Myopathies

Colors of text:
Definitions: Blue.
Examples: Green.
Important: Red.
Extra explanation: Gray. . It is only there to help you understand. If you feel that it didn't add anything to you just skip it.
Diseases names: Underline.

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.

Contents:

- **The definition of motor unit and muscle fiber types.**
- **Myopathies:**
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    1. **Disorders of Neuromuscular Junction**
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            - Other X-Linked and Autosomal Muscular Dystrophies
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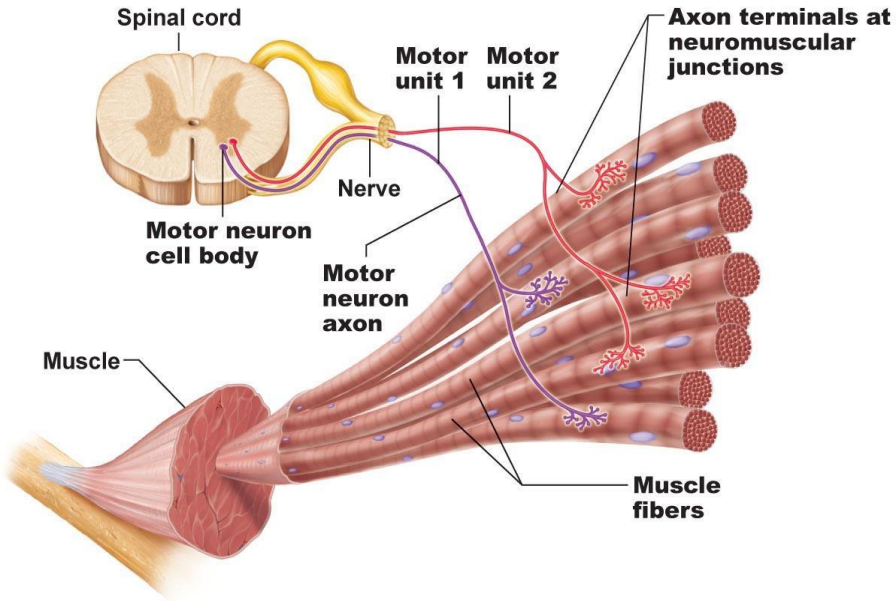
The definition of motor unit and muscle fiber types

[Type One and Type Two Muscle Fibers.]

The principal component of the **motor system** is the **motor unit**, which is composed of :

1. One lower **motor neuron**.
2. Peripheral axon.
3. Neuromuscular junctions.
4. Innervated skeletal muscle fibers.



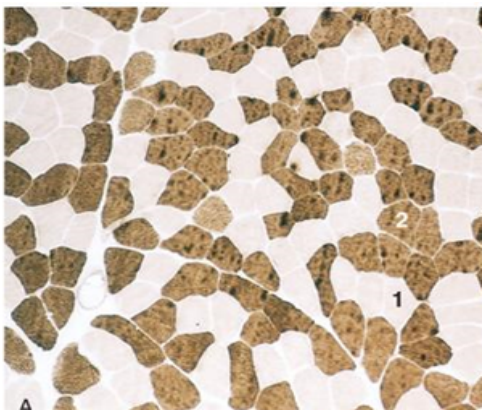
(a) Axons of motor neurons extend from the spinal cord to the muscle. There each axon divides into a number of axon terminals that form neuromuscular junctions with muscle fibers scattered throughout the muscle.

Striated muscles in the skeletal muscles divided into two main subtypes: Type I and Type II.

- **Type I** (RED) muscle fibers have **MORE** Mitochondria than type II (WHITE) muscle fiber.

Types	Type I	Type II
Color	Red It is noticed in on birds' meat where fiber type grouping in different muscles (thigh vs. breast meat) is quite pronounced.	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)

- a way to remember the types of muscles: "I red slowly": type I are red and slow.
- A normal muscle is composed of **both** fibers arranged randomly.
- Under the microscope, their distribution is similar to **checkerboard pattern** شطرنج.
- The different fibers can be identified using specific staining techniques.



Function of both types of fibers depends on the unique [1]protein complexes that make up the sarcomeres and the dystrophin-glycoprotein complex, as well as enzymes that meet the special metabolic requirements of muscle.

- Depending on the **nature of the nerve fiber** doing the enervation[2], the associated **skeletal muscle develops** into one of two major subpopulations.

[1] بروتينات مميزة
[2] قطع العصب

Myopathies

Myopathy: There are lots of different myopathies that have different clinical presentations.

Diseases that affect skeletal muscle (myopathies) can involve any portion of the motor unit:

- Primary disorders of the **motor neuron** or **axon**. (nervous problem)
- Abnormalities of the **neuromuscular junction**.
- Wide variety of disorders primarily affecting the **skeletal muscle** itself .

