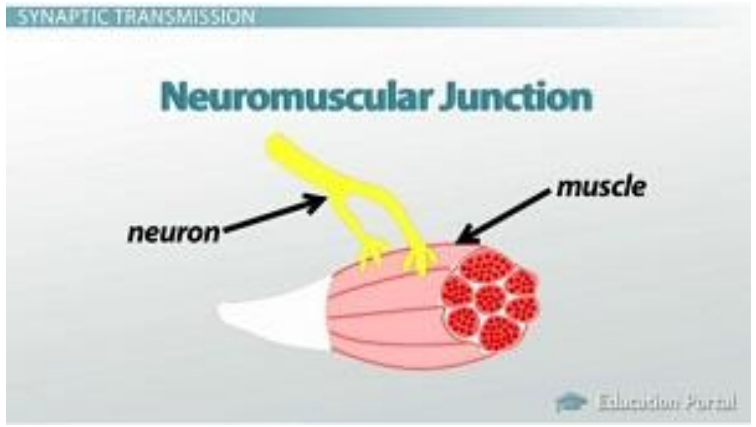
Ashur University
College of Medicine

Grade 2
Neuroscience

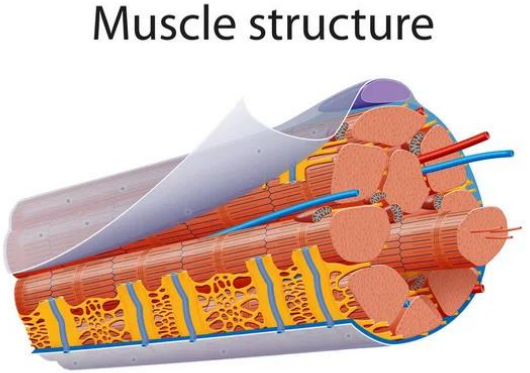
The Neuromuscular junction, The skeletal muscle



Ass. Professor Internal Medicine

Dr.Qasim Razzaq Radhi

30/09/2024



Objectives:

1- Describe the neuromuscular junction and the sequence of events during neuromuscular transmission.

2-Recognize the basic structure and morphology of skeletal muscle.

3-Define sarcotubular system and determine its function.

4- State the electrical characteristics of skeletal muscles.

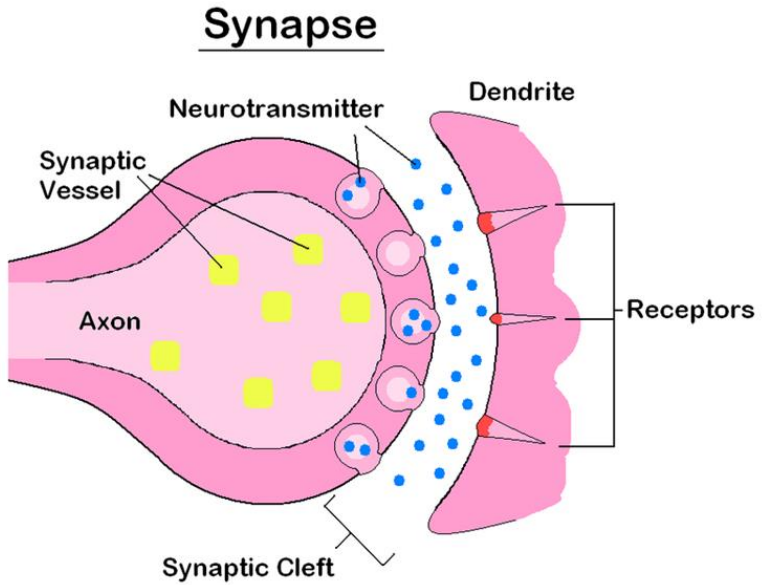
5- State the principles of walk along theory of Skeletal muscle contraction

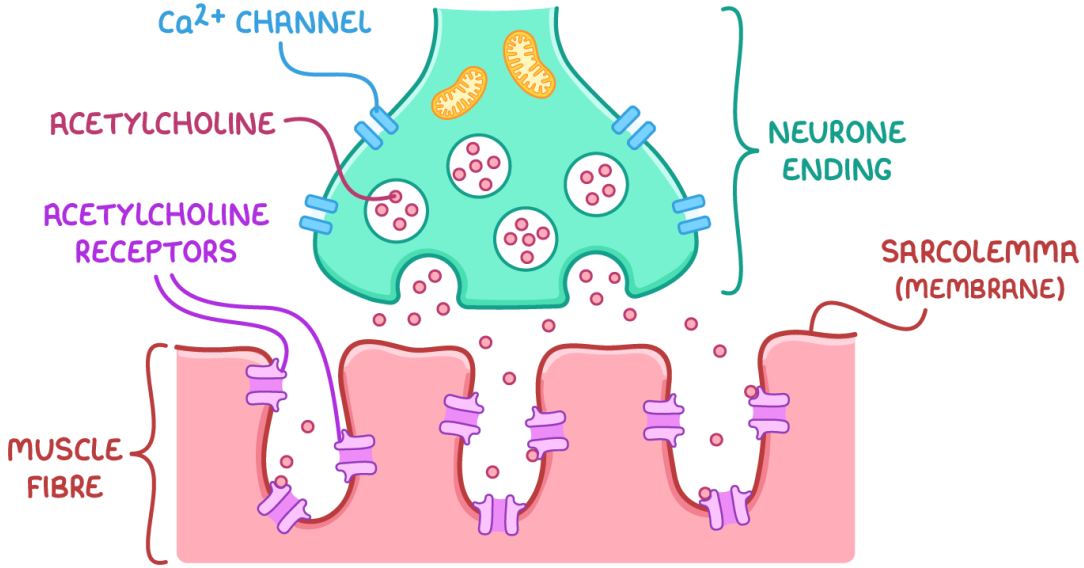
6- List the sources of energy in skeletal muscle.

- **Junction** is the connection between a nerve cell and another tissue (muscle fiber or gland).
- **Synapse** is the connection between 2 nerve cells.
- Each nerve ending makes a junction with the muscle fiber near its midpoint, called the

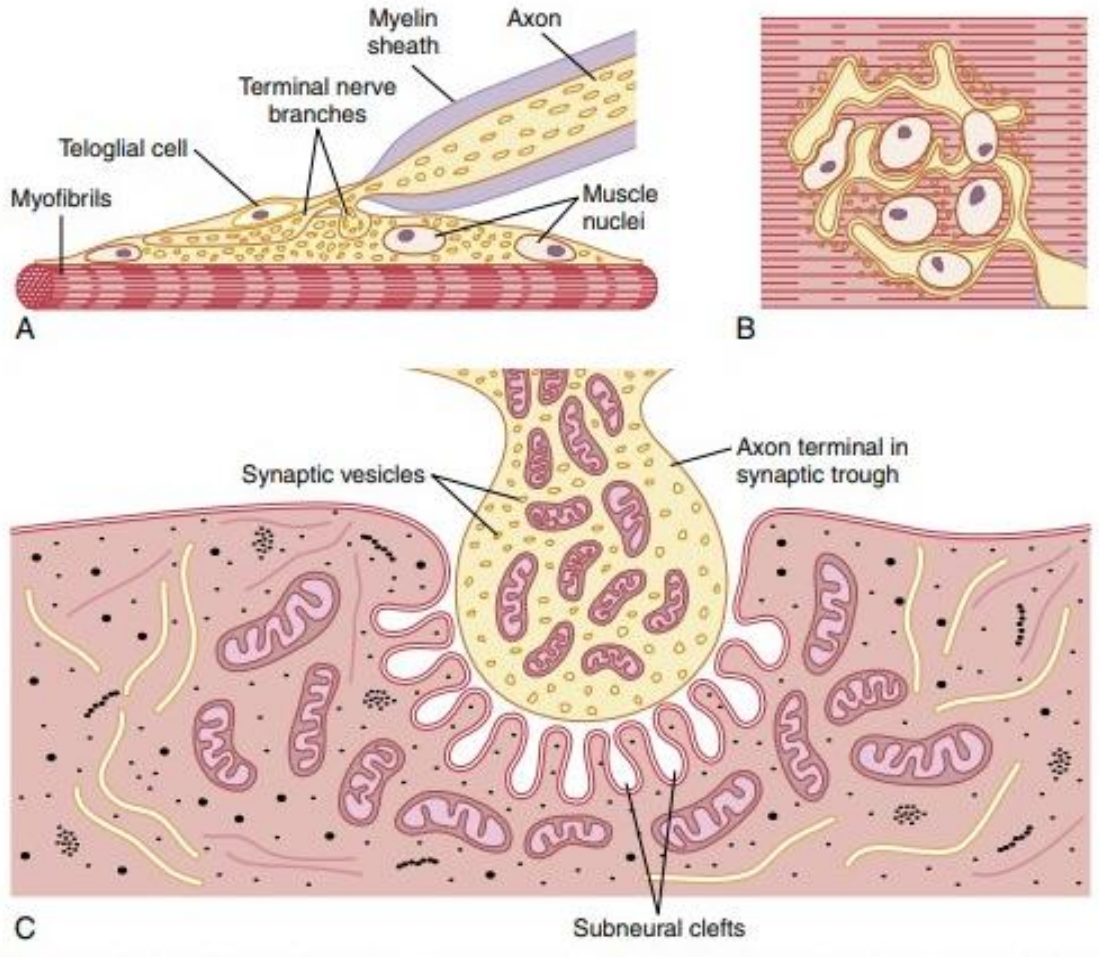
neuromuscular junction.

