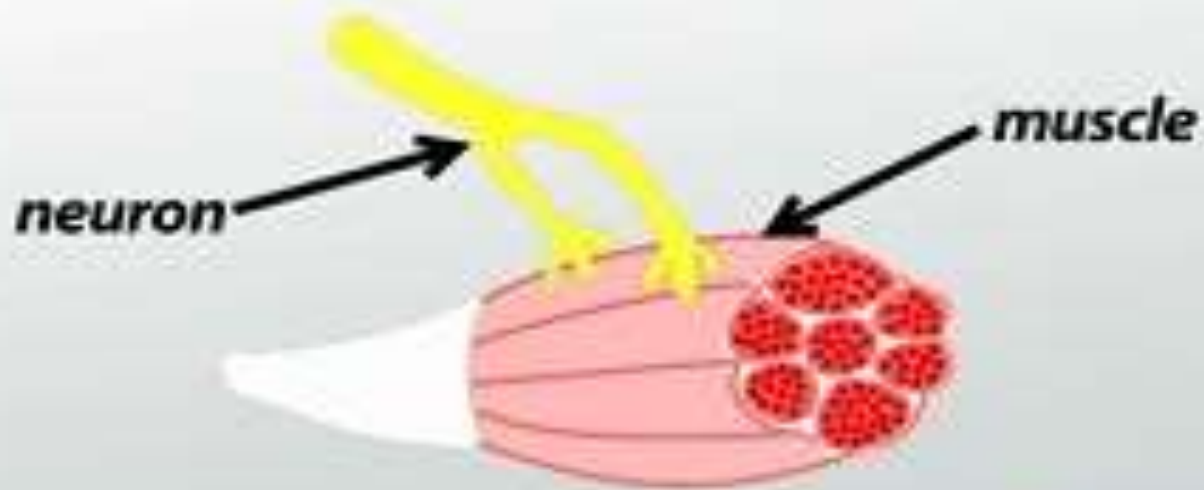


# Neuromuscular Junction

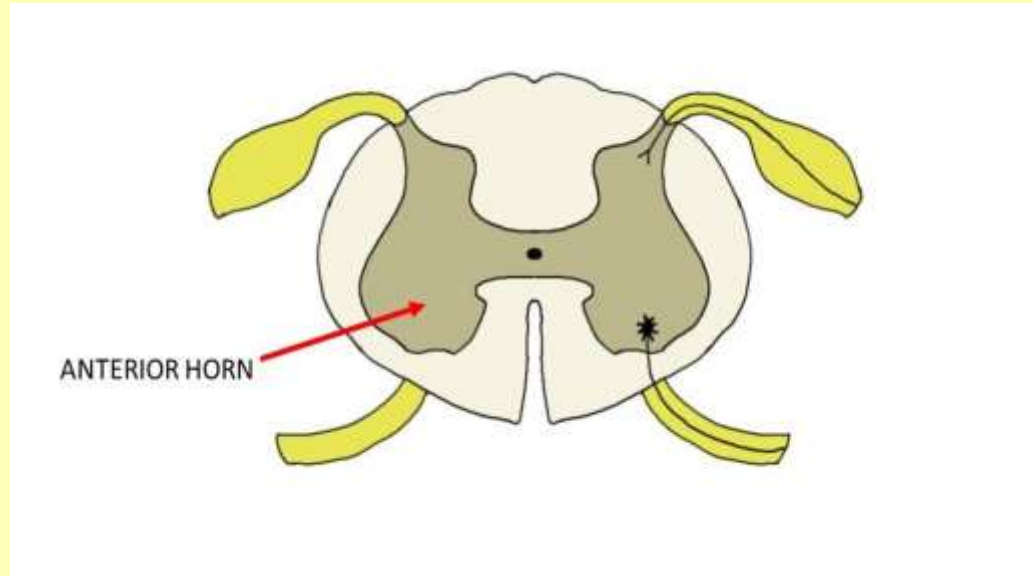
SYNAPTIC TRANSMISSION

## Neuromuscular Junction

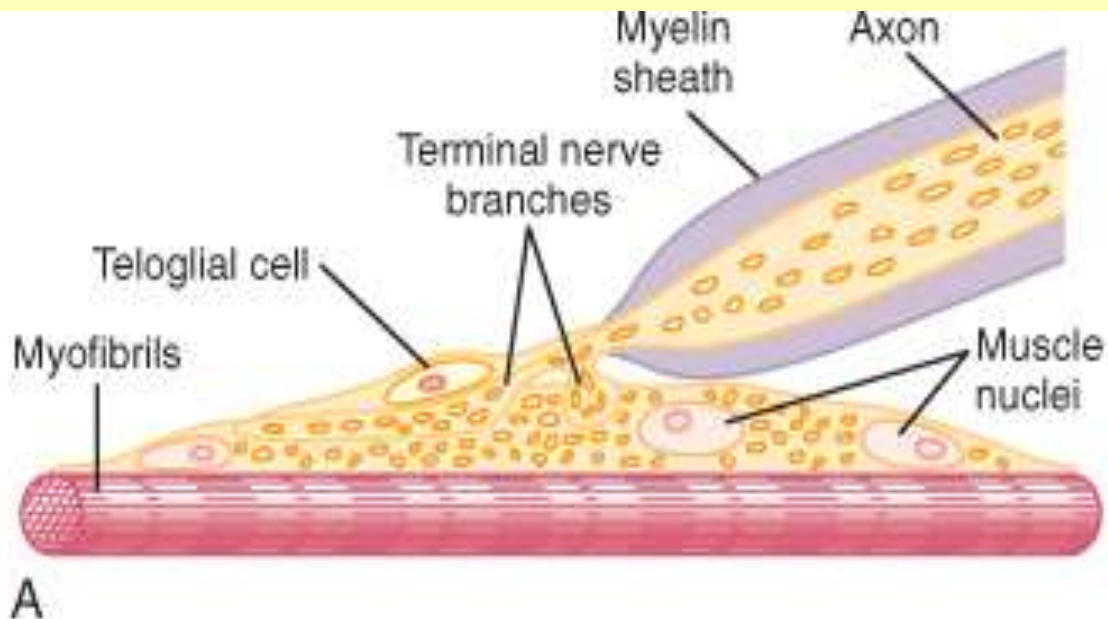


# Introduction

- ❖ **Neuromuscular junction refers to an intimate contact between the nerve endings & the muscle fibers as the nerve endings innervate the muscle fibre**
- ❖ **The nerve fibre originates from Anterior horn of the spinal cord**

