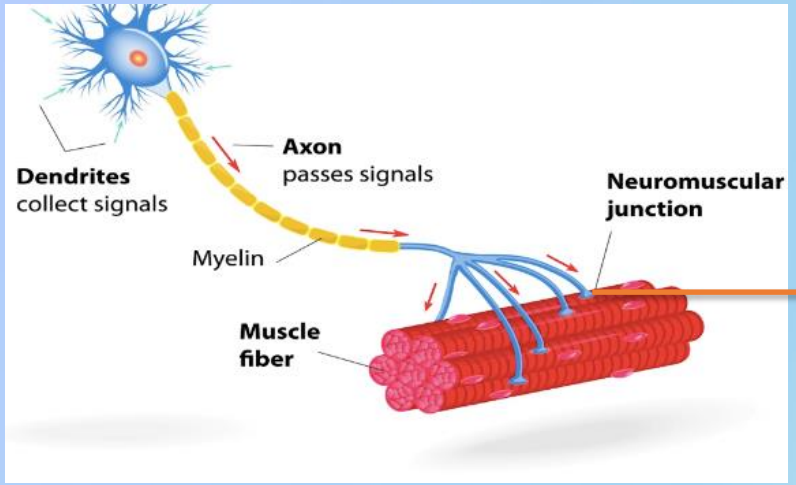
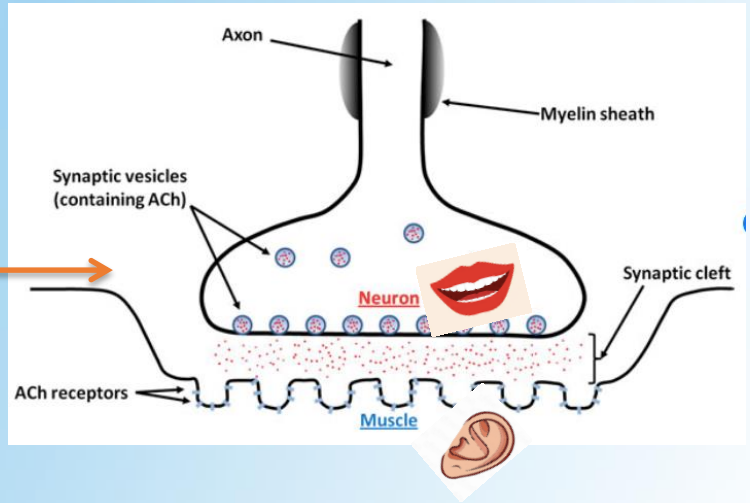
Neuromuscular Junction

What is the neuromuscular junction?

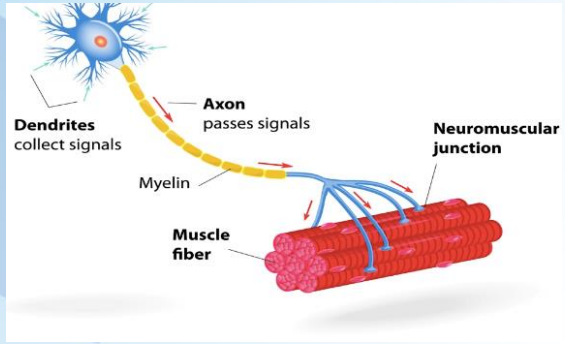




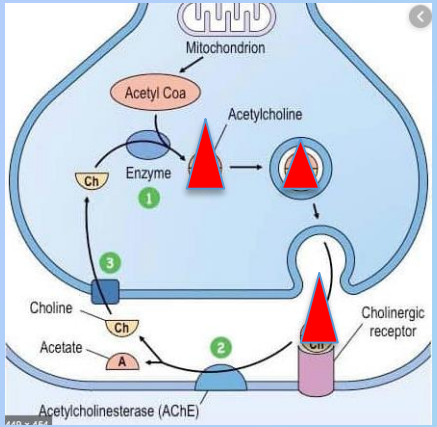
Neuron “talk” to muscle

How is the neuronal electrical message translated into a muscular action?

