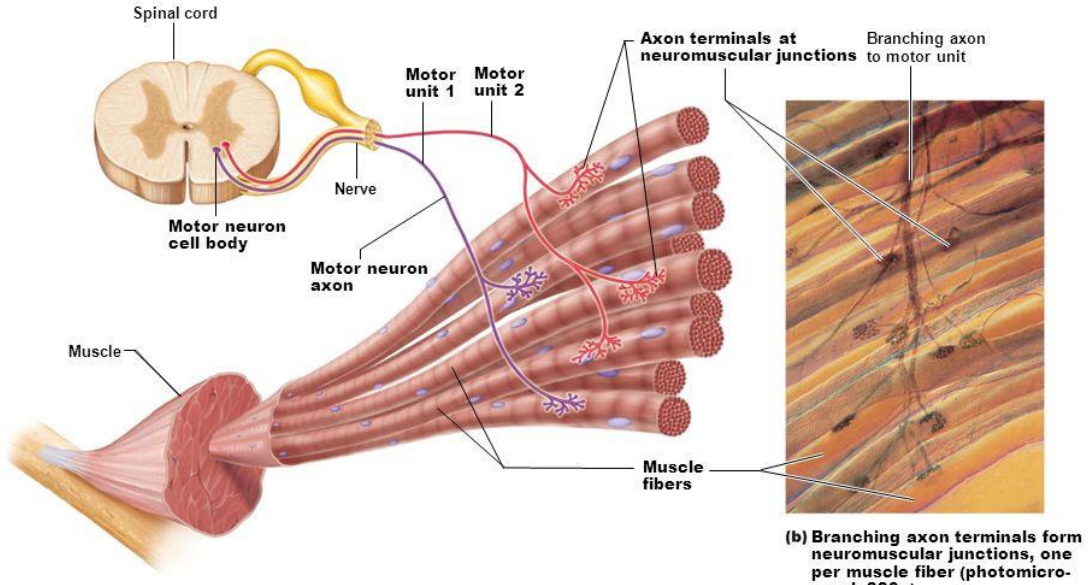
All this slide contain EXTRA information that might help you .

- The principal component of the **motor system** is the motor unit, which is composed of :
  - One lower motor neuron
  - Peripheral axon
  - Neuromuscular junctions.
  - Innervated skeletal muscle fibers.

*Both the **anatomic distribution** of lesions and **specific signs and symptoms** are helpful in **classifying neuromuscular diseases** and in distinguishing them from diseases of the central nervous system.

- جميع مكونات ال motor unit مهمه لوظيفة الmuscle والcontraction
- أي اختلال أو مرض يصيب مكون من ال Motor unit راح يؤدي إلى ضرر بالعضلات ووظيفتها

Figure 9.13 A motor unit consists of one motor neuron and all the muscle fibers it innervates.

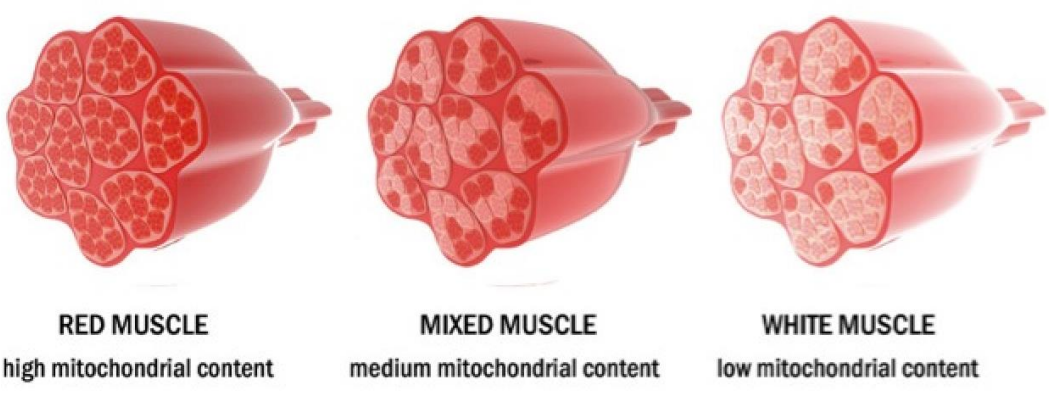


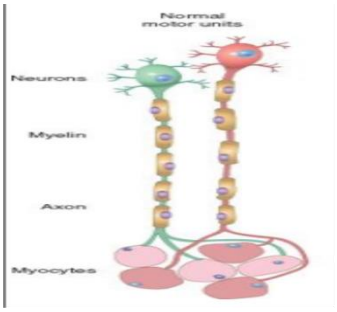
(a) Axons of motor neurons extend from the spinal cord to the muscle. There each axon divides into a number of axon terminals that form neuromuscular junctions with muscle fibers scattered throughout the muscle.

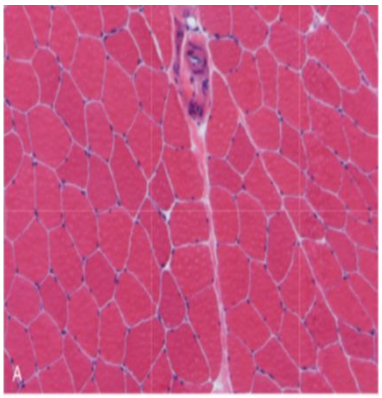
(b) Branching axon terminals form neuromuscular junctions, one per muscle fiber (photomicrograph 330x).

MUSCLE FIBER TYPES :

- Striated muscles in the skeletal muscles divided into two main subtypes**: Type I and Type II.**
  - **The fiber types**, are determined by the **neuron of the motor unit**, and their **properties** are imparted through innervation.
  - A normal muscle is **composed of both fibers arranged randomly**
  - Under the microscope, their distribution is similar to **checkerboard** شطرنج pattern .
  - The different fibers can be identified **using specific staining techniques.**
  - Since the motor **neuron** determines fiber type, **all muscle fibers of a single unit are of the same type.**
  - The fibers of a single motor unit are **distributed across the muscle**, giving rise to a checkerboard pattern of alternating fiber types.







*مثل ما عرفنا أن كل مجموعة من ال muscle fibers يغذيها neuronواحد وهذا ال neuronراح يكسبها نوعها إما كلها تكون type 1أو كلها type 2

*يعني كل neuronيمسك جزئية من ال fibersويحدد نوعها .

