Federal State Budgetary Educational Institution of Higher Education

“Professor V.F. Voino-Yasenetsky Krasnoyarsk State Medical University”,

the Russian Federation Ministry of Health

Prof. A.T. Pshonik Department of Physiology

Instructional guidelines for students (out-of-class work)

for the discipline

**"Normal physiology"**

for students in the specialty Specialty 31.05.01 – General medicine

**FOR PRACTICAL CLASS № 2**

**08.09.2021-14.09.2021**

**SECTION**

 **"PHYSIOLOGY OF EXCITABLE TISSUE"**

**Class No 1. Theme No 1. "GENERAL PROPERTIES OF EXCITABLE TISSUE"**

**Study questions**

**Self-study questions**

1. Structure and functions of membranes. Active and passive transport of substances through membranes.

2. Membrane potential and its origin. The essence of the membrane-ion excitation theory.

3. Action potential, its phases, their origin

4. Galvanic phenomena that occur in the presence of metal inclusions in the oral cavity. Physical basis of these phenomena

5. Mechanisms of nerve impulse conduction along nerve fibers.

6. Change in excitability when excited. The ratio of the phases of excitability with the phases of the action potential.

7 Application of various methods to study the excitability of muscles and nerves in dentistry. Chronaximetry method and its use in dentistry. Electroodontometry and its value

8. Criteria for assessing excitability (threshold force, useful time, chronaxy). The law of the power of time. Accommodation. Lability and its measure. Parabiosis (Vvedensky N.E.)<http://krasgmu.ru/index.php?page%5borg%5d=df_umkd_del_metod_question&question_id=723324&metod_id=660>

9. Criteria for assessing excitability (threshold strength, useful time, chronaxia).The law of the power of time.

10. Action of direct current on excitable tissues (polar law, electroton, cathodic depression).

**Students ' homework.**

Using the program" Virtual physiology", perform the following experiments on the mechanisms of transport of substances through the plasma membrane during home preparation of the material and enter the results in the Protocol notebook:

1. Study of simple diffusion mechanisms

2. Modeling of dialysis

3. Facilitated diffusion

4. Osmosis

5. Filtration

6. Active transport

**Algorithm for performing experiments:**

see Savchenkov Yu. I. et al. "Workshop of the virtual physiological experiment", Instructional guidelines for students. The Krasnoyarsk state medical University, 2011.

**Practical work of students**

Viewing videos on general issues of electrophysiology with subsequent discussion and solution of case problems

**Synopsis**

**Basic concepts of general physiology of excitable tissues.**

  **Biological reactions.** Living organisms and all their cells have irritability, i.e. the ability to respond to environmental influences or disturbances of their state by changing their structure or function, which is inextricably linked with quantitative and qualitative changes in metabolism and energy. Changes in the structure and functions of the body and its cells in response to various effects are called biological reactions, and the effects that cause them are called stimuli Changes in the structure and functions of the body and its cells in response to various effects are called **biological reactions**, and the effects that cause them are called **stimuli**

 The concept of biological reaction includes all types of response of the body, its cells and organs to various influences. The reactions of cells are manifested in changing their shape, structure, growth and division, in the formation of various chemical compounds in them, converting potential energy into kinetic (electrical, mechanical, thermal, light), performing a particular work (moving in space, releasing certain substances, concentrating certain electrolytes in the cell, etc.). Even more diverse are the reactions of the whole organism, especially complex behaviors. In the process of their implementation, the activity of many organs and countless cells are changed, because the body always reacts to various influences as a whole, as a single complex system.

**Stimuli.** Any change in the external environment or internal state of an organism can be an irritant to a living cell or an organism as a whole if it is large enough, occurred quickly enough, and lasts long enough.

 All the infinite variety of possible stimuli can be divided into 3 groups: physical, physico-chemical and chemical. Physical stimuli include temperature, mechanical (shock, prick, pressure, movement, acceleration, etc.), electrical, and light. Physical and chemical stimuli are represented by changes in osmotic pressure, active reaction of the medium, electrolyte composition, and colloidal state. Chemical stimuli include many substances that have different composition and properties, and can change the metabolism of cells (food substances, drugs, poisons, hormones, enzymes, metabolites, etc.).

 The stimuli of cells that cause their activity, which are particularly important in life processes, are nerve impulses. Being natural, i.e. arising in the body itself, electrochemical stimuli of cells, nerve impulses coming through the nerve fibers from the nerve endings in the Central nervous system or coming from it to the peripheral organs cause directed changes in their state and activity.

 According to the place of occurrence, all stimuli are divided into external (Extro-) and internal (Intero-) stimuli, and by physiological value - into adequate and inadequate. Adequate are those stimuli that act on a given biological structure in natural conditions, to the perception of which it is specially adapted by evolution and to which it is usually extremely sensitive (eye-light, ear-sound, etc.). Inadequate are those stimuli that the cell or organ is not specially adapted to perceive, but which, under certain conditions, can cause changes in structure or function (the muscle may contract on impact, heat up quickly, be exposed to an electric current, sudden stretching, acid action, etc.).

 **Excitability.** The cells of the nervous, muscular and glandular tissues are specially adapted to the implementation of rapid reactions to irritation (excite). The cells of these tissues are called excitable, and their ability to respond to various stimuli with excitement is called excitability. **Excitability** is the property of the cell membrane to respond to the action of an irritating (exciting) factor by changing its permeability and its electrical state. This phenomenon is called excitability. Excitation is a complex biological reaction that manifests itself in a combination of physical, physicochemical and functional changes. A mandatory sign of excitation is a change in the electrical state of the surface cell membrane (change in its membrane potential, MP, and the generation of a propagating action potential, AP). Having arisen in one cell or in one of its parts, the excitation spreads to other parts of the same cell or to other cells.

