Neuromuscular junction

OBJECTIVES

At the end of the lecture, students should be able to describe:

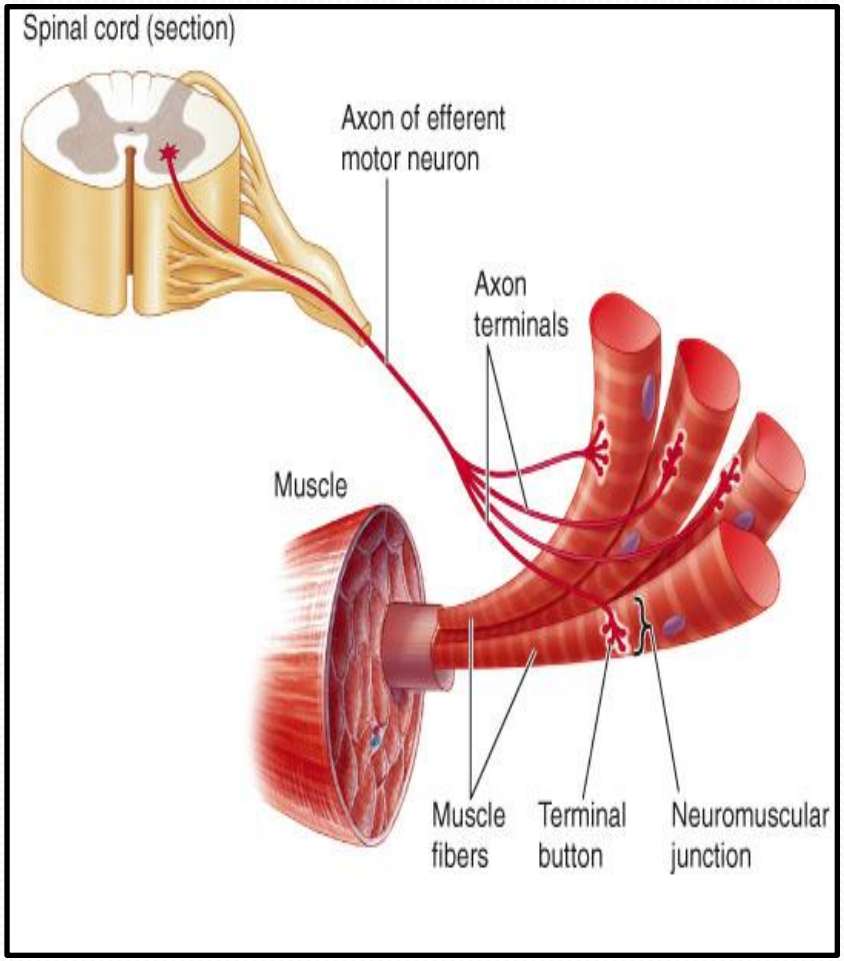
Neuromuscular transmission:

- Physiologic anatomy
- Events
- N-M blocking & its clinical significance
- Applied aspect – myasthenia gravis