For example if the neuron is type 1 all its muscle fibers will be the same type.*

*وأيضاً كل neuronينتشر داخل العضلة ويختار ال fibersبشكل عشوائي مو جنب بعض وهذا الشي اللي يخلي العضلة كأنها بشكل شطرنج .

types	Type 1 fiber	Type 2 fiber
color	**Red** it is noticed n on bird's meat where fiber type grouping in different muscles (tight vs breast meat)	**White**
Contraction speed	Slow	Fast
Conduction velocity	Slow twitch	Fast twitch
Activity	Aerobic	Anaerobic
Duration	Long	Short
Fatigue	Resistant	Easily fatigued
power	Strong	Weak
Storage of energy	More dependent on **fat** catabolism for energy through **mitochondrial oxidative phosphorylation** (aerobic)	More dependent on **glycogen** catabolism for energy through **glycolysis anaerobic**
Enzymes :	high in **myoglobin and oxidative enzyme**s and have many mitochondria	rich in **glycolytic enzymes**
	in keeping with their ability to perform **tonic contraction** (= the long contraction for example : the contraction during standing)	and are involved in **rapid phasic contractions**

*Function of both types of fibers depends on the **unique protein complexes** that make up the **sarcomeres** and the **dystrophin-glycoprotein** complex, as well as **enzymes that meet the special metabolic requirements of muscle.**

Diseases that affect skeletal muscles can involve any portion of the motor unit

- Primary disorder of **the motor neuron or axon**
- Abnormalities of the **neuromuscular junction**
- A wide **variety of disorders primarily affecting** the skeletal muscle itself

*مثل ما قلنا أي جزء يتضرر من ال motor unit يسبب امراض في العضلات ووظيفيتها .

The two principle **pathologic** process seen in skeletal muscles are :

Denervation atrophy :
Which follows loss of axon

Myopathy:
the primary abnormality of the muscle fiber itself

ماذا نسمي المرض اللي يبدأ من العضله ؟ **myopathy**
وماذا نسمي المرض اللي يبدا من ال NEURON ومنه يجي مرض بالعضلات ؟ **Denervation atrophy**
لأن لما تفقد العضلة أي عصب يغذيها بيصير لها ضمور بينما ال myopathy غالبا ما يصير لها ضمور لأن ال neuron يغذيها لكن يكن فيها مشكله إما بعدم الاسجابة أو بالوظيفة..إلخ

- So what is **Myopathy**? as a term may encompasses **a heterogeneous group** of disorders, **both morphologically and clinically** Recognition of these disorders is important for genetic counseling or appropriate treatment of acquired disease.

يعني هي عبارة عن مجموعة امراض كثيره لكن تشترك بنفس الصفات الشكلية والإكلينكية

- And what is **Muscles Atrophy ? A non-specific** response Characterized by abnormally **small myofibers.**

-The type of fibers affected by the atrophy, **their distribution in the muscle, and their specific morphology** help identify the **etiology of the atrophic changes**

-Remember **Atrophy**: loss or shrinkage of muscle fibers. where cells are still alive but **functions significantly fall**

Causes of muscle atrophy:

myopathies

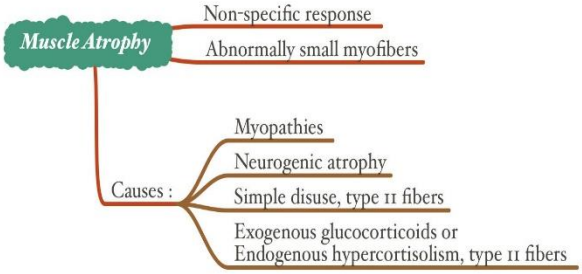
Neurogenic atrophy

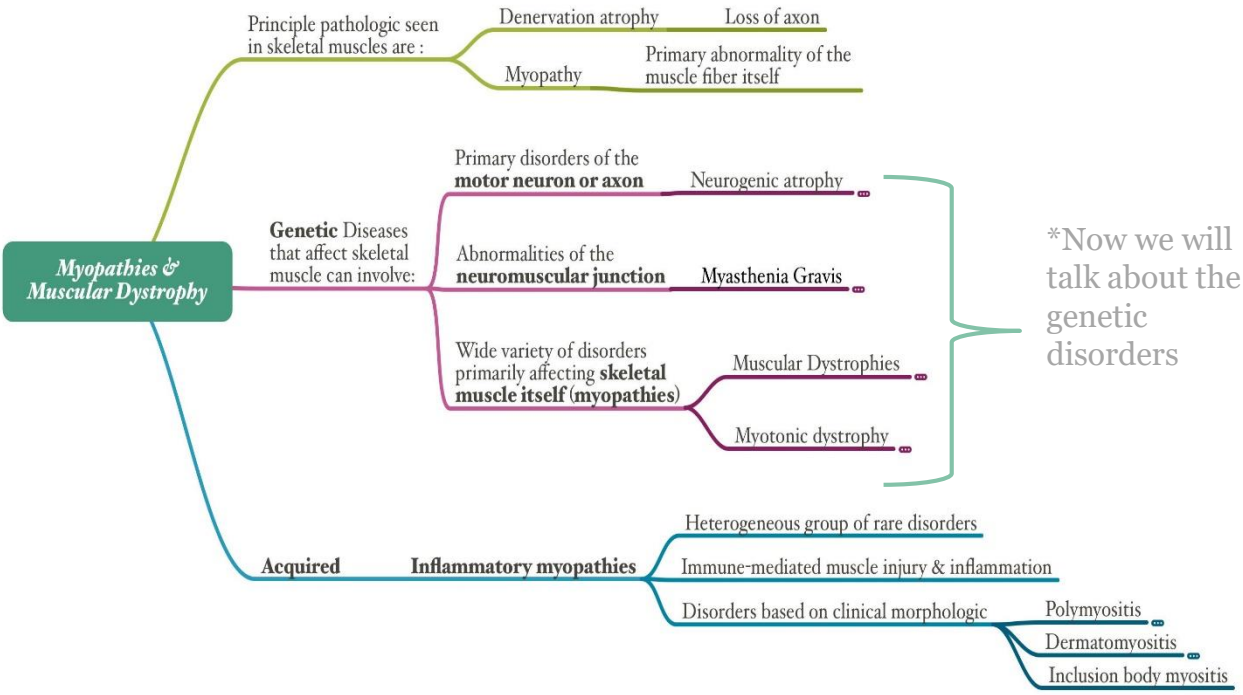
Simple disuse , type 2 Fibers will be effected

Exogenous glucocorticoids or endogenous hypercortisolism (proximal weakness), type II fibers will be effected

Glucocorticoids are naturally produced steroid hormones, or synthetic compounds, that inhibit the process of inflammation (blocking phospholipase A2). Cushing's syndrome is a hormone disorder caused by high levels of cortisol in the blood

- **Cortisol (hydrocortisone)** is a steroid hormone, or glucocorticoid, produced by the adrenal gland. It is released in response to stress and a low level of blood glucocorticoids. Its primary functions are to increase blood sugar through gluconeogenesis; suppress the immune system; and aid in fat, protein and carbohydrate metabolism. It also decreases bone formation. Various synthetic forms of cortisol are used to treat a variety of different diseases