- Electrical signal (AP) -> chemical signal (messenger)-> Electrical signal(AP)
- Chemical messenger: Acetylcholine
- One way communication



ACETHYLCHOLINE



ACETYL CoA + Choline = ACETHYLCHOLINE

(Acetate)

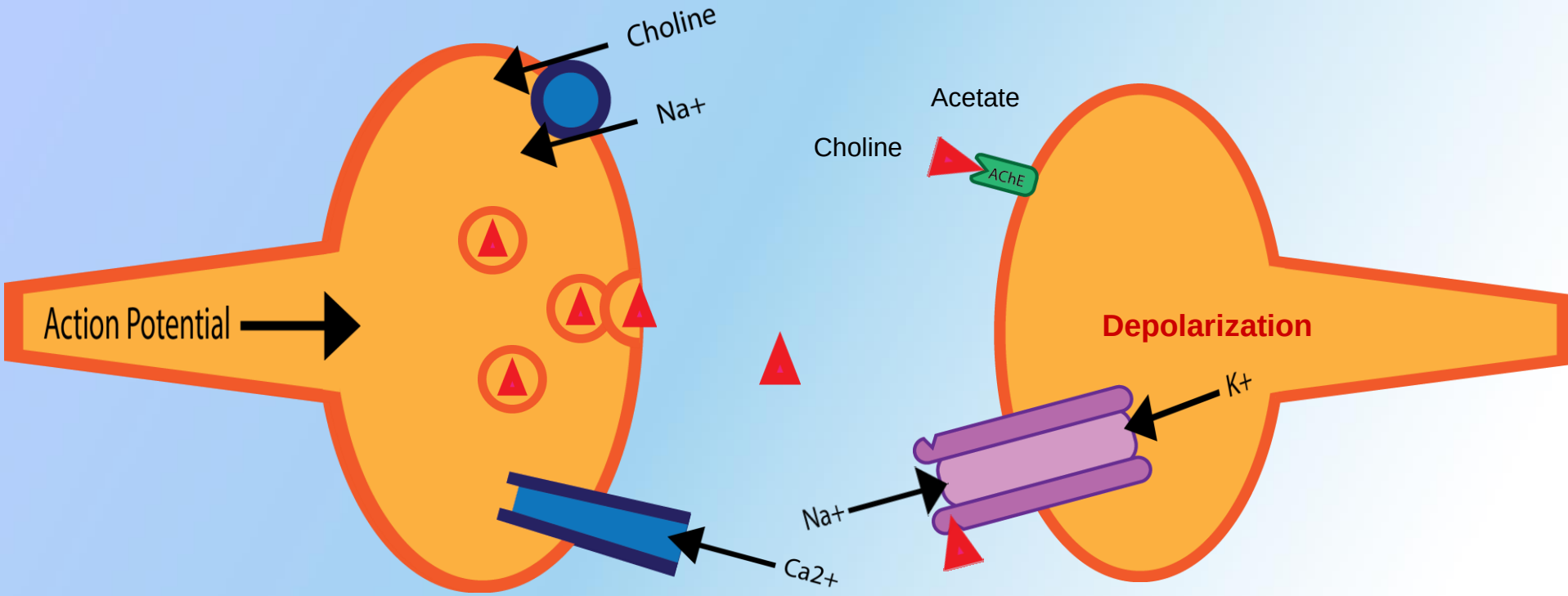
- *Acetyl CoA is produced by mitochondria in the nerve ending*
- *Choline transported from extracellular space*

Acetylcholine (Cholinergic)

- Nicotinic - somatic (skeletal muscle)
- Muscarinic - relating to autonomic (parasympathetic) system

