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STRUCTURAL COMPONENTS OF AUTONOMIC INNERVATION OF MUCOSA OF NASAL CAVITY AND PARANASAL SINUSES

Abstract. *Autonomic innervation of mucosa of the nasal cavity and paranasal sinuses has been studied using complex morphological methods. It was determined that autonomic innervation of the nasal cavity and paranasal sinuses mostly occurs due to the branches of the pterygopalatine ganglion*

Keywords: *nasal cavity, paranasal sinuses, innervation, pterygopalatine ganglion, mucosa, anatomy.*

Introduction. Mucosa of nasal cavity is functionally large receptor surface with a very complex and various reflex connections. It is equipped with lots of blood and lymphatic vessels, which are surrounded with numerous nerve endings. The main factor in the regulation of trophic of the nasal cavity and paranasal sinuses is their autonomic innervation, consisted of trophic (sympathetic) and secretory (parasympathetic) fibers [1, 2].

The autonomic innervation of the nasal cavity is closely linked with the olfactory. Olfactory analyzer is one of the phylogenetically oldest body systems and is the leading analyzer for most mammals. Sense of smell in the human is not as highly developed as in certain animals, but the cerebral mechanisms of smell are closely linked to fundamental mechanisms of formation of needs, motivations and emotions [3, 4]. The peripheral element of olfactory analyzer consists of highly specialized epithelium of the upper nasal passage, short dendrites, which ends with receptors, and

axons form olfactory filaments that enter the olfactory bulb where contact with other neurons [5].

Objective: to study ways of autonomic innervation of mucosa of nasal cavity and paranasal sinuses.

Materials and methods. 32 samples of nasal area of people of all ages were studied by complex of the following morphological methods: histological method, preparation, radiological and morphometric methods. The samples were obtained from corpses of people who died from causes unrelated to the ENT disorders. The study was performed in strict accordance with the Helsinki Declaration of the World Medical Association "Ethical Principles for Medical Research Involving Human Subjects" (1964-2000). The study of the nasal area was carried out in Chernivtsi regional forensic medical bureau and M.G. Turkevych department of human anatomy of SHEI of Ukraine "Bukovinian State Medical University". The side walls of the nose and

formations adjacent to them were dissected consistently with surgical instruments, starting from their posterior. The sphenopalatine foramen and pterygopalatine ganglion were determined, the nerve branches were dissected, and their path and the one of branches that branching from them were traced. Further back nasal branches of pterygopalatine ganglion were studied. The levels of their discharge and syntopy were revealed. Similar studies were carried out on frontal and horizontal autopsy of samples. From some samples the mucosa was dissected for histological study.

Results and discussion. The interest in the detailed study of the autonomic innervation of the mucosa of the nasal cavity and paranasal sinuses increased since the appearance of vidian neurectomy. It is known that the source of parasympathetic innervation of the mucosa of the nasal cavity and paranasal sinuses is a superior salivary nucleus, which belongs to the intermediate nerve, inherent in the reticular formation of pons [6].

Intermediate nerve is closely linked in its course with facial nerve, they go around the back edge of the pons, between the pedunculi cerebellares medii and lower oliva cerebelli. Then it enters the inner ear and deeply in it enters the channel of the facial nerve deep in the temporal bone. In the place where the channel changes its direction from the front side to the back some of parasympathetic fibers – the greater petrosal nerve leaves the channel and falls in the same sulcus on the front surface of the pyramid of the temporal bone, goes to the torn hole and leaves the cranial cavity through it, going into the pterygoid canal. In this place the sympathetic nerve - the deep petrosal nerve – approaches to the greater petrosal nerve, forming a trunk – the nerve of pterygoid canal. The latter, entering the channel and passing it reaches the pterygopalatine ganglion, located in the pterygopalatine fossa.

