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S2.177. Participation of membrane mechanisms in the regulation of electrokinetic properties of erythrocyte populations under stress

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The most important parameter of erythrocytes, which ensures their unhindered movement along the bloodstream, is the negative charge of the surface. The magnitude of the cell charge is usually judged by their electrokinetic potential (EKP) and the experimentally measured speed of cell movement in an electric field - electrophoretic mobility (EPM) (Elblbesy MA, 2017). A decrease in the surface potential of erythrocytes, reducing the forces of electrostatic repulsion of cells, enhances their aggregation, changes blood viscosity, and initiates the process of thrombus formation (Sheremet'ev IuA, 2013). Therefore, maintaining the optimal value of the charge of erythrocytes both at rest and during functional loads is of paramount importance for maintaining suspension stability and the necessary rheological characteristics of moving blood. Naturally, information about the regularities and mechanisms of ensuring such stability is not only of theoretical, but also of practical interest.

Our studies of the electrophoretic mobility of erythrocytes (EPME) in normal and pathological conditions, physical and emotional stress of the body showed that a differential approach to the study of the erythrocyte population can contribute to the solution of these problems (Matyushichev V.B., 2007). From these positions, peripheral blood erythrocytes were considered not as a homogeneous mass of functionally identical cells, but as a cell population, the composition and dynamics of which reflect the membrane functions and metabolism of individual cells, the influence of plasma factors, the activity of erythrocyte production and destruction organs. With this approach, it was possible to establish that the bioelectrical homeostasis of erythrocytes is achieved mainly due to the redistribution of their individual subpopulations in proportions that can ensure the preservation of the optimal total level of EKP.

The aim of the work was to study the contribution of membrane mechanisms to the regulation of the electrokinetic properties of erythrocyte populations under stress.

Methods. A group of students (n=20) aged 18-19 have been examined being under examination stress and in a state of emotional and physical rest. Electrophoretic mobility of erythrocytes was determined by microelectrophoresis in autoplasma diluted in Ringer's medium. The parameters of the EPME distribution shape were used for a quantitative assessment of the qualitative features of the structure of populations. Histogram parameters were taken into account in addition to average values: asymmetry (As) and excess (Ex) coefficients, which make it possible to identify individual erythrocyte subpopulations in the general population and assess the degree of their heterogeneity. The activity of Na, K-ATPase was assessed by means of adding strophanthin 10-5 M.

Results. The primary processes underlying the change in the balance of erythrocyte subpopulations with different charges can be implemented at different levels, from the membrane to the systemic. Taking into account that, along with the relatively passive (surface charge), active component, which reflects the permeability of membranes and the operation of ion pumps, participates in the formation of the EKP of the cell, it can be assumed that ion transport membrane systems are involved in the dynamics of the redistribution processes of erythrocyte subpopulations along their EKP (Krylov VN, 2014). The Na-pump, K-pump are a universal link that performs metabolic self-regulation of the receptor and electrical properties of membranes. The influence of the Na-pump, K-pump on the electrokinetic properties of erythrocytes is evidenced by the presence of correlations between the EPME value and the Na, K-ATPase activity of erythrocyte membranes. EPME of the students under stress increases significantly due to increase of the proportion of cells with increased EKP. EPME decreases due to the inhibition of the pumps of the subpopulation of cells with increased EKP under the influence of strophanthin. In a state of emotional balance the students have no changes in the average values of EPME and distribution parameters under the influence of strophanthin. The ability of strophanthin to suppress the operation of the pump extends only to homogeneous subpopulations (positive Ex), which are characterized by a higher EKP than the population average (negative As). With emotional and physical stress of the body, the proportion of such subpopulations in the total pool increases, indicating an increase in the functions of the Na-pump, K-pump. As for the predominance of cells with a reduced level of EPM in the population, there is both a lack of response to the action of the inhibitor and a slight increase in EKP, indicating a change in the state of the membrane, in particular, its permeability. Among the factors causing destructive changes in the membranes, obviously, one can include the activation of free radical processes, the negative influence of the plasma environment, the pH of the medium, etc.

Thus, under conditions of relative dynamic equilibrium of the erythrocyte production and destruction processes, the autoregulation mechanisms are involved in the redistribution of the balance of subpopulations, acting mainly at the membrane-cellular level. During emotional, physical stress or pathology, additional regulatory elements of a plasma or systemic nature are actively connected to them, the share of which in the control of EPME and the spectrum of influence on the state of the erythrocyte population under specific conditions can vary within fairly wide limits. Our experiments with the use of the Na-pump, K-pump inhibitor strophanthin (10-5 M) in vitro showed that the effect of strophanthin is determined only in relation to the subpopulation of cells with increased EPME.

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S2.178. Peculiarities of AP repolarization in cardiomyocytes of three-week-old rats during application of clonidine hydrochloride