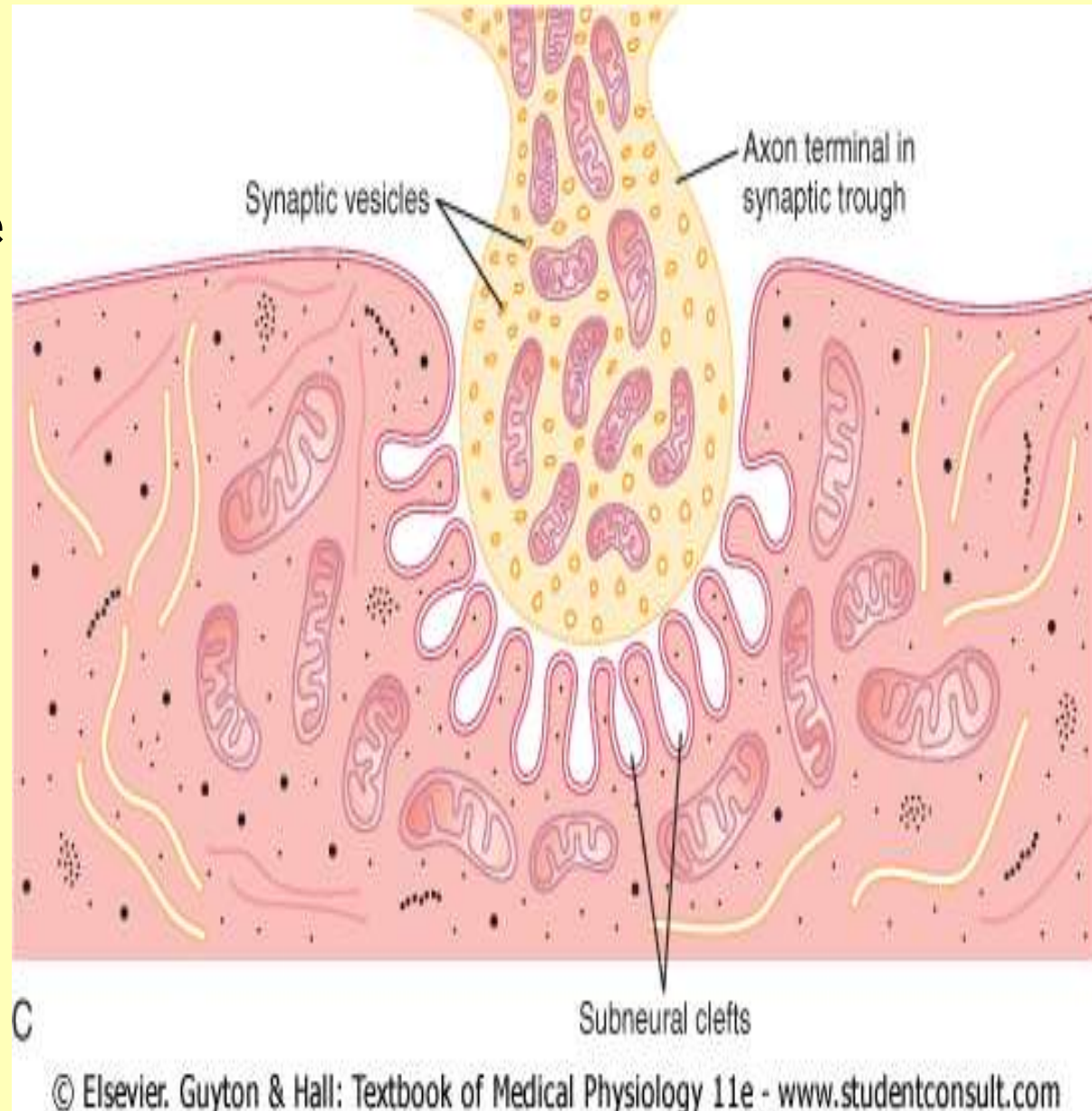


- **Each nerve ending makes a junction with the muscle fibre near its midpoint called neuromuscular junction**