Segmental centers of sympathetic innervation of the mucosa of the nasal cavity and paranasal sinuses lay in the intermediolateral nucleus of the lateral horns of the gray matter of the upper thoracic spinal cord segments. The axons of the nucleus cells go out of the spinal cord as a part of the anterior roots. Departing from the latter, they

form white connecting branches which approach the sympathetic trunk, namely the lower cervical ganglion or the stellate ganglion, the lower cervical and first thoracic ganglions are often connected forming the stellate ganglion. The preganglionic fibers rise by the sympathetic trunk and reach the upper cervical sympathetic ganglion and break up there. The postganglionic fibers that starting from the upper cervical ganglion – the internal carotid nerve, form the internal carotid plexus around the internal carotid artery, from which at the torn hole the branch – the deep petrosal nerve take the start. It should be emphasized that the greater petrosal nerve fibers are preganglionic and the deep petrosal nerve fibers are postganglionic. From this it follows that the nerve of pterygoid canal – which is known in the literature as Vidian nerve, is composed of parasympathetic preganglionic and postganglionic sympathetic nerve fibers.

The direct nerve trunks involved in autonomic innervation of these areas are the branches of the pterygopalatine ganglion.

The postganglionic sympathetic fibers are the part of the nerve trunks. Some of the sensitive fibers of the second branch of the trigeminal nerve, which are also the part of the branches of the pterygopalatine ganglion, also go through the pterygopalatine ganglion. The mucosa of the nasal cavity and paranasal sinuses receives sympathetic innervation, in contrast to parasympathetic one, not only from the pterygopalatine node, but also from the internal carotid plexus, the fibers of which reach the nasal cavity directly with end branches of the sphenopalatine, ophthalmic and ethmoidal arteries.

There are also indications that some of the sympathetic fibers, namely the vasoconstrictors and secretory leaders, pass through the trigeminal ganglion and join its sensitive fibers going to the periphery and penetrating everywhere the latter go.

The branches of the pterygopalatine ganglion form the upper, the medial and lower groups. The upper branches or the orbitales of the pterygopalatine ganglion in most cases are connected with the ciliary ganglion and its branches, as well as participate in parasympathetic innervation of the lacrimal gland. The group of the lower branches is formed

from the large and small palatine nerves, which come directly from the pterygopalatine ganglion and enter into the pterygopalatine canal, where go to the palatine foramina and innervate the blood vessels and glands of the mucosa of the hard and soft palate at the exit of the foramina. The branches of front of these nerves – the greater palatine nerve passes the medial wall of the channel near the back end of the inferior turbinate, enter the mucosa and branch there, and in the mucosa of the middle and lower nasal passages. They are also involved in autonomic innervation of the mucosa of the maxillary sinus.

The medial group consists of the pharynx and upper posterior nasal branches. They depart from the pterygopalatine ganglion, pass through the sphenopalatine foramen and enter the nasal cavity, passing close to the bottom wall of the sphenoid sinus. They end in the mucosa of the lateral surface of the throat, and sometimes can be traced to the pharyngeal opening of auditory tube. Most of these branches go independently from the pterygopalatine ganglion in the number of 3-5, and in some cases go from the total trunk with the back upper nasal branches. Sometimes the pharyngeal branches go directly from the pterygoid canal nerve.

Conclusions: The course, distribution, plant of the autonomic nerve branches in the mucosa of the nasal cavity, features of the innervation of the paranasal sinuses, their syntopy with the adjacent structures are not studied enough. Some studies are devoted to this question, but they are limited, not general and, of course, can serve as a basis for

the development of surgery of autonomic nerves for the nasal cavity.

Prospects for further research. It is planned to study blood supply of nasal area and paranasal sinuses in different periods of human ontogenesis.