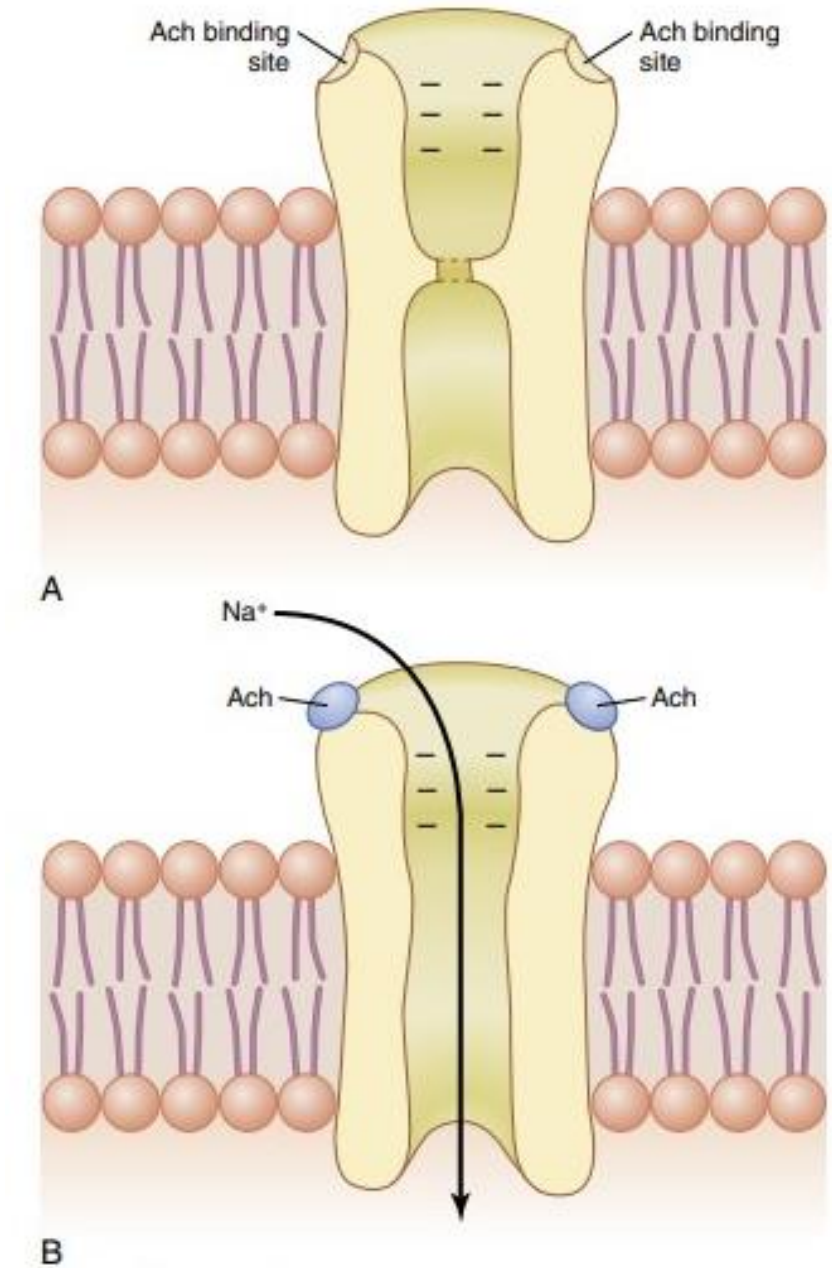
The nerve fiber with its branching plus the thickened muscle surface is called **the motor end plate**.

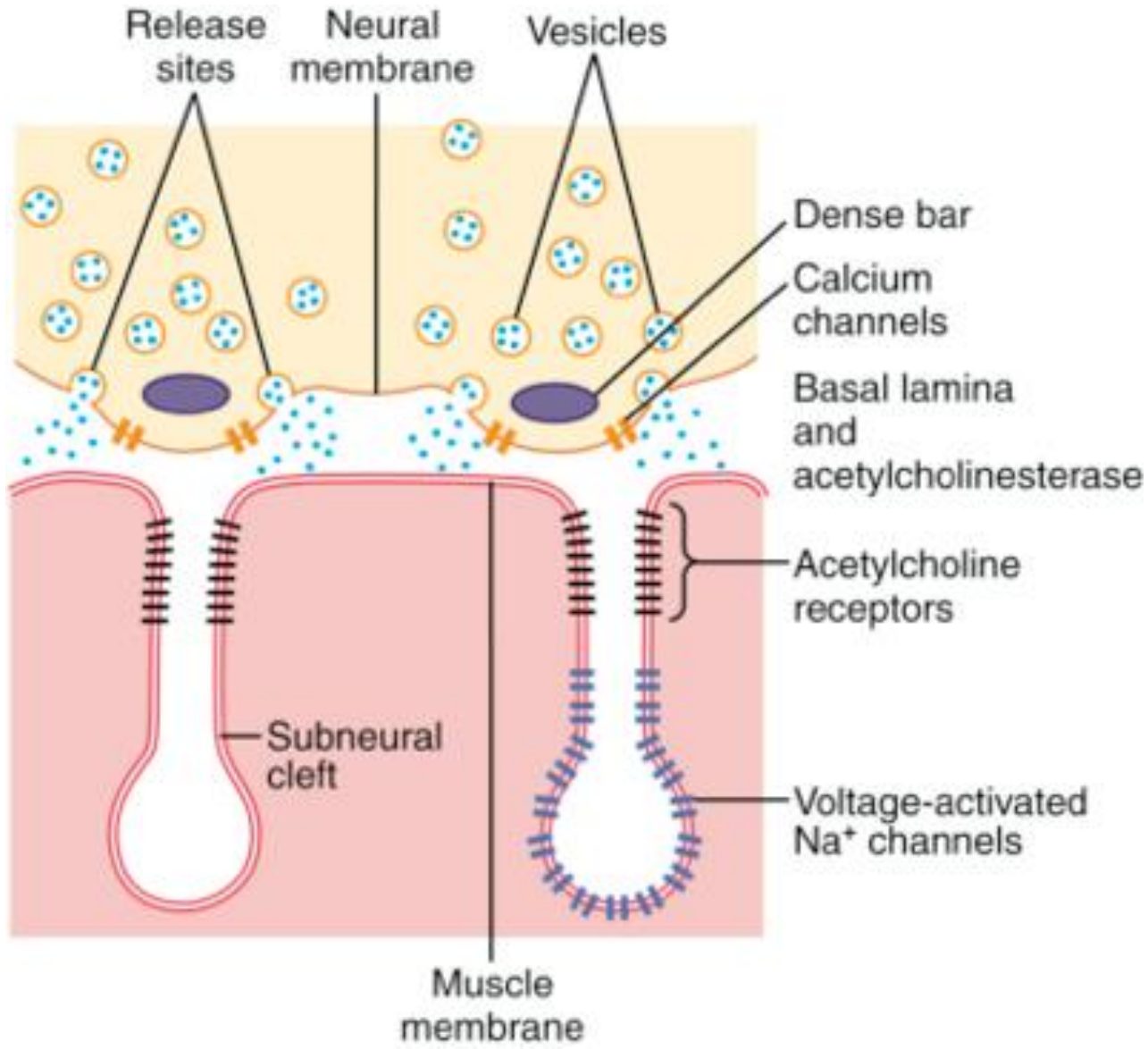




- The invaginated membrane is called the **synaptic gutter**, and the space between the nerve terminal and the fiber membrane is called the **synaptic space or synaptic cleft** (which contains the enzyme acetylcholinesterase, which destroys acetylcholine .
- At the bottom of the gutter are numerous smaller folds of the muscle membrane called **subneural clefts**, which greatly increase the surface area at which the synaptic transmitter can act, and there are also large numbers of **Acetylecholine (Ach) receptors**.




Ach binding site
Ach binding site
A
Na+
Ach
Ach
B


Release sites
Neural membrane
Vesicles
Dense bar
Calcium channels
Basal lamina and acetylcholinesterase
Acetylcholine receptors
Subneural cleft
Voltage-activated Na+ channels
Muscle membrane

• The Neuro-Muscular Junction (NMJ)

NMJ is a synaptic connection between the terminal end of a motor nerve and a muscle (skeletal/ smooth/ cardiac). It is the site for the transmission of action potential from nerve to the muscle.

Structure of Neuromuscular Junction

The presynaptic vesicles,

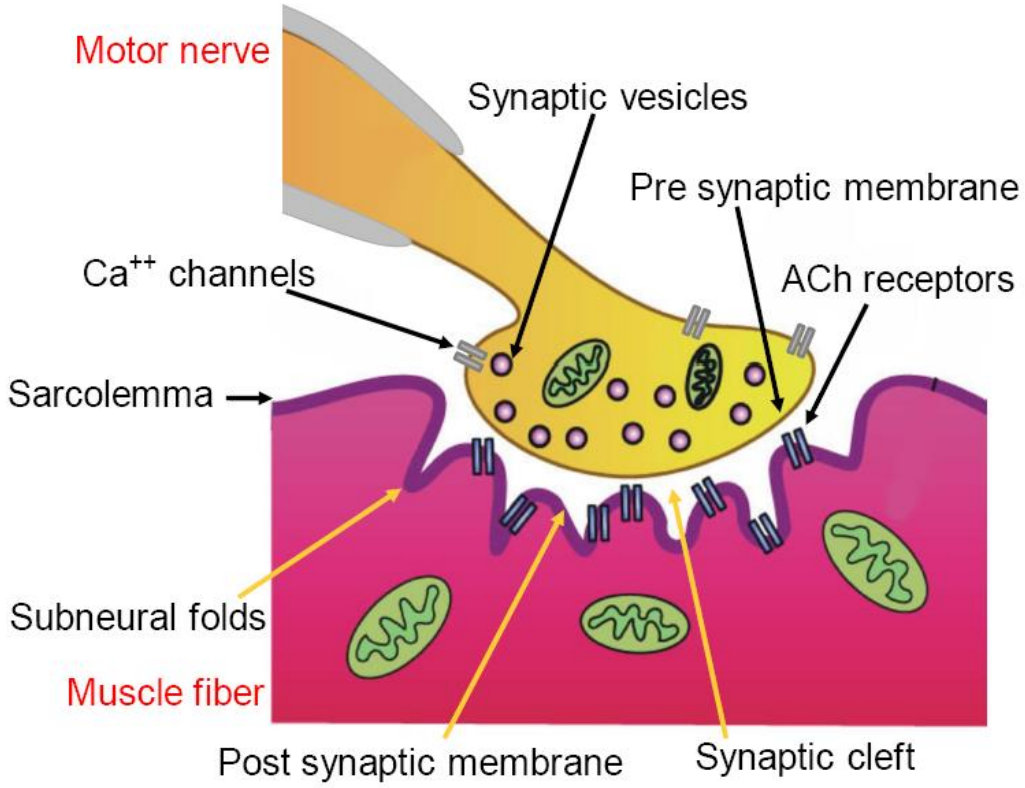
The synaptic cleft, sometimes called the **synaptic junction**, and

The postsynaptic membrane of the skeletal muscle cell containing neurotransmitter receptors.

The postsynaptic membrane of the receptor structure absorbs the chemical messenger.