Muscle Atrophy
Non-specific response
Abnormally small myofibers
Causes :
Myopathies
Neurogenic atrophy
Simple disuse, type II fibers
Exogenous glucocorticoids or
Endogenous hypercortisolism, type II fibers


Myopathies & Muscular Dystrophy
Principle pathologic seen in skeletal muscles are :
Denervation atrophy
Loss of axon
Myopathy
Primary abnormality of the muscle fiber itself
Genetic Diseases that affect skeletal muscle can involve:
Primary disorders of the motor neuron or axon
Neurogenic atrophy
Abnormalities of the neuromuscular junction
Myasthenia Gravis
Wide variety of disorders primarily affecting skeletal muscle itself (myopathies)
Muscular Dystrophies
Myotonic dystrophy
Acquired
Inflammatory myopathies
Heterogeneous group of rare disorders
Immune-mediated muscle injury & inflammation
Disorders based on clinical morphologic
Polymyositis
Dermatomyositis
Inclusion body myositis
*Now we will talk about the genetic disorders

disorder of the motor neuron or axon

Neurogenic Atrophy: *(Important)*

- Characterized by involvement of both fiber types and by clustering of **myofibers into small groups**.

HOW could this happen ?

1) **Loss of a single neuron** will affect all muscle fibers in a motor unit, so that the atrophy tends to be scattered over the field. لأن قلنا ان النيورن يغذي العضلات بشكل عشوائي ومتوزع بينهم

2) However, following **re-enervation**, **adjacent intact neurons** send out sprouts (زي البراعم)(budding) to engage the neuromuscular junction of the previously de-enervated fibers→ **new connection** is established → these fibers assume the type of the innervating neuron →**whole groups of fibers can eventually fall under the influence of the same neuron**, **and become the same fiber type (fiber type grouping)**

3) In that setting, if the relevant enervating neuron now **becomes injured**, rather large coalescent (Grow together) groups of fibers are cut off from the trophic stimulation and wither away **(grouped atrophy)** , a hallmark of recurrent neurogenic atrophy .

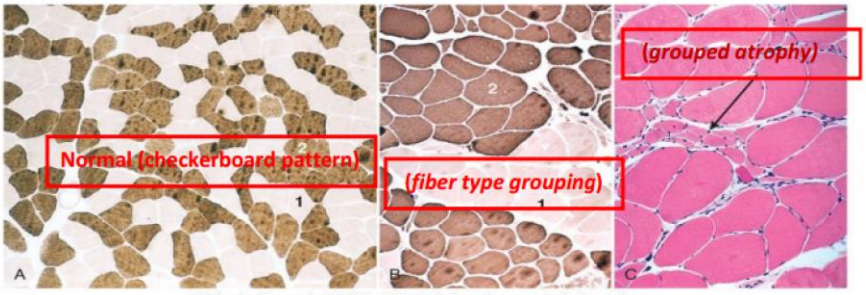


Figure 21-22 **A,** ATPase histochemical staining, at pH 9.4, of normal muscle showing checkerboard distribution of intermingled type 1 (*light*) and type 2 (*dark*) fibers. **B,** in contrast, fibers of either histochemical type are grouped together after reinnervation of muscle. **C,** A cluster of atrophic fibers (group atrophy) in the center (*arrow*).

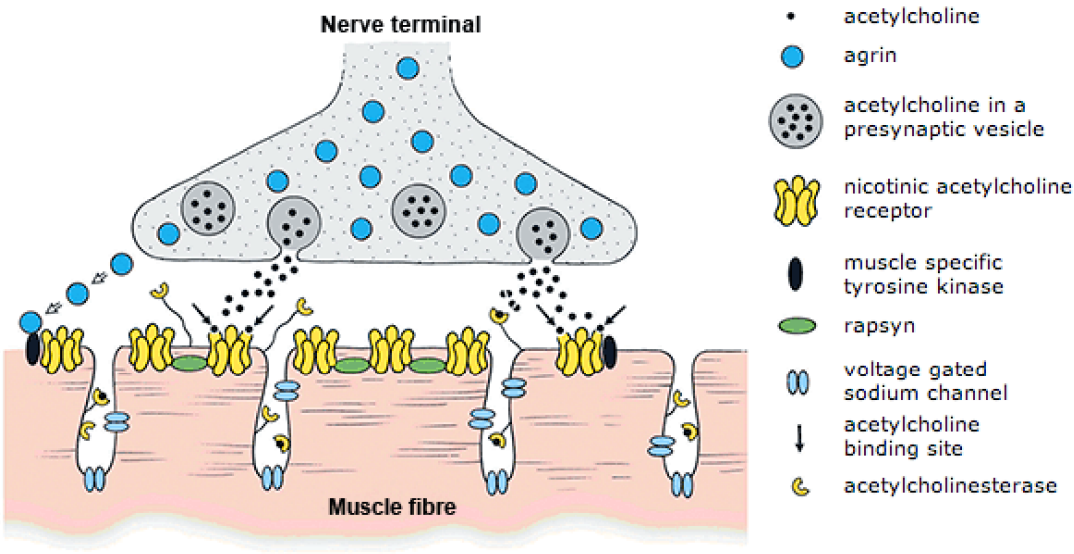
(ATPase is a stain used in pathology.)

*Notice here the stain depend on enzyme reaction not always type 1 is dark because if you stain it with **ATPASE** Stain It will be light.

Here you should remember that fiber follow the nerve supply , so how Neurogenic atrophy happen ? For example we have **axon A** supply type | fiber while **axon B** supply fiber|| , suppose that we have damage in **axon B** ,**the axon A** (as neighbor) help fiber || , then fiber || will change its type because of changes of axon that lead to type grouping .then the damage of axon occur in axon A(the neighbor it self) which lead to group atrophy

Disorders of Neuromuscular Junction

هذي سلايد إضافيه لتوضيح أن لكل جزء للموتر يونت له امراض معينه تصيبه



Neuromuscular junction: a specialized interface between **synaptic nerve endings and muscle fibers**. Usually, disorders of the neuromuscular junction produce functional abnormalities in the absence of any significant changes in the morphology; in other words: the nerve is fine and the muscle also appears healthy, the problem lies in their junction. Those disorders **disrupt the transmission of signals across the neuromuscular junction.**

-The most important Disorder of neuromuscular junction : **Myasthenia Gravis**

Myasthenia gravis is caused **by auto antibodies** that **block the function of postsynaptic acetylcholine receptors** at motor end plates, which results in the degradation and depletion of the receptors.

