Physiology Team

MEDICAL COLLAGE 433

Neuromuscular transmission

Color Index

Red = important

Purple = Addition

Orange = Explanation

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objectives

- To give reasonable comprehension of the mechanism of excitation-concentration coupling with reference to neuro-transmitters, receptors Ca++ and esterase.
- To comprehend muscle contraction on the basis of molecular structures.
- To explain biophysics in terms of length-tension and force velocity-relationship

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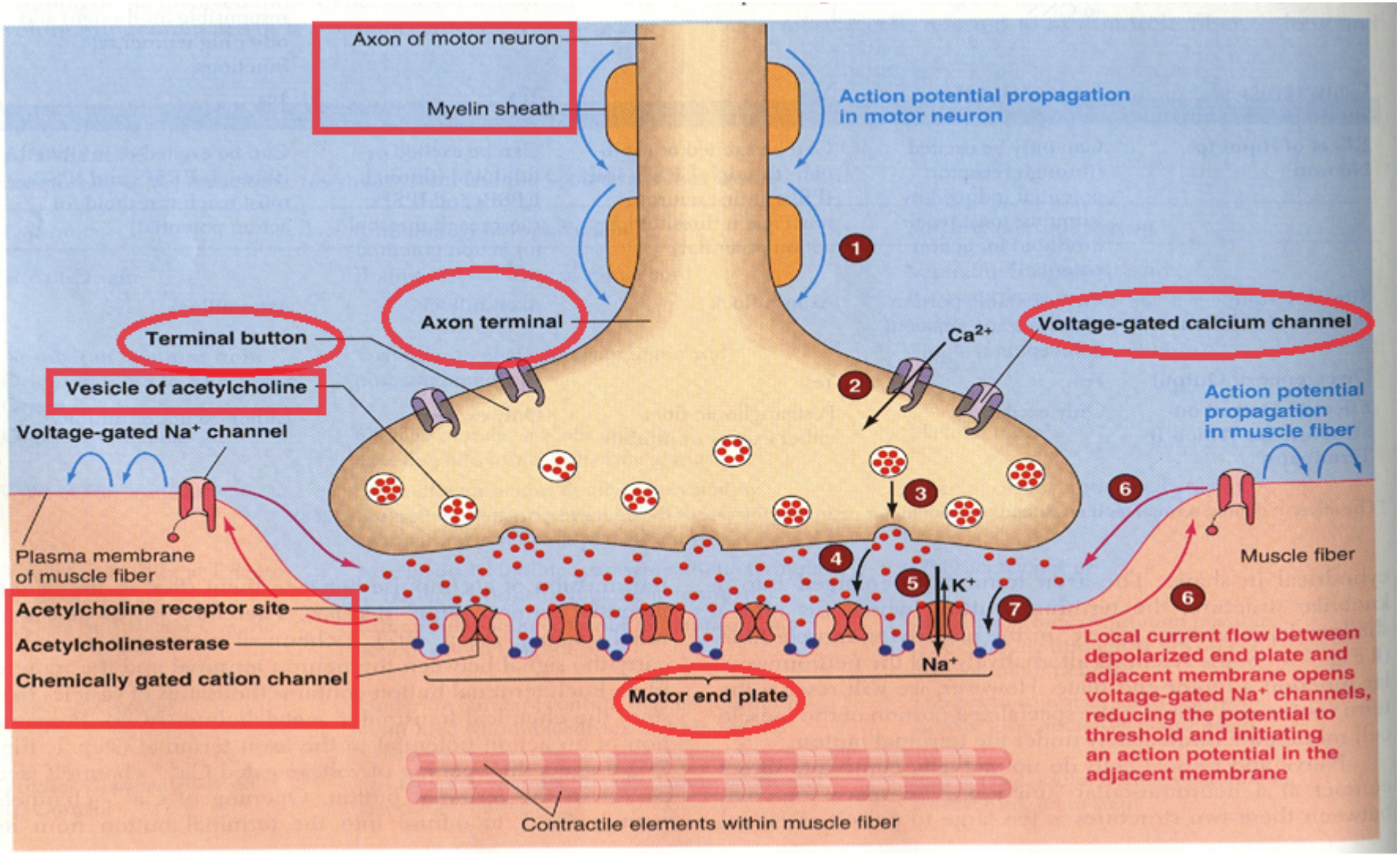
The continent of Neuromuscular junction