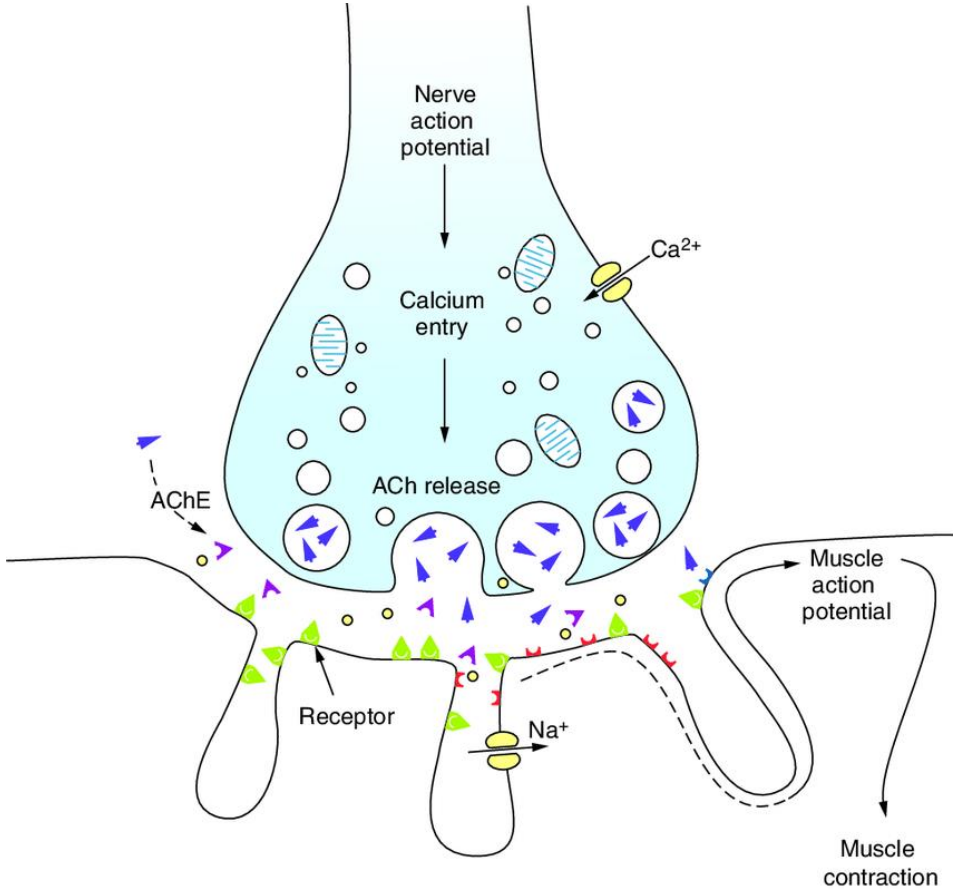
NMJ consists of:

- **Axon terminal**.
-**Synaptic gutter or synaptic trough**.
-**The synaptic space or synaptic cleft**.
-**Subneural clefts, Ach receptors**



Neuromuscular transmission

- **1- Action potential** spreads over the terminal; → channels open and allow **calcium ions** to diffuse to the interior of the nerve terminal.
- **2-** The calcium ions ,exert an attractive influence on the **acetylcholine vesicles**, drawing them to the neural membrane adjacent to the dense bars.
- **3-**The vesicles then fuse with the neural membrane and empty their **acetylcholine into the synaptic space by the process of exocytosis** (Botulinum and Tetanus toxins block the transmitter release)
- **4- Ach will diffuse** to the synaptic cleft and binds with the receptors **(Nicotinic receptors)**, causing activation of the Na and K ionic channels resulting in local depolarization and firing level is reached ,and **action potential is initiated**.
- Neuromuscular transmission is terminated by rapid Ach cleavage by **acetylcholinesterase (AChE)**.



- **Curary** is an arrow poisoning used by the American Indians to paralyze their victims.

Curare has long been used in tropical

South America as an extremely potent **arrow poison**.

Curare is a generic term for arrow poisons that contain tubocurarine and curarine. Most frequently it is derived from the bark of **Strychnos toxifera**.

In medicine, curare has been used as a treatment for tetanus .





Strychnos toxifera

Botulinum toxin

- **Botulism** is a rare but serious illness that attacks your body's nervous system. Types of botulism include **foodborne**, **infant** and **wound botulism**. Botulism is usually caused by a bacteria called **Clostridium botulinum**. Symptoms include muscle weakness and paralysis. Treatment typically includes antitoxin to prevent the toxin from causing more damage.
- **Botulinum toxin** (sold under the trade name **Botox**) inhibits the release of acetylcholine at the neuromuscular junction.
- **Iatrogenic botulism**

Only get Botox injections from licensed medical professionals.

Iatrogenic botulism can happen if too much botulinum toxin is injected for cosmetic reasons, such as for wrinkles. It also can happen if too much of the toxin is injected for medical reasons, such as for migraine headaches.

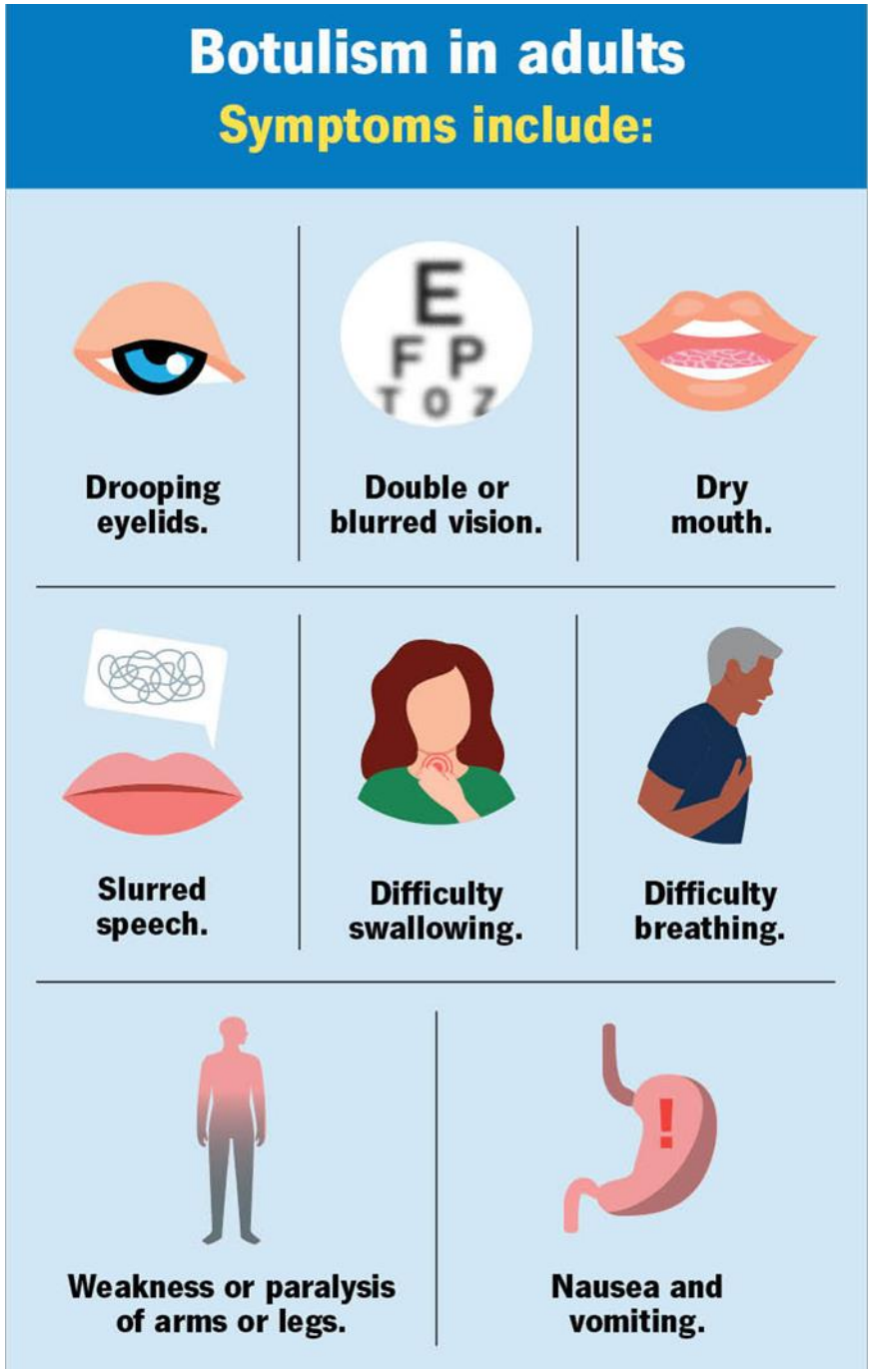
- **Foodborne botulism**
- Foodborne botulism can happen when you eat foods contaminated with ***Clostridium botulinum* spores**. When food is stored improperly, bacteria can grow. As the bacteria grow, they release toxins into your food.
- Though rare, improperly **canned store-bought foods** can also cause botulism. Other sources of foodborne botulism include:
- **Oils infused with herbs.**
- **Potatoes baked in aluminum foil.**
- **Canned cheese sauces.**
- **Bottled garlic.**
- **Canned tomatoes.**
- **Carrot juice.**
- **Foods kept warm or left unrefrigerated for too long.**

- **Treatments and interventions**
- **Antitoxin treatment**. Botulism is treated with antitoxin, which prevents the toxin from causing any more harm.
- **Ventilation**. If your disease is severe, you may have respiratory (breathing) problems.
- **Surgery.** If you have wound botulism,

Prevention :

If in doubt, throw it out!

Do **not** eat food if you do not know whether it was safely canned, preserved, or fermented.



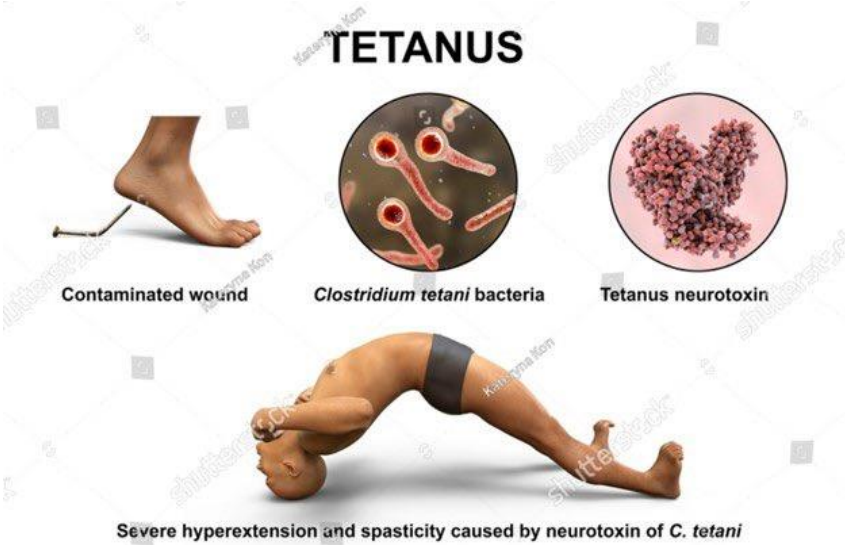
Tetanus toxin

- **Tetanus** is an acute infectious disease caused by spores of the bacterium **Clostridium tetani**.

