

NERVE & MUSCLE

Dr. Neven Makram Aziz

□ Explain Why:

1- Hypokalemia is associated with skeletal muscle weakness.

Hypokalemia \rightarrow \uparrow RMP due to increasing K out flux \rightarrow hyperpolarization \rightarrow decrease excitability \rightarrow muscle weakness.

2- Hypokalemia increase resting membrane potential.

Increasing K out flux and increasing the -ve charge inside leading to hyperpolarization \rightarrow \uparrow RMP

3- Antidromic conduction stops at dendrites.

This is there is no chemical transmitter to be released at dendrites.

4- Acidosis decrease excitability of nervous tissue.

It causes ionization of Ca^{+2} ($\uparrow \text{Ca}^{+2}$ level) that guard the Na^+ channels and prevents its entry \rightarrow decrease excitability.

5- Faradic current is ideal for diathermy.

Because it is of short duration, below minimal time, so it leads to heating of tissues without stimulation.

6- Cell membrane is more permeable for K^+ than Na^+

1. Na^+ channels are closed while K^+ is opened under resting conditions.
2. Na^+ channels are guarded by Ca^{+2} from outside which repel Na^+ .
3. The hydrated Na^+ ion is thicker than the hydrated K^+ ion.

7- Cell membrane is weakly permeable for Na^+ .

1. Its channels are closed at resting conditions.
2. Large hydration energy lead to its large size.

8- Subthreshold stimuli can produce a response when applied in the region of a cathode.

Because catelectrotonus increase the excitability by adding electrons that neutralizes some +ve charges on the outer surface of the membrane → decrease the membrane potential (depolarization) and make it closer to the firing level.

9- Threshold stimuli will not produce a response when applied at the region of the anode.

OR Strong anadol current can produce a nerve block.

Because anelectrotonus decrease the excitability by adding protons that increases the +ve charges on the outer surface of the membrane → increase the membrane potential (hyperpolarization), and this make the membrane potential away from the firing level.

□ Define:

- 1- **Faradic current:** It is a current of high intensity and short duration.
- 2- **Galvanic current:** It is a current of low intensity & long duration.
- 3- **Saltatory conduction:** It is the jumping of depolarization wave from node to node and it is rapid, and consumes less energy.

- 4- **Chronaxie:** It is the time needed by a current of double rheobase to stimulate and used to compare excitability of different tissues. "The shorter the chronaxie, the greater is the excitability".
- 5- **Rheobase:** it is the minimal intensity of a current of a very long duration (as galvanic current) which can stimulate.
- 6- **Relative refractory period:** It is the period during which excitability is starting to return to normal, but still below than normal. A stronger stimulus is needed to excite the fiber during this phase. It corresponds to the last 2/3 of the descending limb of spike.

- 7- **Resting membrane potential:** It is the potential difference between the inside and the outside of the nerve fiber under resting condition. It is written as -70 mV (the negative sign indicates the type of the charge inside the nerve).
- 8- **Action potential:** it is a wave of transient reversal in the membrane polarity which is induced by stimulation of the excitable tissue by its adequate stimulus (the electrical changes that accompany the nerve impulse).
- 9- **Local response:** it is the potential changes that caused by weaker (subthreshold) stimulation of the nerve membrane that are not propagated for long distances and decline rapidly.

□ Mention

1. **The excitability phases during which nerve need strong stimulus to respond:**

A- Relative refractory period that to the last 2/3 of the descending limb of spike.

B- Subnormal phase of excitability that corresponds to the positive after potential.

2. **Properties of Neurons:**

1. Excitability (the most excitable tissue).
2. Conductivity: it is the ability of nerve to conduct the nerve impulse which is an active self-propagation process.
3. The nerve never gets fatigued.

3. The cause of ascending limb of spike (depolarization):

Maximum opening of voltage gated Na^+ channels (firing level) $\rightarrow \uparrow \text{Na}^+$ entry according to concentration and electrical gradients \rightarrow rapid depolarization that overcomes any repolarizing force \rightarrow the membrane reaches the zero potential and Na^+ continues to diffuse in reversing the polarity until reaching +35 mV.