- **Clinically** : myasthenia gravis frequently manifests with ptosis or diplopia due to weakness in the 4 5 extraocular muscles.
- Repetitive use or electrophysiologic stimulation of muscles makes the weakness more severe.
- **Effective treatments** : include cholinesterase inhibitory drugs, immunosuppression.

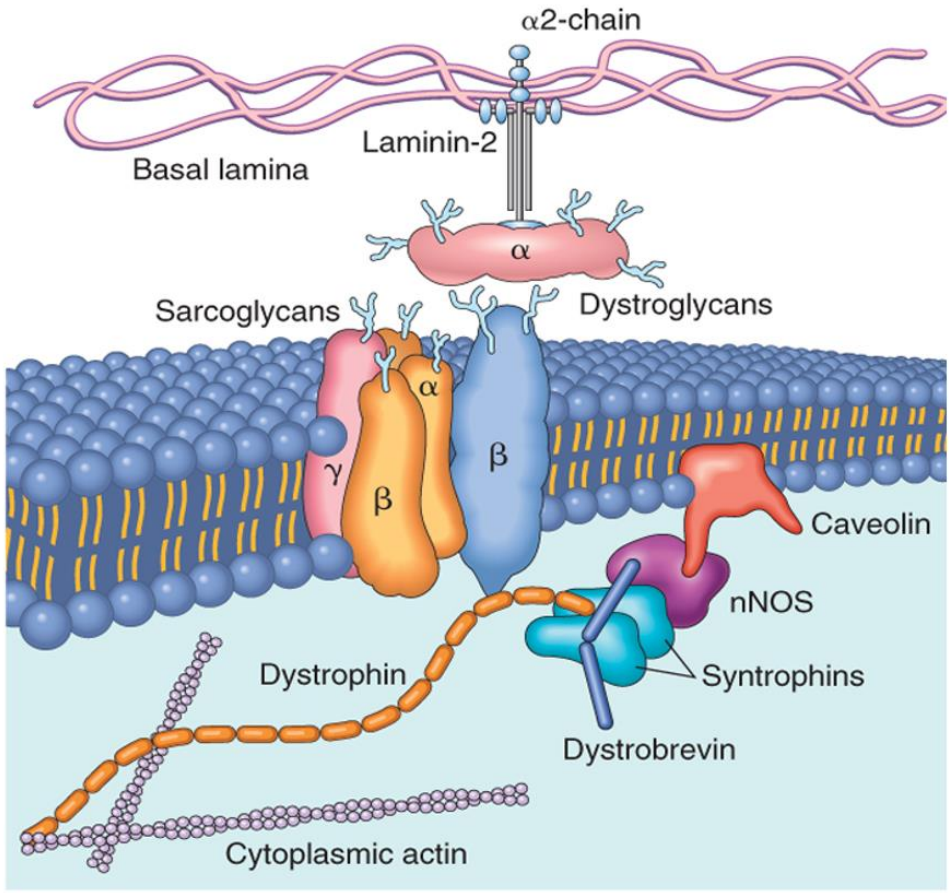
Connect to pharmacology: edrophonium is used to diagnose MS, while neostigmine or pyridostigmine are used to treat it.

DYSTROPHIN PROTEIN :

- As we said before, the Function of types of muscle fibers depends on **the unique protein complexes** that make up the **sarcomeres** and **the dystrophin-glycoprotein complex ,** as well as **enzymes** that meet the special metabolic requirements of muscle.

- **But what is dystrophin?**
  - Dystrophin is a large protein (427 kD). This protein **is located primarily in muscles** used for **movement** (skeletal muscles) and in heart (cardiac) muscle. Small amounts of dystrophin are present in nerve cells in the brain.

  - The dystrophin gene (Xp21) spans (~1% of the total X chromosome: it is an X linked disorder), **making it one of the largest in the human genome**; its enormous size is a probable explanation for its particular vulnerability to **mutations**.



- **What is Dystrophin FUNCTION in the muscle ?** attaches portions of the **sarcomere** to the **cell membrane.** to maintain muscle integrity.
  - This complex **stabilizes** the muscle cell during **contraction** and may be involved in cell **signaling** through **interaction** with **other proteins**.
  - It defects are thought to make muscle cells **vulnerable** "susceptible to physical or emotional attack or harm" to transient **membrane tears** during **contraction** that lead to calcium influx.
  - The result is myofiber **degeneration** that with time outpaces "rise" the **capacity for repair**.
  - So The role of dystrophin in **transferring the force** of **contraction** to **connective tissu**e has been proposed as the basis for the myocyte degeneration that occurs with dystrophin defects, or with changes in **other proteins that interact with dystrophin**
  - It important for cardiac muscle function ; this explains (why **cardio myopathy** eventually develops in many patients)

- So any **mutations** in the **dystrophin gene**, will lead to muscle weakness and loss it's integrity.

  -The most common type of mutations is **deletion mutations.**

  - Approximately **two-thirds** of the cases are **familial**, with the remainder representing new mutations (**sporadic**).

  -In affected **families**, females are **carriers**; they are clinically **asymptomatic** but often **have elevated serum creatine kinase** and can show mild histologic abnormalities on muscle biopsy . **Why** ? Because the cell membrane loss its integrity.

MUSCULAR DYSTROPHIES

- What is **muscular dystrophies?**
  - It's **heterogeneous** group of **inherited disorders** often presenting in **childhood**

=مرض يصيب العضلات مباشرة

- **What is Characters of muscular dystrophies?**
  - progressive degeneration of muscle fibers leading to muscle **weakness** and **wasting**

- **What happened in advanced cases (Histologically)?**
  - cases muscle fibers are replaced by fibrofatty tissue

- **What most common forms of muscular dystrophy?**

Duchenne Muscular dystrophy (DMD) & **BMD (Becker's muscular dystrophy)**

= مرضين يصيبون ويسببون خلل في العضلات مباشره بسبب وجود طفره في بروتين دستروفين

DMD (Duchenne muscular dystrophy) and **BMD (Becker's muscular dystrophy)** are caused by abnormalities in the **dystrophin** gene. Dystrophin supports muscle fiber strength, and the absence of dystrophin reduces muscle stiffness.

The role of dystrophin is transferring the force of **contraction** to connective tissue has been proposed as the basis for the **myocyte degeneration** that occurs with **dystrophin defects**, or with changes in other proteins that interact with dystrophin.