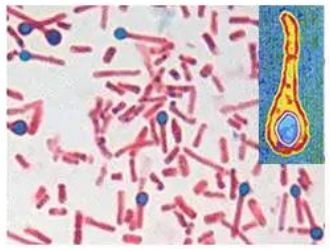
Tetanus toxin, produced by bacteria and causes the disease state, tetanus.It functions is similar to botulinum neurotoxin by attaching and endocytosing into the presynaptic nerve terminal.

It differs from botulinum neurotoxin in that tetanospasmin demonstrates a **rigid / spastic paralysis** as opposed to the **flaccid paralysis** demonstrated with botulinum neurotoxin.

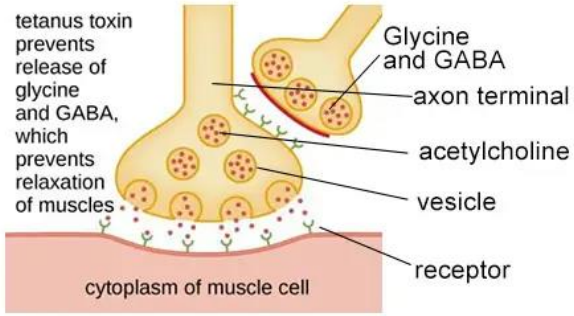
- Tetanus







'Drum Stick' or
'Tennis Racket' appearance



Mechanism of Tetanus Toxin

Clostridium tetani



Opisthonus

microbeonline



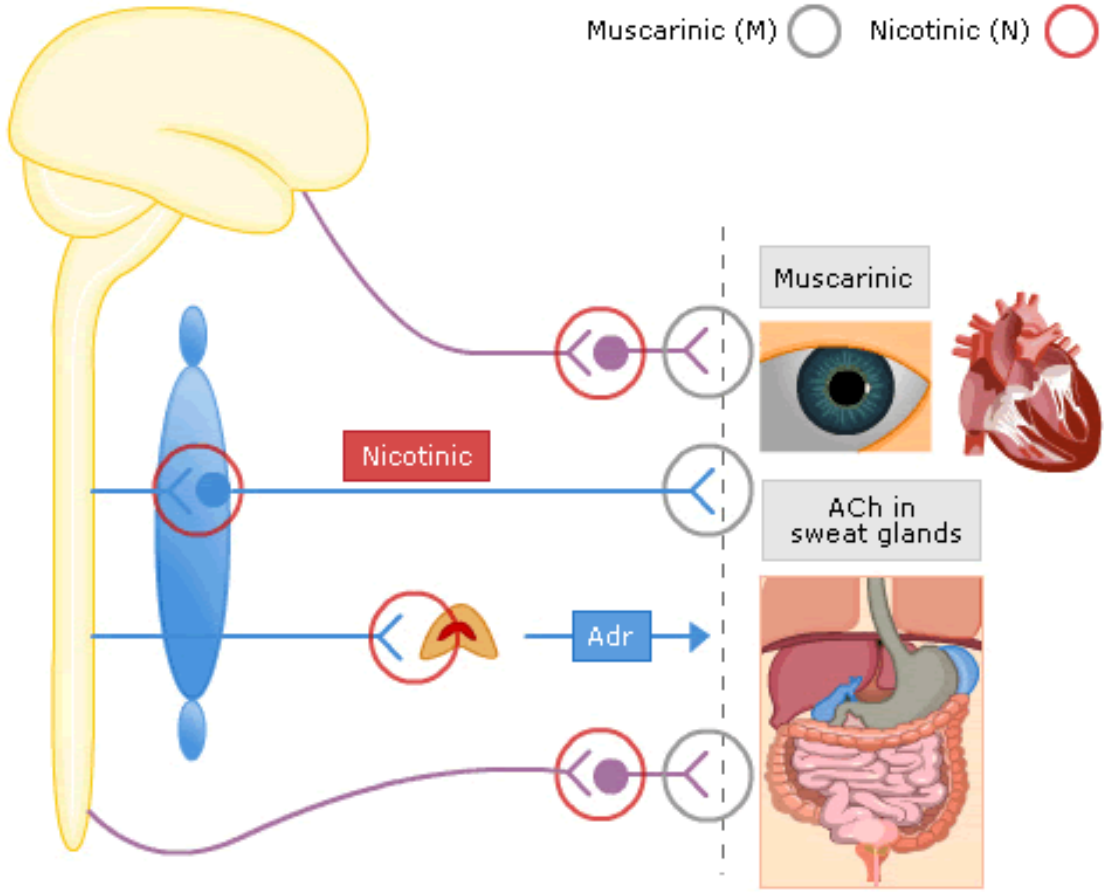
Risus Sardonicus

Acetylcholine Receptors (cholinergic receptors)

- The term **cholinergic** refers to those receptors which respond to the transmitter **acetylcholine (Ach)**

  and are mostly parasympathetic.

- Ach receptors have been divided into **two main types** on the basis of their pharmacologic properties:
- **1- Muscarinic**, found in the plasma membrane of smooth muscle cells, cardiac muscle cells, and the cells of particular glands .
- **2- Nicotinic receptors**, found in specific regions of the brain, in autonomic ganglia and in skeletal muscle fibers.



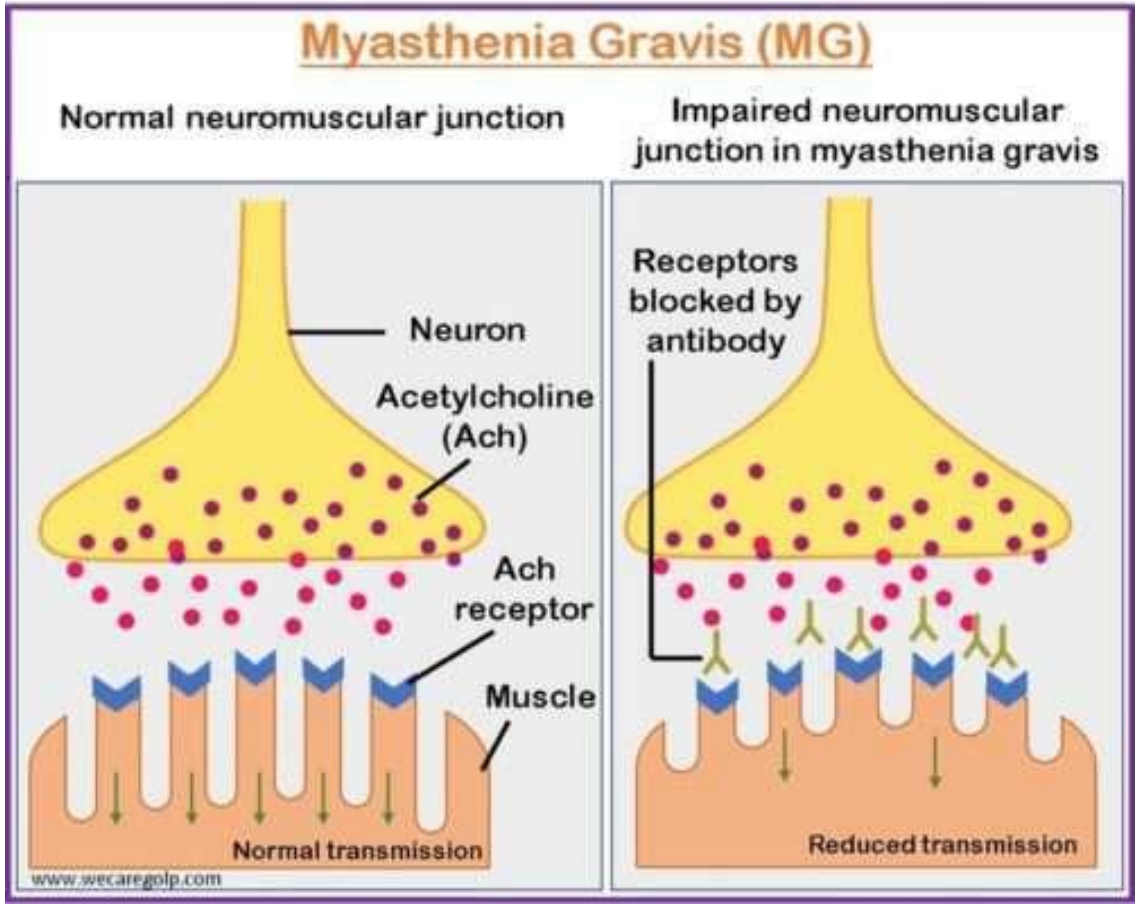
Mysthenia Gravis (MG)

- Myasthenia gravis is an **autoimmune disease**.
- Myasthenia gravis is a **chronic neuromuscular disease** that causes weakness in the voluntary muscles. Voluntary muscles include muscles that connect to a person's bones, muscles in the face, throat, and diaphragm.
- In myasthenia gravis, **antibodies** (immune proteins produced by the body's immune system) **block, alter, or destroy the receptors for acetylcholine**

at the neuromuscular junction,

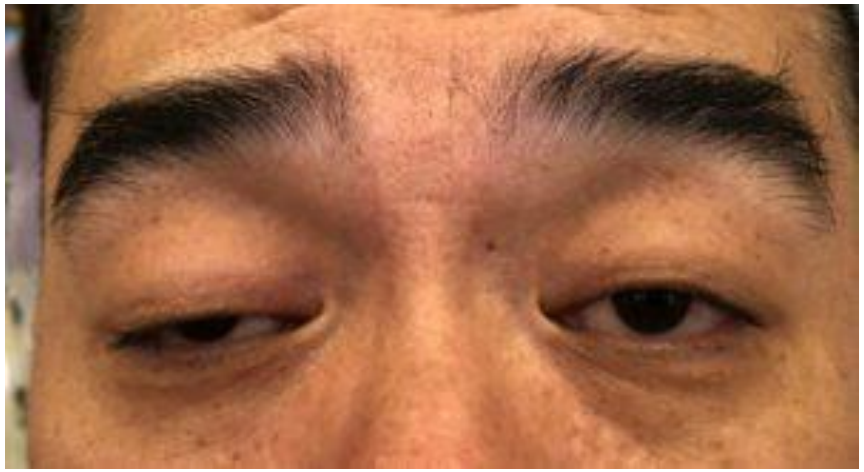
which prevents the muscle

from contracting.



