Physiology 439

MED439
KING SAUD UNIVERSITY

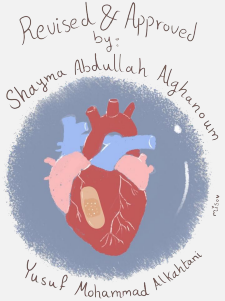
5

Neuromuscular transmission

Editing file

physiology439@gmail.com

Red: Important
Black: In Male & Female slides
Blue: In male slides
Pink: In female slides
Gray: Notes & extra information



Objectives

Know and describe the following:

01 The physiologic anatomy of the skeletal muscle and NM junction.

02 The general mechanism of skeletal muscle contraction.

03 Motor End Plate potential and how action potential and excitation-contraction coupling are generated in skeletal muscle.

04 The molecular mechanism of skeletal muscle contraction & relaxation.

05 Sliding filament mechanism.

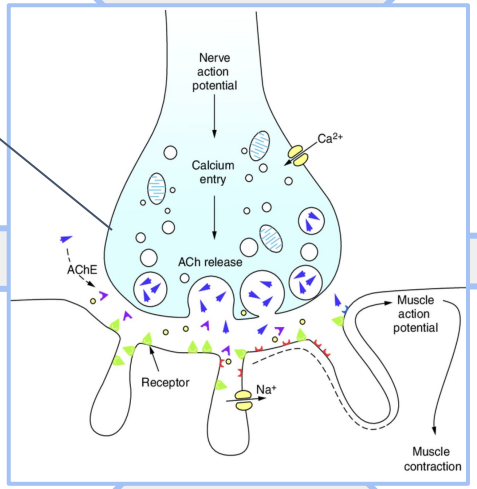
06 Drugs/ diseases affecting the neuromuscular transmission.

helpful video

Neuromuscular transmission

Transmission between motor neurons and muscle cells.

An axon terminal (synaptic knob) can meet another cell, a neuron, muscle fiber, or gland cell.



One neuron will transmit info to a muscle or another neuron or gland cell by releasing chemicals called neurotransmitters.

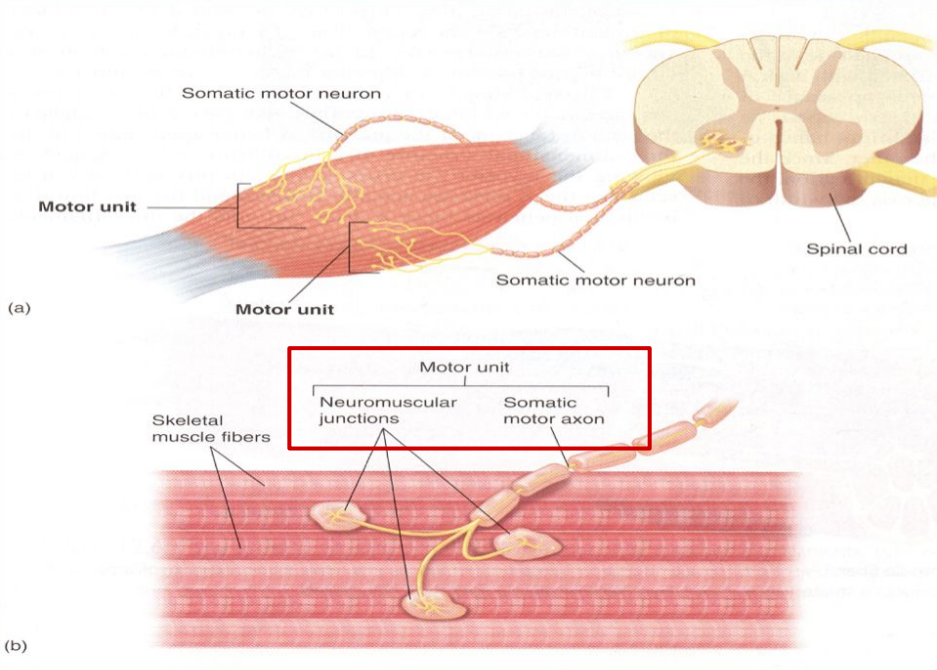
In neuromuscular transmission, the neurotransmitter is acetylcholine.