Disorders of Peripheral Nerves

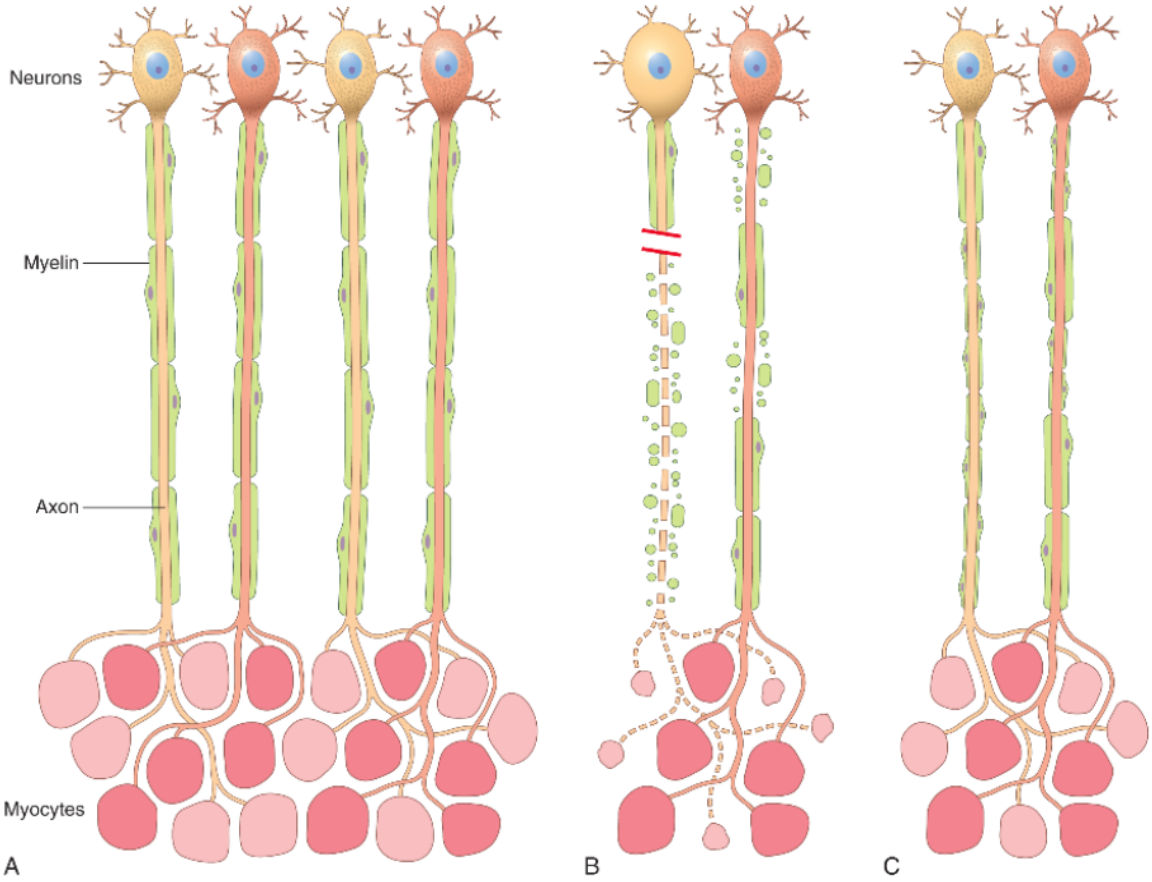
Note: this section wasn't focused on by the doctors. However, it is in our objectives. We recommend you not to spend a lot of time on this section because it is more related to the CNS. This is just to let you understand the fact that damages to the nerve could have an effect on the muscles; causing muscular dystrophies.

Peripheral neuropathy.

The two major functional elements of peripheral nerves:

1. Axonal processes.
2. Myelin sheaths (made by Schwann cells.)

In the case of myelinated axons, one Schwann cell makes and maintains exactly one myelin segment, or internode, along a single axon. Adjacent internodes are separated by nodes of Ranvier. Peripheral nerves contain a mixture of different types of axons.



A: In normal motor units.

B: Acute axonal injury (left axon) results in degeneration of the distal axon and its associated myelin sheath, with atrophy of the denervated myofibers. By contrast, acute demyelinating disease (right axon) produces random segmental degeneration of individual myelin internodes, while sparing the axon.

C: Regeneration of axons after injury (left axon) allows connections with myofibers to re-form. The regenerated axon is myelinated by proliferating Schwann cells, but the new internodes are shorter and the myelin sheaths are thinner than the original ones. Remission of demyelinating disease (right axon) allows remyelination to take place, but the new internodes also are shorter and have thinner myelin sheaths than flanking normal undamaged internodes.

Most peripheral neuropathies can be subclassified as:

- **axonal neuropathies:** caused by insults that directly injure the axon. The entire distal portion of an affected axon degenerates. Axonal degeneration is associated with secondary myelin loss.

The idea here is the same of that we were talking about in anatomy: when there is an injury to one of the nerves' axon there will be damage to the muscle such as paralysis, atrophy, or loss of sensation in the parts the nerve supplies.

- **Demyelinating neuropathies:** damage to Schwann cells or myelin sheath, resulting in abnormally slow nerve conduction velocities.
- **mixed** (axonal and demyelinating).

Peripheral neuropathies fall into several anatomic patterns and may cause:

- sensory damage.
- motor axon damage.
- mixture of both.

- **Polyneuropathies:** Axonal loss. Patients commonly present with loss of sensation and paresthesias[3].
- **Polyneuritis multiplex:** in which the damage randomly affects portions of individual nerves, resulting (for example) in a right radial nerve palsy and wrist drop together with loss of sensation in the left foot.
- **mononeuropathy:** involving only a single nerve most commonly is the result of traumatic injury or entrapment (e.g., **carpal tunnel syndrome**).

Useful Article: **Carpal Tunnel syndrome.**

- Diabetes is the most common cause of peripheral neuropathy.