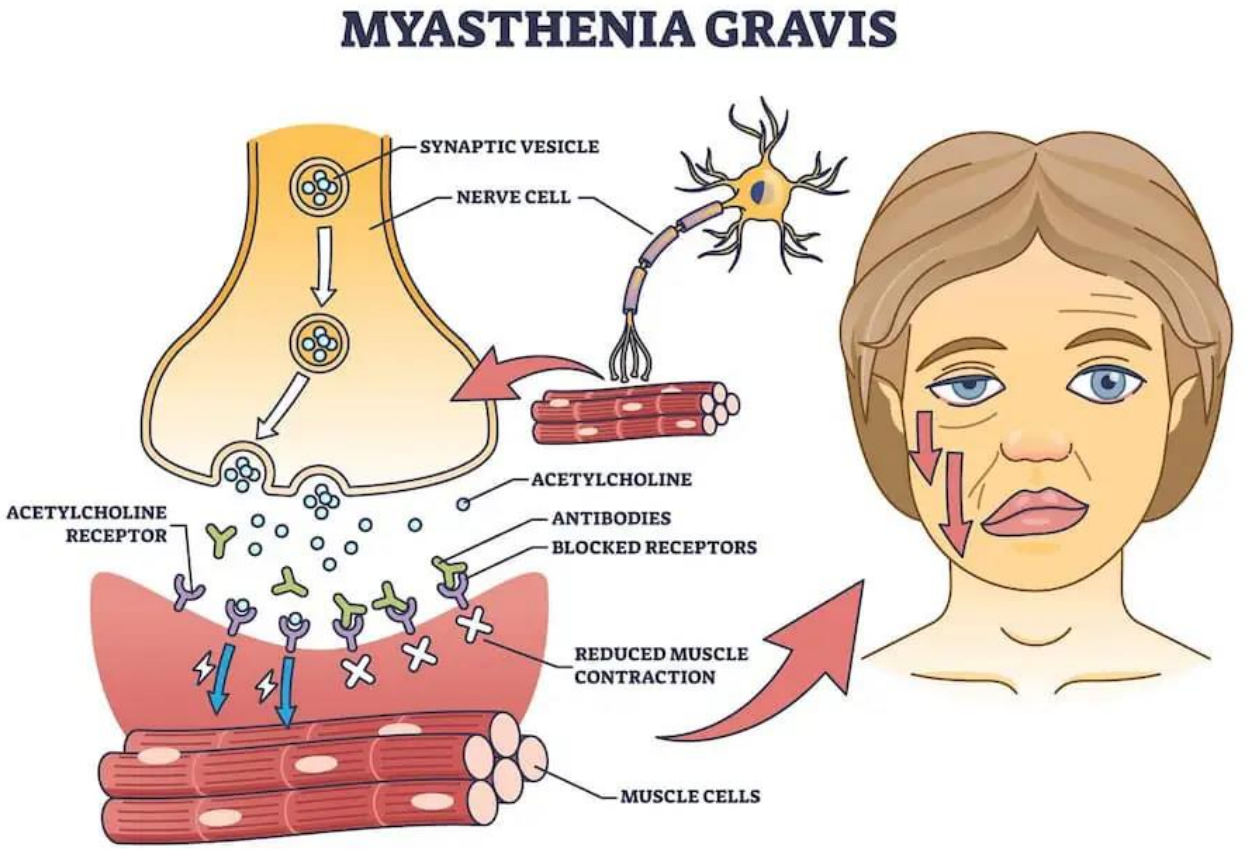
Myasthenia gravis :

Ptosis (Drooping of the eyelid)





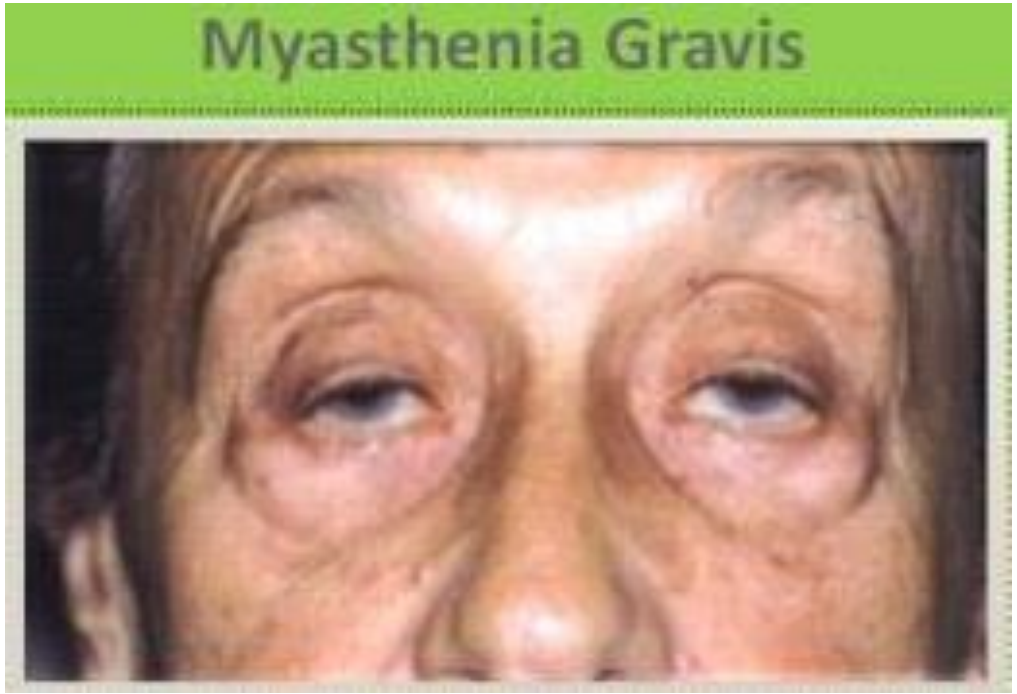
Facial muscle weakness

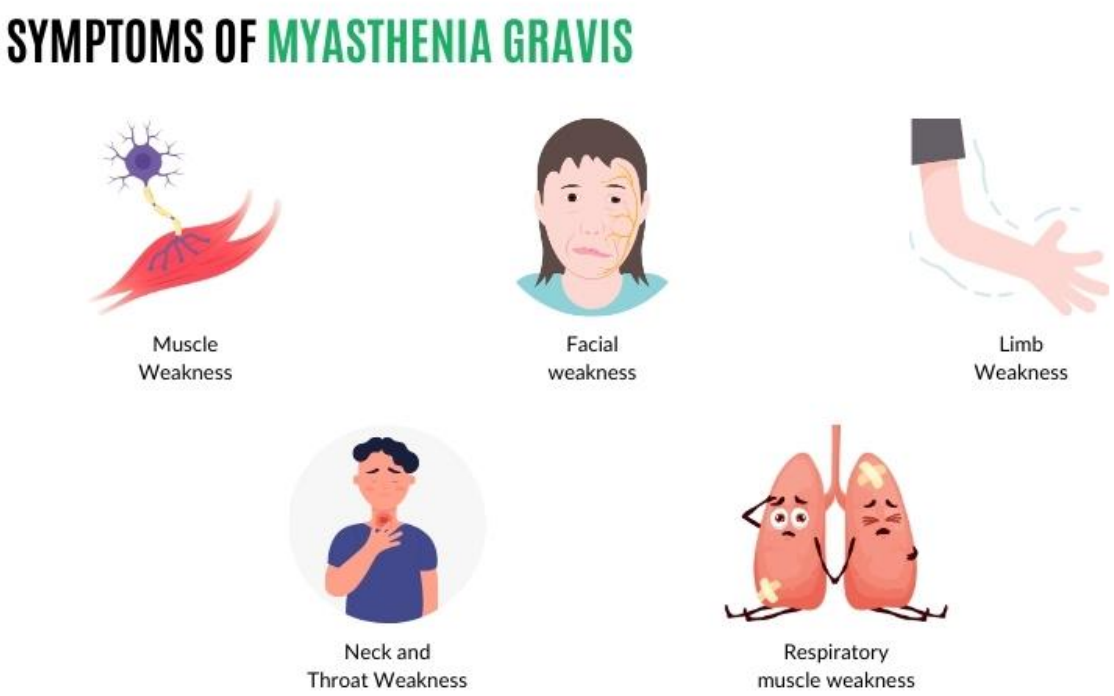


Destruction of the Released Acetylcholine by Acetyl cholinesterase

1-Most of the acetylcholine is destroyed by the enzyme acetylcholinesterase (which is present in the synaptic space), into choline and acetate.

2- A small amount of acetylcholine diffuses out of the synaptic space.





Lambert-Eaton syndrome
Lambert-Eaton myasthenic syndrome (LEMS)

- **Lambert-Eaton syndrome**: is an auto-immune condition caused by antibodies against voltage-gated calcium channels on the presynaptic membrane. This prevents Ca from entering the nerve terminal and triggering the fusion of ACh vesicles with the synaptic membrane.
- Therefore, it essentially prevents the release of ACh into the synaptic cleft and ultimately prevents muscle contraction.



The muscle

- The muscles are excitable cells; they are machines to convert the chemical energy to mechanical energy.There are more than 600 muscles in our body.
- It differs from the nervous system by the fact that it has a contractile mechanism which is activated by Action potential (A.P.).

There are **three major muscle types** found in the human body:

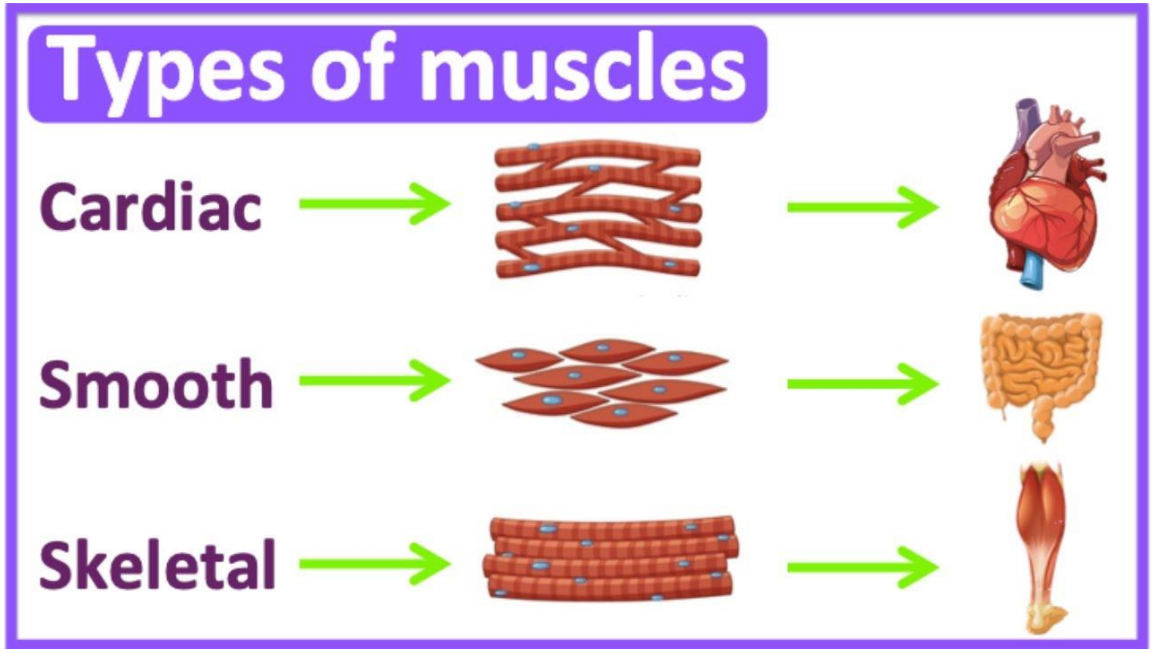
1- Skeletal muscle.