Site: Synapse

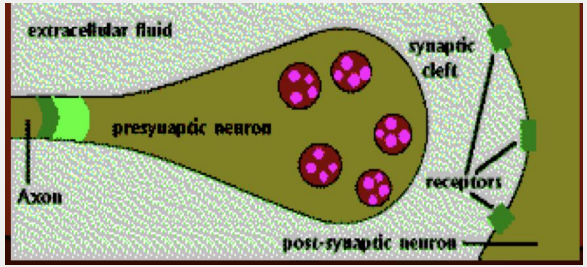
If transmission is between neuron and muscle cell it's called a neuromuscular junction.

In the synaptic knob, the process of **"conversion of electrical signal into a chemical signal"** is called transduction.

Neuromuscular Junction (NMJ)



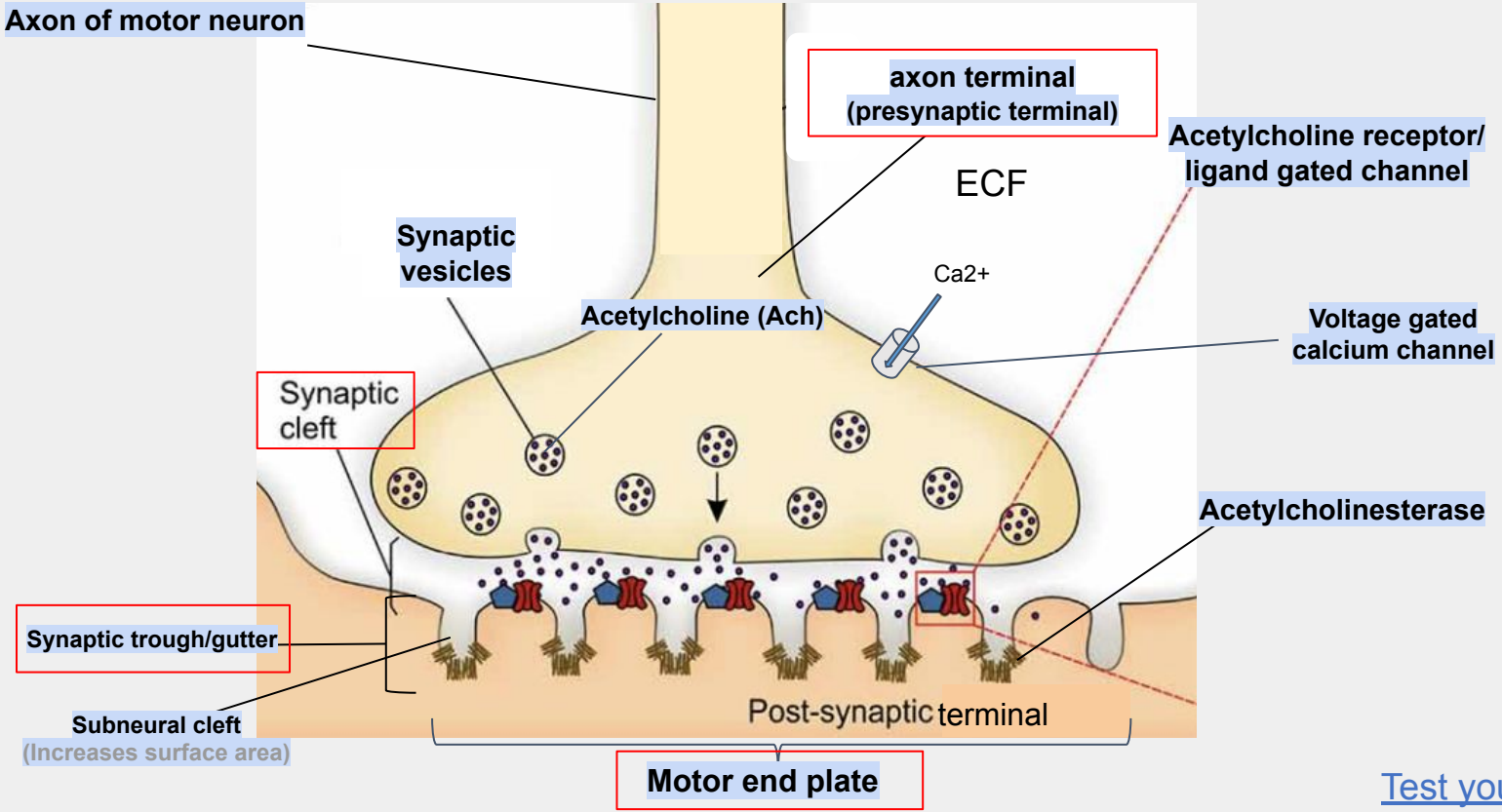
A neuromuscular junction, is a chemical synapse formed by the contact between a motor neuron and a muscle fiber. It is part of a motor unit.
A motor unit is made up of a motor neuron and the skeletal muscle fibers it innervates.