# Structure of Neuromuscular Junction

- **Motor end plate**
- **Synaptic gutter**
- **Subneural cleft**



# Structural Organization of N-M Junction

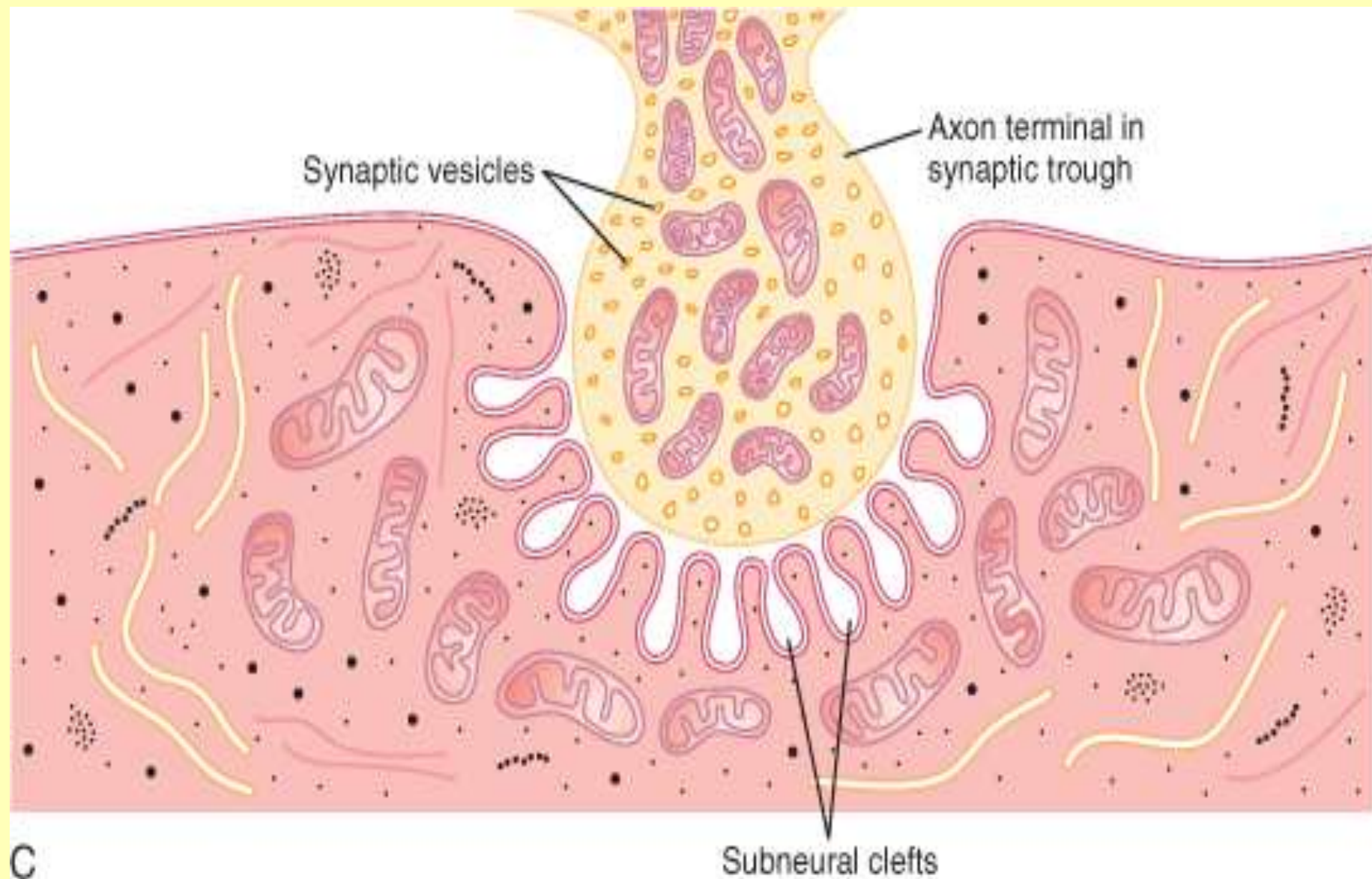
**Terminal Button-** Axon of neuron, supplying a skeletal muscle loses its myelination, gives out branches ending into small swellings (knobs)- Terminal buttons

- These terminal buttons (synaptic knobs) contain large number of vesicles containing Acetylcholine (which is synthesized by mitochondria)
- Also ATP is present

**The invaginating membrane is called synaptic trough/gutter**

**Presynaptic membrane-** Axonal membrane lining the terminal buttons of the nerve ending

**Synaptic Cleft-** 50 to 100 nm wide. It's a space between the presynaptic membrane & postsynaptic membrane



C

**Postsynaptic Membrane**-It is the muscle fibre membrane (sarcolemma).

Thickened & depressed so that the terminal button fits in, they have receptor sites for Acetylcholine

Postsynaptic membrane is thrown into folds- ***subneural clefts (contains enzyme- Cholinesterase)***

