*Materials of Conferences*

## CHANGES OF LEFT VENTRICLE MYOCARDIUM STRUCTURE OF A RAT'S HYPERTROPHIC HEART INFLUENCED BY HYDRA'S PEPTIDIC MORPHOGEN

Fedoseyeva V.A., Pistsova T.V., Pavlovich E.R.
*Russia State Medic University,*
*A.L. Myasnikov Institute of Clinical Cardiology, Russian Cardiology Research-and-Production Complex*
*Moscow, Russia*

It is given that hydra's peptidic morphogen (HPM) in invertebrates organism is a growth hormone, and its role in mammal's organism is unclear. According to substituted data HPM is a tissue nonspecific regulator, stimulating some functions of organs in health and none. Aim of the research is studying of single dosing of HPM into different layers of rat's hypertrophic myocardium. The research is carried out with 9 Wistar rat-males 180-200 gr. HPM is from peptide synthesis laboratory of Institute of Experimental Cardiology of Russian Cardiology Research-and-Production Complex, IP injected in dose 20 mcg/kg of the body in the volume of 1 ml once after coarctation of aorta surgery. Control animals were injected normal saline solution, containing equimolar mixture of aminoacids. The surgery of dosed 50% abdominal aorta coarctation was carried out under Nembutal narcosis. In 10 days chest was opened, heart was perfused with 2% gluteraldehyde and then taken out. Tissue sheets were cut from the middle third of the left ventricle, fixitaed with 1% osmic acid, dehydrated with graded alcohols and embed in Epon resin. Semifine section, dyed in toluidine blue, was evaluated by 1350 times amplification, using morphometric reticle. Morphometric analysis did not show differences between series of operated animals that got and did not get injection of a mixture of aminoacids. There were determined volume fraction of myocytes Vv(m), connective tissue Vv(ct) and capillary Vv(c), surface of myocytes S (m) and capillary S (c), surface density of myocytes per unit of surface of capillary S(m)/S(c), surface of cardiac myocytes per unit of its volume S (m)/Vv (m), volume of myocytes per volume of capillary Vv (m)/Vv (c), and volume of capillary per volume of connective tissue Vv (c)/Vv (ct). The average value of diameter of myocytes was calculated (μm). PC 1640 "Amstrad" was used for statistical processing. Injection of HPM led to change zone decrease, marked in subendocardial layer and moved to ventricular cavity. With that myocyte vacuolization was decreased, and changed cores and abbreviated myocytes were detected rarer. No signs of structure failure were detected in other myocardium layers. Hydrops of subendocardial layer was less expressed than in control. Other myocardium layers did not show hydrops signs. Resetting of myocyte volume fraction was marked in subendocardial layer when HPM injected. Mocyte surface was accurately decreased in comparison to control when average diameter of myocytes was increased. Content of connective tissue was decreased because of hydrop reduction, capillary apparent density came to N. Surface - volume dataofmyocytes came to normal level. Myocyte surface to capillary surface ratio was at control level. Myocyte volume to capillary volume ratio was decreased. When HPM injected more significant part of myocytes was observed in intramural layer of walls of the heart than in subendocardial layer. Average myocyte diameter did not change. Content of connective tissue was decreased because of tissue hydrop reduction. Capillary surface was comparable with the control one. Volume-surface characteristics of capillary in subendocardial and intramural layers of myocardium showed increased volume of blood flow. In subendocardial layer the HPM injection restored specific to normal balance between volume fraction of myocytes and connective tissue. Myocyte diameter was increased with that which shows their earlier involvement into hypertrophy process. Capillary surface and volume decrease showed their decrease of blood supply level in subepicardial layer. It is followed from the represented data that single HPM injection relieved the development of myocardium hypertrophy in subendocardial layer and in less extent in intramural and subepicardial layers, influencing all tissue components.

The work is presented for an International Science Conference "Burning Problems of Science and Education", (Cuba), Varadero, March 20-30, 2010. Received by the editorship on 12.01.2010.

## CONCEPTUAL MODEL OF STRESS-INDUCED DYNAMICS ACID-HEMOLYTIC STABILITY OF ERYTHROCYTE

Mikhailis A.A.
*Stavropol State Medical Academy*
*Stavropol, Russia*

The problem of the adaptation of living organisms to the continuously changing conditions of their environment, occupies one their visible places in the number of those, at which work the specialists of biomedical profile. As key component in the theory of adaptation comes out the concept of stress, created with G. Selye.

According to the contemporary ideas, stress (in man) – this is the typical pathologic process, at basis of which lies the prevailing in the course of evolution standard unspecific general adaptive reaction of the complete organism to the action of ultrapowerful stimulus or its threat, that is the result of integral interaction of the complex of reciprocal psycho-neuro-endocrine-immune and cellular-tissue factors and

mechanisms, which form the stress-realizing and stress-limiting systems, represented by the multilevel and multicomponent regulated totality of the structures, which function relatively antagonistically in the direction of mobilization and redistribution of energy and plastic resources for the purpose of the restoration of the disrupted homeostasis and increase in the local and overall adaptive possibilities of organism.