The response of a living cell to a stimulus, whether in the form of excitation and the associated electrical reaction, or in the form of contraction or secretion, always occurs after some latent period. This is the time period between the onset of the stimulus and the reaction of the tissue to its action. During the latent period, the changes in the state of the tissue necessary for the reaction to occur must pass. The latent period of excitable tissues is shorter than that of non-excitable ones, and the latent period of the electrical reaction of the tissue is shorter than that of muscle contraction and the secretory reaction.

 **History of the discovery of electrical phenomena in tissues.**

In 1786, the Italian physician and physiologist Galvani, after hanging frog legs on the balcony to dry, noticed that when the leg swayed by the wind comes into contact with the metal grating of the balcony, its contraction occurs. Galvani concluded that if a short circuit is established between a nerve and a muscle by means of a metal conductor, and the muscle contracts, this is proof of the manifestation of "animal electricity". He believed that the nerve and muscle are charged oppositely.

 However, the physicist Volta showed the error of Galvani's conclusion by conducting such an experiment: he noticed that the balcony railing was copper, and the hooks on which the legs hung were iron. After trying to apply tweezers to the foot, one part of which was made of copper, and the other of zinc or iron, Volta got a muscle contraction. Therefore, he concluded, the muscles contract not because "animal electricity" is released, but because a current flows between two metals in contact with the electrolyte, which irritates the nerves of the frog's foot.

 Not agreeing with Volta, Galvani set up a second experiment. It consisted of a non-metallic contraction of the muscle. The contraction was achieved by throwing a nerve over the prepared muscle using glass instruments. However, it turned out that contraction could be obtained only when the muscle was damaged, and if the muscle was carefully prepared, without damaging its surface, then with such an experiment, contraction did not occur. Later, German physiologist Hermann showed that if the galvanometer electrodes are applied to an intact muscle, no potential difference can be seen. But if an injury or an incision is inflicted on a muscle or nerve, and one of the electrodes is immersed in this incision, then the galvanometer needle deflects, which shows that an electric current arises between the damaged and undamaged areas of the living muscle, and the damaged area carries a negative charge. This current was called the **rest current**, or **quiescent current.**

In 1837 Matteuchi showed that the resting current of skeletal muscle decreases during its contraction. Matteuchi did one more experiment. He took two neuromuscular preparations and threw the nerve of the 2nd onto the muscle of the 1st. At the same time, it irritated the nerve of the 1st preparation, causing the muscle to contract. It turned out that the 2nd muscle also began to contract. It is impossible to explain this by the influence of the resting current on the nerve, since the contraction of the second muscle occurred only when the first was excited. This experience is even more demonstrative if you take the working heart of a frog instead of the first muscle. When a neuromuscular preparation is applied to the frog's heart with a glass hook, the leg muscle begins to contract in the rhythm of the working heart. The cause of this phenomenon was discovered later.

In 1850, the famous French researcher Dubois-Raymond, irritating the sciatic nerve of a frog, discovered that after the irritation, a wave of electric current runs through the nerve. In 1868, Hermann showed that the reason for this is that the electric current that occurs during irritation reaches an adjacent section, excites it, then reaches the next section and through such contacts, the excitation wave runs along the nerve, like a fire on a Bickford cord.

If you irritate a section of the nerve with single shocks of direct current, and from the next section, drain the current to the galvanometer or to the cathode oscilloscope tube with two electrodes, then at the beginning, at the moment of stimulation, no deviations are recorded, since the same potential is under both discharge electrodes. After some time, the spreading excitation reaches the first discharge electrode, and then the galvanometer registers the potential difference in the form of a negative oscillation-the arrow deviates to the left (on the oscilloscope - down). When the excitation wave is between the electrodes, the arrow returns to its original position. Then the excitation wave reaches the second electrode-the arrow is deflected to the right (the beam is up). When the excitation wave goes further, both the oscilloscope beam and the galvanometer arrow return to their original position.

The following conclusions can be drawn from these facts:

 1. At rest, the potential difference exists only between the undamaged and damaged parts of the tissue (damage current, or rest current).

 2. When the excitation passes through the nerve, an action current arises in it.

 3. This action current does not stay in place, but spreads.

 4. The action current is a negative fluctuation of the potential.

 A more precise study of the mechanisms of electrical changes in tissues at rest and during excitation became possible with the progress of electrical measurement and microelectrode technology. We now turn to the consideration of modern data on electrical processes in tissues.

**Resting potential**. It turned out that there is a potential difference of about 60-90 mV between the outer surface of the cell and its protoplasm at rest, and the cell surface is charged electropositively with respect to the protoplasm. This potential difference is called the membrane potential, or resting potential. Its exact measurement is possible only with the help of intracellular microelectrodes.

 According to the Hodgkin-Huxley membrane-ion theory, bioelectric potentials are caused by different concentrations of K+,Na+,and Cl-ions inside and outside the cell, and different permeability of the surface membrane for them.