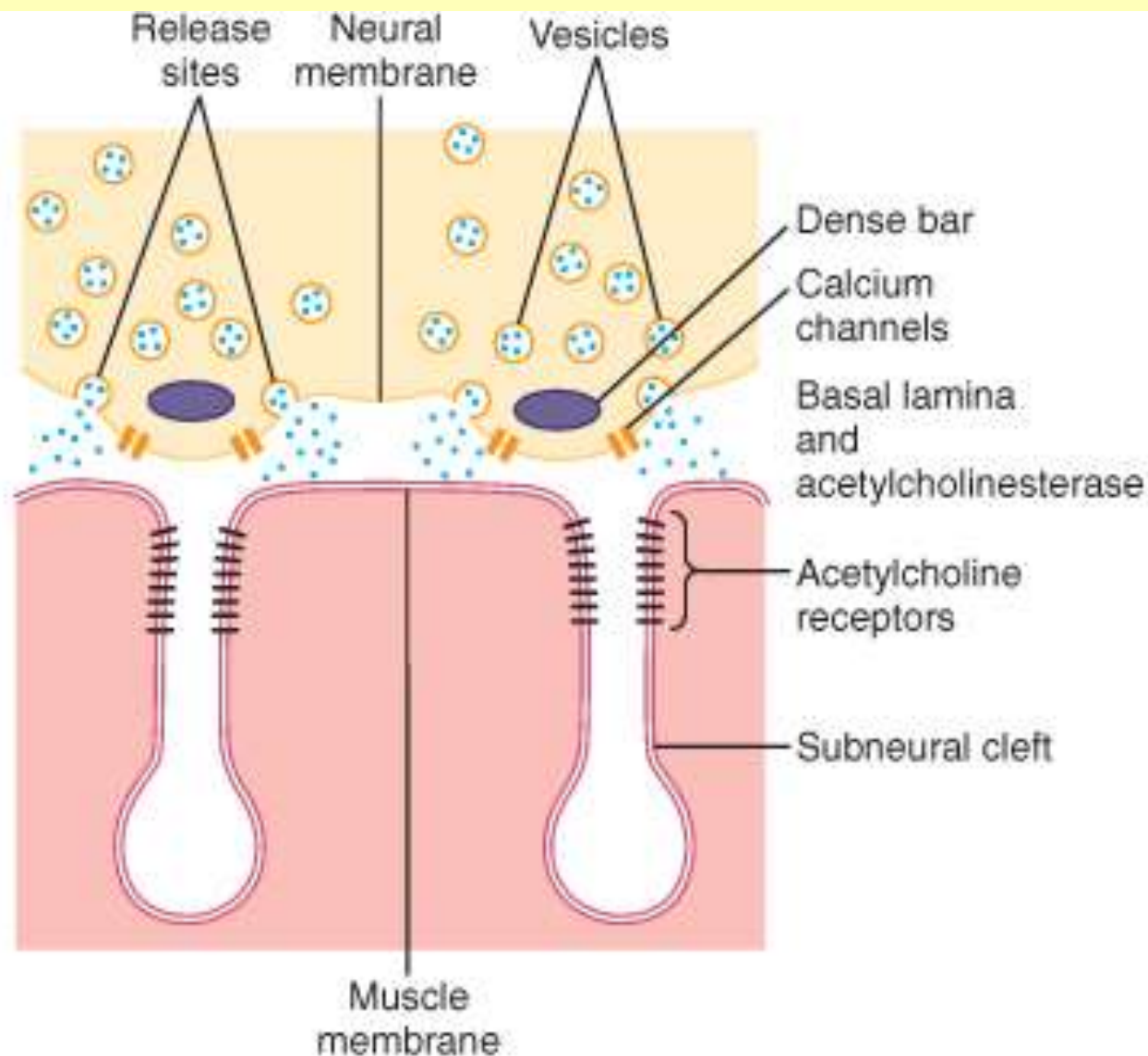
- The nerve fiber branches at its end to invaginate into muscle fiber but lies outside the muscle fiber plasma membrane- entire structure is called **MOTOR END PLATE**

# The sequence of events are:

- ❖ Release of acetylcholine by the nerve terminals
- ❖ Effect of acetylcholine on postsynaptic membrane
- ❖ Development of end plate potential
- ❖ Development of Miniature end plate potential
- ❖ Removal of acetylcholine by cholinesterase
- ❖ Initiation of the action potential in muscle fibre