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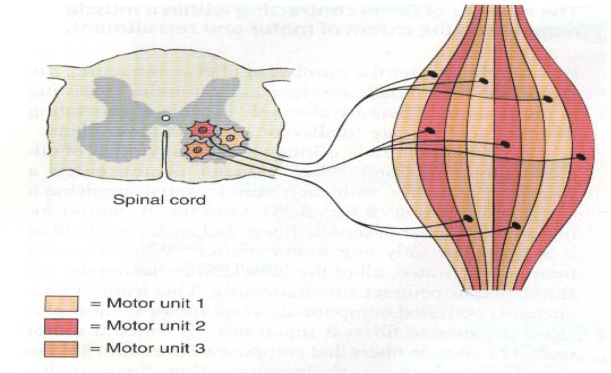
Concepts included in this lecture

- **Motor unit** :
- is the motor neuronand all the muscle fibers
- it supplies all of these fibres will have the same type (either fast twitch or slow twitch). When a motor unit is activated



- **Synaptic transmission** : Synapse is the junction **between two neurones** where electrical activity of one neurone is transmitted to the other

- **Neuromuscular transmission** : Transmission of impulse **from nerve to muscle** (neuromuscular junction)

The Neuromuscular junction

Axon Terminal

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

Synaptic Cleft

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

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 surface area** , allowing for accommodation of **large numbers of ACH receptors.**

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

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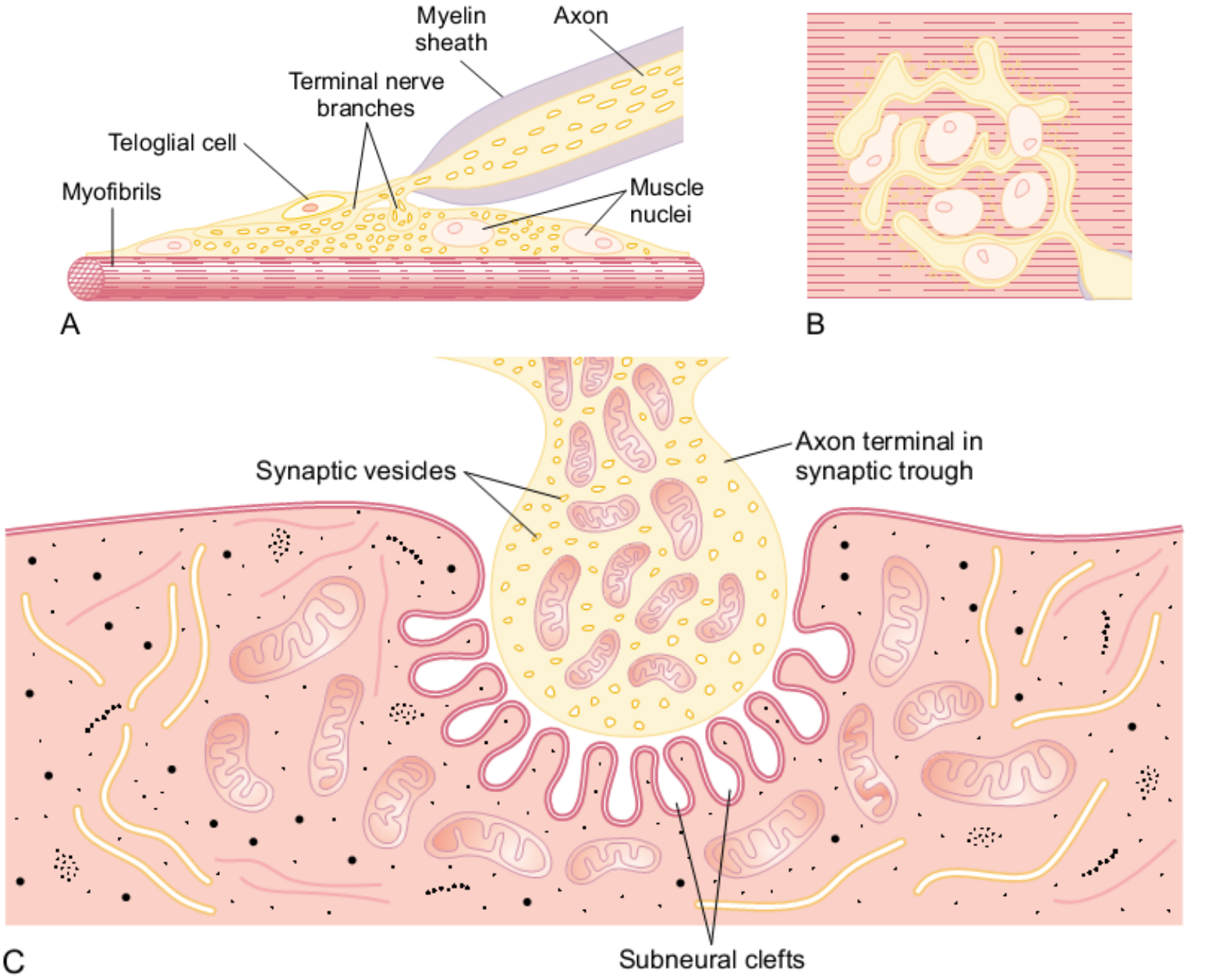