 Based on electron microscopy, chemical analysis, and electrophysiological studies, it is assumed that the membrane consists of a double layer of phospholipid molecules, covered from the inside with a layer of protein molecules, and from the outside with a layer of protein molecules and mucopolysaccharides. It is assumed that the cell membrane has the thinnest channels (pores) with a diameter of several angstroms. Through these channels, water and other substances, as well as ions with a pore-sized diameter, enter and leave the cell. Various charged groups are fixed on the structural elements of the membrane, which gives the walls of the channels a certain charge. Thus, the presence of dissociated phosphate and carboxyl groups in the membrane of nerve fibers is the reason that it (the membrane) is significantly less permeable to anions than to cations.

 The permeability of the membrane for different cations is also not the same and changes regularly at different functional states of the tissue. At rest, the nerve fiber membrane is about 25 times more permeable to K ions than to Na ions, and when excited, the sodium permeability is about 20 times higher than the potassium one.

 In addition to permeability, the ion concentration gradient on both sides of the membrane is of great importance for the appearance of the membrane potential. It is shown that the cytoplasm of nerve and muscle cells contains 30-59 times more K+ ions (500 mEq / l vs. 10 mEq/l), but 8-10 times less Na+ ions (35 mEq/l vs. 350 mEq/l) and 50 times less Cl-ions than extracellular fluid (see table). The value of the resting potential of nerve fibers and cells is determined by the ratio of positively charged K+ ions diffusing outwards from the cell along the concentration gradient per unit time, and positively charged Na+ ions diffusing along the concentration gradient in the opposite direction. Thus, in model experiments on the squid axon, with the K+ concentration gradient that occurs in the nerve fiber, the K+ current value is -120 mV. If only the sodium gradient is modeled in this experiment, then the current value of Na+ is +30 mV. The actual measured membrane potential of the nerve is equal to the sum of these two opposite-directed currents, i.e.-90mv.

Despite the fact that the rate of diffusion of Na + and K + ions through the membrane at rest is small, the difference in their concentration outside the cell and inside it would eventually have to completely equalize if there was no special mechanism in the cell that ensures active release (" pumping out ") from the protoplasm of Na + ions penetrating into it and the introduction (" injection ") of K + ions. This mechanism is figuratively called the sodium potassium pump.

In order to maintain the ion asymmetry, the Na-K pump must perform certain work against the ion concentration gradient. The direct source of energy for the operation of the pump is the breakdown of ATP, which occurs under the influence of ATP-ase localized in the membrane and activated by Na and K ions (the so-called Na-K-dependent ATP-ase). Inhibition of the activity of this enzyme leads to a malfunction of the pump. As a result, the protoplasm is enriched with Na+ and loses K+. A direct consequence of this is a decrease or even complete disappearance of the MP (resting potential, or membrane potential).

Depolarization of the membrane occurs because, due to the concentration gradient, K + goes out, but due to the fact that CL- ions, which are not able to pass through the membrane, electrostatically hold positive ions, an excess of K + is created in the boundary layer, and between the outer and the inner surfaces of the membrane, charged respectively positively and negatively, there is a potential difference of about -90 mV. The membrane is constantly depolarized at rest, since the Na-K pump maintains the desired ion concentration gradient.

 **Action potential.** If a section of a nerve or muscle fiber is exposed to a sufficiently strong stimulus (for example, an electric shock), an excitation occurs in this section, one of the most important manifestations of which is a rapid fluctuation of the MP, called the action potential (AP) With intracellular lead, it can be found that the surface of the excited area for a very short interval, measured in thousandths of a second, becomes charged electro-negatively with respect to the neighboring, resting area, i.e., when excited, the so-called "membrane recharge" occurs. Accurate measurements showed that the AP amplitude exceeds the MP value by 30-50 mV. The reason for this is that upon excitation, not only the disappearance of the AP occurs, but a potential difference of the opposite sign arises, as a result of which the outer surface of the membrane becomes negatively charged with respect to its inner side.

 In AP, it is customary to distinguish between its peak (the so-called spike) and trace potentials. The peak of the AP has an ascending and descending phase. Before the ascending phase, a more or less pronounced so-called local potential, or local response, is registered. Since the initial polarization of the membrane disappears during the ascending phase, it is called the depolarization phase; accordingly, the descending phase, during which the membrane polarization returns to the initial level, is called the repolarization phase. The duration of peak AP in nerve and skeletal muscle fibers varies between 0.4-5.0 msec. The repolarization phase is always longer.

 In addition to the peak, there are two trace potentials in AP - trace depolarization (trace negative potential) and trace hyperpolarization (trace positive potential). The amplitude of these potentials does not exceed several millivolts, and the duration varies from several tens to hundreds of milliseconds. Trace potentials are associated with recovery processes that develop in the muscles and nerves after the end of arousal.

The cause of AP is a change in the ionic permeability of the membrane. At rest, as already mentioned, the membrane permeability for K + exceeds the sodium permeability. As a result, the flow of positively charged ions from the protoplasm to the outside exceeds the opposite flow of Na+. Therefore, the membrane at rest is positively charged from the outside.

When an irritant acts on the cell, the membrane permeability for Na+ ions increases sharply and eventually becomes about 20 times greater than the permeability for K+. Therefore, the flow of Na+ ions into the cell begins to significantly exceed the outward flow of K+. The Na+ current reaches a value of +150 mV. At the same time, the output of K+ from the cell decreases somewhat. All this leads to a distortion (reversion) of the MP, and the outer surface of the membrane becomes charged electro-negatively with respect to the inner surface. This shift is recorded as an ascending branch of the peak of the AP (depolarization phase).

