L 4 :The Neuromuscular Junction (Neuromuscular Synapse)

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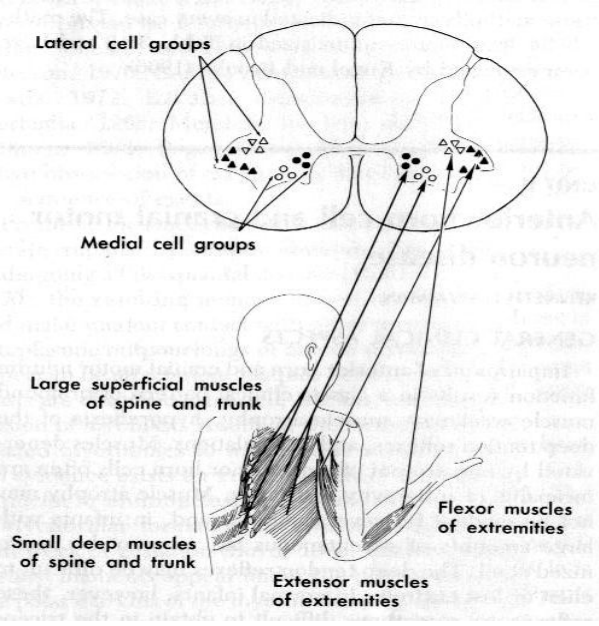
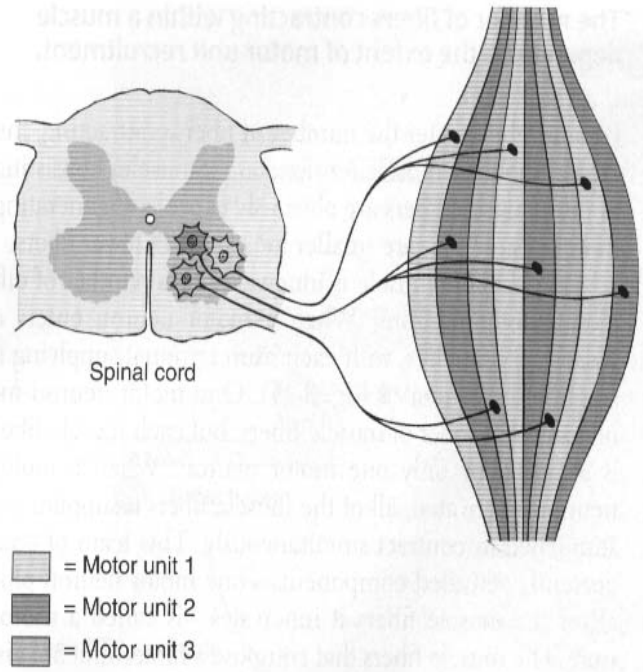
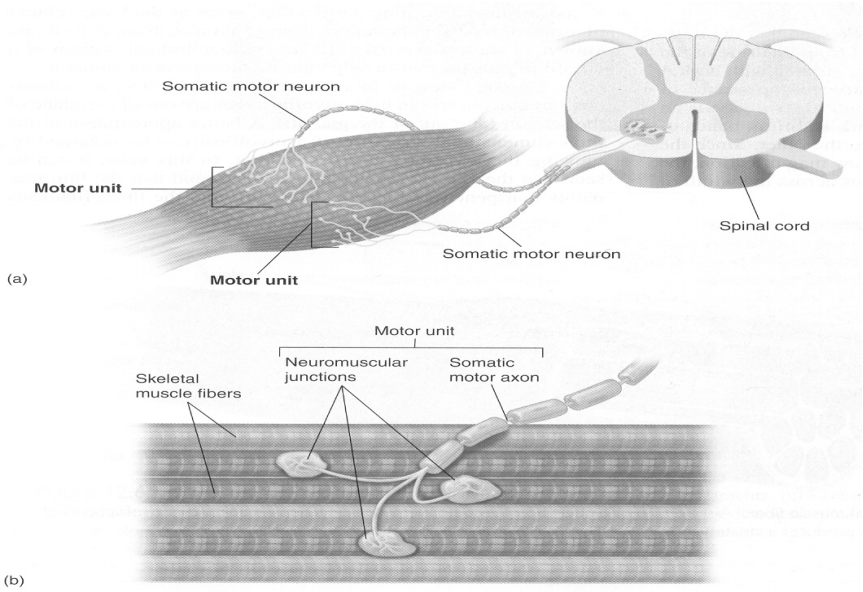
- **Anterior Horn Cells (Motor Neurons).**