In the case of neuron to neuron transmission

Physiologic Anatomy of the Neuromuscular Junction

(Nerve+Muscle)



Test yourself

The Neuromuscular junction consists of

01

Axon terminal

Contains around 300,000 vesicles which contain the neurotransmitter acetylcholine (Ach).

02

Synaptic cleft

20 – 30 nm (nanometer) space between the axon terminal & the muscle cell membrane.

It contains the enzyme acetylcholinesterase which can destroy Ach .

03

Synaptic gutter/ synaptic trough

It is the muscle cell membrane which is in contact with the nerve (axon) terminal.
It has many folds called Subneural Clefts , which:
1: greatly increase the surface area
2: allow for accommodation of large numbers of Ach receptors .

Ach receptors are located here .

- The entire structure of axon terminal , synaptic cleft and synaptic gutter is called " Motor End-Plate "

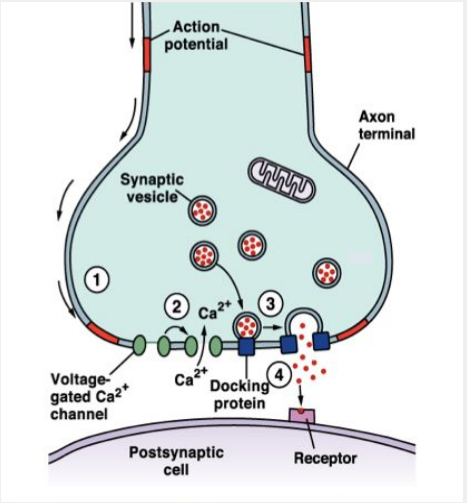
Acetylcholine

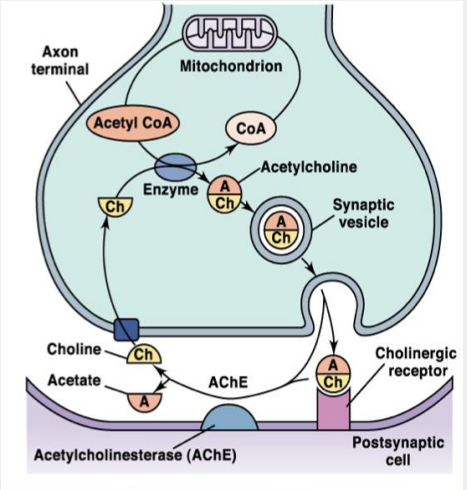
Ach is synthesized locally in the cytoplasm of the nerve terminal , from active acetate (acetyl coenzyme A) and choline.

Then it is rapidly absorbed into the synaptic vesicles and stored there.

The synaptic vesicles themselves are made by the Golgi Apparatus in the nerve soma (cell-body).