Acetylcholine:

1. Ach is synthesized locally in motor end-plate of the nerve terminal, from active acetate (acetylcoenzyme A) and choline acetyl transverase

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

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

acetate is a derivative of acetic acid. This term includes salts and e sters

Golgi transports lipids around the cell

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

5. 5) Each vesicle is then filled with around 10,000 Ach molecules .

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The trip of Acetylcholine:

1. AP (***Action potential)*** at the synaptic knob → Ca channels open (increase Ca permeability)
2. Calcium → release of Ach from **synaptic knob** to **synaptic cleft**
3. Ach combine with receptors on **motor end plate** → Na permeability increase
4. Na ions lead to → local,non-propagated potential called the " End-Plate Potential (EPP)", whose value is 50 – 75 mV.
5. This EPP triggers a muscle AP which spreads inside the muscle to make it contract

Note:
One nerve impulse can release 125 ACh vesicles , which is more than enough to generate produce one End-Plate Potential (EPP)

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Destroying of Acetylcholine:

- After ACh acts on the receptors , it is destroyed (hydrolyzed) by the enzyme **Acetylcholinesterase** (also called **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** .

Examples of Drugs Acting on the NMJ

- Drugs that inactivate Cholinesterase , called Anticholinesterase drugs , preventing it from destroying Ach & hence sparing ACh and allowing Ach to acccunulate & stimulate the muscle .

- Example of this drug category is Tensilon (Edrophonium) which is used in to test for Myasthenia Gravis

Disorder of Neuromusculartransmission :

Myasthenia gravis

Type	autoimmuneneuromuscular disease
Characteristic	Muscle weakness
Cause	circulating antibodies that block acetylcholine receptors at the postsynaptic neuromuscular junction
Leading to	fluctuating muscle weakness and fatigue.
Treatment	Acetylcholinesterase inhibitors: **neostigmine**