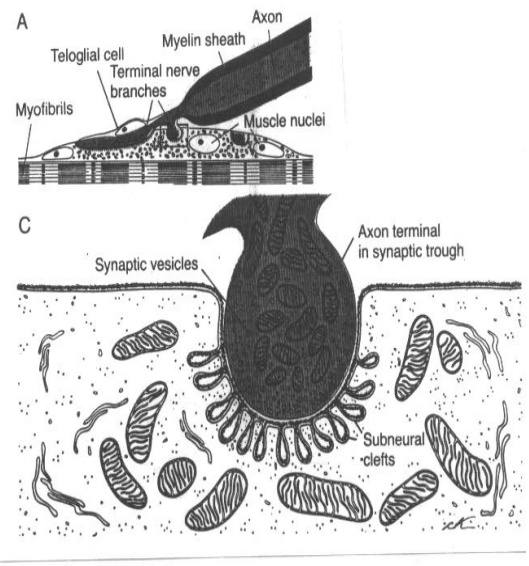
- **Motor Unit : is the motor neuron (Anterior horn Cell) and all the muscle fibers it supplies**



Neuromuscular Junction (NMJ)



The Neuromuscular junction consists of



A/ Axon Terminal : contains around 300,000 vesicles which contain the neurotransmitter acetylcholine (Ach).

B/ Synaptic Cleft :

20 – 30 nm (nanometer) space between the axon terminal & the muscle cell membrane. It contains the enzyme cholinesterase which can destroy Ach .

C/ Synaptic Gutter (Synaptic Trough)

It is the muscle cell membrane which is in contact with the nerve terminal . It has many folds called **Subneural Clefts** , which greatly increase the surface area , allowing for accomodation of large numbers of Ach receptors . Ach receptors are located here .

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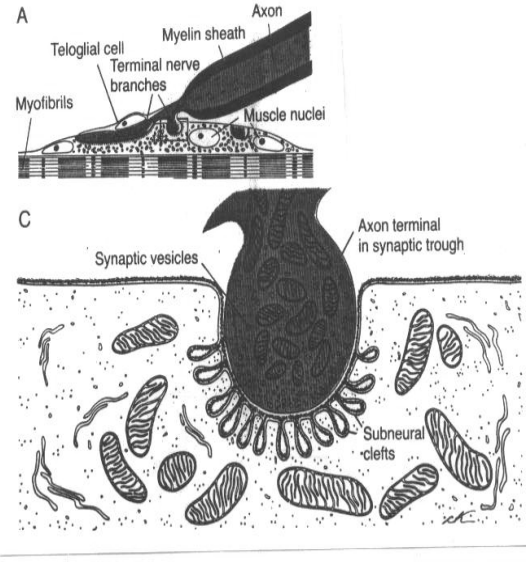
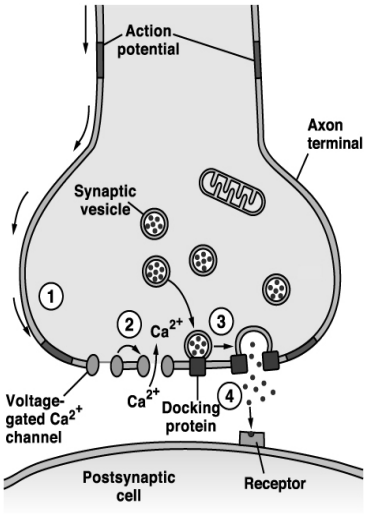