DISORDERS OF SKELETAL MUSCLES (MUSCULAR DYSTROPHIES):

(1)Duchenne Muscular dystrophy (DMD)

most severe and the most **common** form of muscular dystrophy ,ncidence of about 1 per 3500 male births
DMD only affects male, so it is sex-linked disease

-Muscle biopsy specimens from individuals with DMD show little or no dystrophin by both staining and western blot analysis
Dystrophin protein here is absent so when you stain it it will appear negative

-(**5 years**): (DMD) becomes clinically evident
-(**10-12 years**): progressive weakness leading to wheelchair dependence
-(**before 20 age**): death

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(2)Becker Muscular Dystrophy (BMD)

less common and much **less severe**

- -People with BMD, who also have mutations in the dystrophin gene, have diminished amounts of dystrophin, usually of an abnormal molecular weight, reflecting mutations that allow synthesis of an abnormal protein of smaller size
- BMD becomes **symptomatic** later in childhood or adolescence and progresses at a slower and more variable rate.
- Many patients live well into **adulthood** and have **a nearly normal life span.**
- **Cardiac involvement can be the dominant clinical feature** and may result in death in the absence of significant skeletal muscle weakness.

- The histologic alterations in skeletal muscles affected by DMD and BMD are similar except
- that the changes are milder in BMD

Morphology

1- The hallmarks are ongoing myofiber necrosis and regeneration.

loss of يكون فيه مناطق فيها myofibers

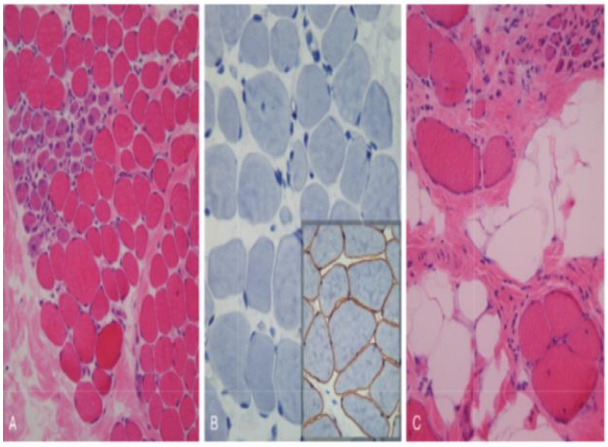
fat وتستبدل هذه المناطق بال

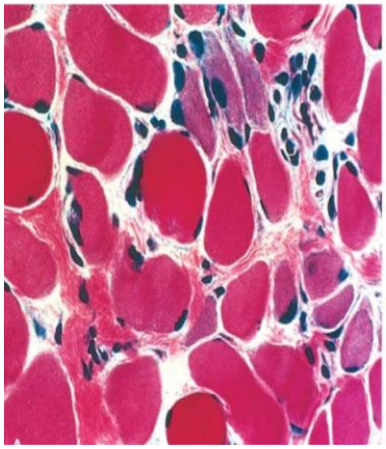
2- Progressive replacement of muscle tissue by fibrosis and fat is the result of degeneration outpacing repair.

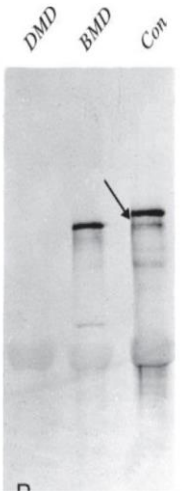
3- marked variation in myofiber size and

4- abnormal internally placed nuclei. (it is normally in the periphery)

- Both DMD and BMD also affect cardiac muscles, which show variable degrees of interstitial fibrosis







CLINICAL FEATURES

- Boys with **DMD**:
  - Normal at birth, and early motor milestones are met on time
  - first symptoms of DMD are clumsiness and an inability to keep up with peers due to muscle weakness
  - Weakness begins in the pelvic girdle muscles and then extends to the shoulder girdle
  - Enlargement of the calf muscles associated with weakness, a phenomenon termed ***pseudohypertrophy***, is an **important clinical finding (replacement of the muscle fibers by fibro fatty tissue)**
    - The increased muscle bulk is caused initially by an increase in the size of the muscle fibers and then, as the muscle atrophies, by an increase in fat and connective tissue في البداية يكون فيه زيادة للألياف ولكن بعدين يصير لها *ديستروفي* ثم تستبدل العضلات بدهون و Connective tissue العضلية..
  - Pathologic changes are also found in the **heart**, and patients may develop heart failure or arrhythmias((عدم انتظام ضربات القلب
  - Walking is often delayed.
  - Cognitive impairment seems to be a component of the disease and is severe enough in some patients to be considered mental retardation (creatine kinase is found in the cells of brain.)
  - Serum **creatine kinase is elevated** during the first decade of life but returns to normal in the later stages of the disease, as muscle mass decreases
  - Death results from **respiratory insufficiency**, **pulmonary infection**, **and cardiac decompensation**

https://www.youtube.com/watch?v=DGOmN6rnsNk

Overview of DMD

https://www.youtube.com/watch?v=o1uhhpjmzkw

To understand pathogenesis of DMD

MYOTONIC DYSTROPHY

- **What is <u>myotonia</u> ?**
  - **sustained involuntary contraction** of a group of muscles, is the cardinal symptom in this disease. (its X linked disease)

- **What are the clinical features and symptoms?**
  - Patients often complain of "stiffness" and have difficulty in releasing their grip, for instance, after a handshake.
  - Myotonia can often be elicited by percussion of the thenar eminence.

- **What are the Pathogeneis ?**
  - Mutations in the gene that encodes the dystrophia myotonica protein kinase (**DMPK).**

The **DMPK** gene provides instructions for making a protein called myotonic dystrophy protein kinase. Although the specific **function** of this protein is unknown, it appears to play an important role in muscle, heart, and brain cells

- **What is the normal function of DMPK ?**
  - In normal subjects, this gene contains fewer than 30 repeats of the sequence CTGe. (CTG-CTG-CTG-CTG.... 30 times). , whereas in severely affected persons, several thousand repeats may be present.
  - Myotonic dystrophy thus falls into the group of disorders associated with trinucleotide repeat expansions
  - Myotonic dystrophy exhibits the phenomenon of ***anticipation***, characterized by worsening of the disease manifestations with each passing generation due to further trinucleotide repeat expansion.

recall from Genetics (Foundation Block) :

that anticipation means that this disease will worsen from one generation from another. In other words, if a patient gets this disease at 15 years of age, the patient's affected children will show this disease at an earlier age; such as 10 years of age.

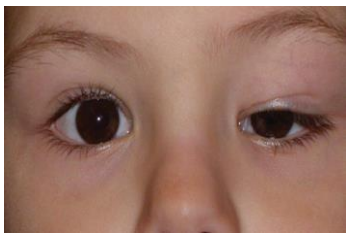
What is the Morphology of myotonia ?