INTRODUCTION

- Motor Unit:-
- **Neuromuscular junction:-**

  = motor end plate

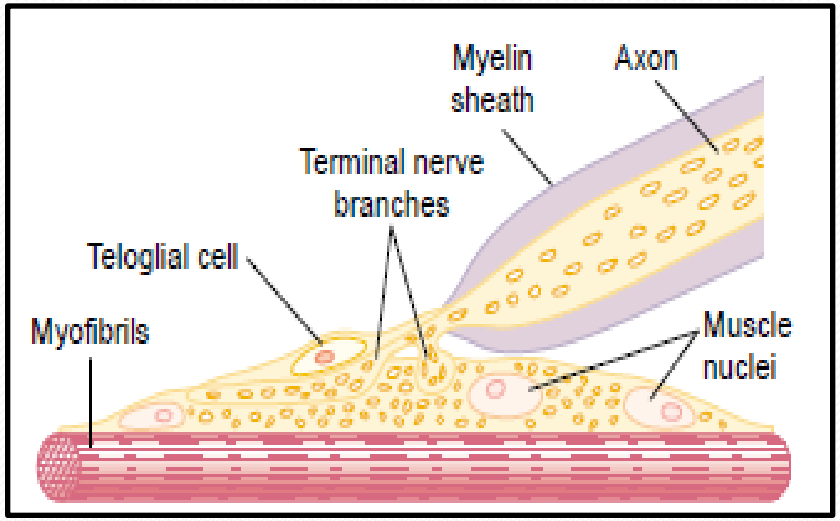


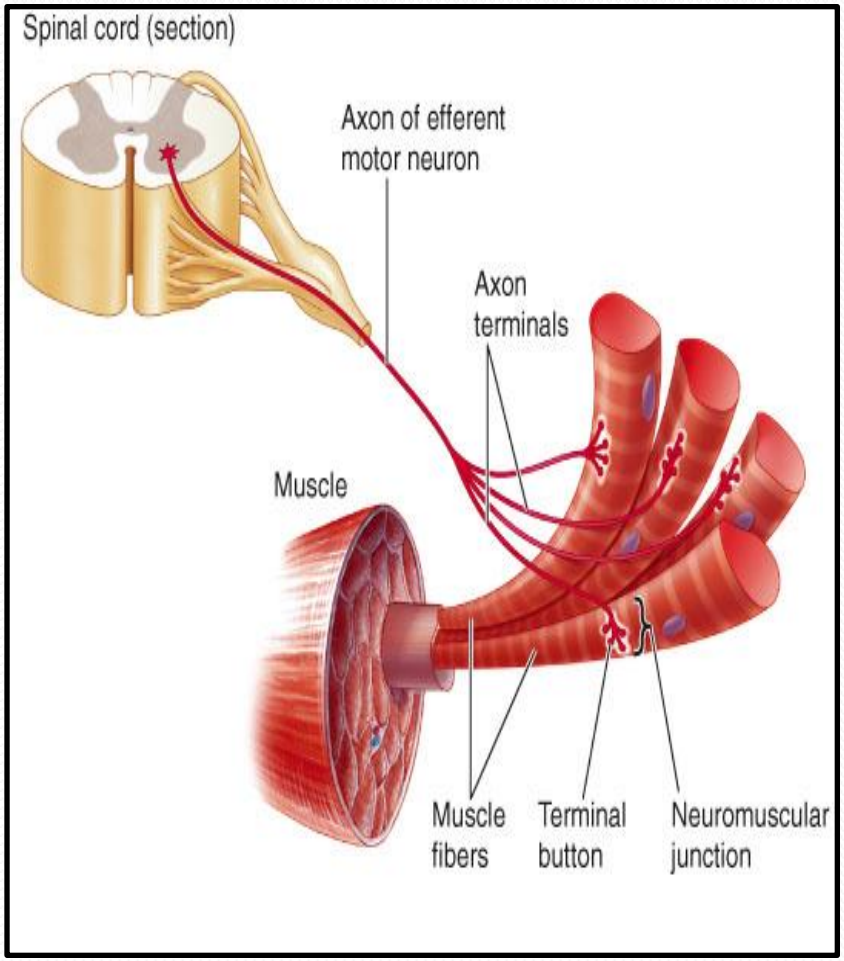
STRUCTURE

- Axon terminal:-

  - Terminal arborizations

- Boutons:-



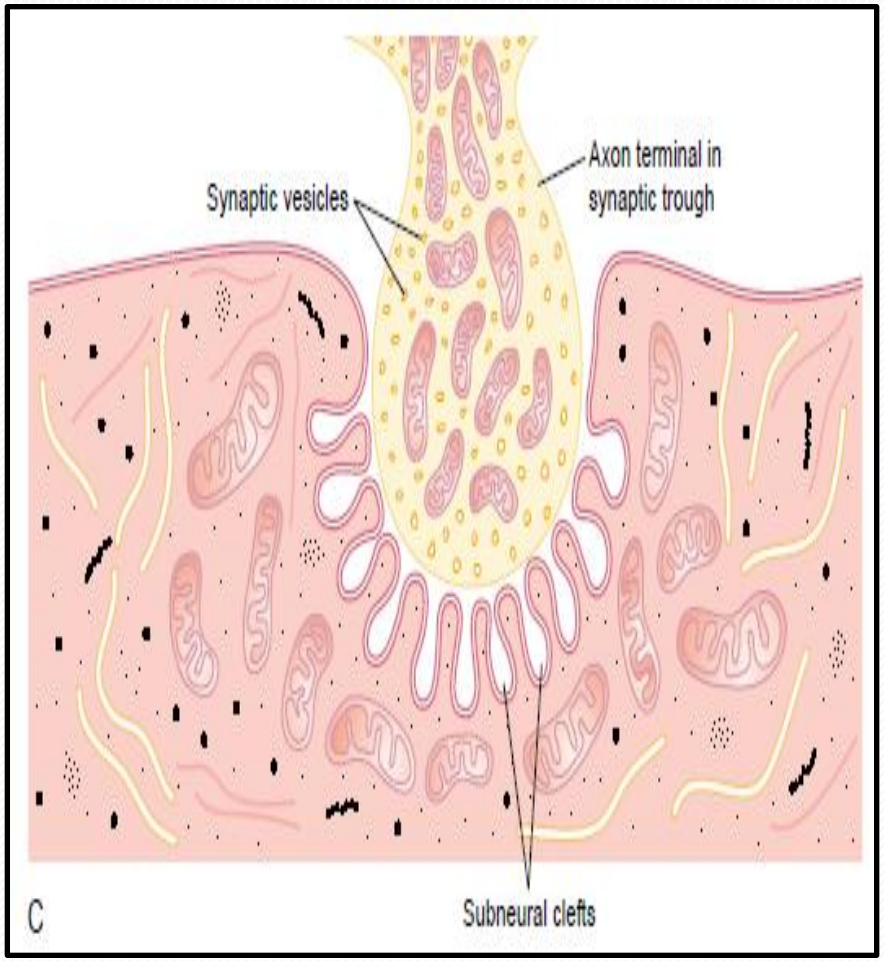


STRUCTURE

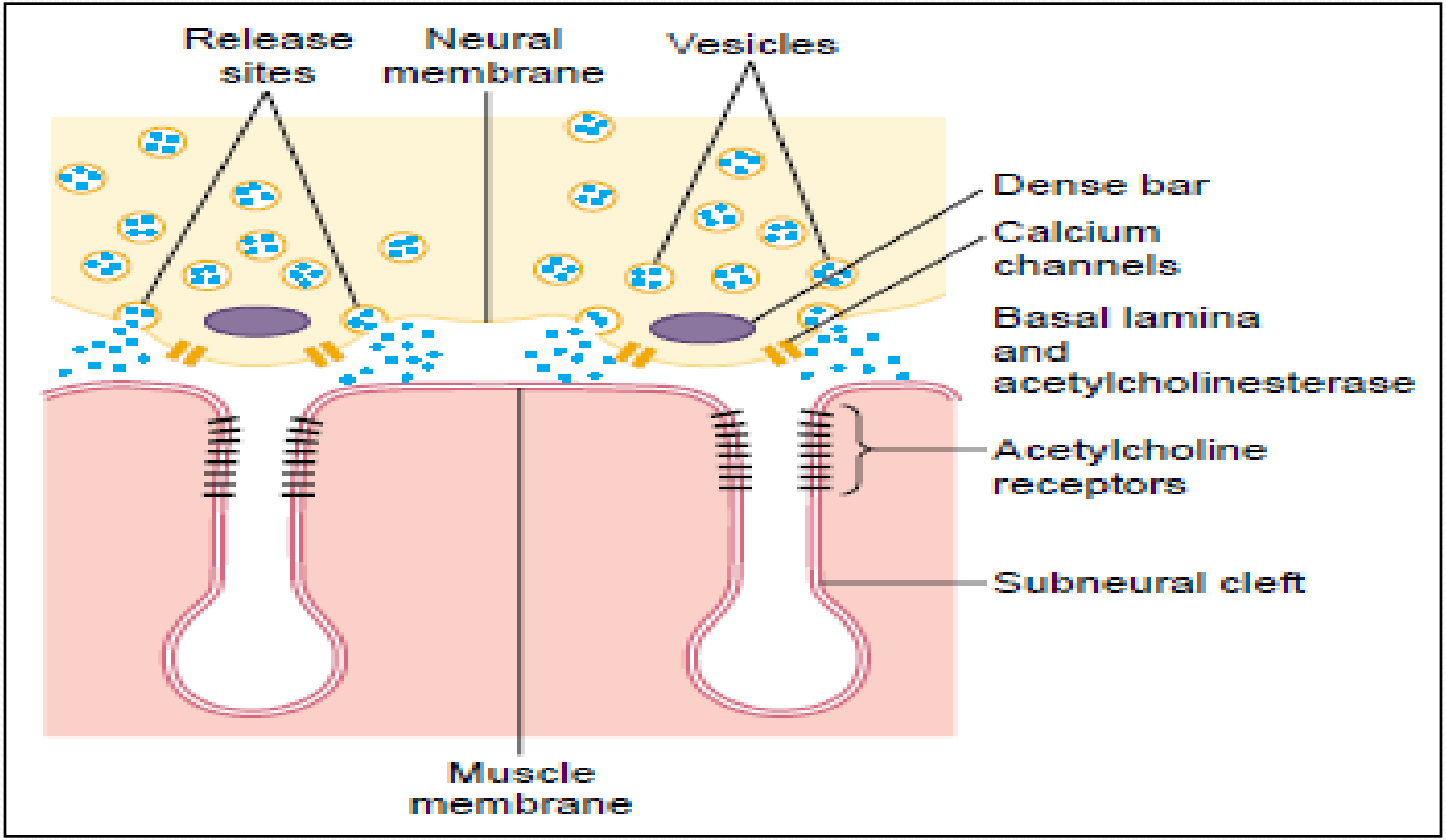
- Axon terminal:-

  3,00,000 Ach vesicles

- Synaptic gutter (trough):-
- Synaptic cleft:-
- Synaptic basal lamina:-
- Subneural clefts:-