- **The entire structure of axon terminal , synaptic cleft and synaptic gutter is called " Motor End-Plate " .**
- **Ach is synthesized locally in the cytoplasm of the nerve terminal , from active acetate (acetylcoenzyme A) and choline.**
- **Then it is rapidly absorbed into the synaptic vesicles and 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 .**

Acetylcholine (1)



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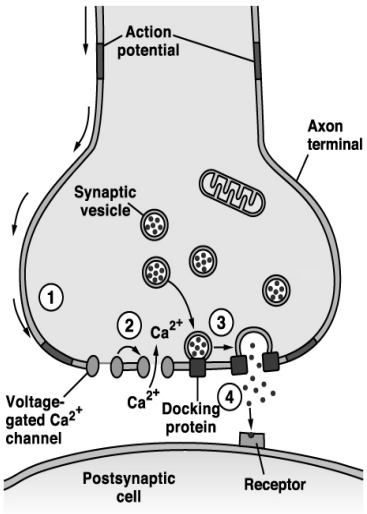
- **The synaptic vesicles themselves are made by the Golgi Apparatus in the nerve soma (cell-body).**
- **Then they are carried by Axoplasmic Transport to the nerve terminal , which contains around 300,000 vesicles .**
- **Each vesicle is then filled with around 10,000 Ach molecules .**

Acetylcholine (2)



- **When a nerve impulse reaches the nerve terminal ,**
- **it opens calcium channels → calcium diffuses from the ECF int the axon terminal → Ca++ releases Ach from vesicles by a process of EXOCYTOSIS**
- **One nerve impulse can release 125 Ach vesicles.**
- **<u>The quantity of Ach released by one nerve impulse is more than enough to produce one End-Plate Potential .</u>**

- Ach combines with its receptors in the subneural clefts. This opens sodium channels → & sodium diffuses into the muscle causing a **local,non-propagated** potential called the " **End-Plate Potential (EPP)",** whose value is 50 – 75 mV.
- This EPP triggers a **muscle AP** which spreads down inside the muscle to make it cntract .