- Skeletal muscle may show variation in fiber size.
- Increase in the number of internal nuclei.
- Another well-recognized abnormality is the ring fiber

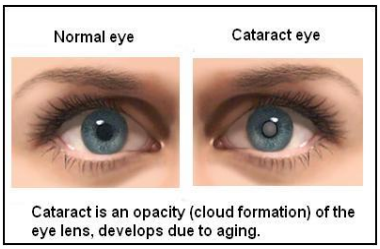
- **What are the clinical Course of myotonia ?**
  - The disease often presents in **late childhood** with abnormalities in gait
  - weakness of **the hand intrinsic muscles and wrist extensors.**
  - Atrophy of **muscles of the face and ptosis** (weakness in eyelid and cause collapse look at pic 1)
  - **Cataracts** (look at pic 2)
  - Other associated abnormalities include frontal balding, gonadal atrophy, cardiomyopathy, smooth muscle involvement, decreased plasma IgG, and abnormal glucose tolerance.
  - **Dementia** has been reported in some cases.

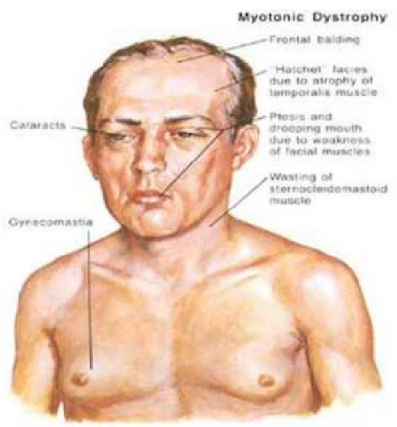
Clinicopathological features: this disease manifests (shows) during late childhood with gait abnormalities (abnormalities in walking). This is because there is a problem in the muscles responsible of dorsiflexion (Dorsiflexion: foot up, Plantarflexion: foot down). After this, the disease progresses and includes weakness of the muscles of the hand, wrist extensors, facial muscles, and ptosis (dropping of the eyelids).