Skeletal Muscle is regulated by **Nicotinic Cholinergic** receptors

SYNAPTIC CLEFT



Presynaptic Nerve Terminal

Motor End Plate

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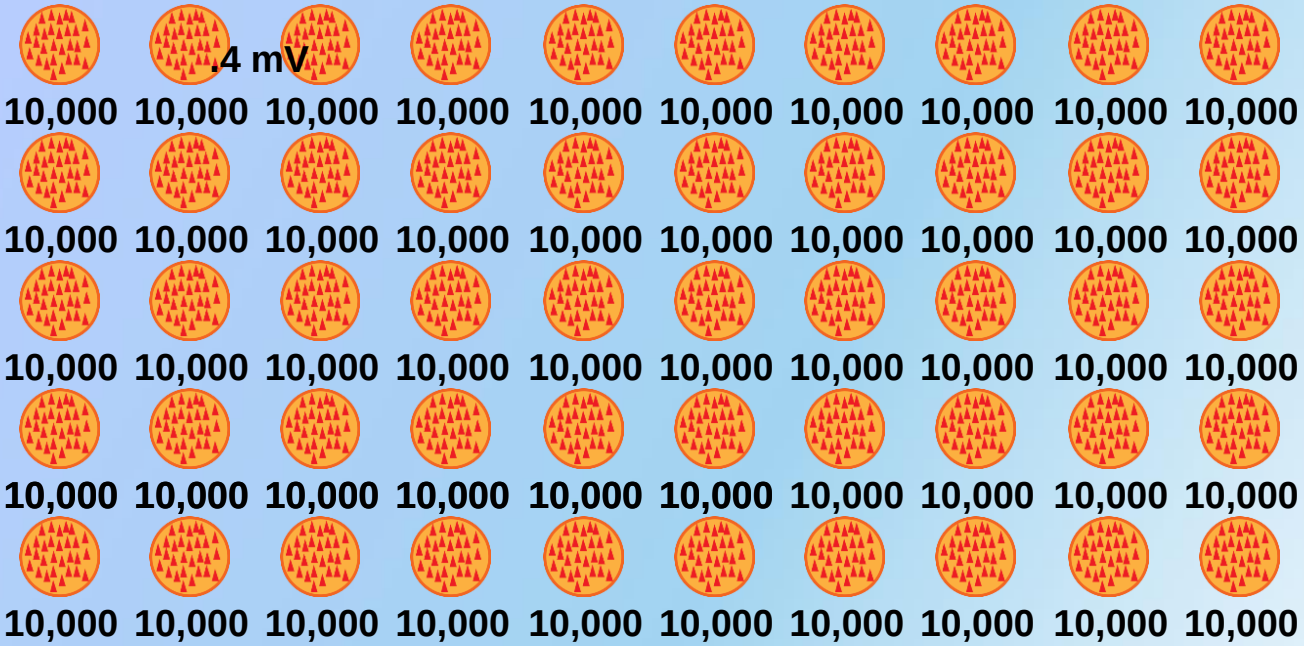
Activity in Motor End Plate

- The amount of ACh in a single vesicle is a quantum
  - The amount of change in membrane by a quantum is a **miniature end plate potential (MEPP)**
    - **Approximately 0.4 mV change**

- MEPPs summate to cause **End Plate Potential (EPP)**
  - Requires a change from about -90 mV to -50 mV

Putting Things in Perspective



4 mV

20 mV

Neuromuscular transmission

1. **AP** (electrical signal) depolarizes nerve ending

1. Voltage-gated Ca2+ channels open = **Calcium influx**

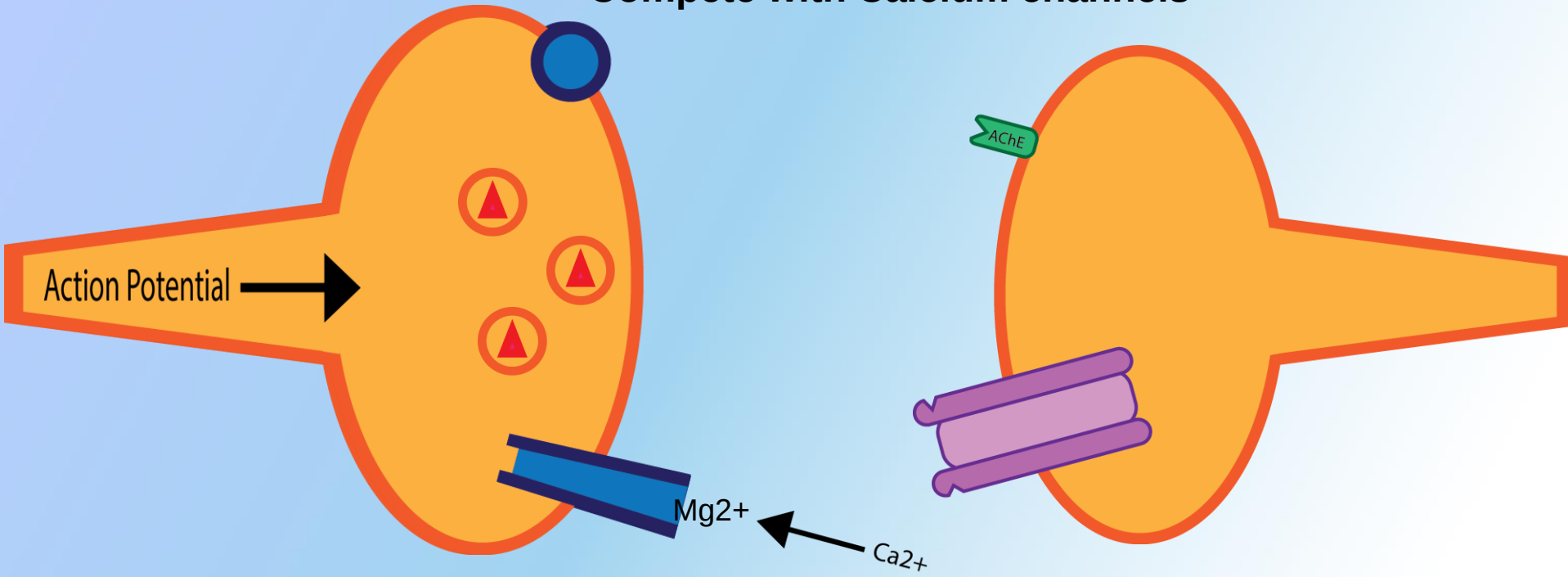
1. Ca allows release of neurotransmitter **Acetylcholine** (chemical signal)