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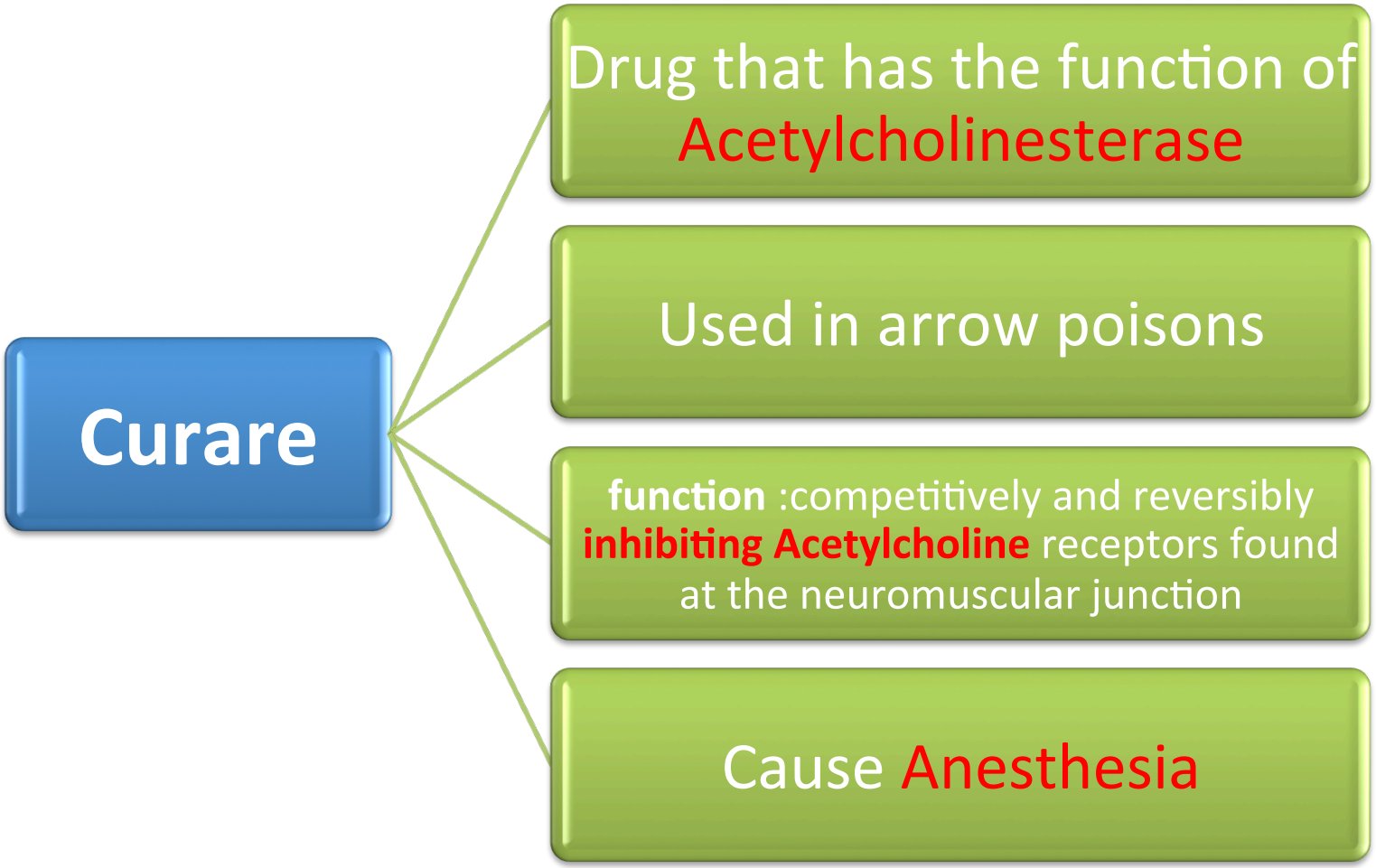
Curare
Drug that has the function of Acetylcholinesterase
Used in arrow poisons
function :competitively and reversibly inhibiting Acetylcholine receptors found at the neuromuscular junction
Cause Anesthesia

Summary

- Motor end-plate composed of :

1-Axon terminal : vesicles contain Ach

2- Synaptic cleft : where choline esterase can be found

3- Synaptic gutter : consist of subneural cleft and where contain receptors

- Ach synthesized by : active acetate (acetylcoenzyme A) and choline acetyl transverase
- Vesicles of Ach synthesized by : Golgi apparatus
- Ach destroyed by : cholienesterease

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Neuromuscular Transmission 1/2

https://www.youtube.com/watch?v=RKhr_YXUVLE

Neuromuscular Transmission 2/2

https://www.youtube.com/watch?v=eKsfoLmoJwE

Multiple Choice Questions

Q1: Which of the following best describes the end-plate potential ?

A. It is the action potential at the muscle cell
B. It is the action potential at the motor nerve
C. It is the graded potential of the motor end-plate

Q2: During neuromuscular transmission, the arrival of nerve AP at the synaptic knob leads to which of the following:

A. Opening of Na channels.
B. Opening of K channels.
C. Opening of Ca channels.

Q3: During neuromuscular transmission, which of the following takes place?

A. Diffusion of calcium ions from the synaptic knob into extracellular fluid.
B. Diffusion of calcium ions from the extracellular space to the synaptic knob.

Q4: Which of the following is the site that synthesis of vesicles take place?

A. Synaptic cleft
B. Golgi apparatus
C. Motor end-plate
D. Axon terminal

Q5:Acetylcholineesterase can be found at?

A. Axon terminal
B. Synaptic Cleft
C. Synaptic gutter
D. Golgi apparatus

Q6 : Ach can binds to receptors at:

A. Synaptic cleft
B. Muscle cell membrane
C. Synaptic gutter
D. Both B & C

Q7: Which of the following enzyme can involve in Ach synthesis?

A. Cholinesterase
B. Acetyl choline transverse
C. Choline synthase
D. None of them

Q8: Anticholinesterase used to cure :

A. myasthenia gravis
B. Rheumatoid arthritis
C. Osteomyelitis

1-C 2-C 3-B 4-B 5-B 6-D 7-B 8- A

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