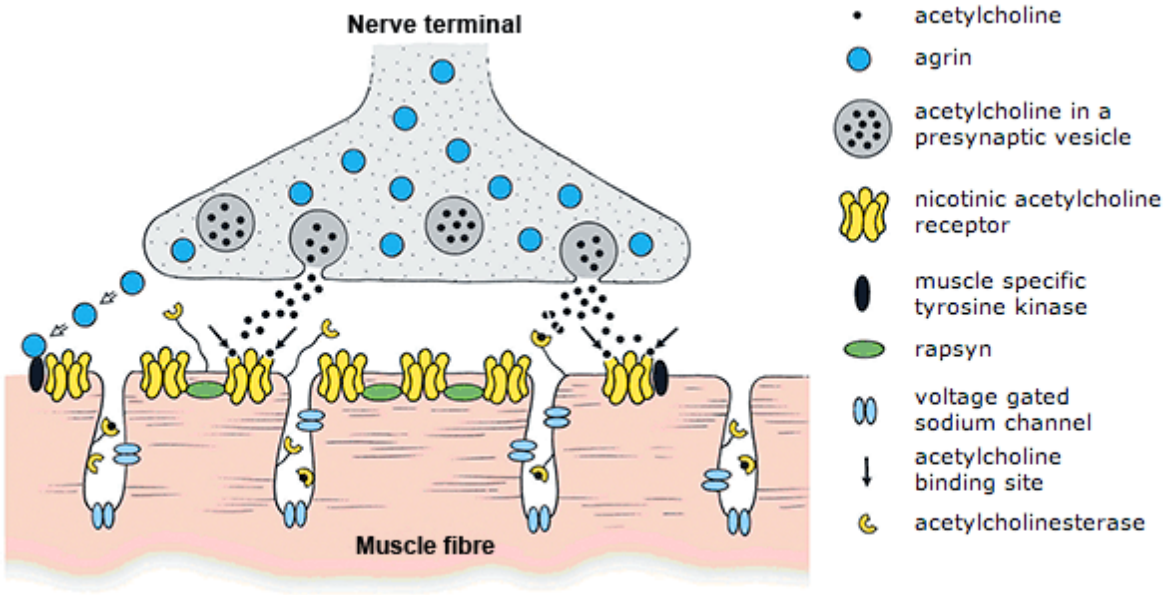
SUMMARY

Peripheral Neuropathies

- Peripheral neuropathies may result in weakness and/or sensory deficits and may be symmetric or consist of random involvement of individual nerves.
- Axonal and demyelinating peripheral neuropathies can be distinguished on the basis of clinical and pathologic features. Some disorders are associated with a mixed pattern of injury.
- Diabetes is the most common cause of peripheral neuropathy.
- Guillain-Barré syndrome and chronic idiopathic demyelinating polyneuropathy are immune-mediated demyelinating diseases that follow acute and chronic courses, respectively.
- Metabolic diseases, drugs, toxins, connective tissue diseases, vasculitides, and infections all can result in peripheral neuropathy.
- A number of mutations cause peripheral neuropathy. Many of these are late-onset diseases that may mimic acquired ones.

[3] sensation of tingling

Disorders of Neuromuscular Junction



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.

Disorders of neuromuscular junction can be divided into:

1- 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** [4]or **diplopia** [5]due to weakness in the 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.

2- Lambert-Eaton Syndrome:

Lambert-Eaton syndrome is caused by **autoantibodies** that inhibit the function of **presynaptic calcium channels**, which reduces the release of acetylcholine into the synaptic cleft.

Connect to physiology: calcium influx in the presynaptic neuron causes the release of ACh vesicles.

Patients with Lambert-Eaton syndrome experience improvement in their muscles throughout the day because there is increased stimulation of the neuron (opposite of patients with Myasthenia Gravis).

It often arises as a **paraneoplastic disorder** (disorders associated with cancer), particularly in patients with **small cell lung carcinoma**.

Treatments: **immunosuppression**, **plasmapheresis**.

*cholinesterase inhibitory drugs are not effective in this case.