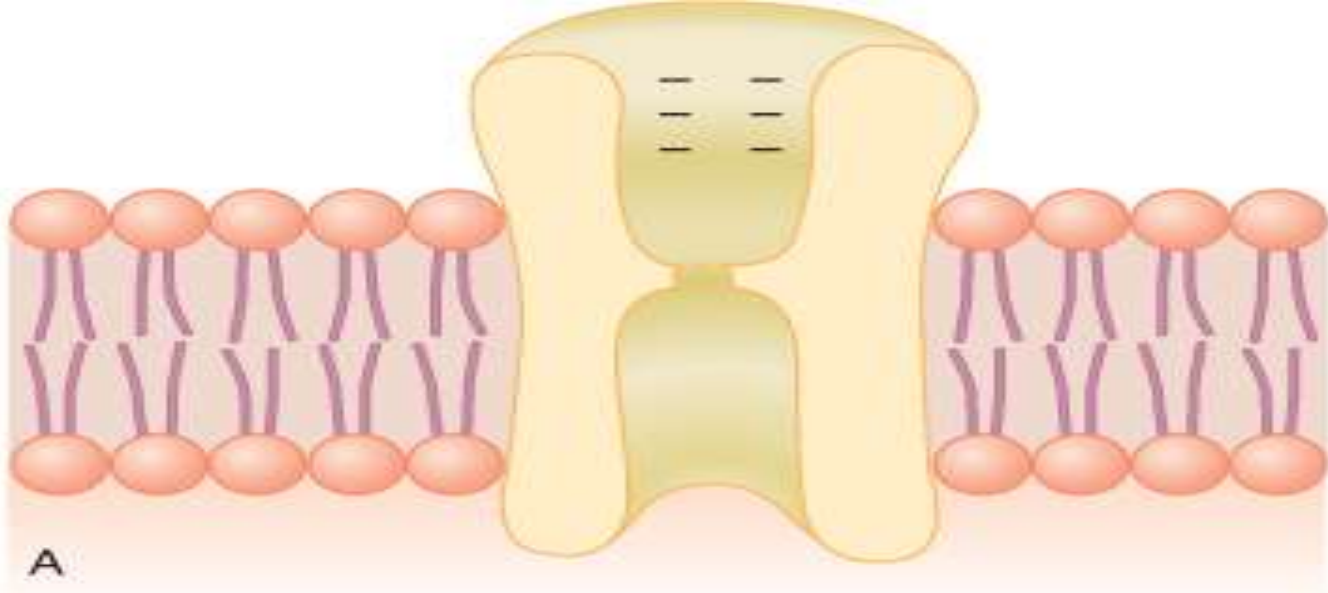
# Release Of Acetylcholine

- Action potential travelling in the nerve fibre (axon) reaches the terminal button
- Voltage gated Calcium channel open up, increasing the calcium permeability
- Ca ions present in ECF of synaptic cleft enter terminal button
- Exocytosis of vesicle (about 125) causes-release of Acetylcholine in synaptic cleft
- Each vesicle has 10,000 molecule of Ach



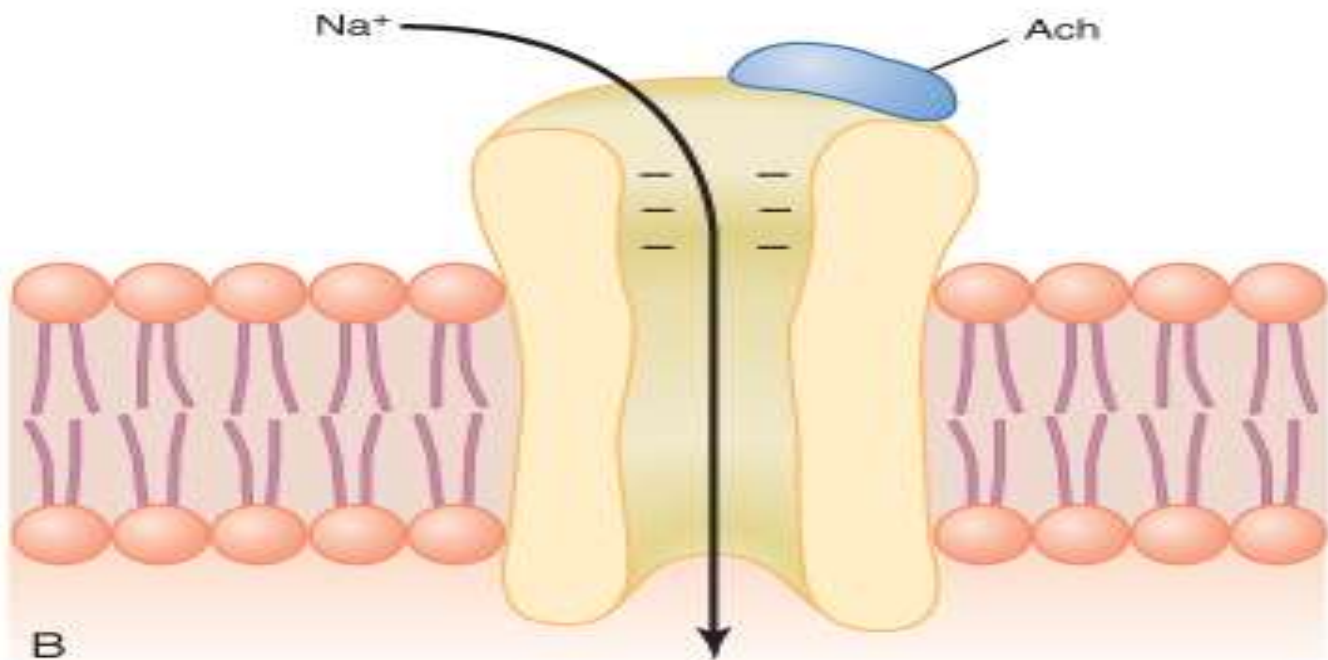
# Effect of Acetylcholine on Postsynaptic Membrane