 The increase in membrane permeability for Na+ ions continues in nerve cells for a very short time. It is associated with the short-term opening of the so-called Na+channels (more precisely, the M dampers in these channels), which is then replaced by the urgent closing of the Na+pores using the so-called N-gates. This process is called sodium inactivation. As a result, the flow of Na into the cell stops.

 The presence of special Na - and K-channels and a complex mechanism for locking and opening gates is well studied by biophysicists. It is shown that there are selective mechanisms that regulate certain channels. For example, the poison tetrodotoxin blocks only Na-pores, and tetraethylammonium blocks only K-pores. It is shown that in some cells, the occurrence of excitation is associated with changes in the membrane permeability for CA++, in others-for Mg+. Research on the mechanisms of changes in membrane permeability continues.

 As a result of Na-inactivation and simultaneous increase in K-permeability, positive K+ ions are released from the protoplasm into the external solution. As a result of these two processes, the polarized state of the membrane is restored (repolarization), and its outer surface again acquires a positive charge. In the future, the processes of restoring the normal ionic composition of the cell and the necessary ion concentration gradient occur due to the activation of the Na-K-pump.

 Thus, in a living cell, there are two different types of ion movement across the membrane. One of them is carried out along the ion concentration gradient and does not require energy consumption, so it is called passive transport. It is responsible for the occurrence of MP and AP and ultimately leads to the equalization of ion concentrations on both sides of the cell membrane. The second type of movement of ions through the membrane, which is carried out against the concentration gradient, consists in "pumping" Na + ions out of the protoplasm and "pumping" K+ ions into the cell. This type of ion transport is possible only if energy is consumed - this is an active transport. It is the result of special enzyme systems (so-called pumps), and thanks to it, the initial concentration difference necessary to maintain MP is restored.

**Conditions for the occurrence of excitation.** For the occurrence of AP, it is necessary that, under the influence of any stimulus, an increase in the ionic permeability of the membrane of the excitable cell occurs. However, excitation is possible only if the agent acting on the membrane has a certain minimum (threshold) value capable of changing the membrane potential (MP, or Eo) to a certain critical level (EK, the critical level of depolarization). Stimuli, the strength of which is below the threshold value, are called subthreshold, above - suprathreshold. It has been shown that the threshold force required for the initiation of excitation **with an intracellular microelectrode is 10 -7 - 10-9 A.**

 **Thus, the main condition for the occurrence of AP is the following: the membrane potential must be equal to or less than the critical level of depolarization** ( EO <= EK)

 The reasons for this phenomenon will become clear to us later, after clarifying some of the mechanisms of action of a constant electric current on excitable tissues.

 In laboratory conditions and in some clinical studies, electrical stimuli are used to irritate nerves and muscles, which are easy to dose both in amplitude and duration, and in form, imitating natural nerve impulses. The mechanism of the irritating effect of current on the tissue is basically the same for all types of stimuli, as close as possible to the mechanism of action of the nerve impulses themselves, but in the most distinct form these mechanisms are revealed when using direct current.

MULTIPLE- CHOICE STUDY QUESTIONS ON THE THEME

"Physiology of excitable tissues"

1. SIMPLE DIFFUSION IS CARRIED OUT

1) along concentration gradient and (or) electrical gradient of the transferred substance \*

2) along the gradient of the concentration of the transferred substance using carrier proteins

3) against the concentration gradient of the transferred substance

4) both along the concentration gradient and against the concentration gradient of the substance

5) by carrier proteins simultaneously with the actively transported substance

2. SECONDARY-ACTIVE TRANSPORTATION IS PERFORMED

 1) against a concentration gradient with the participation of ion pumps and the expenditure of ATP energy

 2) only along the concentration gradient of the transported substance

 3) without energy consumption of ATP

 4) against a concentration gradient using the energy of ionic gradients created by ion pumps

 5) along the concentration gradient of substances with the participation of carrier proteins

3. THE MEMBRANE POTENTIAL OF REST IS

1. the potential difference between the outer and inner surfaces of the cell membrane at functional rest
2. a characteristic feature of only cells of excitable tissues
3. fast oscillation of the cell membrane charge with an amplitude of 90-120 mV
4. the potential difference between the excited and unexcited sections of the membrane
5. the potential difference between the damaged and undamaged membrane sections

4. AN INCREASE IN THE POTASSIUM CURRENT DURING THE DEVELOPMENT OF THE ACTION POTENTIAL CAUSES

1. rapid repolarization of the membrane
2. repolarization of the membrane
3. reversal of the membrane potential
4. trace depolarization
5. local depolarization

5. SPECIFY THE FUNCTIONAL ROLE OF THE RESTING MEMBRANE POTENTIAL

1. its electric field affects the state of protein channels and membrane enzymes
2. it characterizes the increase in cell excitability
3. it is the main unit of information encoding in the nervous system
4. ensures the operation of membrane pumps
5. characterizes a decrease in cell excitability

6. BIOLOGICAL MEMBRANES, PARTICIPATING IN THE TRANSFORMATION OF EXTERNAL STIMULI OF NON-ELECTRICAL AND ELECTRICAL NATURE INTO BIOELECTRIC SIGNALS, PERFORM MAINLY THE… FUNCTION

1. barrier
2. регуляторную
3. cell differentiation
4. transport
5. generation of the action potential