STRUCTURE


Release sites
Neural membrane
Vesicles
Dense bar
Calcium channels
Basal lamina and acetylcholinesterase
Acetylcholine receptors
Subneural cleft
Muscle membrane

MECHANISM OF SYNAPTIC TRANSMISSION

Sir Bernard Katz
(1911-2003)

the quantal / vesicle hypothesis
of neurotransmitter release

nobel prize, 1970

Fatt & Katz, 1952
del Castillo and Katz, 1955

MECHANISM OF SYNAPTIC TRANSMISSION

1. Formation of Acetylcholine
2. Secretion of Acetylcholine
3. Acetylcholine action on post-synaptic membrane
4. Removal of Acetylcholine

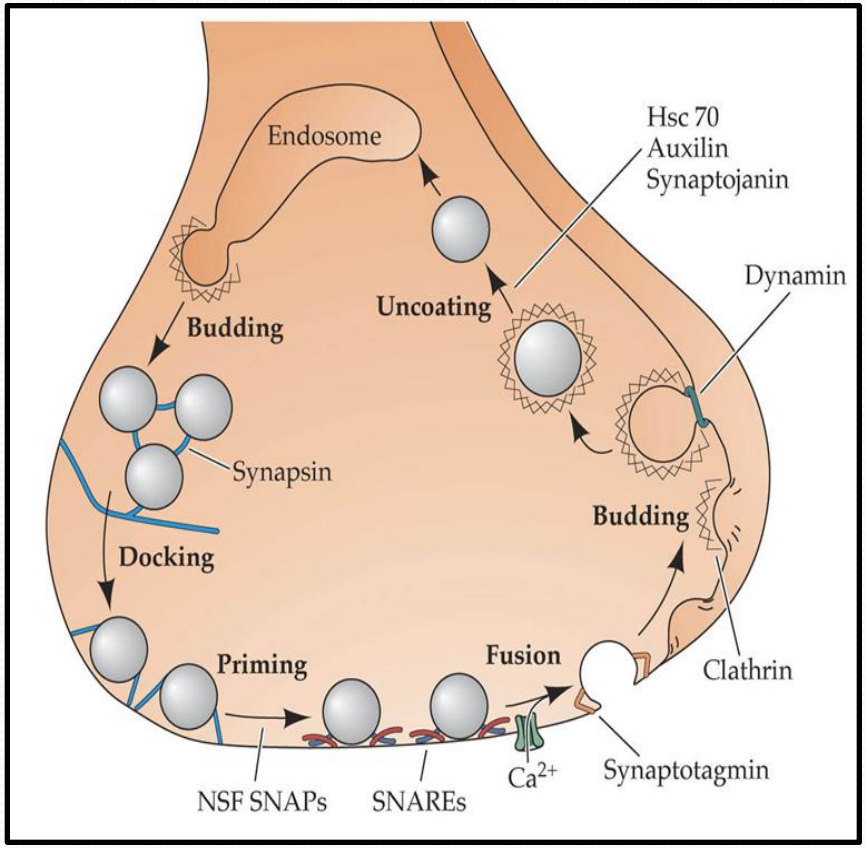
MECHANISM OF SYNAPTIC TRANSMISSION

1. **Formation of Acetylcholine:-**

MECHANISM OF SYNAPTIC TRANSMISSION

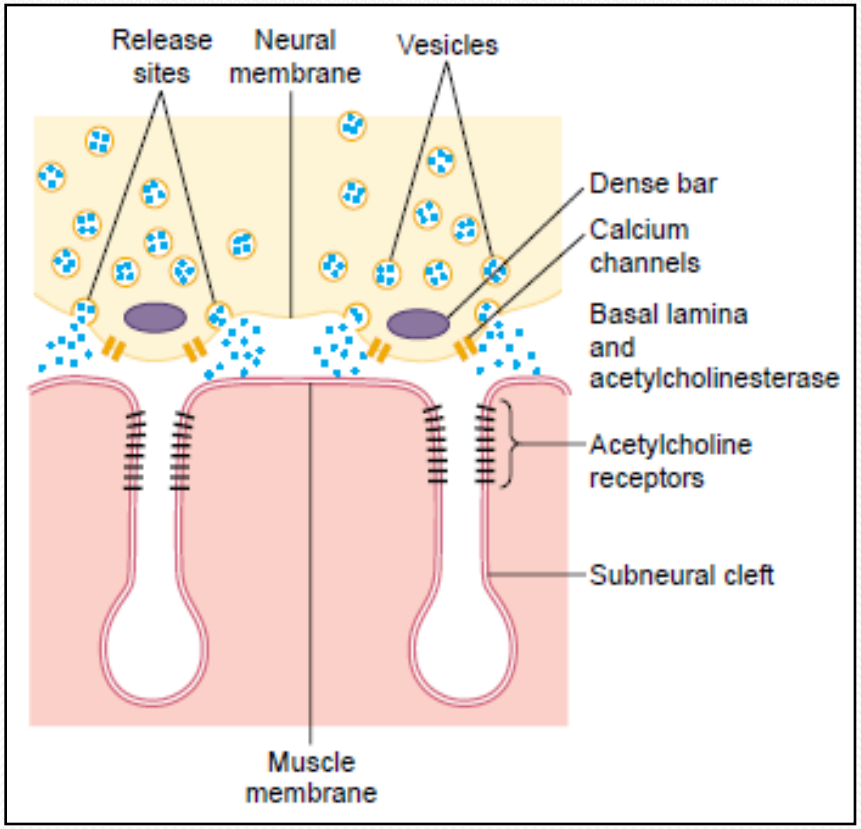
2. **Secretion of Acetylcholine:-**

- Quantal release
- Safety factor > 10



MECHANISM OF SYNAPTIC TRANSMISSION

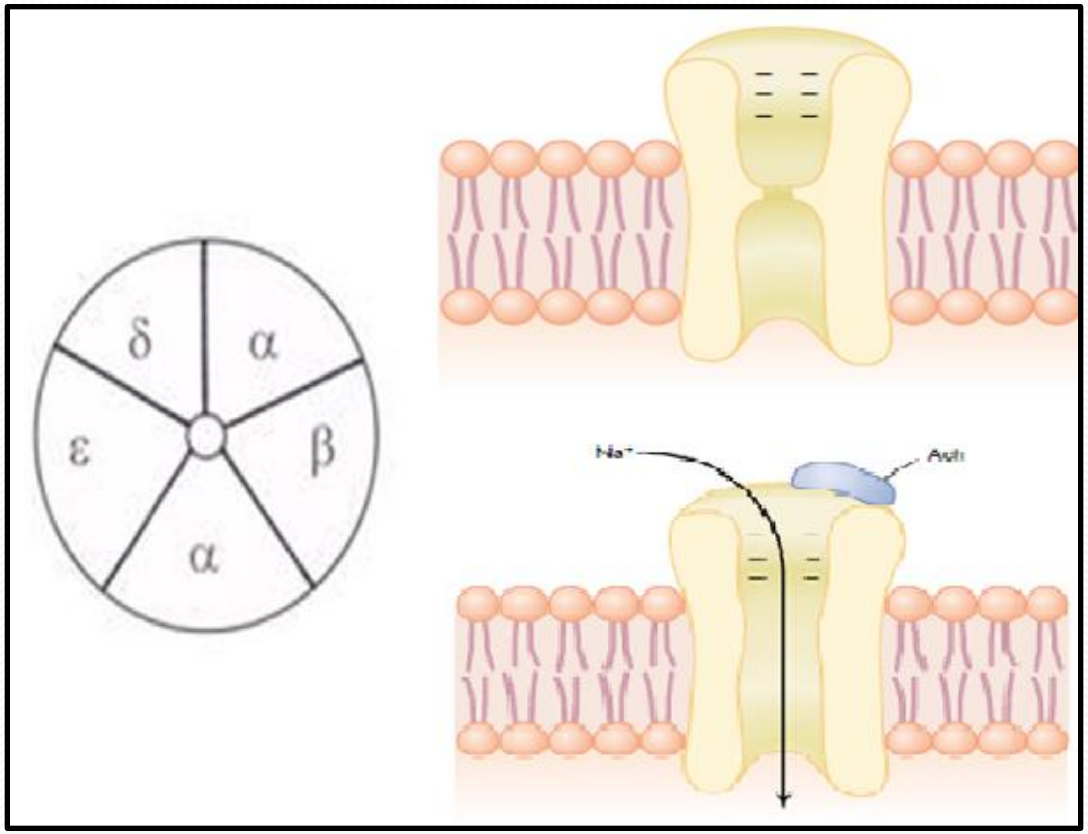
3. **Acetylcholine action on post-synaptic membrane:-**