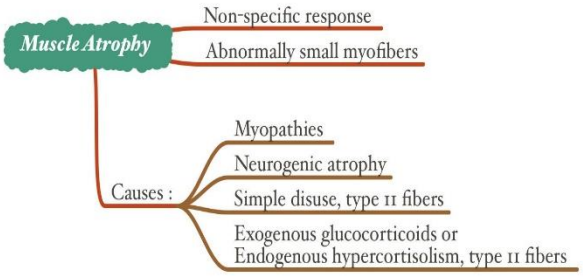
Pic 1: ptosis

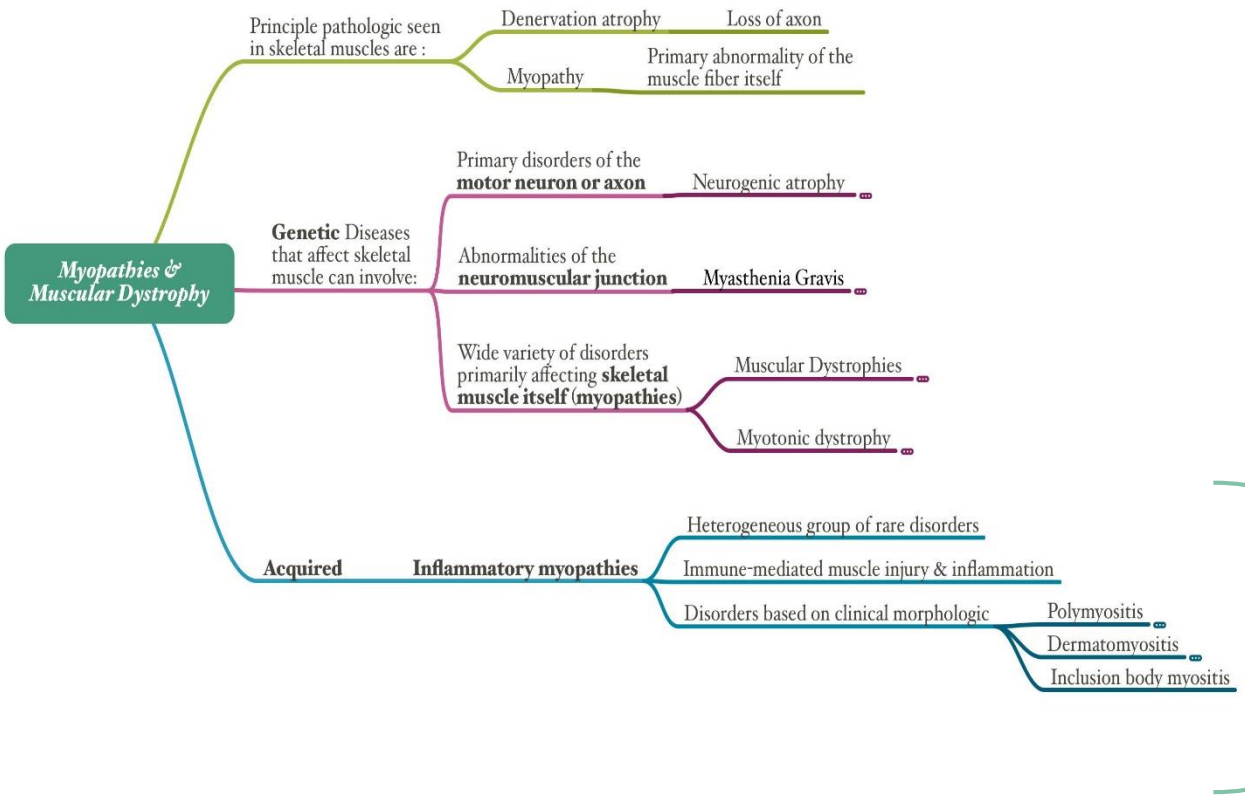


Pic 2: cataracts



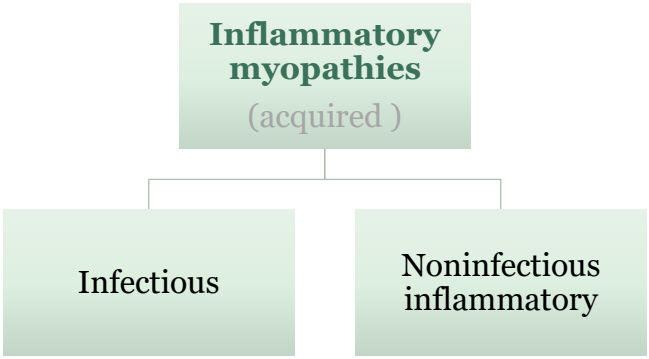






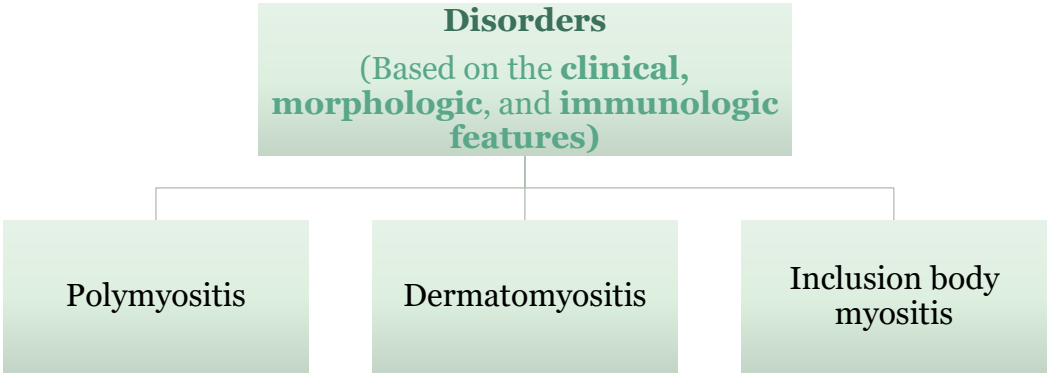
*Now we will talk about the acquired disorders

Acquired Disorders of Skeletal Muscle



Noninfectious Inflammatory Myopathies:

Inflammatory myopathies make up a heterogeneous group of rare disorders characterized by **immune-mediated** muscle injury and inflammation.



Further information :

Occur alone or in conjunction with other autoimmune diseases, such as systemic sclerosis.
- Women with dermatomyositis have a slightly increased risk of developing visceral cancers (of the lung, ovary, and stomach)

Clinically:
- usually symmetric muscle weakness.
- initially affecting large muscles of the trunk, neck and limbs. Thus, tasks such as getting up from a chair or climbing steps become increasingly difficult

Dermatomyositis (affect both children and adults)

- **What is Dermatomyositis ?**

inflammatory disorder of the **skin** as well as **skeletal muscle**.

- **What is the symptoms ?**

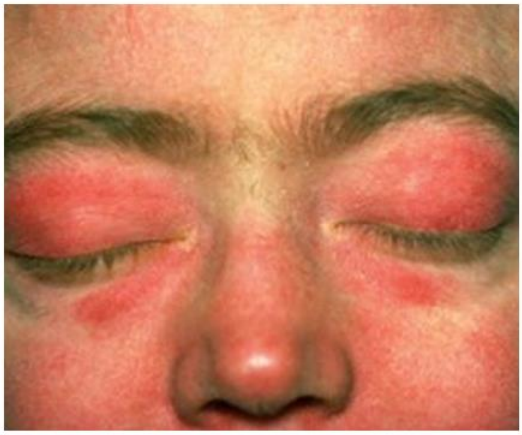
1. **skin rash :** may accompany or precede the onset of muscle disease.
   The classic rash takes the form of
   - ➢ a discoloration of the upper eyelids associated with periorbital edema (look at pic 1 in the next slide)
   - ➢ scaling erythematous eruption over the knuckles(Gottron's lesions) (look at pic 2 in the next slide)

2. **Muscle weakness :** is slow in onset, bilaterally symmetric It typically **affects the proximal muscles first**. As a result, tasks such as getting up from a chair become increasingly difficult.

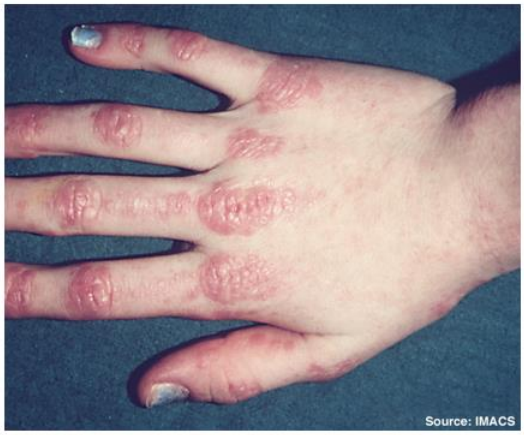
3. **Dysphagia** (difficulty in swallowing)

4. **Extramuscular manifestations**: including interstitial lung disease, vasculitis, and myocarditis, may be present in some cases

5. According to several studies, 20% to 25% of adults with dermatomyositis have **cancer (paraneoplastic)**



Pic1:
Rash and edema



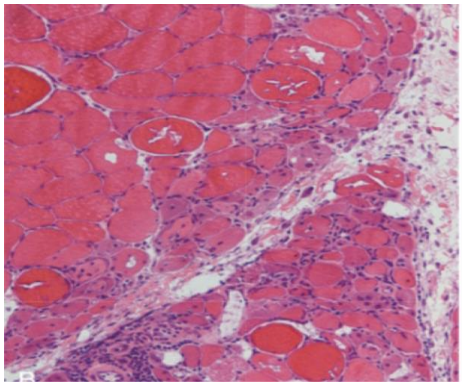
Pic 2:
Rash over the knuckles

MORPHOLOGY

- **Mononuclear inflammatory infiltrate** located predominantly **around small blood vessels.**

- **perifascicular atrophy** : is a Groups of atrophic fibers are particularly prominent at the periphery of fascicles. This is sufficient for **diagnosis**, even if the inflammation is mild or absent.

- marked reduction in the **intramuscular capillaries**



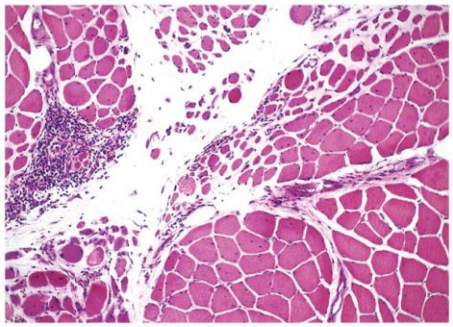


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Figure 5-28 Dermatomyositis. Perifascicular inflammation and atrophy in a skeletal muscle. (Courtesy of Dr. Dennis Burns, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

Further information :

Diagnosis : The diagnosis of these myopathies is based on clinical features, laboratory evidence of muscle injury (e.g., increased blood levels of creatine kinase), electromyography, and biopsy.

NOTE:
- The immunologic evidence supports antibody-mediated tissue injury in dermatomyositis. - Polymyositis and inclusion body myositis seem to be mediated by CTLs (cytotoxic T cells).

Polymyositis (affect adults)

- **What is polymyositis ?**

is an uncommon inflammatory disease that causes muscle weakness affecting both sides of your body.

- **What is characterized by?**

symmetric proximal muscle involvement, similar to that seen in dermatomyositis.

- **What does it differ from dermatomyositis?**

lack of cutaneous involvement and its occurrence **mainly in adults**.