[4] drooping eyelids
[5] double vision

SUMMARY

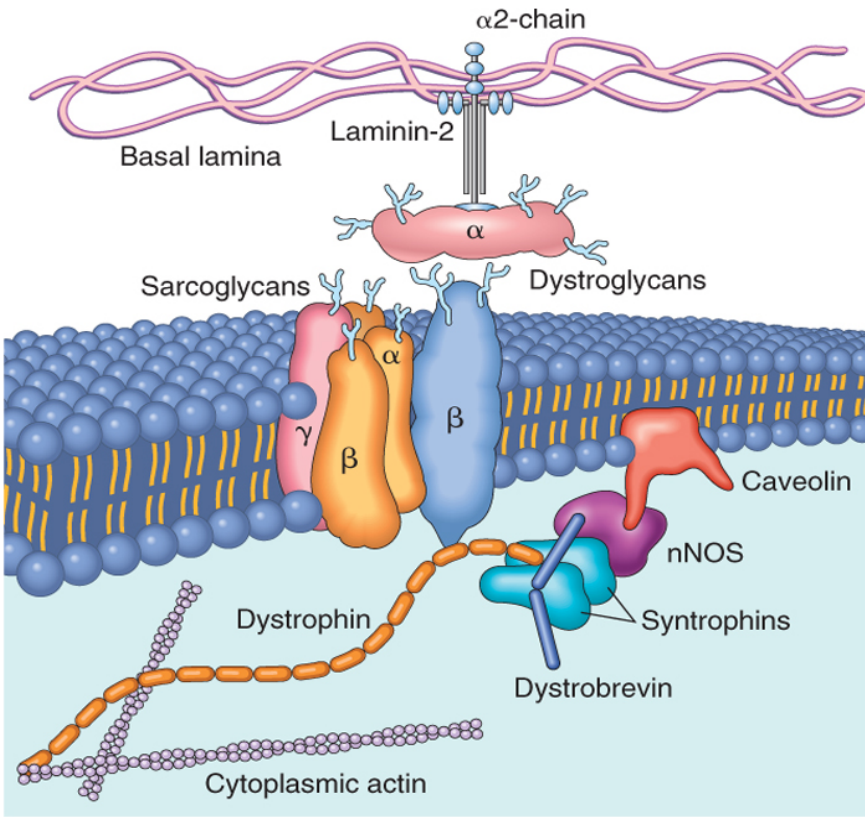
Neuromuscular Junction Disorders

- Disorders of neuromuscular junctions manifest with weakness that often affects facial and extraocular muscles and may show marked fluctuation in severity.
- Both myasthenia gravis and Lambert-Eaton syndrome, the most common forms, are immune-mediated, being caused by antibodies to postsynaptic acetylcholine receptors and presynaptic calcium channels, respectively.
- Myasthenia gravis often is associated with thymic hyperplasia or thymoma. Lambert-Eaton syndrome in a majority of cases is a paraneoplastic disorder; the strongest association is with small cell lung cancer.
- Genetic defects in neuromuscular junction proteins and bacterial toxins also can cause symptomatic disturbances in neuromuscular transmission.

Disorders of Skeletal Muscles

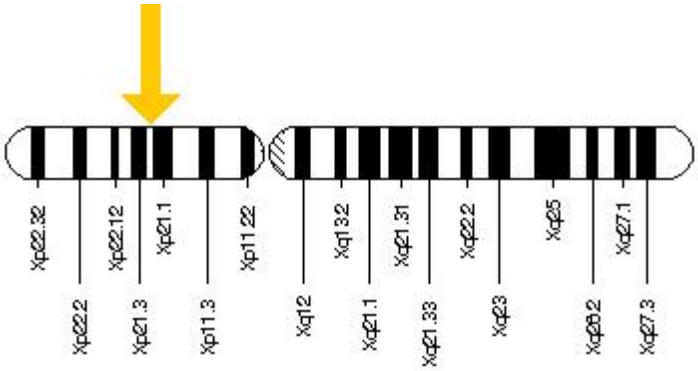
Function of types of muscle fibers depends on the unique **protein complexes** that make up the sarcomeres and the **dystrophin-glycoprotein** complex , as well as **enzymes** that meet the special metabolic requirements of muscle.

Dystrophin (Structure Protein):



Dystrophin is a large protein (**427 kD**[6]). 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**.

Dystrophin attaches **portions of the sarcomere** to the **cell membrane.** 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.

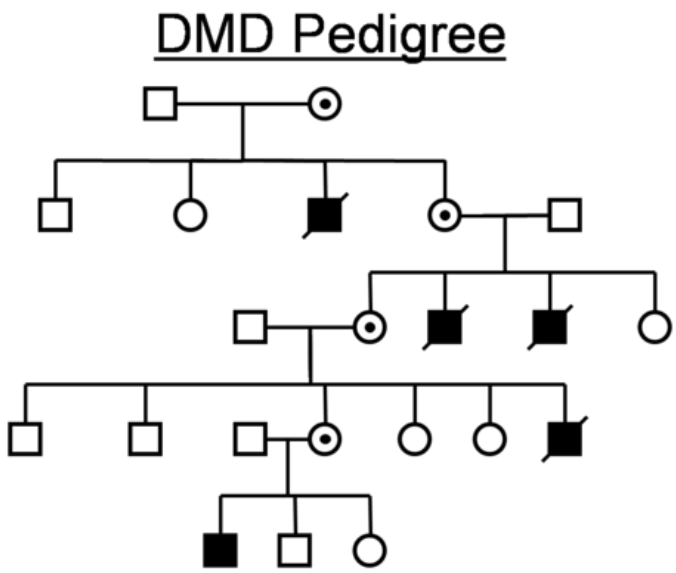


- The most common type of mutations is **deletion mutations**.

[6] kilodalton. Atomic mass unit.

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



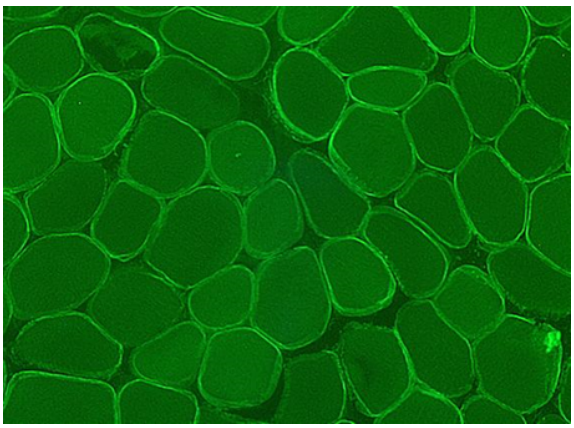
The X chromosome carrying the disease-causing mutation can be tracked through the family. Note: Shaded squares = affected males: dots in circles = carrier females.

Pathogenesis:

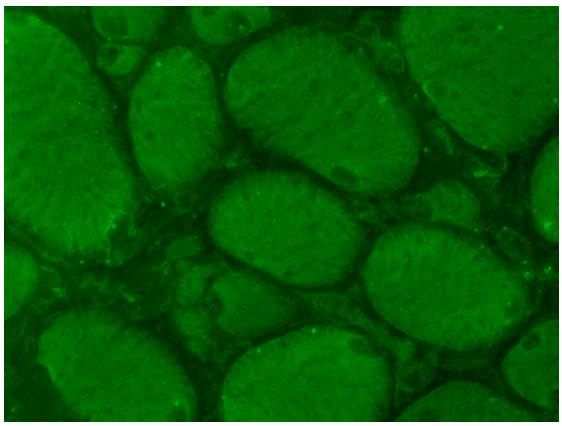
DMD (Duchenne muscular dystrophy) and **BMD** (Becker's muscular dystrophy) are caused by abnormalities in the dystrophin gene.