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Activation of the sympathetic nervous system is responsible for the body's "fight or flight" reaction. The physiological responses to the activation of the sympathetic nervous system and adrenal medulla are mediated through the action of the endogenous catecholamines

norepinephrine (or noradrenaline) and epinephrine (or adrenaline) on adrenergic receptors. Adrenergic receptors belong to the superfamily of G protein-coupled receptors (GPCR). Adrenoceptors are divided into alpha1, alpha2, beta1, beta2 and beta3 receptors. [1] α2 receptors are coupled to inhibitory Gi proteins, that inactivate adenylyl cyclase, decreasing cyclic adenosine monophosphate (AMP) production. In addition to the endogenous ligands epinephrine and norepinephrine, they may be activated by several agonist drugs, including clonidine, brimonidine, and moxonidine. [2]
Purpose . To study the effect of α2-adrenoreceptor stimulation on cardiac electrical activity in three-week-old rats at 10-6 M concentrations.
Material and Methods. The investigation was carried out on three-week-old white mongrel rats. The anesthetic was 25% urethane solution at the rate of 1.2 g/kg of animal weight, which was injected intraperitoneally. The anesthetized animal's chest was opened, the heart was quickly extracted and placed in a petri dish with oxygenated Tirode's solution. The heart was dissected and a multicellular preparation with the auricle of the right atrium, transverse scallop, and fragments of the superior and inferior vena cava were made. Electrical activity of cardiomyocytes was studied using intracellular microelectrode lead on the right atrium preparation at the imposed rhythm with a frequency of 5 Hz. External stimulation was performed through platinum electrodes. The obtained records of myocardial electrical activity were analyzed using the original Elph 3.0 program. The solution of α2-adrenoreceptor agonist clonidine hydrochloride (10-6 M) was applied for 20 min.
Results. In three-week-old animals clonidine hydrochloride in the studied concentration did not cause significant changes in the values of membrane potential, depolarization phase duration, and action potential amplitude. However, application of α2-adrenoreceptor agonist at a concentration of 10-6 M resulted in prolongation of the repolarization phase of the action potential by 50% and 90%.
Conclusion. We have revealed that application of clonidine hydrochloride at a concentration of 10-6M has a positive effect on the amplitude-time parameters of cardiomyocyte electrical activity in 3-week-old rats.
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S2.179. Peroxiredoxin 6 reduces damage to kidney nephrons in the early reperfusion period

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Nephrons are highly sensitive elements of the kidney, which react sharply to hypoxia, leading to the development of pathological changes. Reperfusion saves the cell from hypoxia, but leads to an aggravation of pathological changes due to the activation of free radical reactions. It is at the initial moment of reperfusion that a cascade of pathological processes is triggered. These reactions are detrimental to nephrons, and it is advisable to use antioxidant enzymes to reduce their effect. In this work, the antioxidant enzyme peroxiredoxin 6 (Prx6) is used to protect nephrons from reperfusion injury. Prx6 neutralizes a wide range of hydroperoxides, has good bioavailability and is able to penetrate into cells, increasing their antioxidant status, in addition, it effectively reduces the severity of damage in various free radical pathologies.
The aim of this work is to study the effect of exogenous Prx6 on the state of nephrons in the initial reperfusion period after ischemia. In the experiments, male Wistar rats were used to reproduce the model of ischemia-reperfusion of the right kidney with left-sided nephrectomy. The period of ischemia is 45 minutes, reperfusion - 2, 5 and 24 hours. Prx6 was administered intravenously 15 minutes before ischemia. Recombinant Prx6 was obtained at the Reception Mechanisms Laboratory of the Institute of Cell Biophysics. The peroxidase activity of the exogenous protein is 200 nmol/mg/min for H2O2 and 100 nmol/mg/min for tert-butyl peroxide.
It was shown that structural damage to nephrons occurs after 2 hours of reperfusion: an increase in Bowman's space and expansion of convoluted tubules. The maximum lesion was noted after 24 hours of reperfusion: focal-diffuse dystrophic and necrotic changes in the epithelium of the convoluted tubules are pronounced. During this period, there is a maximum increase in the concentration of urea and creatinine in the blood relative to the control values (by 6 and 3 times, respectively), which indicates a violation of the filtration capacity of the kidney. A restructuring of the nephron apparatus was noted, which is expressed in an increase in the area of the renal corpuscles, the area of the vascular glomeruli, and the area of the Bowman space. Nephrocyte dystrophies and parenchymal foci with an immunosignal for the KIM-1 kidney lesion molecule were noted. When exogenous Prx6 was used, no restructuring of the nephron apparatus was noted already with the onset of reperfusion, and its components were not increased. Reduced immunosignal area for KIM-1 and minimization of nephron dystrophy. The decrease in nephron damage with the onset of the reperfusion period against the background of the use of Prx6 was reflected in an improvement in the functionality of nephrons. The use of Prx6 led to a decrease in the concentration of urea and creatinine already in the early reperfusion period and maintaining at this level for 24 hours. Thus, exogenous Prx6, when administered intravenously before renal ischemia, reduces nephron damage with the onset of reperfusion. This contributes to the improvement of the compensatory-adaptive properties of nephrons during the reperfusion period and the preservation of their functionality. The implementation of Prx6 of its protective properties with the onset of reperfusion is associated with its powerful antioxidant properties, mainly with peroxidase activity, which makes it possible to neutralize the hyperproduction of reactive oxygen species.
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S2.180. Phase transitions in chimeric antigen receptor systems

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The creation of chimeric antigen receptors is one of the most promising technologies for the treatment of oncological diseases [1]. Currently, modifications of chimeric antigen receptors are being actively developed, which aim to increase not only the sensitivity, but also the specificity of recognition of cancer cells [2].
A number of recent works state that the specificity of chimeric antigen receptors is associated with their ability to form clusters [3,4]. The mechanisms of receptor clustering are being actively studied [5, 6]. It was found that, in a number of cases, the mechanism of cluster nucleation has a threshold character.
The ability of chimeric antigen receptors to threshold cluster formation can be assessed from the standpoint of nucleation theory. Due to this, opportunities open up at in vitro stages of development of chimeric antigen receptors to compare their eventual specificity. Currently, specificity is assessed at the stage of in vivo testing [7]. The development