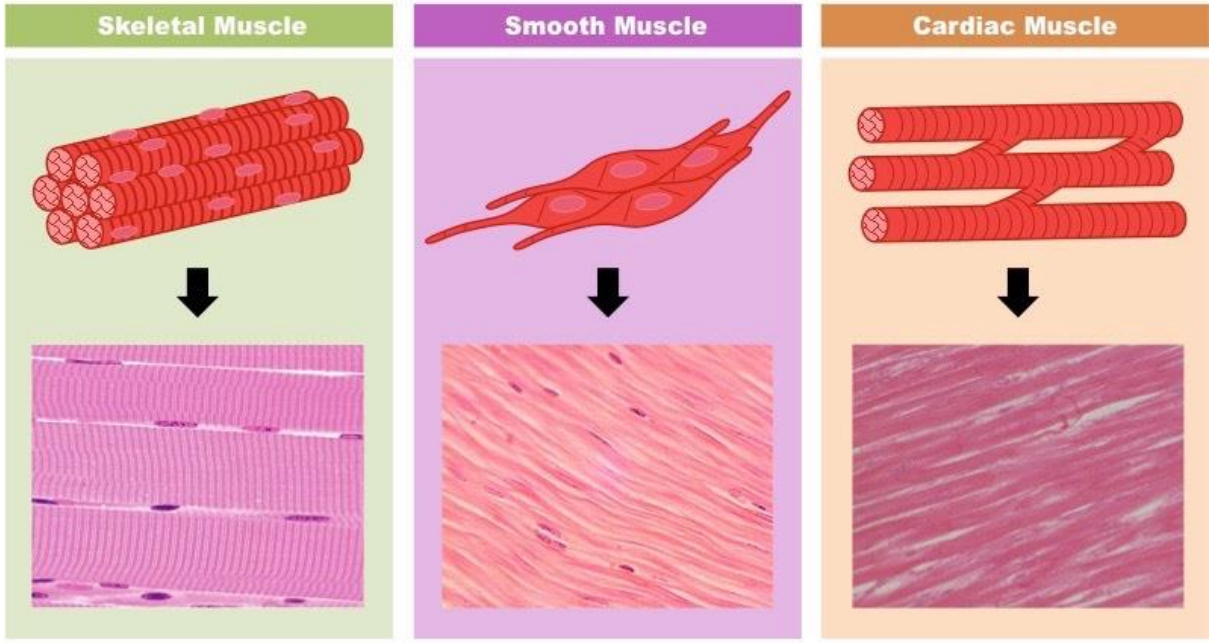
2- Cardiac muscle.

3- Smooth muscle.

Each muscle type has unique cellular components, physiology, specific functions, and pathology. Skeletal muscle is an organ that primarily controls movement and posture.

- Muscles


Types of muscles
Cardiac
Smooth
Skeletal


Skeletal Muscle
Smooth Muscle
Cardiac Muscle

Characteristics of muscle:

1-excitability - responds to stimuli (e.g., nervous impulses)

2-contractility - able to shorten in length

3-extensibility - stretches when pulled

4-elasticity - tends to return to original shape & length after contraction or extension

Functions of muscle:

1-motion

2-maintenance of posture

3-heat production

The skeletal muscle

- It is that type of the muscles that is attached to bones & moves skeleton, **also called striated muscle**. It is voluntary.

The muscle fiber is a cylindrical single cell containing: -

- multiple nuclei.

- **Cell membrane (sarcolemma).**

- Sarcoplasm (intracellular fluid fills the spaces between the myofibrils).

- **Other organ cells** -Small muscle fibrils, which consist of filaments that are made up of contractile proteins **(actin and myosin)**

- **The striations**

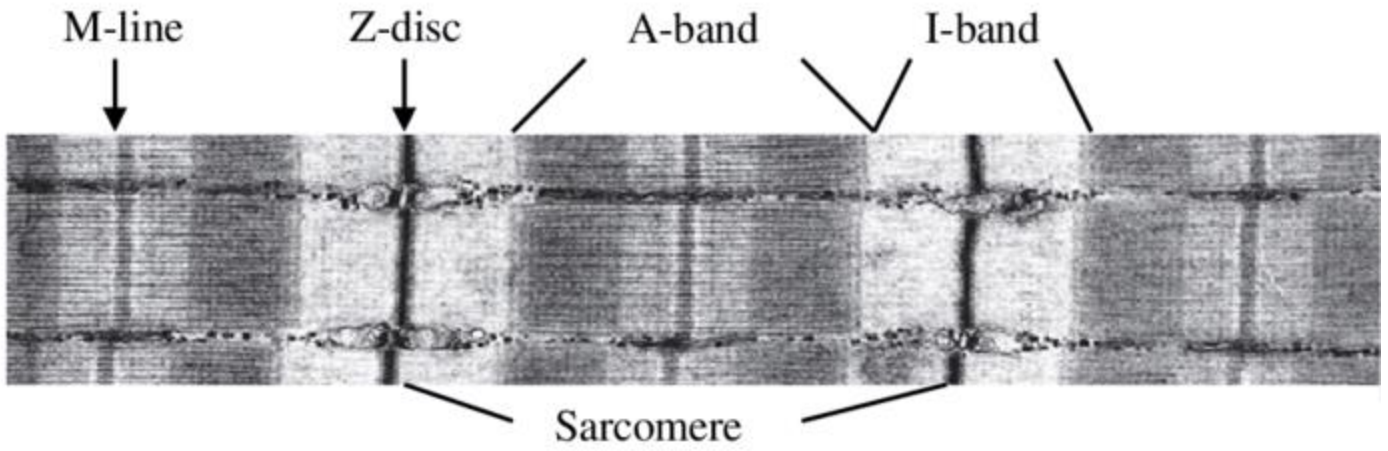
- The myosin and actin filaments interdigitate and cause the myofibrils to have **alternate light and dark bands**.

  The **light bands are only Actin** filaments called **I band**.

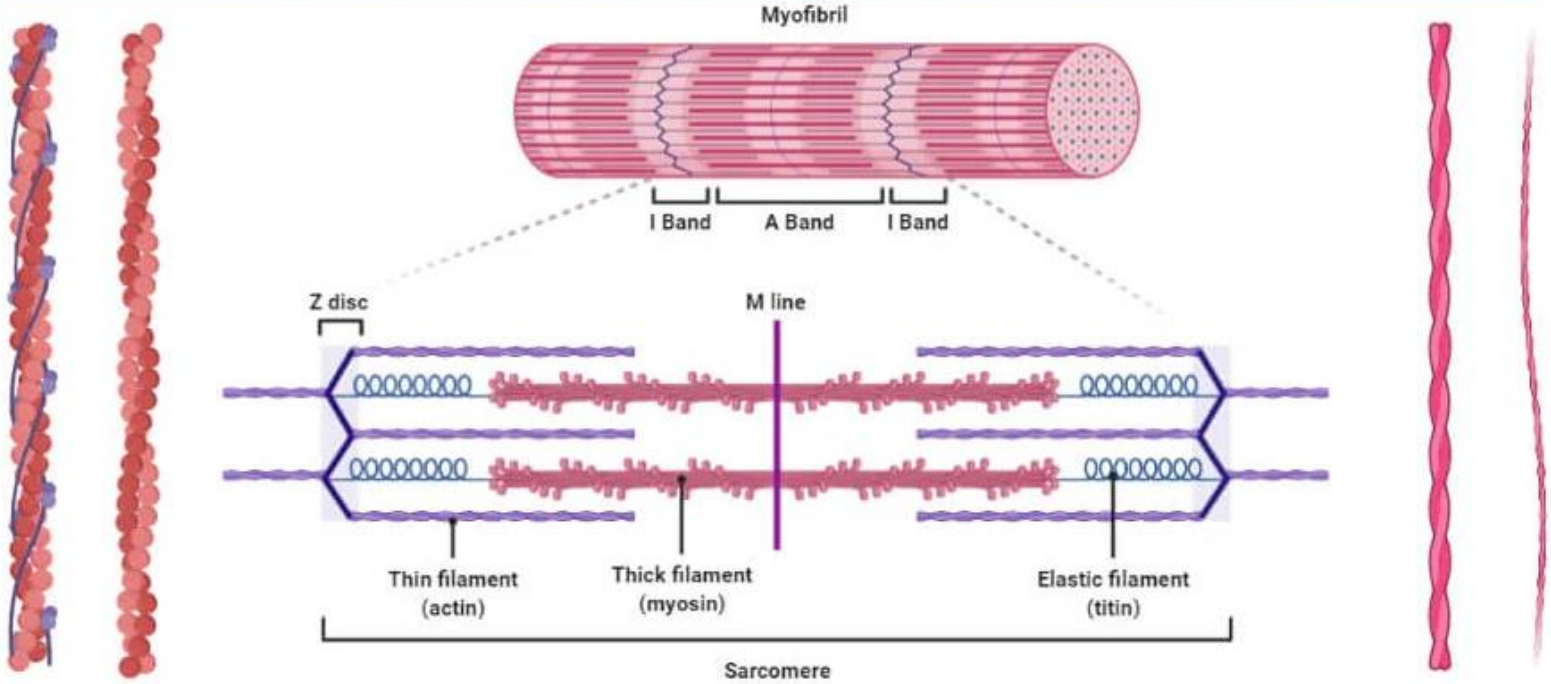
  The **dark bands contain Myosin** (overlap with actin filaments) called **A band.**

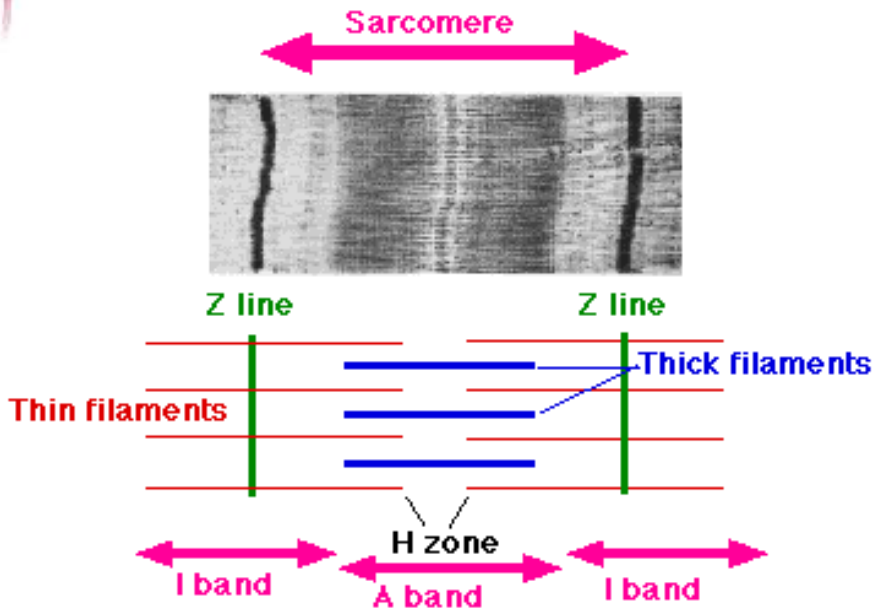
The portion of the myofibrils that is between 2 successive Z discs is called **Sarcomere** which is he smallest functional unit of the muscle.