1. ACh activate **Nicotinic Cholinergic** receptors
2. Na influx – **EPP**
3. EPP stimulate **voltage gated Na+ -channels**
4. **AP** (electrical signal)

Toxins, Disruptions, Fluctuations

Magnesium Ions

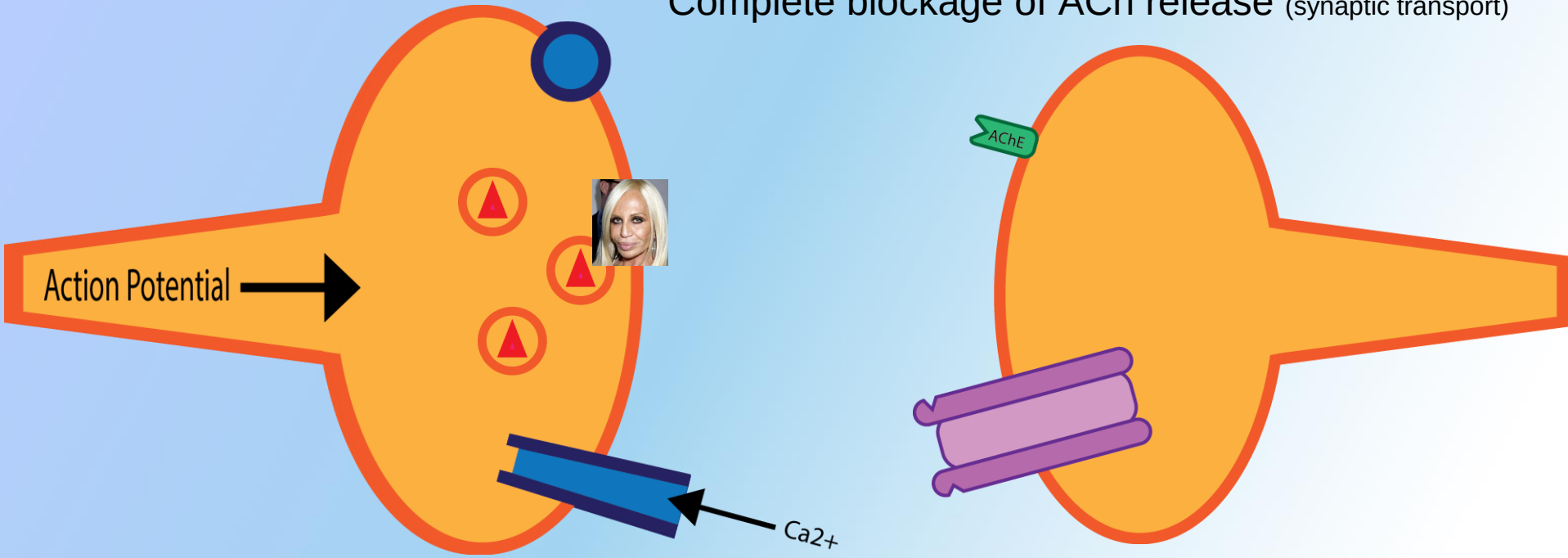
Compete with Calcium channels



Presynaptic Nerve Terminal
Motor End Plate

Botulinus Toxin