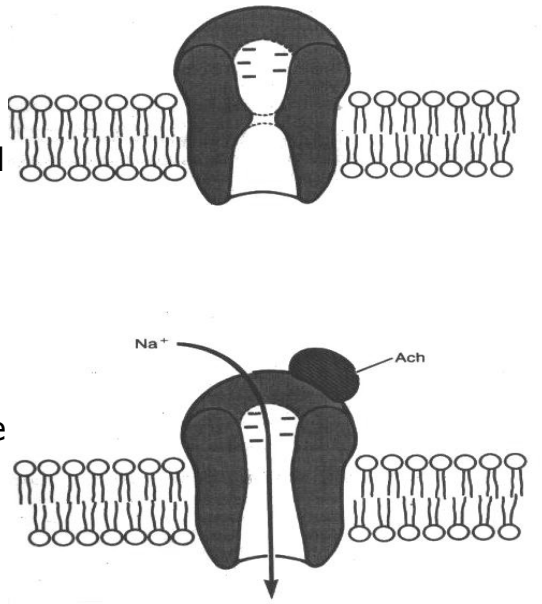
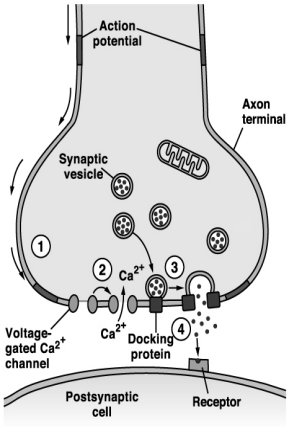
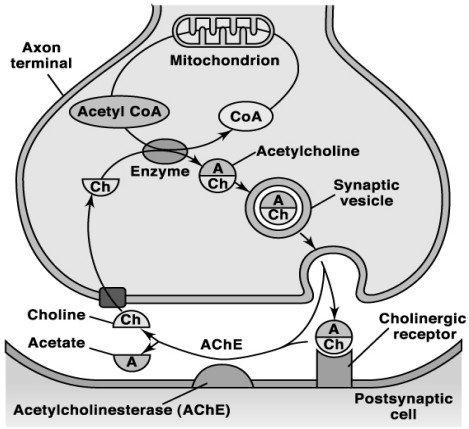
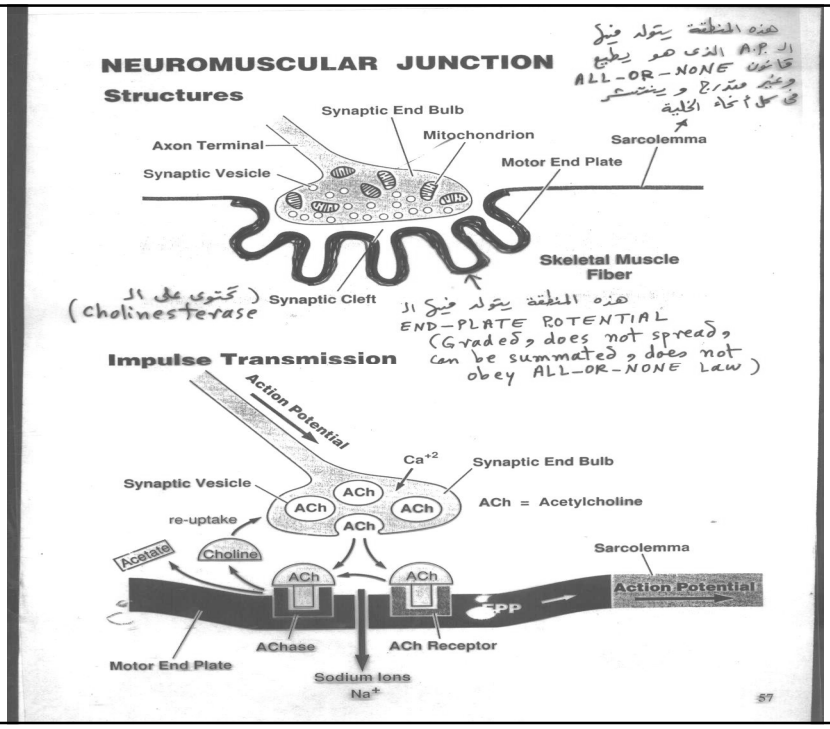


Figure 7–3 The *acetylcholine channel:* Above, while in the closed state. Below, after acetylcholine has become attached and a conformational change has opened the channel, allowing excess sodium to enter the muscle fiber and excite contraction. Note the negative charges at the channel mouth that prevent passage of negative ions.





- 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 .



Myasthenia Gravis

- Auto-immune disease
- Antibodies against Ach receptors destroy many of the receptors → decreasing the EPP , or even preventing its formation → weakness or paralysis of muscles (depending on the severity of the disease) .
- → patient may die because of paralysis of respiratory muscles.
- <u>Treatment</u> : Anti-cholinestersae drugs . These drugs inactivate the cholinesterase enzyme (which destroys Ach) and thereby allow relatively large amounts of Ach to accumulate and act on the remaining healthy receptors → good EPP is formed → muscle contraction .

Drugs Acting on the NMJ

- Drugs that stimulate the muscle cell by Acetylcholine-like action : nicotine , methacholine , carbachol .
- Drugs that block neuromuscular transmission : Curare and curare-like drugs (curariform drugs) . They have a chemical structure similar to ACh , but can not stimulate the receptors . They occupy acetylcholine receptors and thereby prevent ACh from acting on its receptors → muscle weakness or paralysis . Example : Tubocurarine. It is used during some surgical operations .
- Anticholinesterase drugs : e.g. Neostigmine (Prostigmin) , Physostigmine , Pyridostigmine (Mestinon) Used in treatment of Myasthenia Gravis . These drugs inactivate the cholinesterase enzyme (which destroys Ach) and thereby allow relatively large amounts of Ach to accumulate and act on the remaining healthy receptors → good EPP is formed → muscle contraction .