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THE DEPENDENCE OF THE CYTOKINE HOMEOSTASIS STATE ON THE CYTOTOXICITY OF H. PYLORI STRAINS IN PATIENTS WITH PEPTIC GASTRIC AND DUODENAL ULCER COMBINED WITH HYPERTENSION AND TYPE 2 DIABETES MELLITUS

Abstract. *The article demonstrates the prevalence of CagA+, VacA+ strains and their combinations in patients with peptic gastric and duodenal ulcer combined with arterial hypertension and type 2 diabetes mellitus. The changes in the state of the cytokine homeostasis have been revealed. The changes are accompanied with an increase in the IL-6, IL-12, IL-18 content and a decrease in the IL-10 content, which parameters depend on the presence of H.pylori (CagA+, VacA+) strains and their combinations.*

Key words: *gastric ulcer, IL-12, IL-10, IL-6, IL-18, diabetes mellitus 2, arterial hypertension, cytokine homeostasis.*

Introduction. The wide spread and increasing incidence of gastric and duodenal ulcer, high probability of development of severe complications, increase in mortality and disability of patients justify the urgency of search for new pathogenic mechanisms of the disease. In recent years, the numerous data appeared, which show that chronic inflammation is due not only features of the H. pylori pathogen persistence and its damaging effects on the mucosa, but also due to the development of immunodeficiency state or immunopathological aggression [1,2]. Changes in the content of IL-6, IL-10, IL-12, IL-18 is a diagnostic criterion of the frequency of relapses and the disease stage.

Objective: to study the dependence of the state of the cytokine homeostasis on the H. pylori toxic strains in patients with peptic gastric and duodenal ulcer combined with hypertension and type 2 diabetes mellitus.

Materials and methods. 71 patients were examined (33 patients with PGU and PDU (18 patients with H.pylori-associated diseases with CagA+VacA+ toxigenic strains (group1a), 15 patients with H.pylori-associated diseases with CagA+VacA-/CagA-VacA+ toxigenic strains (group 2a) and 38 patients with peptic gastric (PGU) and duodenal ulcer (PDU) combined with arterial hypertension (AH) and type 2 diabetes mellitus (DM2) (22 patients with H.pylori-associated

diseases with CagA+VacA+ toxigenic strains (group 1b), 16 patients with H.pylori-associated diseases with CagA+VacA+/CagA-VacA+ toxigenic strains (group 2b) and 20 apparently healthy people (AHP). The criteria for inclusion of the patient in the study were the following: Hp-associated peptic gastric and duodenal ulcer; AH of I and II stage, of 1st and 2nd degree; DM2 of low severity, compensated, of medium severity, and subcompensated. CagA, VacA H. pylori strains in the biopsies were determined using the PCR reagents "Khelikopol" ("Litekh", Russia). Cytokine series was determined by ELISA using the reagents IL-6, IL-10, IL-12, IL-18 (Benher MedSystems GmbH, Austria).

Results and discussion. As a result of the study of H. pylori strains it was found out that there is a presence of (SagA + VacA +) in 18 patients with PGU and PDU (54.54%) (group 1a), and a presence of (SagA + VacA- / SagA-VacA +) in 15 patients (45.45%) (group1b). In the group of patients with PGU and PDU combined with AH and DM2 the results are similar: (SagA + VacA +) is observed in 22 patients (57.89%) (group 1b), (SagA + VacA- / SagA-VacA +) is observed in 16 patients (42.11%) (group 2b). It is proved that the presence of CagA and VacA is an additional risk factor for chronic gastritis, PGU and PDU, gastric cancer in patients infected with H. pylori. The combination of VacA and SagA strains is a marker of the disease severity [3].

Evaluating the state of the cytokine homeostasis (Table 1) it was established that in patients with PGU and PDU with the presence of CagA+VacA+ *H. pylori* strains there is a significant increase in the IL-6 content in 2.3 times, in the IL-12 content - in 3.88 times, in the IL-18 content - in 2.3 times and a decrease in the IL-10 content in 1.37 times compared with the group of AHP. In groups 1b, 2a, 2b there is an increase in the IL-6 content in 5.23 times, in 8.2 times, in 9.91 times accordingly compared with the group of AHP; the IL-12 content increases in 2.13 times, in 2.95 times

and in 9.71 times in groups 1b, 2a, 2b accordingly compared with the group of AHP; the IL-18 content increases in 2.11 times, in 9.74 times and in 3.37 times in groups 1b, 2a, 2b accordingly compared with the group of AHP; and in groups 1b, 2a, 2b there is a decrease in the IL-10 content of 16.11%, in 3.4 times and in 1.92 times accordingly.