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.



Normal Dystrophin



Defect in dystrophin

Inherited Disorders of Skeletal Muscle

Genetic disorders affecting skeletal muscle include:

1. Muscular dystrophies:

Muscular dystrophies are inherited diseases that result in progressive muscle injury in patients who usually appear **normal at birth**.

- the **Duchenne** and **Becker** muscular dystrophies are good examples.

2. Congenital muscular dystrophies:

Congenital muscular dystrophies are progressive, early-onset diseases. Some are also associated with central nervous system manifestations.

3. Congenital myopathies:

Congenital myopathies are a heterogeneous group of inherited diseases that often have a perinatal or early childhood presentation and result in relatively static deficits.

- Remember the difference between congenital and inherited diseases. Inherited are in the genes but congenital disease occur during embryogenesis.

Dystrophinopathies: Duchenne and Becker Muscular Dystrophy

Recessive **X-Linked** Muscular Dystrophy caused by a mutation in the **dystrophin gene** located in short arm of x21 chromosome (Deletion).

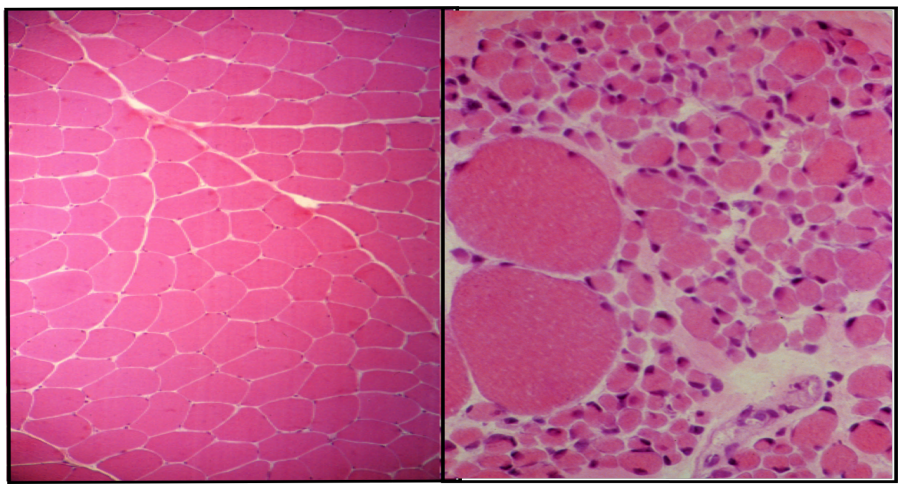
Duchenne Muscular Dystrophy (DMD) is the most severe and the most common form of muscular dystrophy, with an incidence of about 1 per 3500 live male births. It leads to rapid muscle degeneration.

Becker muscular dystrophy (BMD) is very similar to DMD but it takes **longer time to develop**. It leads to slow muscle weakness.

DMD becomes clinically evident by age of 5, a progressive weakness leading to **wheelchair dependence** by age 10 to 12 years and death by the early 20s.

- Although the same gene is involved in both BMD and DMD, BMD is **less** common and much **less** severe. Because in Duchenne muscular dystrophy no functional dystrophin is produced.

A way to remember this: "Du**chenne** is شين, while Becker is **Better"**



The picture at your left shows a normal skeletal muscle, while the other is for a patient with DMD or BMD.

Morphology

- ❏ The histologic features of **DMD** and **BMD** are similar exept changes are milder in BMD.
- ❏ Marked variation in muscle fiber size, and abnormal interenally placed nuclei caused by myofibers' hypertrophy and atrophy.
- ❏ Progressive replacement of muscle tissue by fibrosis and fat as a result of degeneration.
- ❏ **Note:** this is why a patient may looks as if he or she has been weight lifting, but actually there is no muscle, but actually fat and fibrosis. In other words, this fat and fibrosis may increase the size of the patients' body; making it look as if they have been excercising.
- ❏ **Connective tissue** is increased throughout the muscle.

Other X-Linked and Autosomal Muscular Dystrophies

1- Myotonic muscular dystrophies:

Myotonic dystrophy: sustained involuntary contraction of a group of muscles; patients find it difficult to release their grip after a handshake.

Pattern of inheritance: autosomal dominant; problem in the gene encoding for **dystrophia myotonica protein kinase** (DMPK).

What is the problem or mutation in this gene?

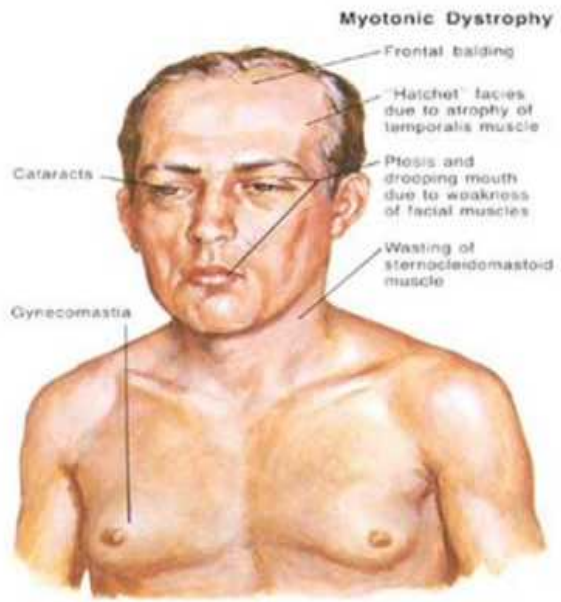
In normal people, this gene has **less than 30 CTG sequence**. (CTG-CTG-CTG-CTG…. 30 times). In affected individuals, there are more repeats (**thousands**) resulting in a mutation in dystrophia myotonica protein kinase.