- Acetylcholine so released in synaptic cleft binds to Nicotinic Ach receptors (Protein in nature having 2 Alpha, one Beta, Gamma & Delta units) located on folds of motor end plate (postsynaptic membrane)
- Opened Ach channel have diameter of 0.65 nm



A

© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)



B

© Elsevier. Guyton & Hall: Textbook of Medical Physiology 11e - [www.studentconsult.com](http://www.studentconsult.com)

# Development of End-Plate Potential

- Opening of the Ach gated channels causes movement of large amount of positively charged ions- Na, K & Ca to enter into muscle fibre from ECF
- RMP of postsynaptic membrane - -80 to -90 Mv
- Na ions cause depolarization- Local Positive Potential is developed- ***End Plate Potential***

- At -60 mV the end plate potential- triggers development of Action potential in the muscle fibre
- Thus leading to muscle contraction

***SAFETY FACTOR- impulse arriving at NMJ causes about 3 times as much end plate potential as that required to stimulate muscle fiber.***

# Removal Of Acetylcholine

- Ach released into the synaptic cleft (remains for about 1 ms)

## Removal Process:

- ❖ Ach is destroyed by enzyme Acetylcholinesterase present in the synaptic cleft
- ❖ A small amount diffuses out of synaptic space

# Drugs Affecting Neuromuscular Junction

## Neuromuscular Blocker:

Curare drugs (receptor blockers)

Bungarotoxin

Succinylcholine

Botulinum toxin

# Neuromuscular Stimulators:

Drugs having acetylcholine like action- e.g.  
Methacholine, Nicotin

Drugs that inactivate the enzyme  
cholinesterase- e.g. Neostigmine,  
Physostigmine

# Disorders of Neuromuscular Junction

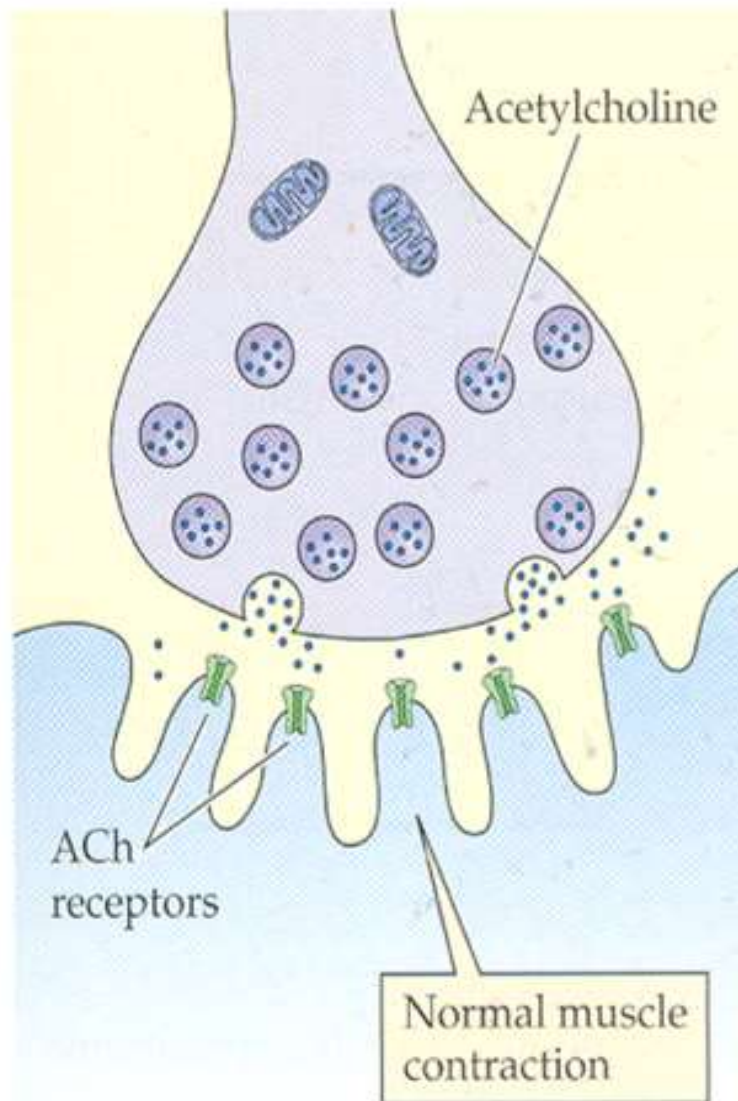
## Myasthenia Gravis:

- ❖ Autoimmune disorder
- ❖ Antibodies are produced against the Ach-channels
- ❖ Paralysis (paralysis of respiratory muscles)

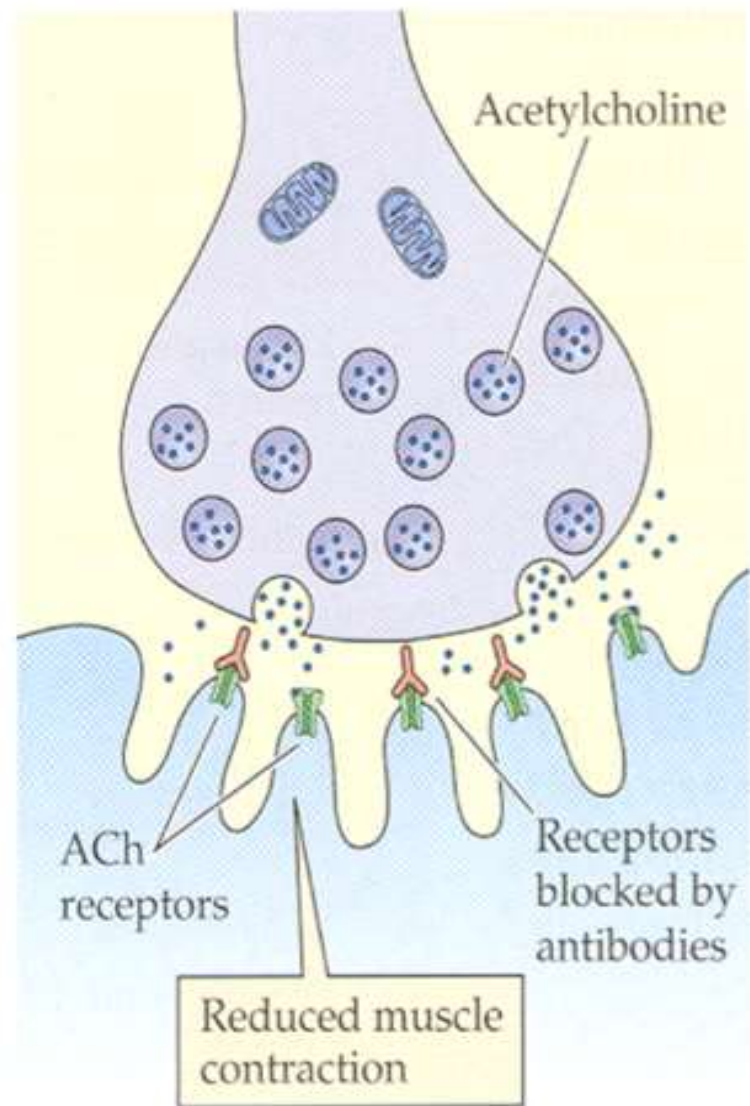
## Lambert-Eaton syndrome:

- ❖ Antibodies against Calcium channels are produced

Normal neuromuscular junction



Neuromuscular junction in myasthenia gravis





## SYMPTOMS:

- The first noticeable symptom is weakness of the **eye muscles**, difficulty in swallowing and slurred speech may also be the first signs.
- Muscles that control eye and eyelid movement, facial expressions, **chewing, talking and swallowing** becomes weaker.
- The muscles that control **breathing** and neck and limb movements can also be affected.



**Myasthenia Gravis (MG disease)**