MECHANISM OF SYNAPTIC TRANSMISSION

3. **Acetylcholine action on post-synaptic membrane:-**

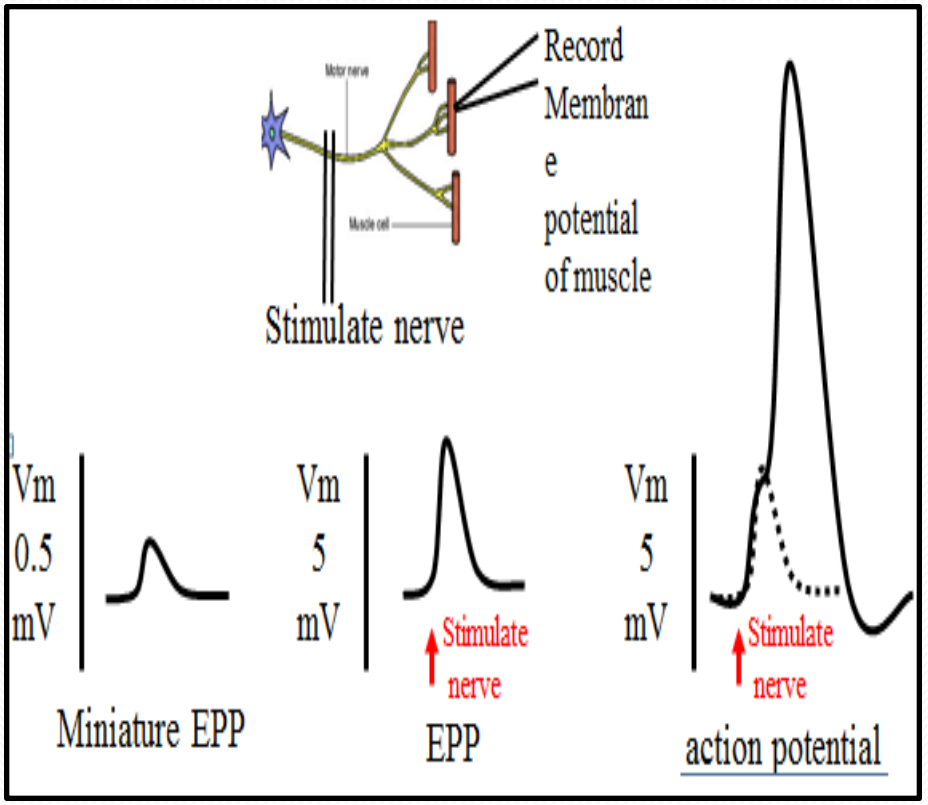
- Ach receptor:-

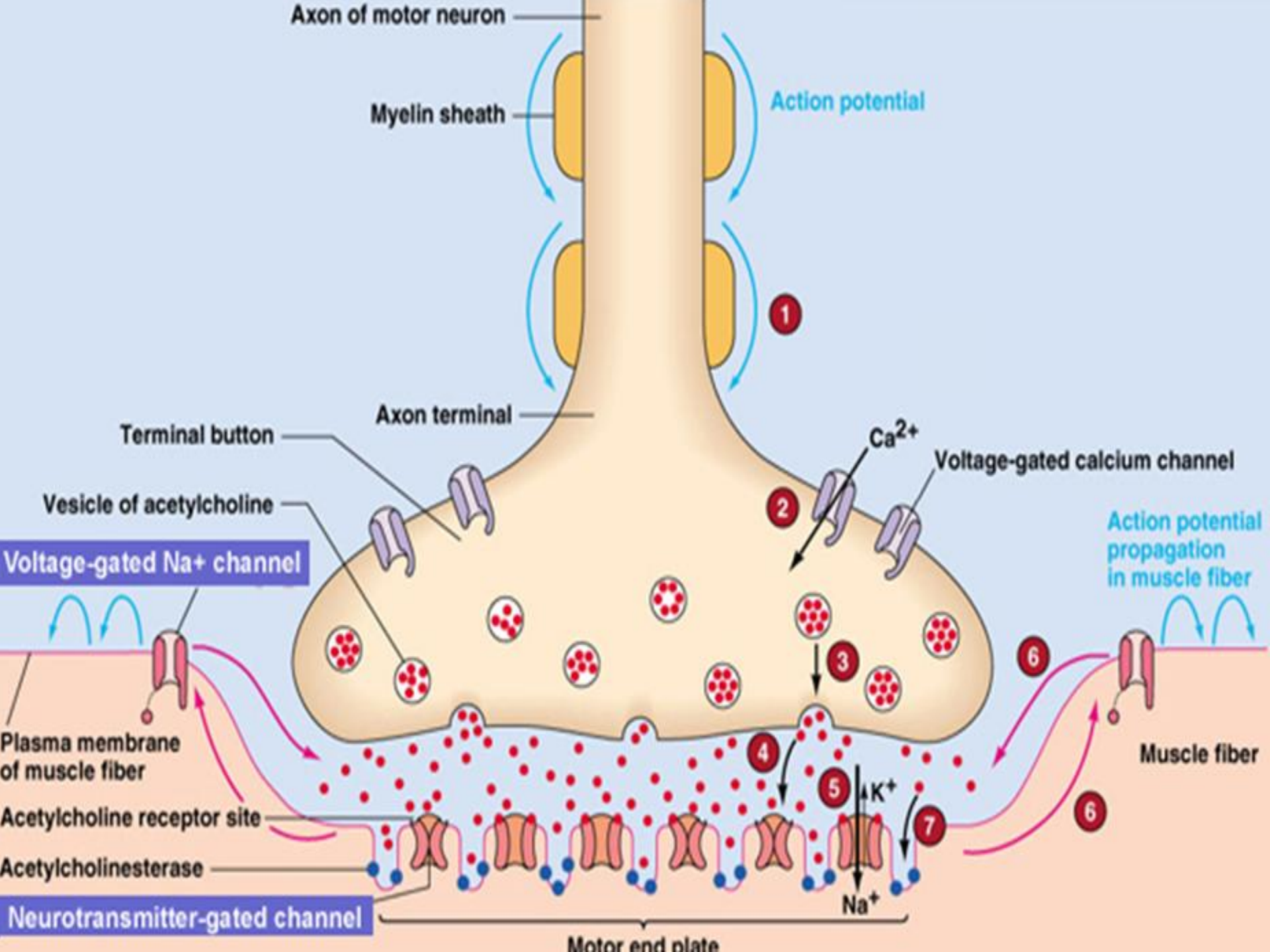


MECHANISM OF SYNAPTIC TRANSMISSION

3. **Acetylcholine action on post-synaptic membrane:-**

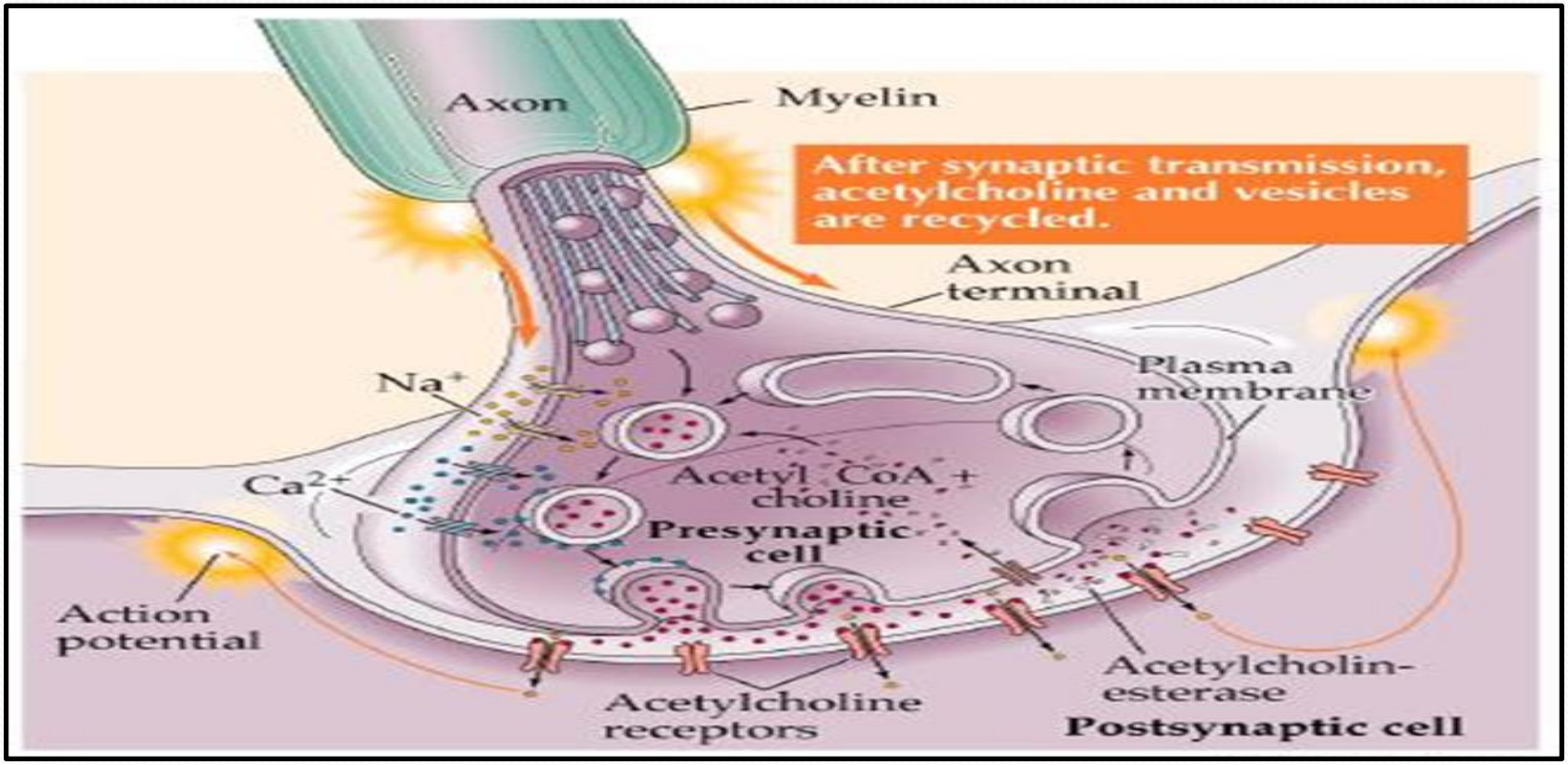
- End plate potential:-
- Miniature EPP:-
- Safety factor = 3




Axon of motor neuron
Myelin sheath
Action potential
1
Axon terminal
Terminal button
Ca2+
Voltage-gated calcium channel
Vesicle of acetylcholine
2
Action potential
propagation
in muscle fiber
Voltage-gated Na+ channel
3
6
Plasma membrane
of muscle fiber
4
Muscle fiber
5
K+
Acetylcholine receptor site
7
6
Acetylcholinesterase
Neurotransmitter-gated channel
Na+
Motor end plate

MECHANISM OF SYNAPTIC TRANSMISSION

4. **Removal of Acetylcholine:-**



CASE

A 35 years old woman presented with progressive weakness for the last 2 months. She has also noticed intermittent drooping of both of her eye lids and progressive facial muscles weakness while speaking. She also complains of weakness and tiredness while climbing the stairs of her office and has difficulty while typing lengthy official replies to their clients.