7. THE SYSTEM OF MOVEMENT OF IONS THROUGH THE MEMBRANE ALONG THE CONCENTRATION GRADIENT, WHICH DOES NOT REQUIRE DIRECT ENERGY CONSUMPTION, IS CALLED

1. pinocytosis
2. passive transport
3. active transport
4. persorption

 exocytosis

8. THE LAW ACCORDING TO WHICH THE EXCITABLE STRUCTURE RESPONDS TO THRESHOLD AND SUPER-THRESHOLD STIMULI WITH THE MAXIMUM POSSIBLE RESPONSE IS CALLED THE LAW

1. of force
2. "all or nothing"
3. of force-duration
4. of accommodation
5. polar

9. THE LAW ACCORDING TO WHICH THE EXCITABLE STRUCTURE RESPONDS TO THRESHOLD AND SUPER-THRESHOLD STIMULI WITH THE MAXIMUM POSSIBLE RESPONSE IS CALLED THE LAW

1)of force

1. "all or nothing"
2. of force-duration
3. of accommodation
4. polar

10. THE ADAPTATION OF THE TISSUE TO A SLOWLY INCREASING STIMULUS IS CALLED

1. lability
2. functional mobility
3. hyperpolarzation
4. accommodation
5. braking

.11. LIGHTWEIGHT DIFFUSION IS PERFORMED

1) against the concentration gradient with the participation of ion pumps

2) along the gradient of the concentration of the transferred substance using carrier proteins \*

3) along the concentration gradient without the participation of carrier proteins

4) with direct consumption of ATP energy or sodium gradient energy

5) by an electrochemical gradient

12. A POSITIVE SHIFT (DECREASE) OF THE MEMBRANE REST POTENTIAL UNDER ACTION OF AN IRRITANT IS CALLED

1. hyperpolarization
2. repolarization
3. exaltation
4. depolarization
5. static polarization

13. THE VALUE OF THE REST POTENTIAL IS CLOSE TO THE VALUE OF THE EQUILIBRIUM POTENTIAL FOR ION

1)potassium

2) chlorine

3) calcium

4) sodium

5) magnesium

14. MEMBRANE PERMEABILITY FOR NA+ IN THE PHASE OF DEPOLARIZATION OF THE ACTION POTENTIAL

1. increases sharply and a powerful sodium current enters the cell
2. sharply decreases and there is a powerful sodium current coming out of the cell
3. does not change significantly
4. is balanced with the permeability for K+
5. there is no correct answer

15. WHEN THE INCREASE IN THE K+ CONCENTRATION INCREASES IN AN EXTRACELLULAR MEDIUM WITH A RESTING MEMBRANE POTENTIAL… WILL OCCURS IN AN EXCITABLE CELL

1. depolarization
2. hyperpolarization
3. the transmembrane potential difference will not change
4. stabilization of the transmembrane potential difference
5. there is no correct answer

16. THE PARADOXICAL PHASE OF PARABIOSIS IS CHARACTERIZED BY

1. a decrease in the response with an increase in the strength of the stimulus
2. a decrease in the response with a decrease in the strength of the stimulus
3. an increase in the response with an increase in the strength of the stimulus
4. the same response with an increase in the strength of the stimulus
5. lack of reaction to any stimuli in strength

17. SODIUM CHANNELS HAVE "GATES"

1. slow activation
2. fast inactivation
3. slow activation and fast inactivation
4. slow activation and slow inactivation
5. fast activation and slow inactivation

18. LOCAL RESPONSE IS DISTRIBUTED

1. decrementally (with attenuation)
2. incrementally (without attenuation)
3. abruptly
4. without changing the amplitude

19. AS A RESULT OF BIOCHEMICAL PROCESSES, THE PERIOD OF GENERATION OF THE ACTION POTENTIAL IS ACCOMPANIED BY THE RELEASE OF

1) 2-3 % of heat

2) 12-13 % of heat

3) 97 – 98 % of heat

4) 50% of heat

20. THE LAW ACCORDING TO WHICH THE EXCITABLE STRUCTURE RESPONDS TO THRESHOLD AND SUPER-THRESHOLD STIMULI WITH THE MAXIMUM POSSIBLE RESPONSE IS CALLED THE LAW

1. of force
2. of "all or nothing"
3. of force-duration
4. of accommodation
5. polar

21. THE ABILITY OF LIVING TISSUE TO RESPOND TO ANY TYPE OF IMPACT BY CHANGING THE METABOLISM IS CALLED

 1) conductivity

 2) lability

 3) excitability

 4) irritability

5) automation

22. PRIMARY ACTIVE TRANSPORTATION IS PERFORMED

1. against the concentration gradient with the participation of ion pumps and the energy consumption of ATP
2. only along the concentration gradient of the transported substance
3. without energy consumption of ATP
4. directly with the energy consumption of ionic gradients, but without the direct participation of ion pumps and the energy consumption of ATP
5. along the electrochemical gradient with the energy consumption of ATP

23. IN THE STATE OF PHYSIOLOGICAL REST, THE INNER SURFACE OF THE MEMBRANE OF EXCITABLE CELL WITH REGARD TO THE EXTERNAL ONE IS CHARGED

1. positive
2. as well as the outer surface of the membrane
3. negatively
4. has no charge
5. there is no right answer

24. AT THE COMPLETE BLOCKADE OF FAST SODIUM CHANNELS OF THE CELL MEMBRANE, … IS OBSERVED

1. decreased excitability
2. a decrease in the amplitude of the action potential
3. absolute refractoriness
4. exaltation
5. trace depolarization