Myotonic dystrophy shows anticipation: recall from genetics 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.

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).

Other tissues may be affected (I don't believe this is important but we put it to be complete):

- cataracts: the eyes become white like a cat's (look at a picture of cataracts)
- arrhythmias, testicular atrophy, balding[7] of certain areas of the head… etc.



[7] صلع

2- Autosomal Muscular Dystrophies:

Other forms of muscular dystrophy share many features of DMD and BMD but have distinct clinical and pathologic characteristics .

Some of these muscular dystrophies affect specific muscle groups, and the formal diagnosis is based largely on the clinical pattern of muscle weakness.

Limb Girdle Muscular Dystrophies

Limb girdle muscular dystrophies can be inherited either as autosomal dominant or autosomal recessive disorders. Mutations of the **sarcoglycan complex** of proteins are a classic example of limb girdle muscular dystrophy.

muscles affect	genetic basis	subtypes	mutations
proximal musculature of trunk and limbs	heterogeneous (many genes affecting it)	6 autosomal Dominant subtypes . 12 autosomal Recessive subtypes .	1- mutations affect components of Dystrophin Glycogen Complex other than Dystrophin (because if it affected dystrophin we would call it DMD or BMD) 2-mutations affect Proteins involved in vesicle transport and repair of cell membrane after cell injury.

Channelopathies, Metabolic Myopathies, and Mitochondrial Myopathies

1. Inherited mutations of ion channels (channelopathies):

Ion channel myopathies are a group of familial disorders characterized by myotonia(myotonia is inability to relax voluntary muscle after vigorous effort). These diseases stem from inherited defects in genes encoding ion channels.

e.g. Hyperkalemic periodic paralysis: results from mutations in the gene encoding the skeletal muscle sodium channel protein **SCN4A .**

2. Inborn errors of metabolism (exemplified by glycogen and lipid storage diseases)

These Myopathies are due to inborn errors of metabolism include disorders of glycogen synthesis and degradation , and abnormalities in lipid handling. These storage diseases can manifest in many disorders including:

- **Systemic disease.**
- **Ongoing muscle damage and weakness.**
- **Acute renal failure.**

- patients with this type of disorders must avoid episodes of massive exercise or fasting due to their damage on his muscles.

3. Mitochondrial myopathies.

Can involve mutations in either mitochondrial or nuclear DNA that encodes mitochondrial constituents.

Mitochondrial myopathies typically present:

- in young adulthood.
- with proximal muscle weakness.
- sometimes with severe involvement of the **ocular musculature** (external ophthalmoplegia).

In the case of mitochondrial myopathies, there might be **neurologic signs**, **lactic acidosis**, and **cardiomyopathy.**

The most consistent pathologic findings in skeletal muscle are **irregular muscle fibers** and **aggregates of abnormal mitochondria**. The abnormal mitochondria give a red appearance to the muscle fiber on a special stain, that is why they are called **ragged red fibers.**

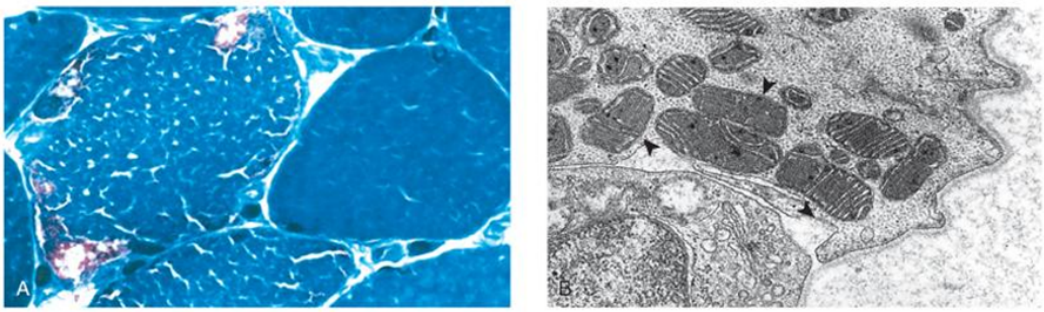


Figure 21-25 **A,** Mitochondrial myopathy showing an irregular fiber with subsarcolemmal collections of mitochondria that stain red with the modified Gomori trichrome stain *(ragged red fiber)*. **B,** Electron micrograph of mitochondria from biopsy specimen in **A** showing "parking lot" inclusions (*arrowheads*).

The electron microscopic appearance is also often distinctive: there are **increased numbers** of, and **abnormalities** in, the **shape** and **size** of mitochondria, some of which contain alterations in the structure of the cisternae such as a parking lot appearance.

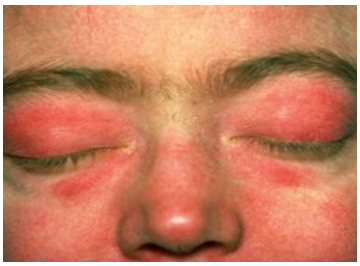
Acquired Disorders of Skeletal Muscle

1- Toxic Myopathies:

Important subcategories include disorders caused by **intrinsic exposures** (e.g. thyroxine) or **extrinsic exposures** (e.g., alcohol, therapeutic drugs).

- Thyrotoxic myopathy can present as either acute or chronic proximal muscle weakness, and can precede the onset of other signs of thyroid dysfunction. Findings include myofiber necrosis, regeneration, and interstitial lymphocytes.
- Ethanol myopathy can occur with alcohol abuse. Acute toxic rhabdomyolysis with accompanying myoglobinuria that can cause renal failure. On histology, there is myocyte swelling and necrosis, myophagocytosis, and regeneration.
- A drug called **chloroquine** can also produce proximal myopathy.