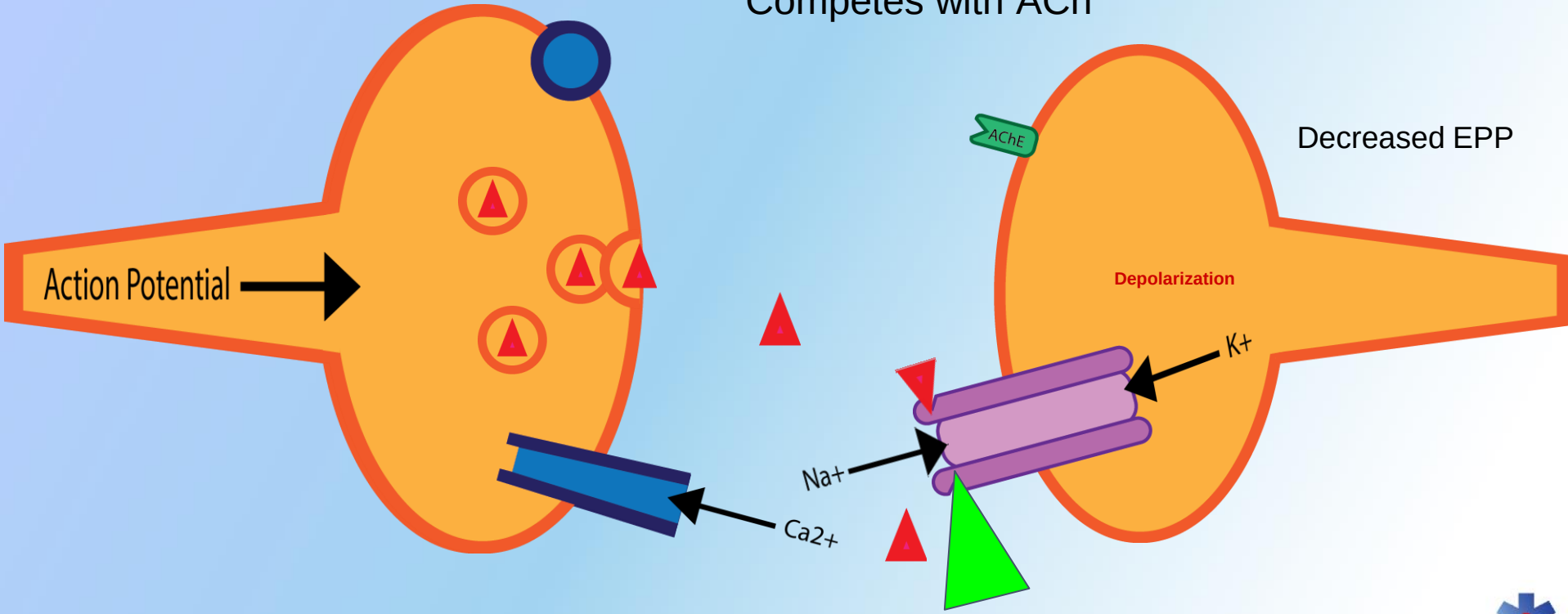
Complete blockage of ACh release (synaptic transport)



Presynaptic Nerve Terminal
Motor End Plate

Curare

Competes with ACh



Presynaptic Nerve Terminal
Motor End Plate

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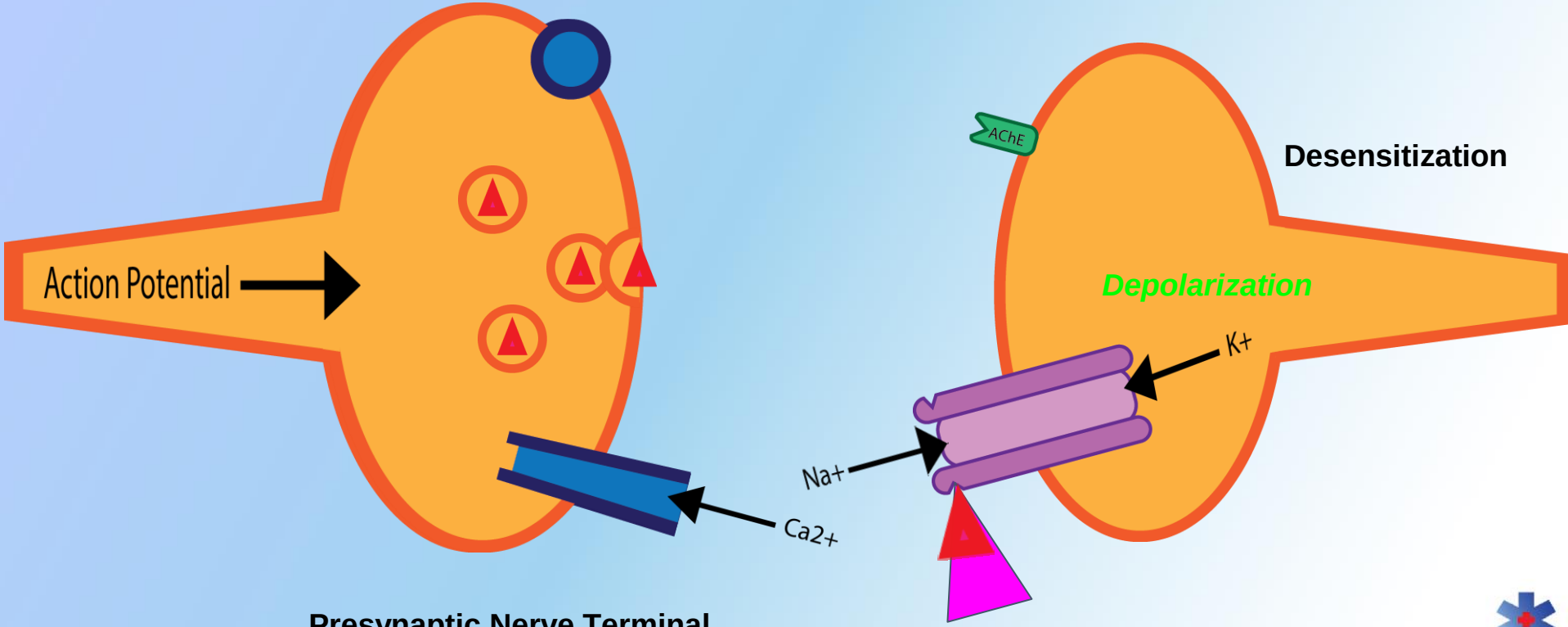
Suxamethonium chloride