In the group of patients with PGU and PDU combined with AH and DM2 there is a statistically significant increase in the IL-6,

Table 1

The dependence of the cytokine homeostasis state in patients with peptic gastric and duodenal ulcer combined with hypertension and type 2 diabetes mellitus on the *H. pylori* toxic strains

Parameters	PGU and PDU (group 1) (n=33)		PGU and PDU combined with AH and DM2 (group 2) (n=38)		AHP (group 3) (n=20)
	CagA+ VacA+ (group 1a) (n=18)	CagA+ VacA- /CagA- VacA+ (group 1b) (n=15)	CagA+ VacA+ (group 2a) (n=2a)	CagA+ VacA- /CagA- VacA+ (group 2b) (n=16)	
IL-6	28.72±0.59 $p_1 \leq 0.001$	28.67±0.71 $p_1 \leq 0.05$	66.36±3.68 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.001$	54.31±1.35 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_4 \leq 0.05$	5.48±0.22
IL-10	1.49±0.11 $p_1 \leq 0.001$	1.78±0.11 $p_1 \leq 0.001$ $p_2 \leq 0.05$	0.6±0.6 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.05$	1.06±0.04 $p_1 \leq 0.001$ $p_2 \leq 0.05$ $p_3 \leq 0.05$ $p_4 \leq 0.05$	2.04±0.12
IL-12	6.17±0.2 $p_1 \leq 0.001$	3.39±0.33 $p_1 \leq 0.001$ $p_2 \leq 0.05$	53.89±11.02 $p_1 \leq 0.001$ $p_2 \leq 0.001$ $p_3 \leq 0.001$	16.36±3.05 $p_1 \leq 0.001$ $p_2 \leq 0.05$ $p_3 \leq 0.05$ $p_4 \leq 0.001$	1.59±0.19
IL-18	163.17±9.58 $p_1 \leq 0.05$	146.67±17.6 $p_1 \leq 0.001$	678.41±101.69 $p_1 \leq 0.001$ $p_2 \leq 0.05$ $p_3 \leq 0.05$	235±23.14 $p_1 \leq 0.001$ $p_2 \leq 0.05$ $p_3 \leq 0.05$ $p_4 \leq 0.05$	69.63±4.72

Note. p_1 – the parameters are statistically significant compared with the group of healthy persons; p_2 – the parameters are statistically significant compared with the group 1a; p_3 – the parameters are statistically significant compared with the group 1b; p_4 – the parameters are statistically significant compared with the group 2a.

IL-12 and IL-18 content and a decrease in the IL-10 content at the presence of the CagA+VacA+ strains in 1.22 times, in 3.29 times, in 2.89 times and in 1.77 times accordingly compared with the

group of patients with PGU and PDU combined with AH and DM2 at the presence of combination of CagA+VacA- / CagA-VacA+ strains.

Conclusion. 1. In patients with peptic gastric

and duodenal ulcer combined with arterial hypertension and type 2 diabetes mellitus there is a higher prevalence of strains CagA+VacA+ and the lower prevalence of combinations of strains CagA+VacA-/ CagA-VacA+.

2. The presence of CagA+VacA+ *H. pylori* strains in patients with peptic gastric and duodenal ulcer is accompanied by the violation of the state of the cytokine homeostasis (an increase in the IL-6 content ($p \geq 0.001$, $p \geq 0.05$), the IL-12 content ($p \geq 0.001$, $p \geq 0.05$), the IL-18 content ($p \geq 0.001$, $p \geq 0.05$) and a decrease in the IL-10 content ($p \geq 0.001$, $p \geq 0.05$) and combination of this pathology with arterial hypertension and type 2 diabetes mellitus complicates the course of the underlying disease, diagnostic criteria and treatment.