2-Inflammatory Myopathies:




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

Based on the clinical, morphologic, and immunologic features, three disorders:

- Polymyositis.
- Dermatomyositis
- Inclusion body myositis

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.

In dermatomyositis: an associated rash (classically described as a lilac or heliotrope discoloration) affects the upper eyelids and causes periorbital edema.

Histologically

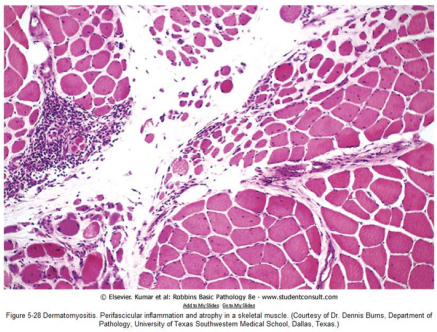


Figure 5-28 Dermatomyositis. Perifascicular inflammation and atrophy in a skeletal muscle. (Courtesy of Dr. Dennis Burns, Department of Pathology, University of Texas Southwestern Medical School, Dallas, Texas.)

- infiltration by lymphocytes.

- degenerating and regenerating muscle fibers.

The pattern of muscle injury and the location of the inflammatory infiltrates are fairly distinctive for each subtype

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).

SUMMARY

Disorders of Skeletal Muscle

- Skeletal muscle function can be impaired secondarily because of problems with muscle innervation or by a primary myopathy that can be inherited or acquired.
- The genetic forms of myopathy fall into several fairly distinct clinical phenotypes, including muscular dystrophy, congenital myopathy, and congenital muscular dystrophy.
- Dystrophinopathies are X-linked disorders caused by mutations in the dystrophin gene and disruption of the dystrophin-glycoprotein complex. Depending on the type of mutation the disease may be severe, such as Duchenne muscular dystrophy, or mild (e.g., Becker dystrophy).
- Acquired myopathies have diverse causes, including inflammation and toxic exposures.

Muscle atrophy

What's the difference between muscle atrophy and muscle dystrophy ?

Muscular dystrophy: Loss of function.
Atrophy means shrinkage of cell size from loss of its intracellular substance, atrophy can rise from a number of different reasons, where cells are still alive but functions significantly fall. It is a non-specific response.

- **Characterized** by abnormally small myofibers
- The type of fibers affected by atrophy, their distribution in the muscle, and their specific morphology[8] help identify the **etiology** of the atrophic changes

Causes of muscle atrophy:

- Simple **disuse**[9] (e.g., prolonged bed rest, immobilization to allow healing of a bone fracture.. etc.) can cause profound atrophy.
- Exogenous **glucocorticoids or endogenous hypercortisolism** (e.g., in Cushing syndrome) are another cause of muscle atrophy, typically involving proximal muscle groups more than distal ones.

- **Disuse- and steroid-induced atrophy** primarily affects **the type II fibers** and causes a random distribution of the atrophic myofibers.
- **Atrophic myofibers** are also found in myopathies

Note: **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.**

The finding of additional morphologic changes, such as myofiber degeneration and regeneration or inflammatory infiltrates are features that suggest a myopathic etiology

Neurogenic Atrophy:

- Characterized by involvement of **both fiber types** and by clustering of myofibers into **small groups,** Deprived of their normal enervation, skeletal fibers undergo progressive atrophy.
- **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.
- However, following re-enervation, adjacent intact neurons send out sprouts(**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) fig B**
- 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) fig C** , a hallmark of recurrent neurogenic atrophy .

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[8] the study of the form and structure and their specific structural features
[9] the state of not being used.

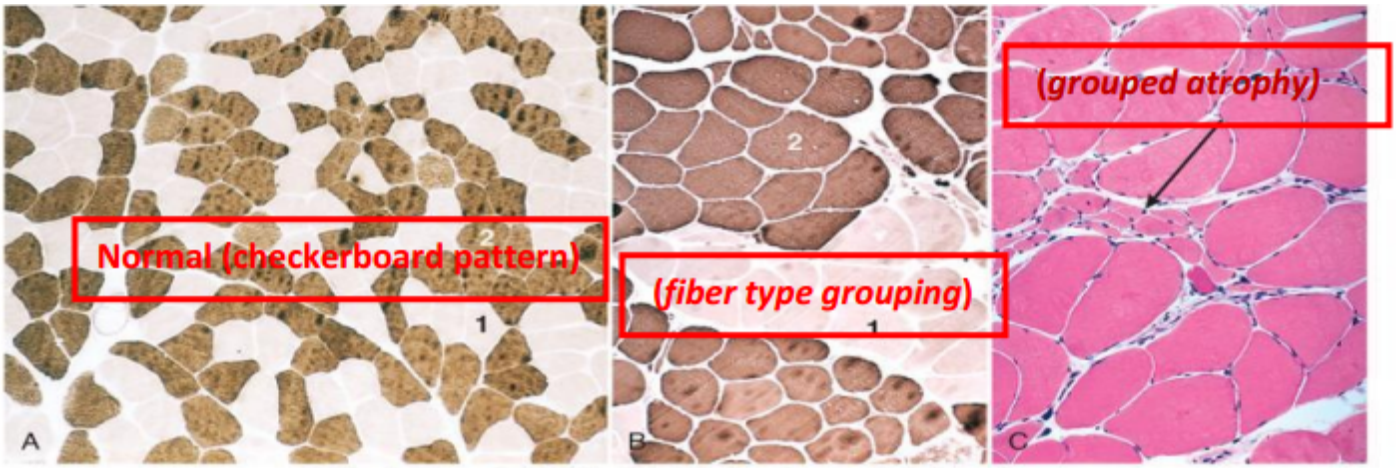

Figure 21-22 **A,** ATPase histochemical staining, at pH 9.4, of normal muscle showing checkerboard distribution of intermingled type 1 (*light*) and type 2 (*dark*) fibers. **B,** in contrast, fibers of either histochemical type are grouped together after reinnervation of muscle. **C,** A cluster of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

(ATPase is a stain used in pathology.)