The process of adaptation is universal and, in spite of the variety of nosologic forms, it is logical to assume existence of general, fundamental regularities in a change in the properties of erythrocytes with the acute stress of any origin. In fact, in the works explosivesV.V. Novitskiy, N.V. Ryazantseva, E.A. Stepovaja and other are described the standard mechanisms of changes in the molecular organization of the membranes of erythrocytes, general for the very different pathology (tumor, vascular defeats, inflammatory processes, dismetabolies and the disease of disregulation, infection and intoxication, burn injury and postoperative period).

In the number of integral characteristics, which give idea about the system shifts in the organism, can prove to be one of the parameters of the system of erythron, which lies at the basis of the hemolytic durability of its cells and determined by the method of acidic erythrograms. This method was developed in its time as the method of hematologic studies for studying the changes in the properties erythrocytes with gemoblastoses, anemias and intoxications with the defeat of the system of the red blood. With the aid of it was evaluated the heterogeneity of erythrocytic population in the dependence on the age, since the acidic durability erythrocytes esides in all, and as the function of the age of erythrocytic cell.

The works, in which method of acidic erythrograms goal directed would adapt for the dynamic estimation of the course of the diseases of nongematological profile, which are accompanied by acute stress, in the accessible literature are not encountered. But those, in which it is used in conjunction with other methods out of the sphere of hematology, are not numerous, contradictory and bear the separate nature, that does not make it possible to obtain the integral idea about the stress-induced dynamics of the acid resistance of erythrocytes (ARE), its factors and mechanisms. In the pathophysiology as the method of studying specific hematologic and unspecific general organismal laws governing the acute stress in the early postagressive period it also is not used.

The purpose of a study it was on the basis of the experimental and clinical data about the stress-induced dynamics of the hemolytic durability of erythrocytes to study the special features of the functioning of the system of erythron in the early postagressive period from the positions of interaction of the adaptive systems of organism.

The experimental part of the work was carried out on the white rats, the mice, the dogs. ARE was fixed with the following forms of acute stress: hypoxia, immobilization, operation, the injection of turpentine, acute coronary insufficiency, the magnetic storm, mechanical injury. ARE was determined to stressing, during it (in several series) immediately after, through 1, 2, 3, 6, 12, 24 hours and then every 24 hours for a period of 3-7 days (in a number of cases – for a period of 2-3 weeks) employing classical procedure.

In the clinical part of the work was used the blood of patients with the acute nongematological pathology or the aggravation of chronic (hypertensive crises and acute coronary insufficiency, stroke and craniocerebral injury, assault of bronchial asthma and pneumonia, pyelonephritis and renal colic, the fractures of the bones of extremities and postoperative period, hepatic colic and cholecystitis, ulcer and pancreatitis, acute thrombophlebitis and the gangrene of extremity). ARE was fixed during the day of rotation and then every 24 hours within a week. With the acute coronary insufficiency in man (unstable stenocardia, Q-positive and Q-negative myocardial infarction), besides ARE, was determined an also whole series of generalgematological and biochemical indices, then the analysis of functional interrelations was produced.

Statistical processing and graphic mapping of results was conducted with the use of standard programs of Microsoft Of Excel XP and batch of programs for the statistical analysis of Statistika 6,0. The authenticity of the differences between the groups was evaluated with the aid of the criteria of Student and Wilcockson-Mann-Whitney. The quantitative expression of the similarity of the dynamics of indices was obtained with the aid of the correlation coefficient of Pirson.

Basic results are reduced to the following. In the first 1-3 hours from the moment of the action of stress factor proceeds a decrease ARE. The degree of this decrease is directly proportional to the force of stress-factor action. Then occurs increase ARE. On the maximum numbers it is held 24-48-72 hours, depending on gravity of stress. Its decrease occurs after this. The degree of a decrease, the degree of increase and the speed of recovery ARE to the initial values directly depends on gravity of stress, what is the expression of the stress factor of the effect of reaction dose-dependent from the value, according to the law of Wilder (Arndt-Shultz). A decrease ARE slows down with the appearance of complication, stops or again it appears its increase. With the unfavorable flow of basic pathologic process and the progressive loading of stress ARE steadily it increases up to the day of the loss of a patient or experimental animal. The fundamental difference in the stress-induced dynamics ARE with the enumerated pathologic processes and the states is absent, i.e., the discussion deals with its nosologic nonspecificity. Occurs the interspecies similarity of the trajectories of acidic-hemolytic erythrograms in the early postagressive period, i.e., the discussion

deals also with the specific nonspecificity of the stress-induced dynamics ARE. Phase character remains, independent of floor and the age of patients. With the presence of complication and its successful treatment occurs daily shift in the dynamics ARE.

The highest positive correlation ARE is noted with components or indices of the work of the stress-realizing system or of the answer of acute phase (hydrocortisone, general cholesterol, LPL, sodium, calcium, glucose and glikogemoglobin, globulins, amylase, Alt and Ast, C-RP, fibrinogen, erythropoietin, the total quantity of leukocytes and neutrophils. In turn, the highest inverse correlation ARE is noted with components or indices of the work of the stress-limiting system (total protein, albumin, insulin, trijodtironin, potassium, magnesium, the eosinophils and lymphocytes).