Then they are carried by Axoplasmic Transport to the nerve terminal , which contains around 300,000 vesicles





- Each vesicle is then filled with around 10,000 Ach molecules

AP = Action potential.
EPP = End-plate potential.
NMJ=Neuromuscular Junction.

Transduction in NMJ

01

When a nerve impulse (action potential) reaches the nerve terminal ,it opens calcium channels (they are voltage gated)

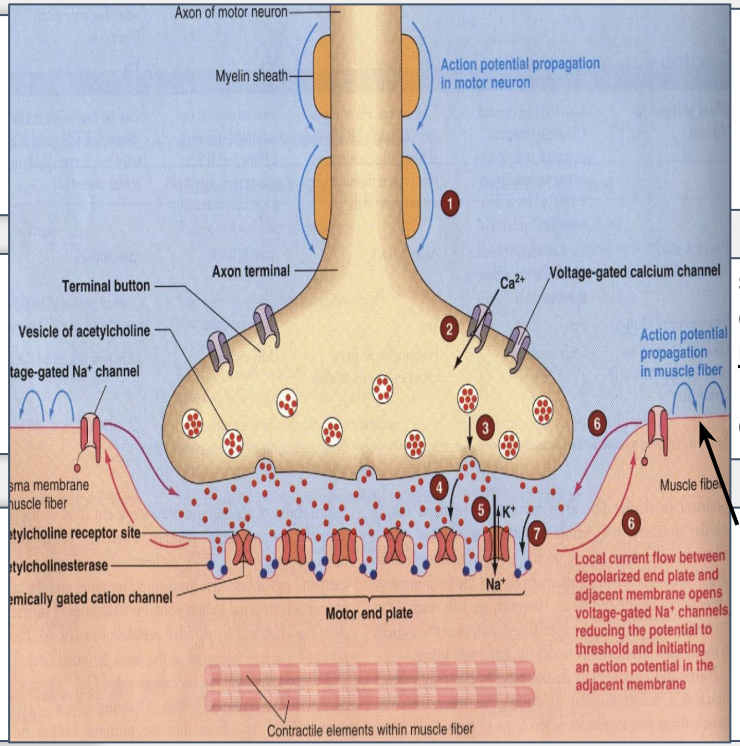
02

Calcium diffuses from the ECF into the axon terminal.

03

Ca++ releases Ach from vesicles by a process of EXOCYTOSIS

(Release from vesicles into synaptic cleft)



04

Ach combines with its receptors in the subneural clefts. This opens sodium channels.

(Ligand gated channel)

05

sodium diffuses into the muscle causing a local,non- propagated potential called the " End-Plate Potential (EPP)" in the motor end plate

EPP is weaker than AP.

06

If there is sufficient Na influx, this EPP triggers a muscle AP which spreads down/ propagat inside the muscle (sarcolemma) to make it contract.

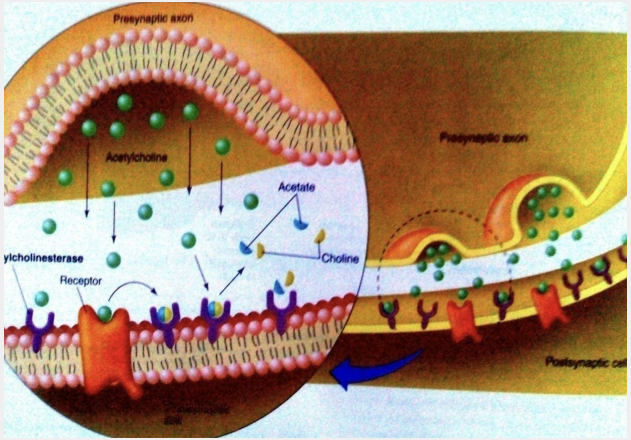
*One nerve impulse can releases 125 Ach vesicles.
*The quantity of ACh released by one nerve impulse is more than enough to produce one EPP.