CASE

On examination:

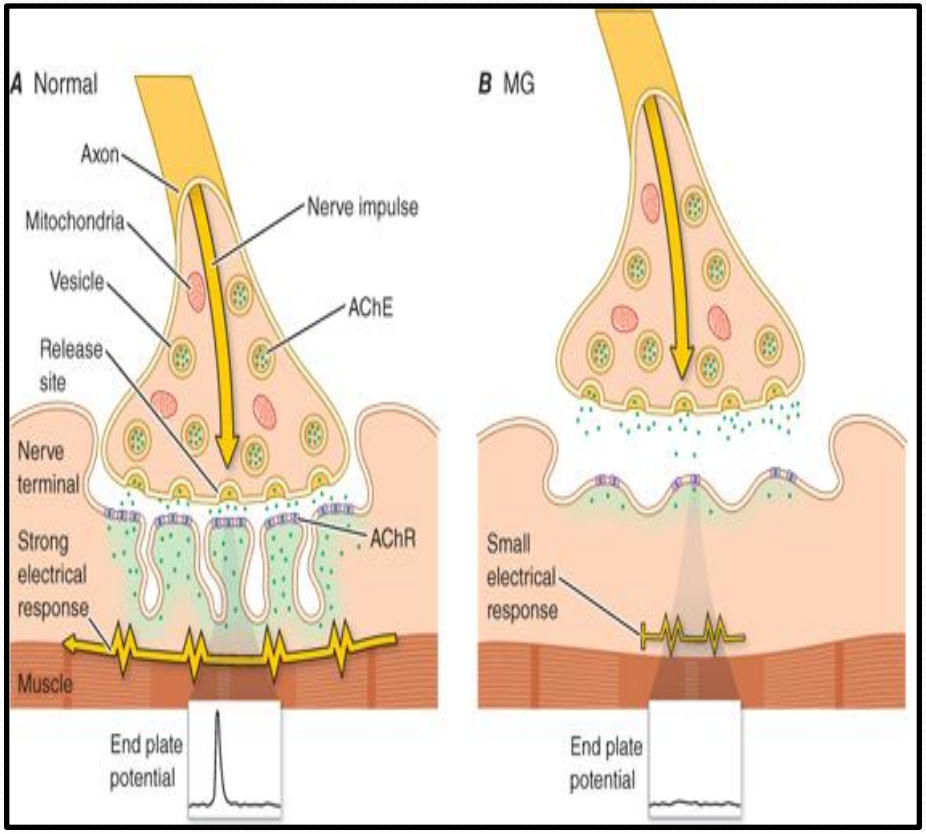
- Pulse - 82/min, BP - 120/80 mmHg, Temp - 98 F, RR - 16/min
- Drooping of both eyelids (Ptosis +)

Lab investigations - positive anti-choline receptor antibodies

MYASTHENIA GRAVIS

- **Introduction:-**
  - Mys = muscle,

    Ashenia = weakness
  - Bimodal distribution



- **Pathophysiology:-**
  - Autoimmune disorder

MYASTHENIA GRAVIS

- Clinical features:-
  - Diplopia
  - Ptosis
  - Husky voice
  - Fatigue

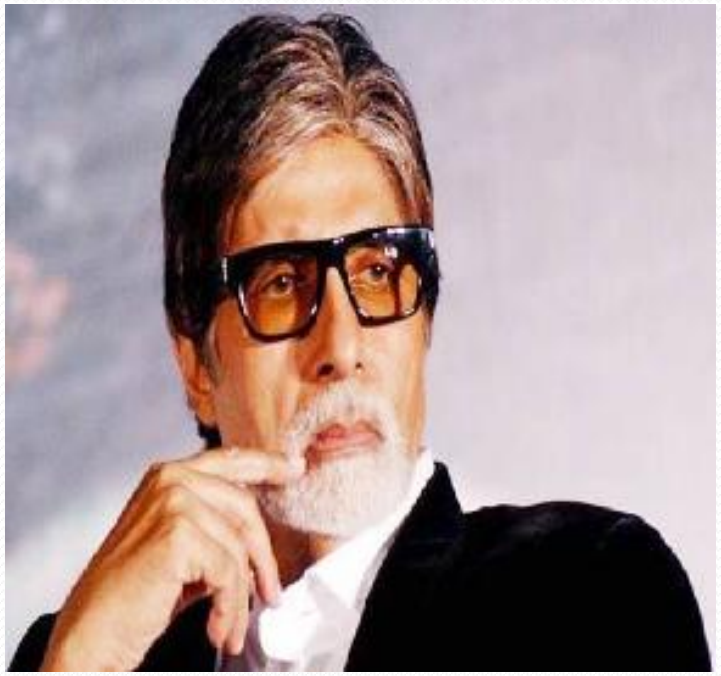
  - Involvement of respiratory muscles → death