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THE STRUCTURE AND FORMATION OF TOPOGRAPHY OF THE VENOUS DUCT IN HUMAN PRENATAL ONTOGENESIS

Abstract. *Using a complex of morphological methods, we have studied the venous duct development in human prenatal ontogenesis. It was established that the venous duct is formed in the embryo on the fifth week of fetal development by combining intrahepatic sinusoids. Later the venous duct anastomoses with the umbilical vein and in the fetuses it becomes its final branch together with the portal sinus.*

Key words: *venous duct, umbilical vein, portal sinus, prenatal period, human fetus.*

Introduction. The anatomical location of the venous duct (VD) is strategically important because it carries oxygenated blood coming from the placenta, bypassing the liver to the fetal heart and its brain. About 30% of the oxygenated blood from the umbilical vein runs through the venous duct [1, 2].

Doppler assessment of blood flow in the VD is becoming more common in clinical obstetrics [3]. Estimation of the fetal development includes ultrasonic Doppler examination of the umbilical artery, the medial cerebral artery and the thoracic descending aorta as well as blood flow in the VD [4, 5].

According to the current views, intrauterine fetal hypoxia is the leading cause of perinatal pathology. It results in the intrauterine growth restriction. In turn, inborn errors of trophism and old prenatal hypoxia is the main background status and a cause of a child's later neurological and somatic pathology [6, 7].

Absence of the venous duct should be excluded in the fetus with unexplained megalocardia or umbilical vein dilatation, that of systemic veins or venous sinuses [8, 9].

Objective: To establish structural features and venous duct morphogenesis at different stages of the fetal development. To follow the dynamics of morphological changes in the structure of the venous duct depending on the age of the fetus through a set of modern morphological techniques.

Materials and methods. The study was conducted on 36 specimens of human embryos, pre-fetuses and fetuses. The material was taken

from obstetrical clinics of Chernivtsi. Several series of histological sections were borrowed from the museum of M.H. Turkevych Department of Human Anatomy of HSEI of Ukraine «Bukovinian State Medical University» Fetal specimens weighing more than 500 g were studied directly in the postmortem department of Chernivtsi Regional Children's Hospital.

The fetal specimens were measured first and fixed in 10-12% solution of formaldehyde for 2-3 weeks, after which they were stored in a 3-5% solution of formaldehyde.

Using several morphological methods: histological, fine dissection and corrosion we studied the formation and structure of the venous duct in human prenatal ontogenesis.

Results and discussion. During the fifth week of fetal development the right umbilical vein and the proximal part of the left umbilical vein reduce. In the body of the fetus the right umbilical vein as the vessel that goes to the liver stops functioning and all the blood from the placenta is directed to the left umbilical vein. The width of the lumen of the umbilical vein in the embryo with 6.5 mm of crown-rump length (CRL) is 250 microns.

Entering the liver, the umbilical vein branches anastomose with the hepatic sinusoids to create a new channel. The flow through these early anastomoses plays an important role in organogenesis of the venous structures and human liver segmentation.

With the increased volume of blood entering the liver, sinusoids, when combined, form a large vessel – the venous (Arantius') duct. The width of the lumen in the VD of the embryo with 6.0 mm of

CRL is 200 microns. Through this vascular channel the flow of blood coming from the umbilical vein to the liver in its bulk is carried away by the hepatic capillaries and hepatic portal veins and this way from the umbilical vein directly to the inferior vena cava.

The sizes of the pre-fetuses aged 11-12 weeks of fetal development are sufficient (54 -79.0 mm of CRL) to study their basic anatomical structures, including the VD.

The main trunk of the umbilical vein at the end of the pre-fetal period (12 week old pre-fetuses) is $6,2 \pm 0,8$ mm long, the outer diameter at the edge of the liver is $0,90 \pm 0,15$ mm and at the site of branching it is $1,70 \pm 0,25$ mm long.