Inhibitor of Postsynaptic Depolarization



Presynaptic Nerve Terminal
Motor End Plate

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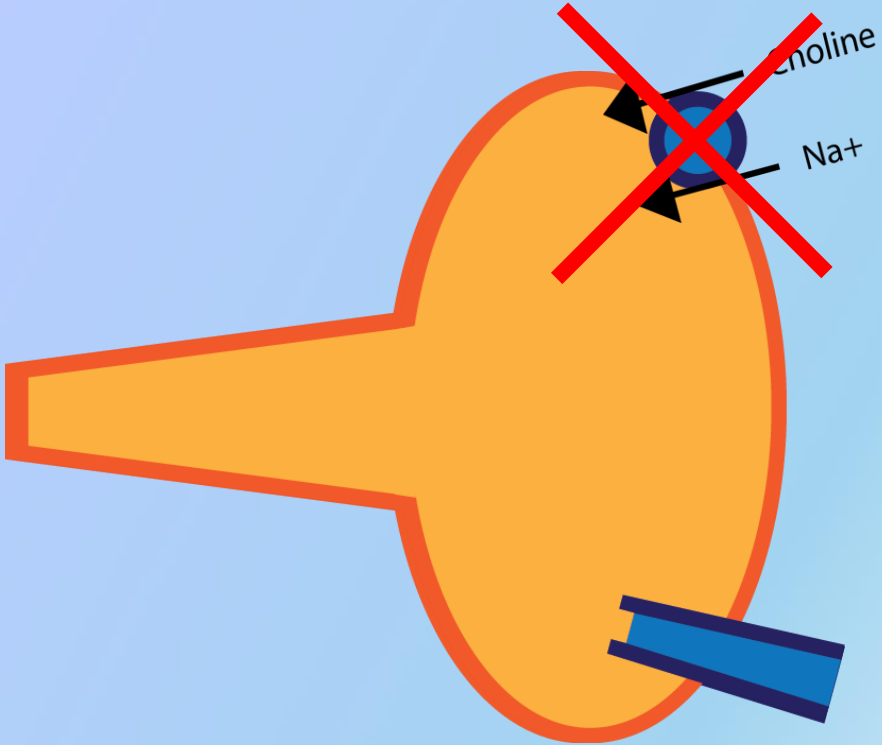
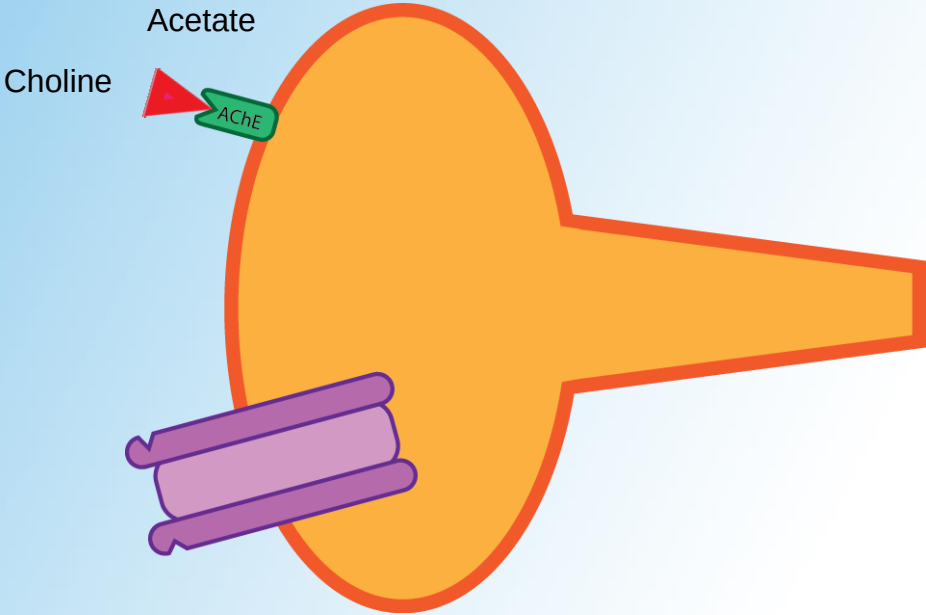
Hemicholinium