MYASTHENIA GRAVIS

- **Differential diagnosis:-**

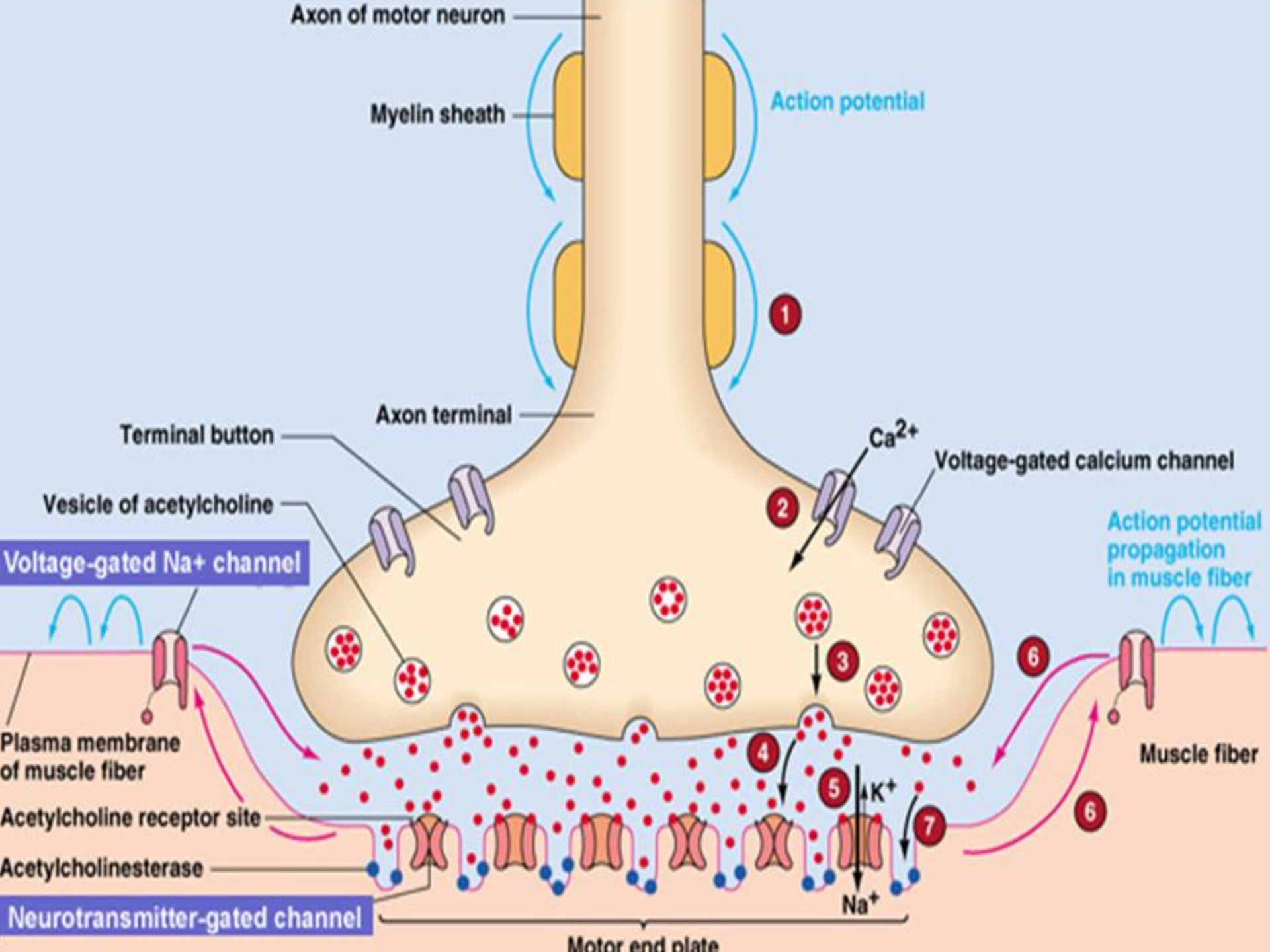
Lambert – Eaton syndrome

- **Test:-** Repeated stimulation



MYASTHENIA GRAVIS

- **Treatment:-**
  - Thymectomy
  - Drugs – AchE inhibitors – Neostigmine, Physostigmine
  - Immunosuppression – Steroids, Plasmpheresis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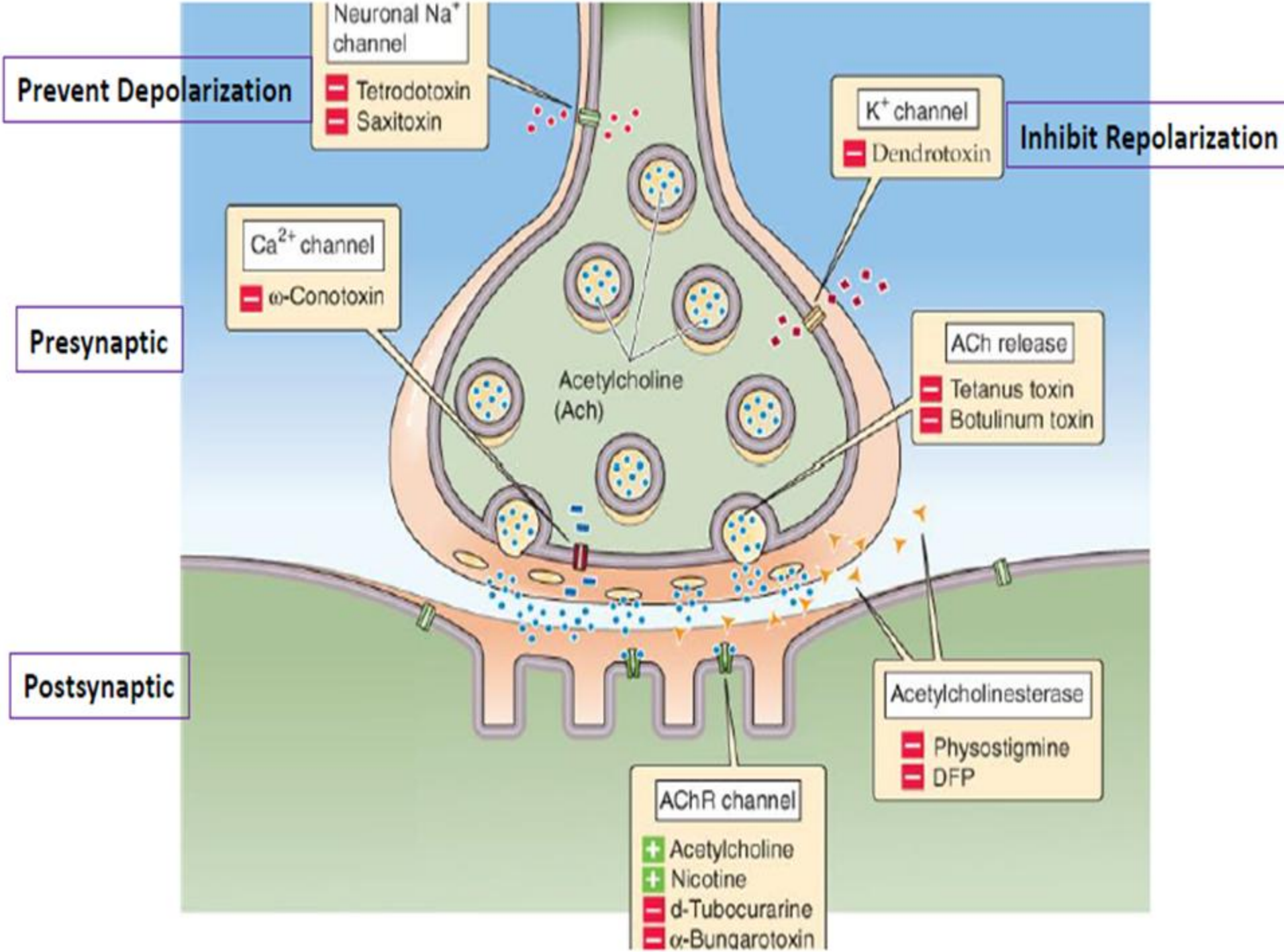
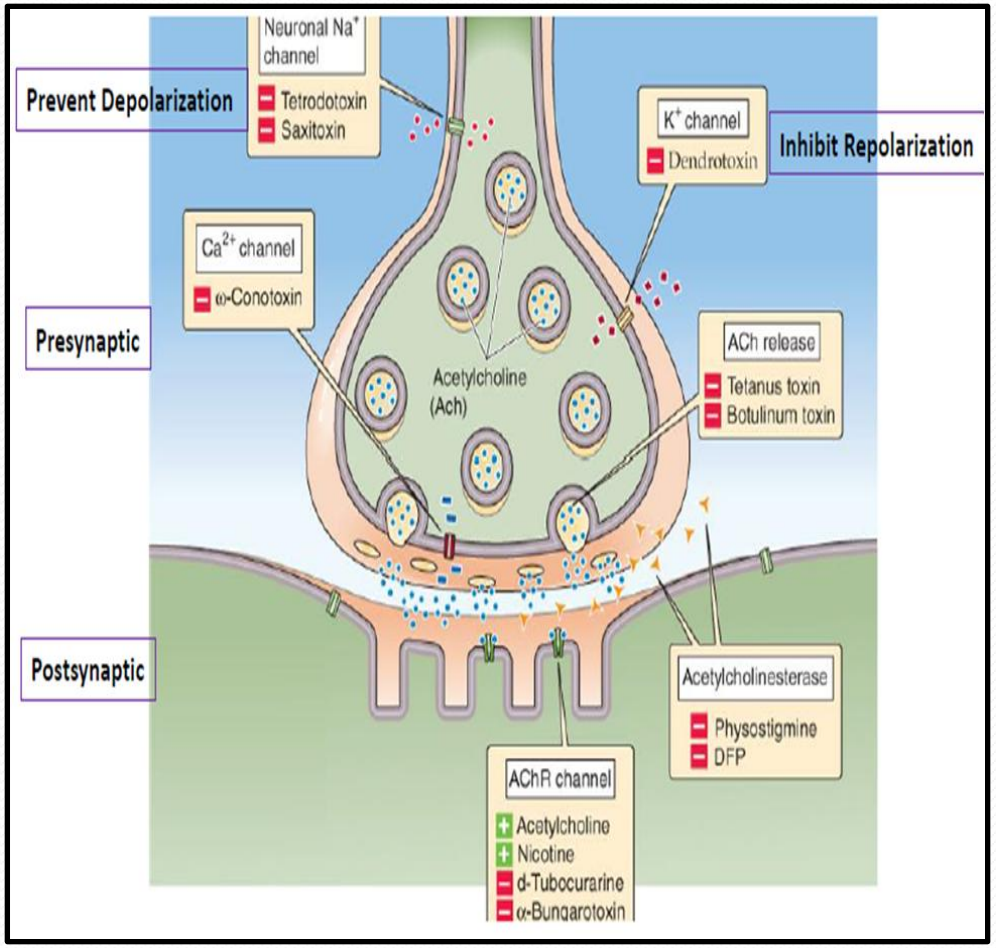
Na+
Motor end plate