OR The cause of rapid repolarization, negative after potential or positive after potential.

4. Three properties of nerve impulse.

- × Obeys the all or none rule.
- × It has an absolute refractory period.
- × Conduction in myelinated nerve fiber occurs by saltatory conduction which needs energy.

5. Three causes of nerve stabilization;

- × High calcium concentration in the extracellular fluid.
- × Low potassium concentration in the extracellular fluid.
- × Local anesthetics and acidosis.

6. The action of Na^+ - K^+ pump:

It is an active pump responsible for the development of the RMP by transmitting 3 Na^+ ions to the exterior for each 2 K^+ ions transmitted to the interior thus creating negativity inside and positivity outside the nerve membrane.

7. Effect of low extracellular Ca^{2+} concentration on nerve excitability:

It increases Na^+ entry \rightarrow partial depolarization \rightarrow \uparrow excitability.

8. Normal extracellular Na^+ and intracellular K^+ concentrations:

✘ Extracellular Na^+ : 142 mEq/L

✘ Intracellular K^+ : 140 mEq/L

9. The opening volt for sodium and potassium channels in the nerve:

✘ Sodium channel → gradual opening up to maximal opening at -55mv (firing level).

✘ Potassium channel → +35 mv.

10- Effects of hypocalcemia and hypokalemia on resting membrane potential and excitability:

- ✗ Hypocalcemia: increase permeability to Na^+ → ↑ excitability with little effect on RMP.
- ✗ Hypokalemia → ↑ RMP → decrease excitability.

11- Causes of RMP:

Unequal distribution of ions that caused by:

1- *Active Na^+/K^+ pump.*

2- *Selective permeability of the membrane:*

A- The resting membrane of the nerve is 50-100 time more permeable to K^+ than to Na^+ .

B- Non diffusible ions (proteins, sulfate and phosphate) remain inside being greater than the positive ions (they are not neutralized by the +ve ions) so the inside become negative while the outside become positive developing RMP.

Skeletal Muscle

□ Explain Why:

1- Muscle relaxation is an active process.

As in relaxation, calcium must be pumped by **Ca²⁺-Mg²⁺ pump** into sarcoplasmic reticulum to be released from troponin C >>> release of actin from myosin active site.

2- There is a summation of the mechanical response in the skeletal muscle.

Because the contractile mechanism does not have a refractory period.

3- Fibrillations occur after complete damage of the motor nerve.

Due to spontaneous discharges by circulating acetylcholine that producing action potentials in denervated muscle (**denervation hypersensitivity**).

4- The muscles concerned with fine movements have multiple motor units.

To allow gradation of contraction (higher central control).

□ Define :

1- Motor end plate:

It is the area of contact between the nerve fiber and the muscle fiber.

2- End Plate Potential (EPP):

It is a process of partial depolarization at the MEP caused by acetylcholine release due to a nerve impulse in the motor nerve.

3- Physiological contracture:

It is a state of sustained muscle contraction that is not initiated by an action potential. It occurs when the muscle is overworked or fatigued.

4- Oxygen Debt :

It is the difference between O_2 needed for the exercise and O_2 available.

5- Muscular hypertrophy:

It is increase in the muscles size as a result of continuous training (within 6- 10 weeks) and their content of ATP, CP and glycogen will increase and the muscle power and ability to do more work will improve.

6- Fasciculations:

It is spontaneous contractions of the motor units in the muscle, sufficient to be seen under the skin occurs immediately after the damage of the motor nerve and before complete degeneration of the nerve fibers.

7- Fibrillations:

It is contractions of separate muscle fibers, occurring after complete degeneration of the motor nerve fibers. These contractions cannot be seen under the skin, but can be felt by the patient.

8- Reaction of degeneration:

It is the changes in the response of denervated muscle to electrical stimulation.

9- Myasthenia gravis:

It is a hereditary disease that affects females more than males that is characterized by marked progressive weakness and easy fatigability of muscles.

□ Mention

1- Properties for neuromuscular transmission:

1. Unidirectional.
2. It has a delay of 0.5 ms.
3. Easily fatigued.
4. Blocked by curare (competes with acetylcholine for the cholinergic (Nicotinic) receptors in the muscle and inhibits it).
5. Mg^{+2} prevent the release of acetylcholine at the MEP.