Blocks choline reuptake

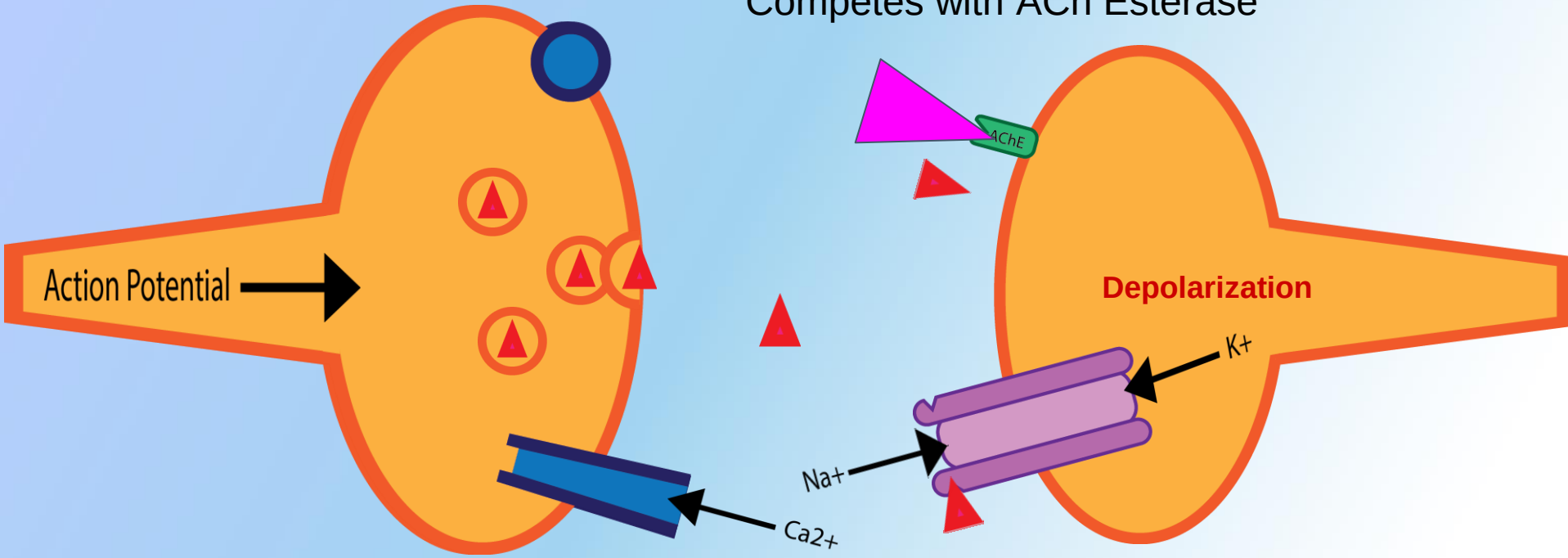




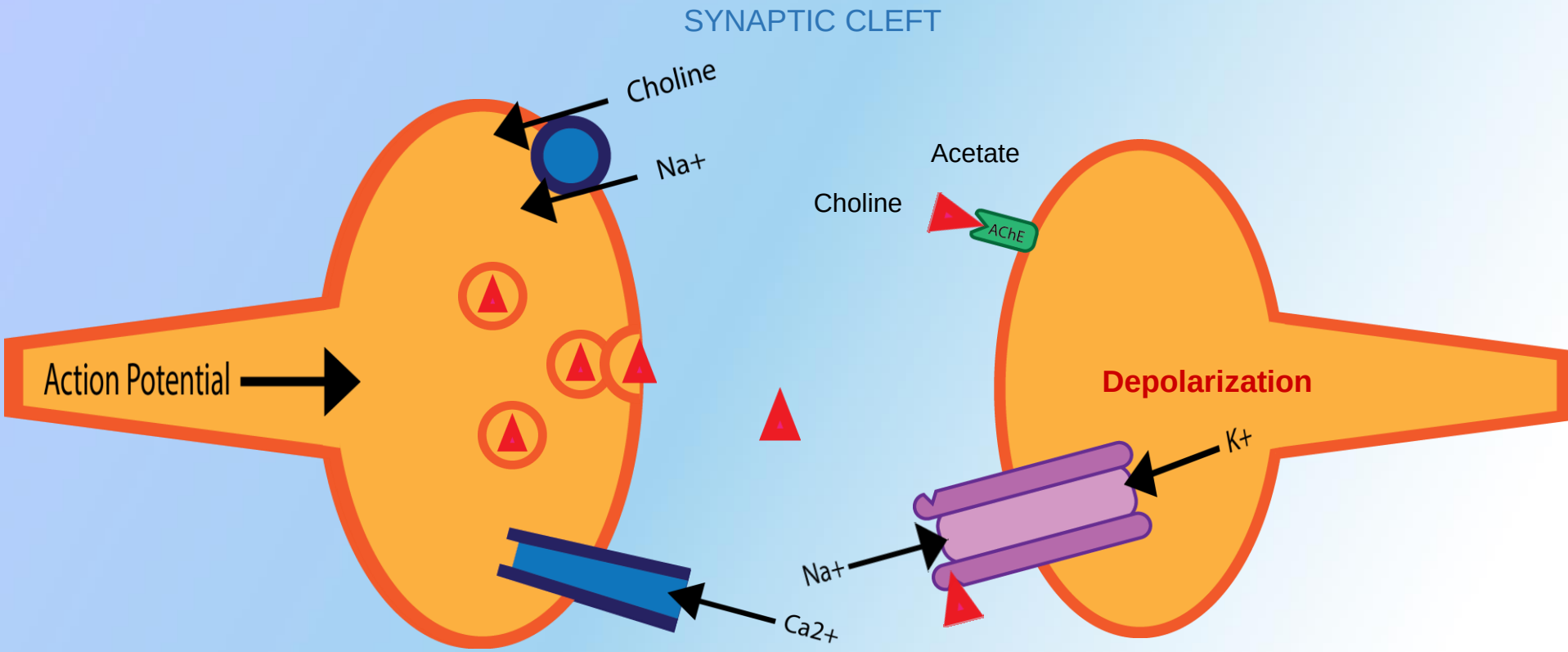
Presynaptic Nerve Terminal
Motor End Plate

AChE inhibitors (e.g. neostigmine, physostigmine)

Competes with ACh Esterase



Presynaptic Nerve Terminal
Motor End Plate


SYNAPTIC CLEFT
Choline
Na+
Acetate
Choline
AChE
Action Potential
Depolarization
K+
Na+
Ca2+
Presynaptic Nerve Terminal
Motor End Plate

Thank you☺

Sample Q

- Which of the following is responsible for the undisturbed transmission of the signal between the pre synaptic nerve terminal and the MEP of a muscle fiber?
  - A. Adrenergic cholinergic
  - B. Musarinic adrenergic
  - C. Nicotinic adrenergic
  - D. Nicotinic cholinergic
  - E. Nicotinic acetylcholine
  - F. D and E are correct
  - G. A is incorrect, C is correct, E is correct sometimes

Sample Q

Botulinum toxin, derived from the clostridium species, exerts its inhibitory function on NMJ activity through which of the following mechanisms?

A. Prevents ACh release
B. Interacts with the SNARE protein and disallows proper function of exocytosis of vesicles
C. Binds to curare and inhibits ACh
D. C is incorrect
E. None of the options are correct, except C

Sample Q

Magnesium ions disrupts NMJ activity through which of the following mechanisms?

A. Competes with Ca2+ release
B. Inhibits postsynaptic depolarization
C. Binds to Na+ ligand gated channel
D. A is not incorrect
E. A and D are not wrong