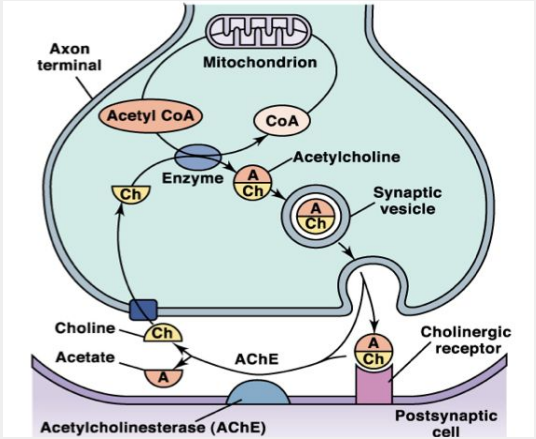
In this step, the AP spreads down the sarcolemma and opens more Na voltage gated channels. Na is diffused into muscle cell, generating a stronger AP = contraction.

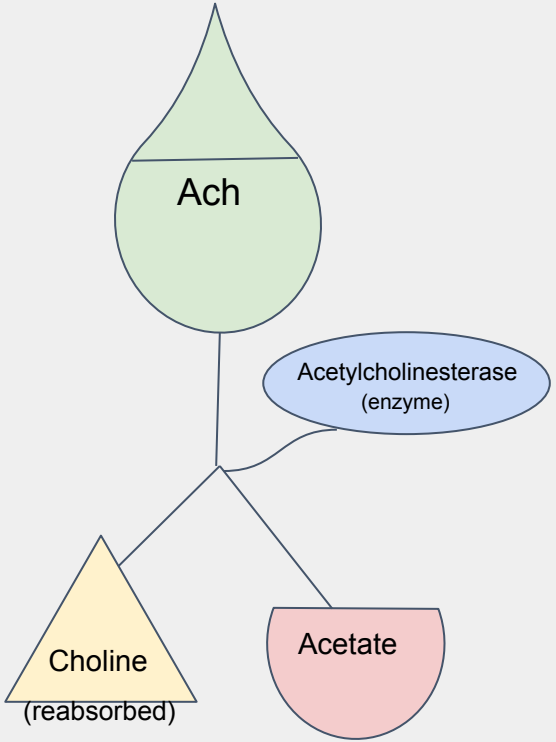
ms= milliseconds

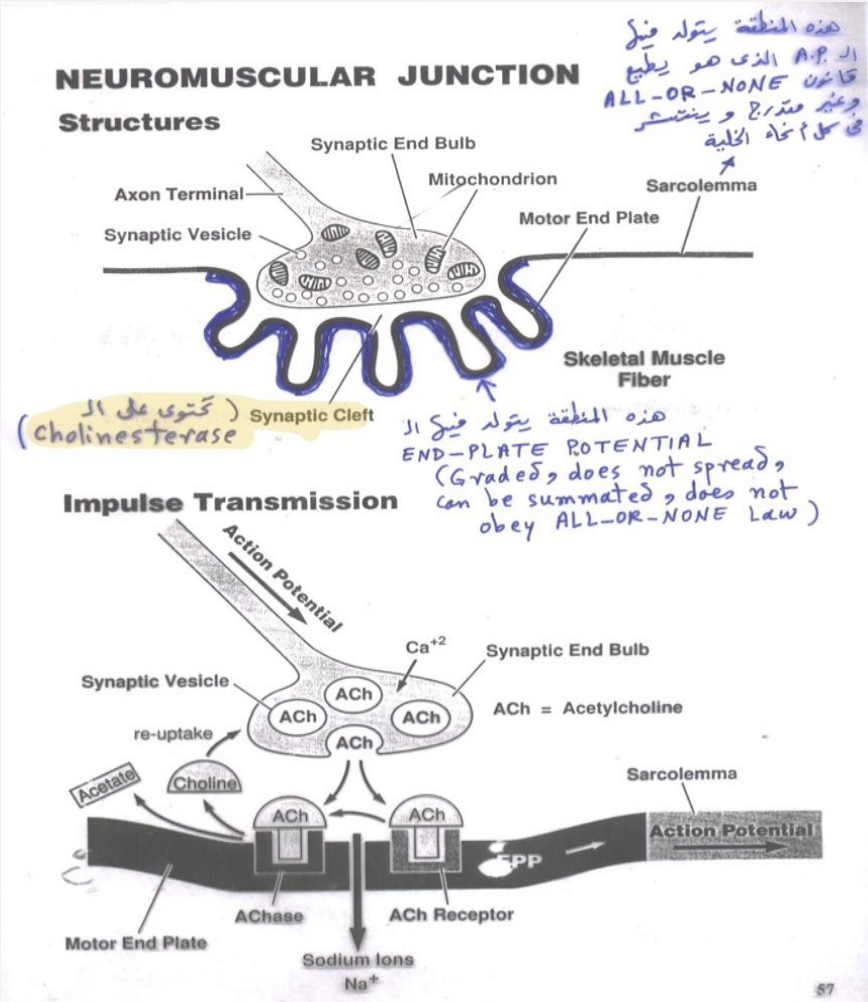
Destruction of Acetylcholine

- After ACh acts on the receptors , it is hydrolyzed by the enzyme Acetylcholinesterase (cholinesterase) into Acetate & Choline .
- The Choline is actively reabsorbed into the nerve terminal to be used again to form ACh.
- This whole process of Ach release, action & destruction takes about 5-10 ms .









End-Plate Potential	Action Potential
In motor end plate	In sarcolemma
Graded	Non graded
Does not spread rapidly	Spreads rapid (propagates)
Can be summated (added)	Cannot be summated
Does NOT obey all-or-none law	Obeys all-or-none law
Doesn't need to reach threshold (is about -40) .any small stimuli will produce response.	Doesn't produce respond until it reach threshold point
Found only on the postsynaptic membrane of the muscle cell	In neurons and muscle cells
Caused by the ligand-gated acetylcholine receptor channels	Maintained by voltage-gated Na and K channels

Drugs That stimulate or Block Transmission at the Neuromuscular Junction

drug stimulates by 2 ways:

1- stimulate muscle fiber by Ach-like action:

e.x: Methacholine, Carbachol, and Nicotine.

- **act for minutes or hours.**
- **NOT destructed by cholinestrase.**

2- stimulate NMJ by inactivating Acetylcholinesterase:

e.x:

A- Neostigmine, Physostigmine.
(inactivate Ach-estrase for hours)

B- diisopropyl fluorophosphate "nerve gas poison":
(inactivate Ach-estrase for weeks and can cause death by respiratory muscle spasm)

blocking drugs

Curare & Curariform like-drugs:

- Prevent passage of impulses from the nerve ending into the muscle by blocking the action of Ach on its receptors.
- act by competitive inhibition to Ach at its receptors & can not cause Depolarization.

Botulinum toxin:

Bacterial poison that decreases the quantity of Ach release by the nerve terminals.

Myasthenia Gravis

01

- It’s an **Autoimmune disorder**.
- patients develop antibodies which block or destroy their own Ach receptors.
- decreasing the EPP , or even preventing its formation.
- weakness or paralysis of muscles.
- patient may die because of paralysis of respiratory muscles.
- Occurs in about 1 in every 20,000 persons.

02

signs of Myasthenia Gravis:

- Presents with ptosis, dysarthria, dysphagia, and proximal limb weakness in hands & feet.

-in adult females affects eyelid, extra ocular bulbar and proximal limb muscles.