- **What is the Similarities between polymyositis and dermatomyositis ?**

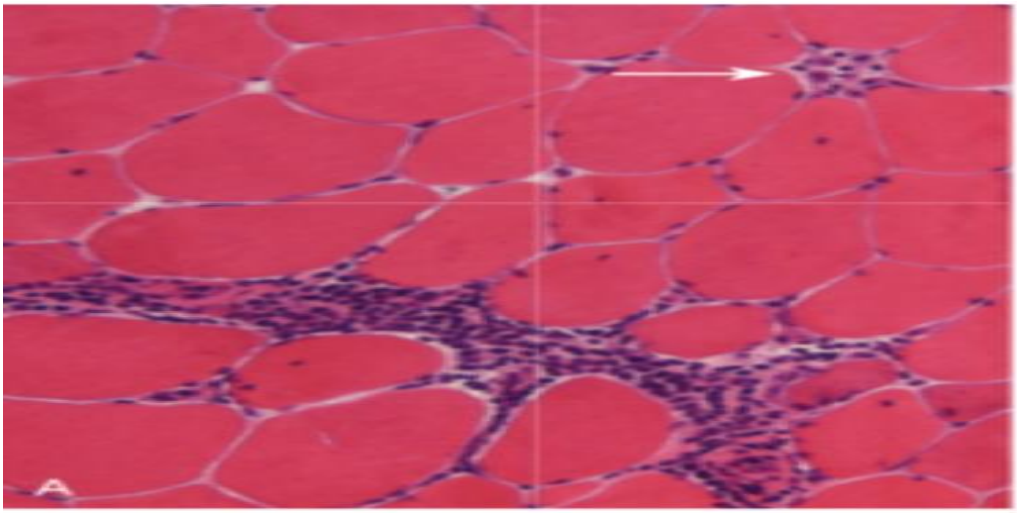
may be inflammatory involvement of **heart**, **lungs**, and **blood vessels.**

MORPHOLOGY

- lymphocytes surround and invade healthy muscle fibers.

- Both necrotic and regenerating muscle fibers are scattered throughout the fascicle, **without** the perifascicular atrophy seen in dermatomyositis.

- **There is no evidence of vascular injury in polymyositis.**



Study smart ! And read this:

	Etiology	Pathogenesis	Clinical features
Neurogenic atrophy	**Genetic** disease affects the motor neuron • Involve both fibers types (1,2). • Clustering of myofiber into small groups.	1. Loss of single neuron 2. Re-enervation 3. Grouped atrophy	
Myasthenia gravis	**Genetic** disorder affect the neuromuscular junction Caused by autoantibodies that block the function of post synaptic Ach receptors which results in degradation & depletion of receptors.	• autoimmune attack. occurs when autoantibodies form against the nicotinic acetylcholine postsynaptic receptors at the neuromuscular junction of skeletal muscles	1. Ptosis or diplopia due to weakness in the 4 5 extraocular muscles. 2. Repetitive use of muscles make the weakness mor severe. 3. More commonly seen in women. **4. Effective treatment:** cholinesterase inhibitory drugs, immunosupperssion.
Muscular dystrophies	• **Genetic** disorder in muscle itself. • Degenerative disorder characterized by muscle wasting & replacement of skeletal muscle by adipose tissue. • Due to mutations of dystrophin gene.	• Duchenne muscular dystrophy (DMD) : deletion of dystrophin. • Becker muscular dystrophy (BMD) : mutated dystrophin protein of smaller size. • Present in childhood.	**DMD :** 1. Proximal muscle weakness at 1 year of age, progress to involve distal muscles. 2. Death results from cardiac or respiratory failure, myocardium is commonly involved. BMD 1. Results in milder disease 2. cardiac involvement can be the dominant.
Myotonic dystrophy	• **Genetic** **Sustained involuntary contraction** of a group of muscles, is the cardinal symptom in this disease.	• Mutations in the gene that encodes the dystrophia myotonica protein kinase (**DMPK**). • Present in late childhood**.**	1. Stiffness & difficulty in releasing the grip. 2. Weakness of the hand intrinsic muscles & wrist extensor. 3. Atrophy of muscles of the face and ptosis. 4. Cataracts & Dementia.
Polymyositis	**Acquired** Uncommon inflammatory disease.	• Affect and seen mainly in adults.	1. Symmetrical proximal muscles weakness. 2. Lack of cutaneous involvement. 3. Inflammatory involvement of heart, lungs and blood vessels.
Dermatomyositis	**Acquired. Unknown etiology** Inflammatory disorder of the skin and skeletal muscles.		1. Skin rash. 2. Muscle weakness. 3. Dysphagia. 4. Extramuscular manifestations. 5. Cancer (paraneoplastic).

MCQs

Taken from 433

1) 5 years old boy displays muscular weakness. He is unable to play with the other children. Quickly becoming tired and unable to keep up. The serum creatine kinase level is elevated. A muscle biopsy is performed, and it has the appearance shown her at low magnification. Which of the following laboratory test finding would be most appropriate to determine the diagnosis?
A. Serum Acetylcholinesterase Antibodytiter
B. Immunuohistochemical Staining for Dystrophin
C. Eosinophil Count in Blood
D. Presence of Oligoclonal Bands of Immunoglobulin In Cerebrospinal Fluid
Answer: B

2) A 35-year- old man has experienced increasing weakness of pelvic and shoulder girdle muscles over several years time. A western blot analysis of affected muscles showed reduced amounts of dystrophin with an abnormal molecular weight.
Amyotrphic Lateral Sclerosis
B. Becker Muscular Dystrophy
C. Dermatomysitis
D. Duchenne Muscular Dystrophy
Answer: B

3) A 56- year-old female has had increasing generalized muscle weakness for the past 2 months. On physical examination: She has 3/5 motor strength in both upper and lower extremities. She is afebrile but has a blood pressure of 155/90 mm hg. A gastrocnemius muscle biopsy is performed and histochemical staining of the biopsy shows type 2 muscle fiber atrophy . Which of the following conditions is the most likely to have?
Cushing Syndrome
B. Mcardle Disease
C. Duchenne Muscular Dystrophy
D. Myasthenia Gravis
Answer:A

4) A 44-year- male, who has worsening congestive heart failure for the past year. Has muscular weakness involving upper arms and legs .A deltoid muscle biopsy is performed, and the immunuohistochemical staining pattern with antibody to dystrophin is shown here (A, normal: B, patient). Which of the following conditions does he most likely have?
A. Werding – Hoffmann Disease
B. Polymyositis
C. Becker Muscular Dystrophy
Answer: C

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Kindly contact us if you have any questions/comments and suggestions:

* EMAIL: pathology437@gmail.com
* TWITTER : @pathology437

GOOD LUCK!

Resources:-

1- Females slides
2- Robbin's Basic Pathology

Pathology

teamwork 437