25. ABILITY OF CELLS TO RESPOND TO THE ACTION OF IRRITANTS BY A SPECIFIC REACTION CHARACTERIZED BY RAPID, REVERSIBLE DEPOLARIZATION OF THE MEMBRANE AND CHANGE OF METABOLISM IS CALLED

 1)irritability

 2) excitability

 3) lability

 4)conductivity

5) automation

26. THE MINIMUM IRRITANT STRENGTH NECESSARY AND SUFFICIENT FOR THE OCCURRENCE OF A RESPONSE IS CALLED

1. threshold
2. overthreshld
3. submaximal
4. subthreshold
5. maximum

27. THE MOST SIGNIFICANT CHANGE WHEN EXPOSED TO A FAST SODIUM CHANNEL BLOCKER WILL BE

1. depolarization (reduction of the resting potential)
2. hyperpolarization (increased resting potential)
3. reducing the steepness of the depolarization phase of the action potential
4. deceleration of the repolarization phase of the action potential
5. there is no correct answer

28. THE ADAPTATION OF THE TISSUE TO A SLOWLY INCREASING STIMULUS IS CALLED

1)lability

2)functional mobility

3)hyperpolarization

4)accommodation

5) braking

29. THE CONCENTRATION OF SODIUM IONS IN THE CYTOPLASM IS LESS THAN THE CONCENTRATION OUTSIDE BY

1) 8-10 times

2) 10-20 times

3) 30-50 times

4) 300-1000 times

30. THE PHASE OF THE ACTION POTENTIAL THAT OCCURS IMMEDIATELY AFTER THE MAIN PRONG IS CALLED

1. latent period
2. inversion
3. trace positive potential
4. trace negative potential

 \*

31. AN IRRITANT TO THE PERCEPTION OF WHICH THE CELLS DURING THE EVOLUTIONAL PROCESS ACQUIRED SPECIALIZED STRUCTURES IS CALLED

1) inadequate

2) subthreshold

3) adequate

4)threshold

5) maximum

32. EXCITABLE TISSUES INCLUDE

1) integumentary epithelium

2) connective (fibrous and skeletal)

3) connective (reticular, fatty and mucous)

4) nervous, muscular, glandular epithelium

5) blood and lymph

33. A NEGATIVE SHIFT (INCREASE) OF THE MEMBRANE REST CAPACITY IS CALLED

1. depolarization
2. repolarization
3. hyperpolarization
4. exaltation
5. reversion

34. THE DESCENDING PHASE OF THE ACTION POTENTIAL (REPOLARIZATION) IS ASSOCIATED WITH INCREASED PERMEABILITY OF THE MEMBRANE FOR IONS OF

1. sodium
2. calcium
3. chlorine
4. potassium

5)magnesium

35. the ACTION POTENTIAL IS

1. a stable potential, which is established on the membrane when two forces are in balance: diffusion and electrostatic
2. the potential between the outer and inner surfaces of the cell in a state of functional rest
3. fast, actively propagating, phase oscillation of the membrane potential, accompanied, as a rule, by recharging of the membrane
4. a slight change in the membrane potential under the action of the subthreshold

irritant

long-term, stagnant membrane depolarization

36. THE MOLECULAR MECHANISM ENSURING THE EXTRACTION OF SODIUM IONS FROM THE CYTOPLASM AND THE INTRODUCTION OF POTASSIUM IONS INTO THE CYTOPLASM IS CALLED

1. potential-dependent sodium channel
2. nonspecific sodium-potassium channel
3. a chemically dependent sodium channel
4. sodium-potassium pump

 5)leakage channel

37. THE LEVEL OF THE MEMBRANE POTENTIAL AT WHICH THE ACTION POTENTIAL OCCURS IS CALLED

1. the resting membrane potential
2. the critical level of depolarization
3. trace hyperpolarization
4. zero level
5. trace depolarization

38. THE VALUE OF THE LOCAL RESPONSE, DEPENDING ON THE STRENGTH OF THE SUBTHRESHOLD STIMULUS IS SUBJECT

1. the law of gradualness
2. the "all or nothing" law
3. the law of force-time

4) the law of isolated conduction

39. THE TRACE ELECTROPOSITIVITY PHASE IS CHARACTERIZED BY THE FACT THAT THE MEMBRANE POTENTIAL

1. reaches the initial level
2. exceeds the value of the resting membrane potential
3. always is equal to the rheobase
4. is less than the value of the resting membrane potential

40. THE PHASE OF REDUCED EXCITABILITY DURING THE ACTION POTENTIAL MEETS

 1) the main wave

 2)trace electronegativity

 3)trace electropositive \*

 4) local response

41. THE CONCENTRATION OF… IONS INSIDE THE CELL IS HIGHER THAN IN THE INTERCELLULAR FLUID

1. chlorine
2. sodium
3. calcium
4. potassium
5. magnesium

42. NEGATIVE CHARGE ON THE INNER SIDE OF THE CELL MEMBRANE IS FORMED AS A RESULT OF DIFFUSION OF

1) K + from the cell and the electrogenic function of the K-Na-pump

2)Na + into the cell

3)C1 - from the cage

4)Ca2 + into the cell

5)there is no right answer

43. THE RISING PHASE OF THE ACTION POTENTIAL IS ASSOCIATED WITH THE INCREASED PERMEABILITY FOR IONSOF:

1. potassium
2. there is no correct answer

 3)sodium

 4) chlorine

5) magnesium

44. SURFACE OF AN EXCITED SECTION OF A CELL (TISSUE) WUTH RESPECT TO THE UNEXCITED ONE IS CHARGED

* 1. positively

2) the same as unexcited

 3) not charged

4) negatively \*

45. HYDROLYSIS OF ONE ATP MOLECULE FOR THE ENERGY SUPPLY OF THE NA-K PUMP PROVIDES TRANSMEMBRANE TRANSPORT AGAINST THE CONCENTRATION GRADIENT OF