Prevent Depolarization
Neuronal Na+ channel
Tetrodotoxin
Saxitoxin
K+ channel
Dendrotoxin
Inhibit Repolarization
Ca2+ channel
ω-Conotoxin
Presynaptic
Acetylcholine (Ach)
ACh release
Tetanus toxin
Botulinum toxin
Postsynaptic
Acetylcholinesterase
Physostigmine
DFP
AChR channel
Acetylcholine
Nicotine
d-Tubocurarine
α-Bungarotoxin

TOXINS AFFECTING SYNAPTIC TRANSMISSION

1. Tetradotoxin
2. Dendrotoxin
3. omega - conotoxin
4. alpha - bungarotoxin
5. Tetanus toxin
6. Botulinum toxin



DRUGS AFFECTING SYNAPTIC TRANSMISSION

1. **Agonists:-**

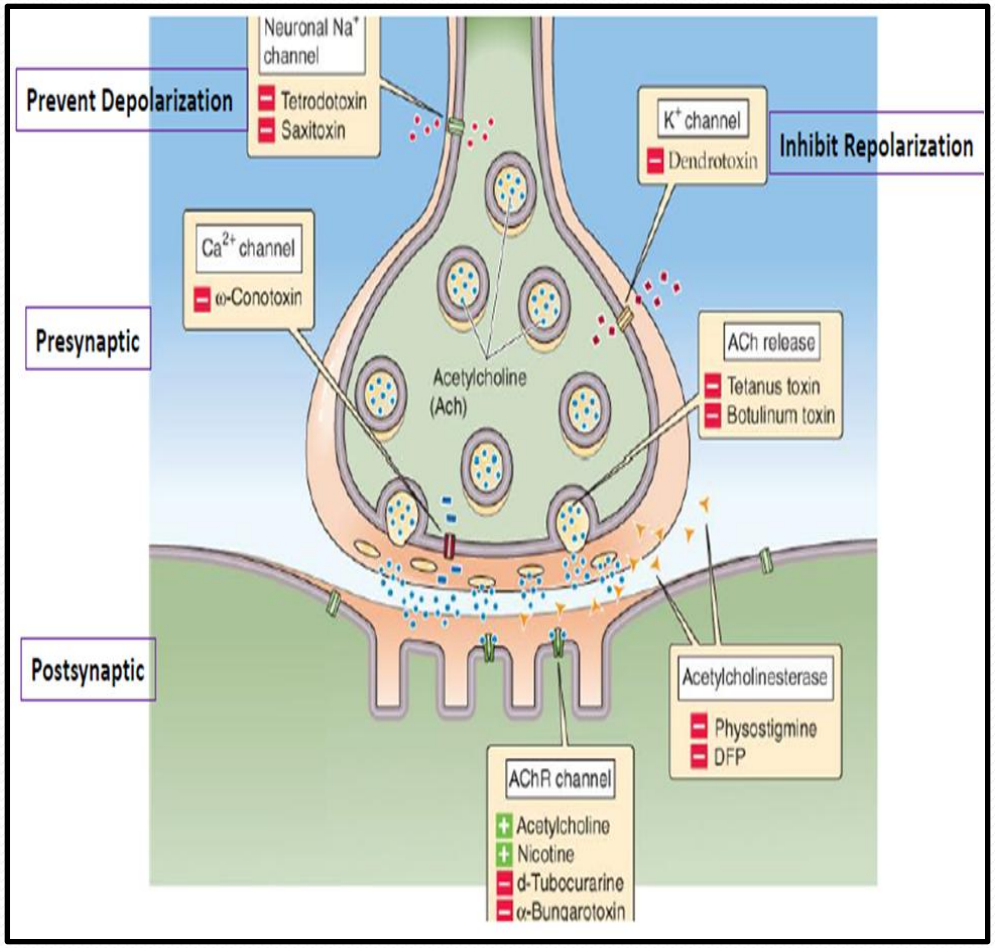
   - e.g. Nicotine

2. **Antagonists:-**

   - e.g. d-tubocurarine

3. **AchE inhibitors:-**

   - e.g. Physostigmine, Neostigmine, Organophosphates




Thank you