2- The cause of Duchenne muscular dystrophy?

It is a serious form of muscular dystrophy in which the dystrophin protein is absent from muscle causing progressive weakness of skeletal muscle.

3- The cause and treatment of the Myasthenia gravis?

- It is due to formation of auto-antibodies that lead to

1- Destruction of acetylcholine receptors at the MEP \rightarrow \downarrow the response to Ach.

2- Destruction of calcium channels in the wall of nerve terminals \rightarrow \downarrow calcium influx \rightarrow \downarrow acetylcholine release \rightarrow \downarrow neuromuscular transmission (Lambert-Eaton syndrome).

- It is treated by prostigmine (reversible anti-cholinesterase) \rightarrow preserve acetylcholine \rightarrow better neuromuscular transmission (repeated stimulation of the muscle).

4- The cause of physiological contracture?

Because there is no sufficient energy for the active Ca^{2+} - Mg^{2+} pump responsible for relaxation \rightarrow maintained interaction between actin and myosin \rightarrow contracture.

5- Types of Muscle Rigor?

1- Myosin rigor in excitation-contraction coupling.

2- In physiological contracture, when muscle fibers are completely depleted of ATP and CP, they develop a state of rigidity called rigor .

3- Heat rigor in **excessive heating of the muscle** \rightarrow Damage of muscle proteins (Irreversible) \rightarrow maintained contraction.

4- Rigor mortis, this is occurs after death (after 4-5 hours) and start to disappear after 12 hours with complete muscle relaxation after 24 hours.

6- Describe the mechanism of skeletal muscle relaxation.

Shortly after contraction, calcium is pumped back into the sarcoplasmic reticulum by an active pump (Ca-Mg ATPase) → ↓ Ca^{+2} concentration in the sarcoplasm → release of Ca^{+2} from troponin C → troponin I binds strongly with actin and tropomyosin covers the active sites of actin → stopping the interaction between actin and myosin → relaxation.

7- Action of Ca^{2+} - Mg^{2+} pump.

Muscle relaxation because it is an active pump present in sarcoplasmic reticulum act by uptake of calcium from sarcoplasm in skeletal muscle lead to release of calcium from troponin C so stop interaction between actin & myosin.

8- pH changes in muscles during contraction?

1. Acidic due to release of inorganic phosphate from breakdown of ATP.
2. Alkaline due to creatine accumulation during the re-synthesis of ATP.
3. Acidic due to pyruvic and lactic acids formed as a result of muscle glucose breakdown.

9- Causes of O₂ debt?

- 1- Accumulation of lactic acid.
- 2- Exhaustion of energy stores (e.g. ATP and CP).

✘ Importance (significance) of O₂ debt?

O₂ debt allows the muscles to do severe exercise for short periods in case of O₂ lack (hypoxia).

10- Functions of lactic acid produced during exercise?

1. Part of lactic acid oxidized aerobically will give energy to restore ATP and CP in the muscle.
2. Lactic acid will be also converted to liver glycogen which is the source of blood glucose, needed for metabolism of heart, brain and muscles.
3. Lactic acid can be used as a fuel for cardiac muscle.
4. Locally, it dilates skeletal blood vessels to increase their blood supply.
5. Lactic acid when passing to the general circulation will produce slight acidosis, which will stimulate the respiratory and cardiovascular centers to increase respiration rate and heart rate.
6. Lactic acid accumulated during exercise, will determine the amount of oxygen debt and enables the body to take this oxygen debt during the whole period of exercise recovery.

• COMPARE BETWEEN ISOTONIC AND ISOMETRIC CONTRACTIONS?

	Isotonic	Isometric
Shortening	The muscle shortens (there is much sliding of myofibrils)	The muscle contract without shortening (no change in length and less sliding of actin over myosin)
Tension	No or minimal change	increased
Work	The muscle performs external work	No work done
Energy	consumed	No energy consumed
Example	Biceps lifting weight against gravity	Biceps lifting weight that is too heavy to be lifted