03

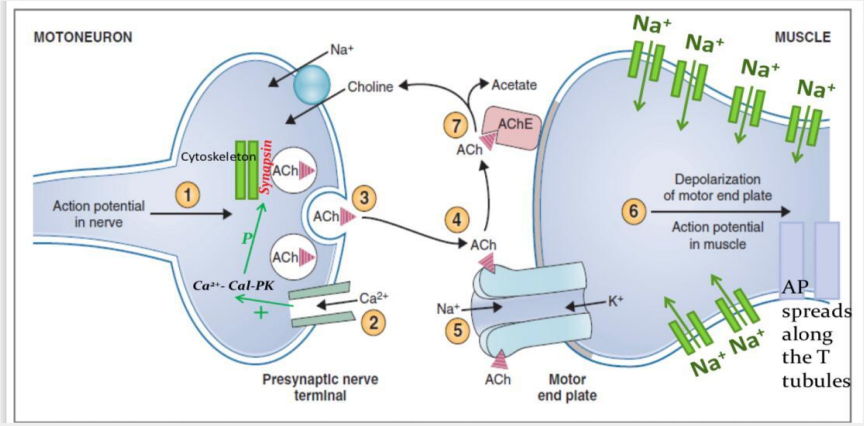
Treatment:
- Administration of anticholinesterase drugs such as Neostigmine which allows larger than normal amounts of Ach to accumulate in the synaptic space.

- Corticosteroids and Immunosuppressant drugs to inhibit the immune system, limiting antibody production.

Myasthenia Gravis (MG disease)

SUMMARY

1. Action potential reaches terminal axon
2. Calcium voltage channels in synaptic knob open
3. Calcium diffuses in axon terminal and moves synaptic vesicle closer to presynaptic terminal
4. Exocytosis of ACh in neuromuscular junction
5. ACh reaches post synaptic terminal which is the motor end plate
6. Ach links with the receptor and open Ligand gated channel
7. sodium diffuses causing a local, non- propagated potential called EPP
8. when there is sufficient Na influx, EPP triggers a muscle AP which propagate inside the muscle to make it contract.



QUIZ!

MCQs

Q1: process of the conversion of an electrical signal into a chemical signal?			
A) NMJ	B) neurotransmitters	C) synaptic knob	D) transduction
Q2 : what is the function of Subneural cleft?			
A) Increases Voltage gated calcium channel	B) Increases surface area	C) decrease surface area	D) Increases neurotransmitters action
Q3 : The synaptic vesicles are made by?			
A) Golgi apparatus	B) mitochondria	C) sarcoplasm	D) nerve cytoplasm
Q4 : Ach combines with its receptors in the subneural clefts, This opens?			
A) muscle AP	B) calcium channels	C) Ligand gated channel	D) potassium channels
Q5 : After ACh acts on the receptors , it is hydrolyzed by the enzyme Acetylcholinesterase into?			
A) Acetate & Choline	B) ester & Choline	C) Acetate & ester	D) Acetate & Cholinesterase
Q6 : An axon terminal can meet another cell, a neuron, muscle fiber, or gland cell called?			
A) NMJ	B) presynaptic terminal	C) Synaptic vesicles	D) synaptic knob

SAQ

Q1: mention two features of EPP and two features of AP ?

Q2: what does NMJ means and what is the site?

MCQs key answer :
1) D
2) B
3) A
4) C
5) A
6) D

SAQ answer key :
1) slide 10

2) NMJ is transmission is between neuron and muscle cell
site: synaps

فيه أسئلة ممتازة بكتاب ليندا من صفحة ٥٣ ارجعوا لها للتدريب، الطبعة السابعة

Physiology 439

THANK YOU

TEAM LEADERS

Abdulrahman Alswat | Haya Alanazi

REVIEWED BY

Meshal Alhamed | Ghada Alothman

TEAM MEMBERS

- Mishal Althuanyan
- Basel Fakeeha
- Mohammad Beyari
- Abdulaziz Alsuhaim
- Mohammad Alsalman
- Abdulrahman Addweesh
- Morshed Alharbi
- Ahmad Alkhayatt
- Abdulaziz Alguligah
- Omar Alhalabi
- Sumo Alzeer
- Noura Alshathri
- Renad Alhomaidi
- Yasmin Alqarni
- Lama Alahmadi
- Alaa Alsulmi
- Farah Albakr
- Hind Almotywea
- Sarah Alqahtani
- Duaa Alhumoudi

Question bank