1. 2 sodium ions and 3 potassium ions
2. 3 sodium ions and 2 potassium ions
3. 3 sodium ions and 2 chlorine ions

4) 3 sodium ions and 3 potassium ions

46 THE FORMATION OF TRACE ELECTROPOSITIVITY CAUSES THE CURRENT OF… IONS

1. sodium
2. chlorine
3. potassium
4. calcium

47. THE ABILITY OF EXCITABLE TISSUE TO REPRODUCE THE MAXIMUM NUMBER OF IMPULSES PER UNIT OF TIME IS CALLED

1)excitability

2) lability

3) anelectron

4) refractoriness

5) accommodation

48. THE MINIMUM TIME DURING WHICH A CURRENT EQUAL TO DOUBLE RHEOBASE (DOUBLE THRESHOLD FORCE) CAUSES EXCITATION, IS CALLED

1. useful time
2. accommodation
3. adaptation
4. chronaxia
5. lability

49. THE THRESHOLD OF IRRITATION IS AN INDICATOR OF

1)excitability

2) contractility

3) lability

4) conductivity

5)automatics

50. UNDER THE ACTION OF A SUBTHRESHOLD STIMULUS, THERE IS

1. a number of physicochemical shifts without visible effects (local response)
2. maximum visible response
3. maximum visible responsev
4. change in the function of excitable tissue
5. greater response than minimal

STUDY QUESTIONS FOR SELF-CONTROL

1.List the excitability parameters.

 Correct answer: Stimulation threshold, latent period, useful time, chronaxia

2.What is the amplitude and duration of trace potentials?

Correct answer: Amplitude is several millivolts, duration is from several milliseconds to one second.

3.What are the differences between the local response and the action potential?

Correct answer: It does not spread across the tissue, does not have a clear threshold, and does not comply with the all-or-nothing law.

4. Is the excitability of the tissue increased or decreased during the local response?

 Correct answer: Increased.

5. What is the ratio of membrane permeability for K and Na ions at rest?

 Correct answer: The permeability for K ions is 20-100 times greater than Na.

6. What causes the local response?

 Correct answer: Increased sodium permeability of the membrane causes the local response.

1. How does the amplitude of the local response depend on the strength of stimulation?

 Correct answer: The stronger the stimulus, the greater the local response is.

1. Which two values determine the value of the threshold of irritation?

Correct answer: The initial level of the membrane potential and the critical level of depolarization determine the value of the threshold of irritation.

1. What changes in membrane properties cause the depolarization phase?

 Correct answer: A sharp increase in membrane permeability to Na ions causes the depolarization phase.

1. How will tissue excitability change if the membrane potential approaches the critical level of depolarization?

 Correct answer: Excitability increases.

1. Does the magnitude of the action potential depend on the strength of irritation?

 Correct answer: It does not depend.

1. When does a local response develop into an action potential?

 Correct answer: When the critical level of depolarization is reached, the local reaction develops into an action potential

1. What are the advantages of electric current as a stimulus?

Correct answer: Its action manifests itself at a value that does not cause tissue damage, quickly begins and stops, and is easily dosed in terms of strength, duration and frequency.

1. How does the membrane charge change with increasing diffusion of Na ions?

Correct answer: The diffusion of Na ions gives a positive charge to the inner surface of the membrane, and a negative charge to the outer surface.

15. Draw a diagram of the local response of the nerve fiber and its development into

an action potential.

Correct answer:

16.What is chronaxie?

Correct answer: The shortest time during which a current equal to two rheobases causes excitation is chronaxie

17. What changes in the properties of the membrane cause the repolarization phase?

 Correct answer: A decrease in sodium permeability and an increase in potassium cause a repolarization phase.

18. Draw the Goorweg-Weiss force-time curve.

Correct answer:

19.What is called the threshold potential or depolarization threshold?

Correct answer: The threshold potential or depolarization threshold is the minimum shift of the membrane potential required for the membrane depolarization from the initial value of the polarization level to reach a critical level.

1. What is called the accommodation of excitable tissue?

Correct answer: Adaptation of excitable tissue to a slowly increasing stimulus is the accommodation of excitable tissue.

1. What is good time (time threshold)?

Correct answer: The minimum time during which a current equal to the rheobase causes excitation is good time (time threshold)

1. What phases of changes in excitability are observed in the nervous and muscular tissue during excitation?

Correct answer: Absolutely refractory, relative refractory, supernormal, / exaltation /, subnormal phases of changes in excitability are observed in the nervous and muscle tissue upon excitement.

1. What is chronaxia?

Correct answer: Chronaxia is the shortest time during which an electric current equal to twice the rheobase must act on the tissue in order to induce arousal.

1. Draw a graph of the change in the excitability of the nerve when it is excited.

Correct answer:

1. What is the critical level of depolarization?

Correct answer: The level of membrane depolarization at which an action potential occurs is the critical level of depolarization

1. What is a local response?

Correct answer: The local response is active subthreshold membrane depolarization.