The **A band** is divided by the **lighter H band**, in the middle of it a there is a line called **M line**.



Differences between Actin and Myosin





- The thin filament is made of **actin** ,**torponin** and **tropomyosin**.
- **Troponin** It is a protein attached intermittently at regular intervals along the sides of tropomyosin molecules. It is a complex of **3 protein subunits**:

1- Troponin I has a strong affinity for **actin** (F actin) inhibits the interaction between myosin to actin **2-Troponin T** binds troponin **to tropomyosin**.

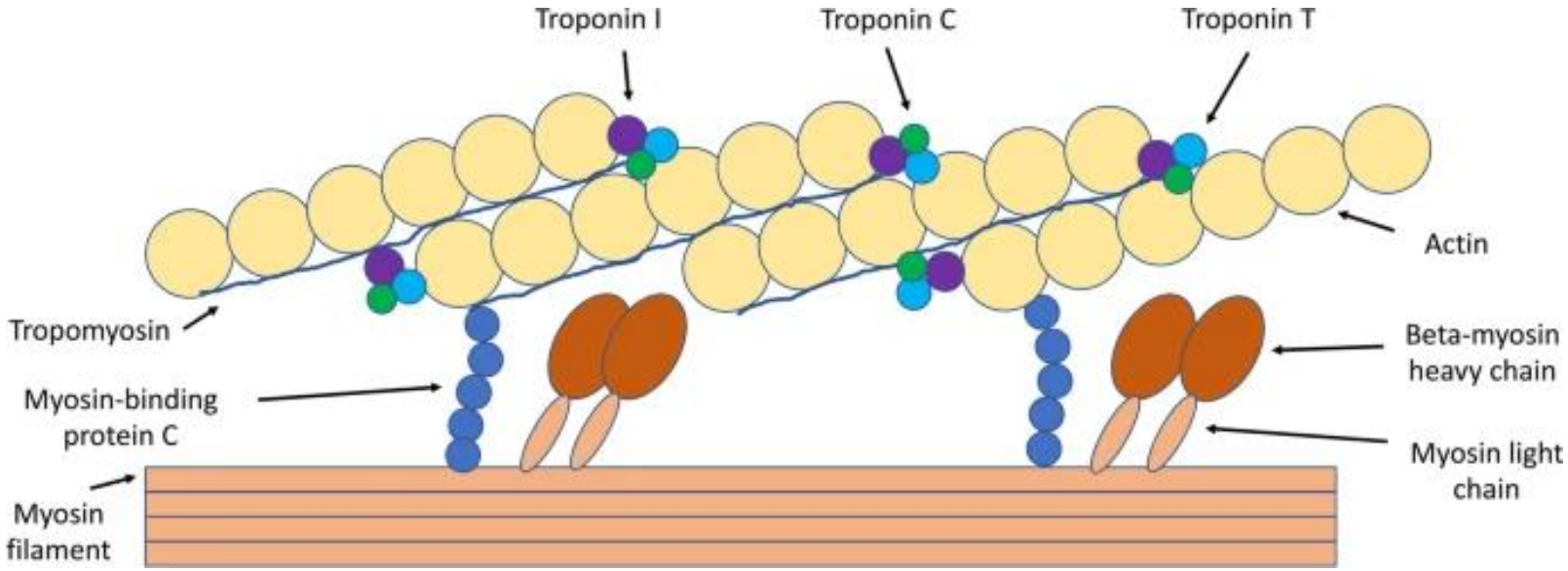
3-Troponin C contains binding sites for **calcium** ions that initiate contraction.

Troponin formed by :

1. Troponin I attached to F actin

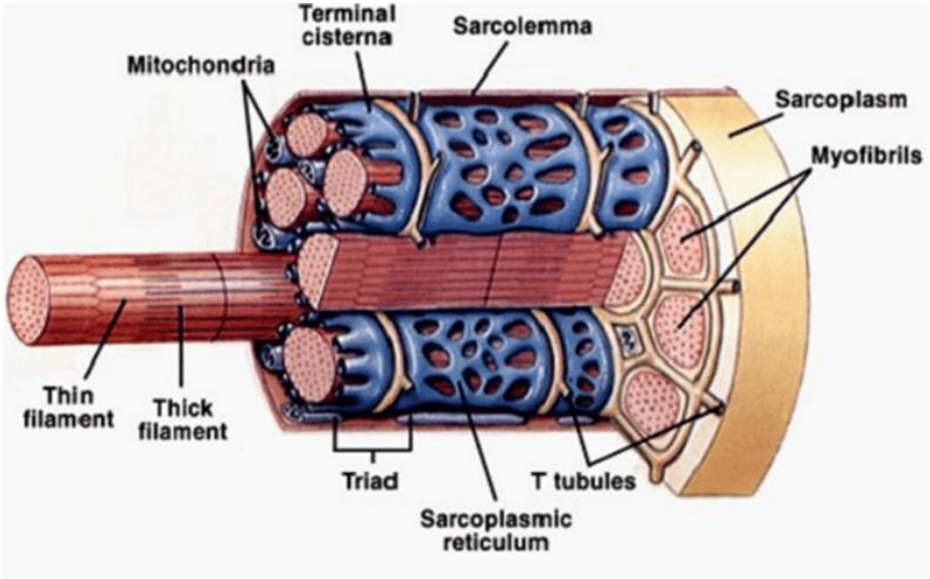
2. Troponin T attached to tropomyosin

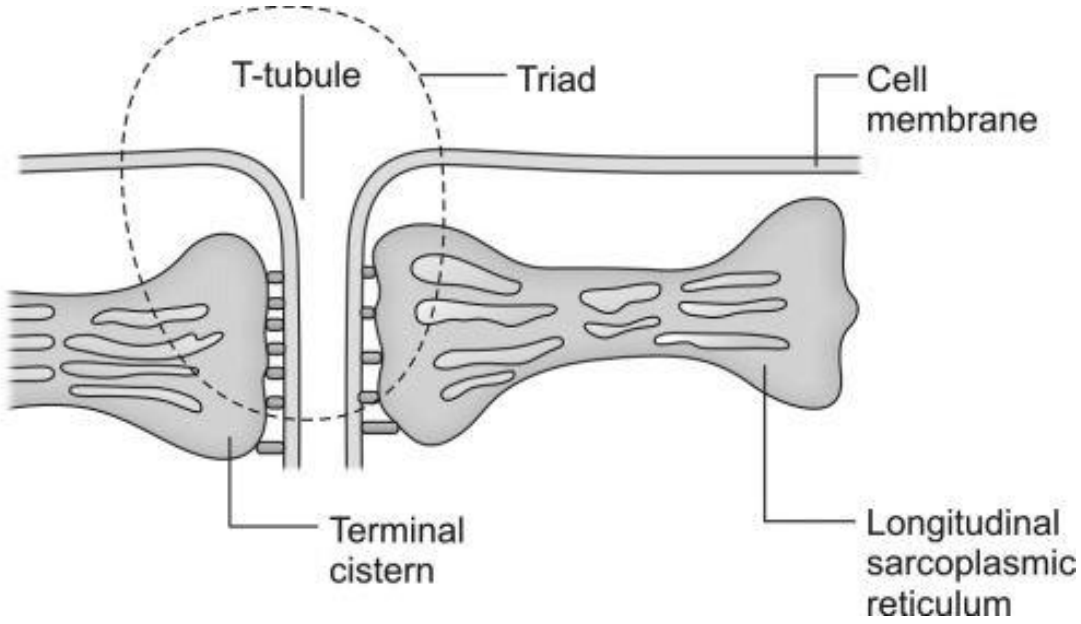
3. Troponin C attached to calcium ions.