Clinical Cases

Duchenne Muscular Dystrophy (DMD)

Its caused by a loss of function mutation in the dystrophin gene in the short arm of the X chromosome Xp21 (X-linked)

Normal at birth, and early motor milestones are met on time. Walking is often delayed

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

-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

Pathologic changes are also found in the heart, and patients may develop heart failure or arrhythmias

the severity of the disease is correlated with the degree of deficiency

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Becker Muscular Dystrophy (BMD)

Its caused by a loss of function mutation in the dystrophin gene with less severity than DMD

Boys with BMD develop symptoms at a later age than those with DMD. The onset occurs in later childhood or in adolescence, and it is accompanied by a generally slower and more variable rate of progression

Although cardiac disease is frequently seen in these patients, many have a nearly normal life span.

MCQ's

1- Which one of the following histologic findings on muscle biopsy would be most indicative of an active polymyositis:

A- Marked fiber hypertrophy
B- Many fibers undergoing degeneration and regeneration
C- Grouping of atrophic fibers
D- accumulations of adipose tissue.

2- Hyperkalemic periodic paralysis is :

A- Sporadic mutation disease
B- Mitochondrial disease
C- Metabolism abnormalities
D- Channelopathies

3- Which one of the following intrinsic exposures is associated with increased risk of toxic myopathies :

A- Alcoholism
B- Glucocorticoids
C- Thyroxine
D- Calcitonin

4- Polymyositis is mediated by:

A- Natural killer cell
B- Cytotoxic T cell
C- Macrophages
D- B-cells

5- Which one of the following muscle types is affected in muscular atrophy :

A- Type I which is fast twitching muscle
B- Type I which is slow twitching muscle
C- Type II which is slow twitching muscle
D- Type II which is fast twitching muscle

6- 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 Antibody Titer
B- Immunohistochemical Staining for Dystrophin
C- Eosinophil Count in Blood
D- Presence of Oligoclonal Bands of Immunoglobulin In Cerebrospinal Fluid

7- 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.

A- Amyotrophic Lateral Sclerosis
B- Becker Muscular Dystrophy
C- Dermatomyositis
D - Duchenne Muscular Dystrophy

8- 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 immunohistochemical staining pattern with antibody to dystrophin is shown here (A,normal: B, patient). Which of the following conditions does he most likely have?

A- Werdnig – Hoffmann Disease
B- Polymyositis
C- Becker Muscular Dystrophy
D- Myasthenia Gravis

9- A 35-year-old man has experienced increasing weakness of the pelvic and shoulder girdle muscles for several years. On physical examination, he has 4/5 motor strength in all extremities. There is no pain or deformity, and his range of motion is normal. He has no gait abnormality and no tremors. There are no focal neurologic deficits. He is afebrile. A deltoid biopsy is performed, and Western blot analysis shows reduced amounts of dystrophin with an abnormal molecular weight. Which of the following is the most likely diagnosis?

A. Duchenne muscular dystrophy
B. Becker muscular dystrophy
C. Lambert-Eaton syndrome
D. Myotonic dystrophy
E. Myasthenia gravis

Answer: B

This patient has Becker muscular dystrophy. This congenital condition is similar to Duchenne muscular dystrophy in that it has an X-linked pattern of inheritance and there is a mutation in the dystrophin gene. However, in Becker muscular dystrophy, dystrophin is abnormal, not absent, resulting in less severe muscle disease than that of Duchenne muscular dystrophy. The typical patient is a middle-aged man. Amyotrophic lateral sclerosis is a progressive disease with a neurogenic form of muscle atrophy resulting from loss of motor neurons. Lambert-Eaton syndrome is a myasthenia-like paraneoplastic condition. McArdle disease is caused by a deficiency in muscle phosphorylase and does not produce progressive weakness. Myasthenia gravis results from acetylcholine receptor antibody and leads to progressive weakness. Myotonic dystrophy is an X-linked disorder characterized by facial and upper body weakness, cataracts, gonadal atrophy, cardiomyopathy, and dementia. Polymyositis is an autoimmune disorder with myalgia. Werdnig-Hoffman disease is a spinal muscular atrophy resulting from loss of motor neurons in infancy.

Answers:

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

True and false questions

1- A 20-year old male come to the clinic with a redness of the upper eyelid and periorbital edema . the clinical examination and laboratory findings indicate that he has Dermatomyositis . which of the following is true and which is not ?

A- He may develop vascular cancers
B- Histologically you may see fibrosis
C- If you ask about his family history you probably find someone with the same disease
D- Dermatomyositis is an antibody mediated injury

Answers:

A- FALSE , because he is a male .
B- FALSE , you may see lymphocytes and degeneration and regeneration muscular fibers
C- FALSE , because it is an inflammatory disease
D- True

2- A 13-year old boy with Duchenne muscular dystrophy :

A- He may have enlargement of calf Muscle
B- He would probably have a normal life span
C- The etiology may be sporadic mutation or familial disease
D- He would probably experience respiratory failure

Answers :

A- TRUE , because of the accumulations of adipose tissue in the muscle
B- FALSE , they usually die in early 20s
C- TRUE
D- TRUE

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Good Luck!

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