1. Why should energy be spent for the operation of the sodium-potassium pump?

Correct answer: The energy should be spent for the operation of the sodium-potassium pump since the work of the pump is associated with the movement of Na and K ions, against the concentration gradient.

1. What is called lability?

Correct answer: Lability is the rate of elementary reactions that underlie the excitation cycle.

1. What is called excitability?

Correct answer: Ability of tissue to respond to stimuli by changing metabolism in the form of a specific response is called excitability

1. Draw a diagram of the action potential for extracellular lead.

Correct answer:

##  10 Case problems with keys

 1. How will the membrane potential change if the flow of sodium into the cell increases, but the amount of potassium remains the same?

2. How will the membrane potential of a nerve fiber change if the sodium channels are closed?

 3. How will the membrane potential change if the Na-K-dependent ATPase is blocked?

 4. Irritating current threshold is 3 V. The tissue is irritated by a current of 10 V., but there is no excitation. In what case can this be observed?

 5. Does propagating excitation occur in the nerve if it is known that the membrane potential is 90 mV, the critical depolarization level is 30% lower, and the irritating current shifts the membrane potential in one case by 10 mV, in the other by 30 mV?

 6. How will the excitability of the tissue change if the critical level of depolarization remains the same during hyperpolarization of the membrane?

 7. How will the excitability of the tissue change if the membrane potential has increased by 20%, and the critical level of depolarization by 30%? Initial values: Eo = 90 mV., (EK) = 60 mV.

 8. As a result of prolonged irritation with direct current, the critical level of depolarization (EK) dropped by 20%. The amount of depolarization is 10% of the level of the membrane potential (Eo). The initial values are Eo = 100 mV7, Ek = 70 mV. How will the excitability of the nerve change in this case?

 9. How and by what amount should the critical depolarization level shift so that the anode is excited when a DC current is opened, which will increase the EO by 10 mV.? Take Eo = 100 mv., Ek = 70 mv.

 10. The threshold of irritation under the anode when opening is 2 V. Will a muscle contract when closing and opening if a neuromuscular preparation is stimulated with an ascending current of 1.9 volts?

## KEYS TO CASE PROBLEMS ON THE TOPIC: "PHYSIOLOGY OF EXCITABLE TISSUES".

1. There will be a depolarization of the membrane and a decrease in the membrane potential.

2. The membrane potential will increase (hyperpolarization), since the potassium current will no longer decrease due to the opposite sodium current, as it was before the experiment.

3. In this case, the Na-K pump is turned off, and the polarisation of the membrane will gradually disappear, as the concentrations of sodium and potassium on both sides of the membrane will be equalized.

4. It can be observed If the duration of irritating current will be very short (see curve Hoorweg - Weiss).

5. Excitation occurs if the membrane potential is less than or equal to the critical depolarization level. Therefore, in this case, propagating excitation will occur only if the membrane potential decreases by an amount greater than 27 mV. (by 30%).

6. Excitability will decrease, since in this case more force and more time are needed to shift the membrane potential to a critical level.

7. In this case, the new membrane potential was 108 mV, and the critical depolarization level was 78 mV. The initial values of these indicators are 90 mV and 60 mV. Consequently, the initial difference between the membrane potential and the critical depolarization level did not change and remained 30 mV. This means that the excitability of this membrane has not changed.

8. In this case, the initial excitability of the membrane corresponds to the difference between EO and Ek of 30 mV. At the beginning of depolarization, when the membrane potential was equal to 90 mV, and the difference between EO and Ek = 20 mV, excitability increased by one third. After prolonged irritation, the critical depolarization level reached 54 mV. Since in this case the difference between EO and Ek was 34 mV, it is clear that the excitability of the tissue fell. This phenomenon is called Verigo "cathodic depression".

9. The membrane potential under the anode increases, and when the current is turned off, it returns to its original level. Consequently, in order for excitation to occur under the anode upon opening, it is necessary to increase the critical level of depolarization by such an amount that it becomes equal to the initial membrane potential. This shift does not depend on the magnitude of hyperpolarization, but is mainly determined by its duration. The required shift is 100-70 = 30 mV.

10. When closing, the muscle will contract, since the threshold of the DC closing shock is less than the breaking one. When opened, there will be no contraction.

**11. TRAINING STANDARDS**

 **(**On the topic "Physiology of excitable tissues", the program does not provide for practical skills that a first-year student of the faculty of "Pharmacy" must acquire.The student should have an understanding of chronoreflexometry.)

**12. Topics for students' scientific research:**

1. History of the discovery of electrical phenomena.

2. Membranes. Active and passive transport.Природа мембранного потенциала.

 3. Excitability. Parameters of excitability.

4. Lability. Parabiosis.

 **Course textbooks and manuals**

1. Dunn, R. B. USMLE Step 1. Lecture Notes. Physiology / R. B. Dunn ; ed. D. E. Fitzovich. - [S. l.] : Kaplan, 2006. - 576 p.

2. Hall, J. E. Guyton and Hall Textbook of Medical Physiology / J. E. Hall. - 13th ed., Int. ed. - Philadelphia : Elsevier, 2016. - 1145 p.

3. Silbernagl, S. Color Atlas of Phisiology / S. Silbernagl, A. Despopoulos. - 7th ed. - Stuttgart : Thieme, 2015. - 458 p.