Is interesting the fact that in proportion to the loading of damage and degree of the manifestation of the coronarogenic stress and postagressive reaction as a whole, is noted an increase in the portion of close couplings and by the decrease of the portion of weak bonds, correspondingly, with an increase in the generalized correlation coefficient.

The discovered regularities make it possible to make following conclusions.

1. The stress-induced dynamics of the hemolytic durability of erythrocytes both in the experiment and under the clinical conditions, bears phase nature, it does not have specific, sexual and nosologic specificity, which makes it possible to consider it as the standard reaction of the system of erythron to the unspecific damage in the organism.

2. The stress-induced dynamics of the hemolytic durability of erythrocytes has the specific temporary organization on the maximum numbers it is found on the elongation of 24-48-72 hours from the moment of the action of stress factor and depends on its force.

3. Temporary organization, phase nature and nonspecificity of the stress-induced dynamics of the hemolytic durability of erythrocytes are caused by temporary organization, phase nature and nonspecificity of stress reaction itself as interactions of stress-realizing and stress-limiting systems.

4. Predominance in interaction of the adaptive systems of the stress-realizing mechanisms in the initial stages of stress reaction is accompanied by reduction in the portion of low-steadfast forms as a result of their destruction and by total increase in the stability of erythrocytes to the acidic hemolysis. Roportion to reduction in the stress-realizing activity and increase in stress-limiting, occurs the recovery of acidic erythrograms to the original values.

5. With the complicated course of postagressive period, independent of its nature, occurs the delay of a decrease or an increase in the hemolytic durability of erythrocytes. The favorable course of postagressive period is accompanied only by daily shift (absence of a decrease) in the dynamics ARE. The unfavorable course of postagressive period, connected with the progression of basic pathologic process or complication, is characterized by a steady increase in the time of acidic hemolysis.

6. The coronarogenic stress is accompanied by strengthening the degree of the coupling of interaction between different systems of organism, which is manifested by the increase in the correlative connections between the acidic durability of erythrocytes and by other indices, in this case the positive correlation of the dynamics of the parameter is noted for the indices of the work of the stress-realizing system, and negative – for the indices of the stress-limiting system.

The carried out experimental and clinical experiments, and also the data analysis of literature, make it possible to as follows describe the conceptual model of changes ARE with the acute stress.

The action of stress factor leads to the activation of sympathoadrenal system and the ejection of catecholamines with the cerebral substance of the adrenal glands. Catecholamines strengthen free-radical processes, which leads to the damage of the membranes erythrocytes, and this is accompanied by the lysis of least resistance cells. In the remained cells the activity of antioxidant systems rises, and hypercatecholaminemia it is changed by hypercortisonemia, that renders the membranostabilistive action. Under the action of the hormones of stress is strengthened the lipolysis, which leads to the increase in the blood of the level of cholesterol and LPL, thanks to which in the membrane erythrocytes changes the spectrum of phospholipids – begin to predominate the difficultly oxidizable forms (sphingomyelins and cholinephosphatides), due to the cholesterol entering from the plasma of the blood of surplus. Catecholamines cause the generalisative vascular spasm, including and the arteries of kidneys. This leads to ischemia of nephritic tissue and strengthening of the formation of erythropoietin, which possesses the membranostabilisative activity. Under the action of the high concentrations of erythropoietin the erythropoiesis considerably is strengthened, and the younger cells of an erythroid number, which possess higher resistance, begin to enter into the blood. Furthermore, under the action of all these neurohumoral reactions is included the stress-erythropoiesis, result of which is the formation of the stress-erythrocytes, which have smaller sizes and deformability, but possessing anomalously high resistance. With the positive dynamics of stress the activity of the stress-realizing system is gradually decreased, but grows the activity of the stress-limiting system, that also leads to the opposite neurohumoral and metabolic shifts, which are correspondingly reflected in the dynamics ARE (it is lowered).

Thus, to the standard mechanisms of increase ARE with any stress can be attributed following: 1) destruction least resistance erythrocytes as a result of strengthening of the peroxide oxidation of the lipids of their membranes; 2) the output of the less ripe and in-

tact forms from the depot; 3) change in the relationship of different fractions of lipids, proteins, polysaccharides of the membranes erythrocytes, which leads to modulation of the activity of ferments and their complexes, fixed in the membrane or connected with it, and also to a change in its physical chemistry properties; 4) an increase in the antioxidant activity and stability erythrocytes (influence of its own and plasma factors, erythropoietin, glucocorticoids); 5) the stress-stimulation of erythropoiesis with the formation of the stress-erythrocytes, which possess anomalously high resistance. The mechanisms of a decrease ARE with the stress are, apparently, connected with the oppositely directed processes.

The work was submitted to international scientific conference «Prospects for the development of university science», (Sochi), September 22-25, 2010, came to the editorial office on 01.07.2010.