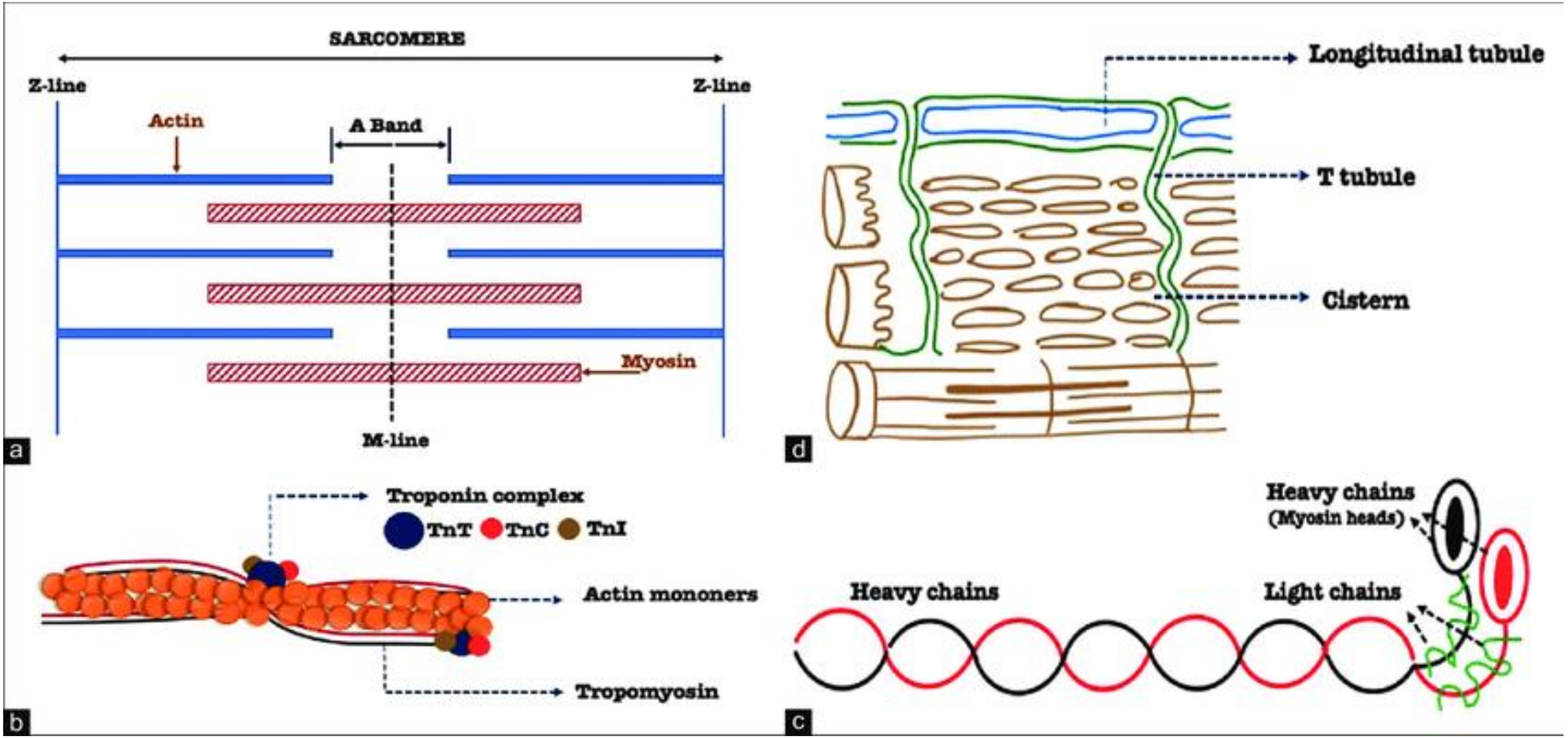


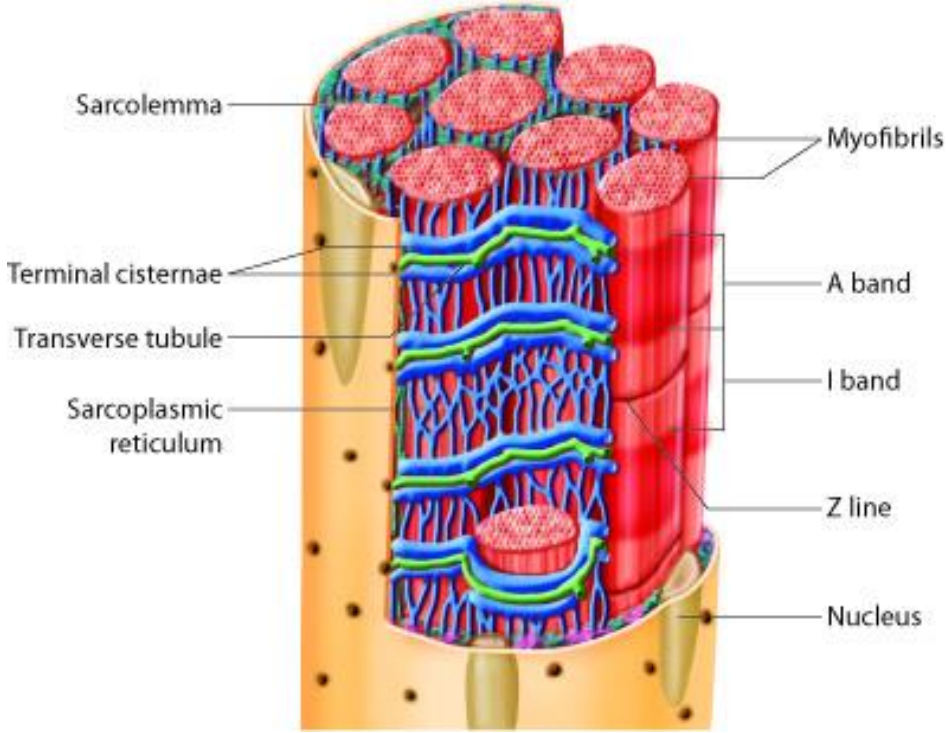
The Sarcotubular System

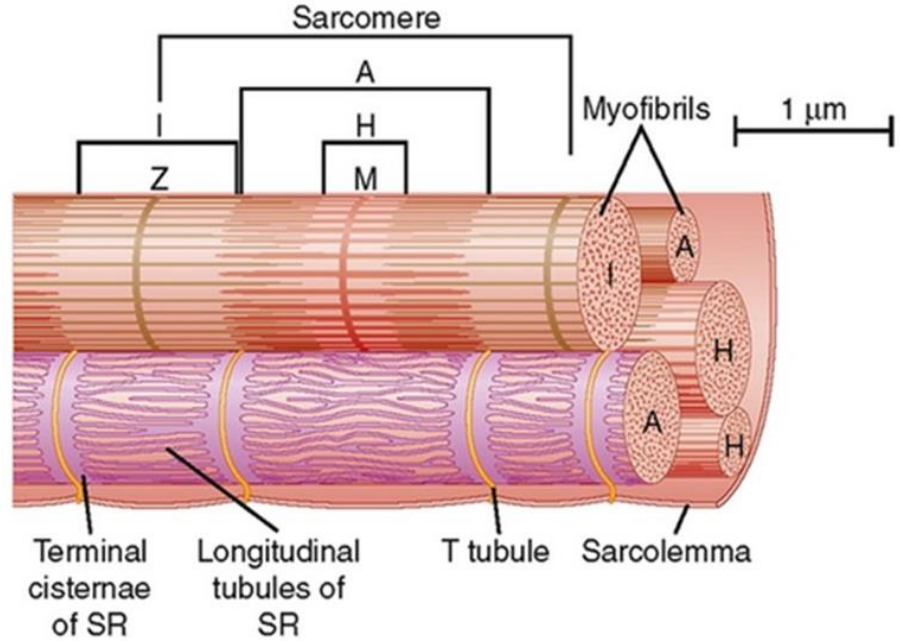
- The sarcotubular system is formed mainly by **two types** of structures:
- **1. ‘T’ tubules** .
- **2. ‘L’ tubules** or **sarcoplasmic reticulum**.
- **The T system (transverse tubules):** it is a system of transverse tubules in the **form of letter T** which is continuous with the membrane of the muscle fiber.
- **The sarcoplasmic reticulum** : it forms an irregular system of tubules surrounding the myofibrils it has an enlarging ends or chambers called **terminal cisterns**.
- The arrangement of the **T system** with **the ciatern** of the endoplasmic reticulum at either side called **Triad** of skeletal system.

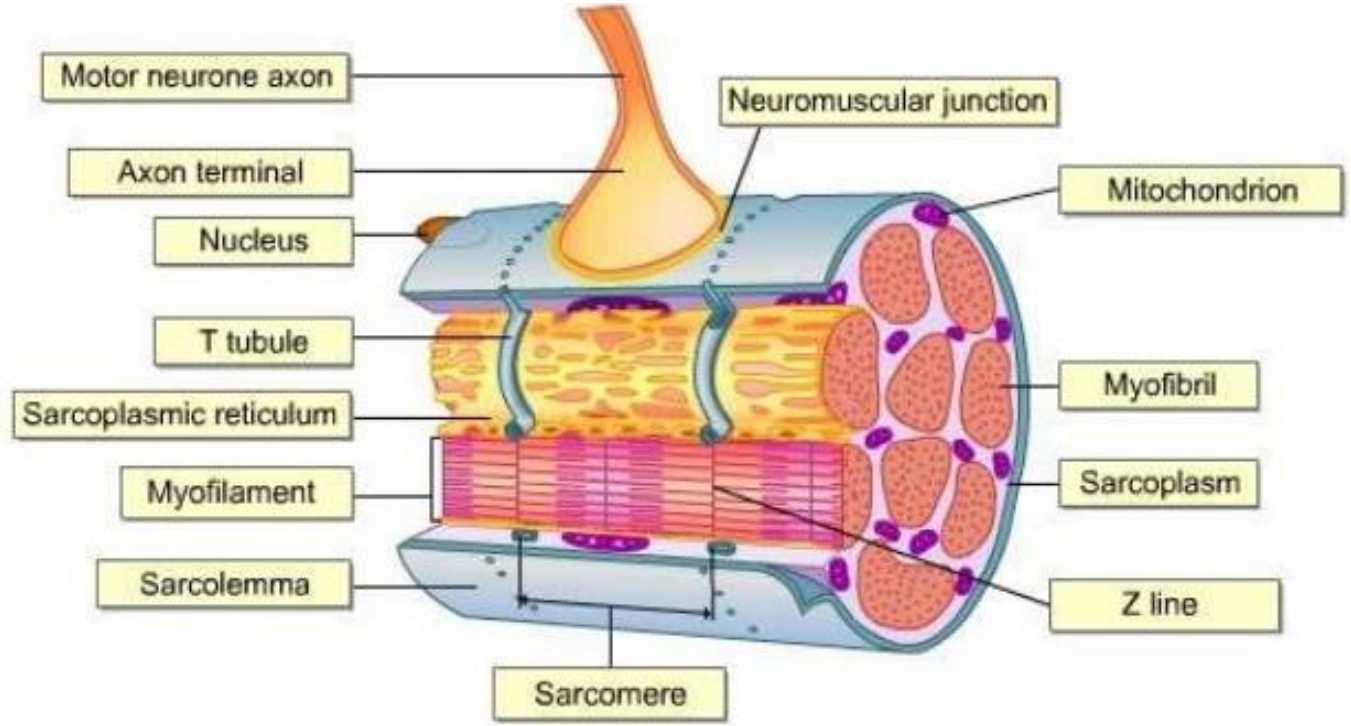





SARCOMERE
Z-line
Z-line
Actin
A Band
Myosin
M-line
a
Longitudinal tubule
T tubule
Cistern
d
Troponin complex
TnT
TnC
TnI
Actin mononers
Tropomyosin
b
Heavy chains
(Myosin heads)
Heavy chains
Light chains
c


Sarcolemma
Myofibrils
Terminal cisternae
A band
Transverse tubule
I band
Sarcoplasmic reticulum
Z line
Nucleus


Sarcomere
A
I
H
Z
M
Myofibrils
1 µm
Terminal cisternae of SR
Longitudinal tubules of SR
T tubule
Sarcolemma


Motor neurone axon
Neuromuscular junction
Axon terminal
Mitochondrion
Nucleus
T tubule
Myofibril
Sarcoplasmic reticulum
Myofilament
Sarcoplasm
Sarcolemma
Z line
Sarcomere



Thank you!