After the side branching the umbilical vein divides into two end branches at the level of the transverse fissure: the VD and the portal sinus.

The VD runs in the back part of the left sagittal sulcus in the anterior-posterior direction, it is a direct continuation of the umbilical vein and flows into the inferior vena cava. On its way, it does not branch or adds vessels. The duct is conical, its narrowed end is located near the site of division of the umbilical vein. Diameter of the duct increases towards the inferior vena cava.

The VD in 12 week old pre-fetuses(CRL 67,0-79,0 mm) is $5,7 \pm 0,4$ mm long and the outer diameter near the portal end - $1,30 \pm 0,13$ mm at the caudal one- $1,70 \pm 0,12$ mm long.

The portal sinus located in the transverse fissure of the liver goes somewhat awry from the left to the right and from the top to the bottom and connects with the left partial branch of the portal vein, which forms the right 1/3 of the portal sinus, then it becomes an anastomotic vessel between the systems of umbilical and portal veins.

In the transverse fissure of the liver the portal sinus is located deeper than the partial left branch of the portal vein and the hepatic artery proper. In its course the sinus does not branch out or accept branches, it is cylindrical in shape, its diameter is somewhat larger than the diameter of the left partial branch of the portal vein.

At the end of the pre-fetal growth period the portal sinus is $2,6 \pm 0,2$ mm long, and its outer diameter is $0,77 \pm 0,03$ mm long.

In the early fetal period two venous systems are found in the liver. The first one is afferent and

consists of the umbilical and the portal veins, through which the blood accumulates from the placenta and the intestines in the liver. The second one is the efferent venous system, consisting of the hepatic veins for blood outflow from the liver parenchyma to the heart. Through the venous duct the oxygenated blood flows to the heart from the umbilical vein system, bypassing the liver.

In four-five month old fetuses (with CRL 81,0-185 mm) the umbilical vein entered the abdominal cavity in the middle of the falciform ligament in the upward direction at an angle to the liver. Through the anterior edge of the organ the vessel passes cranially through its lower surface. Later it joins the venous sinus. The venous sinus is presented as an L-shaped broad vessel, connecting the right and the left branches of the intrahepatic part of the portal vein.

In this group of fetuses the VD originates from the venous sinus, which is located at an almost right angle to the right lobe of the liver. The vessel is hourglass-shaped, does not give the branches, runs in an upward direction towards the diaphragm. The opening of the VD corresponded to that of the umbilical vein.

The VD in 6-7 month old fetuses is mainly conical in shape and is located at the back of the left sagittal fissure of the liver between its left and caudate lobes. The length of the duct in this group of fetuses ranges from 7.0 to 12.0 mm. The diameter of the vessels varies along its length: the umbilical end is narrower (from 2.0 to 3.5 mm in diameter) in the direction of the inferior vena cava the duct gets dilated (from 3.0 to 4.0 mm in diameter).

In most observations (75%) the VD is a direct continuation of the umbilical vein in 25% of them it departed from the umbilical vein at an obtuse angle. In most cases the duct entered the inferior vena cava by itself, slightly above the site of confluence of the hepatic veins, in some cases it formed a common trunk with the left hepatic vein, and it entered the inferior vena cava.

The portal sinus, one the end branches of the umbilical vein, is located in a transverse fissure of the liver, where it is connected to the left branch of the hepatic portal vein. From outside it is surrounded by a connective tissue sheath which is also common for the bifurcations of the left

branch of its own hepatic artery and the bile ducts. The portal sinus leaves the main trunk of the umbilical vein at an obtuse angle (120-140 °). Only in one observation there was no portal sinus. In this case, the main trunk of the umbilical vein connected directly to the hepatic portal vein at the level of the transverse fissure.

Conclusions. VD is formed in the embryo on the fifth week of the fetal development by combining intrahepatic sinusoids. Later the VD anastomoses with the umbilical vein and already in the fetuses it becomes its end branch combined with the portal sinus.

Prospects of further research. We are going to study the venous duct in human infants later.

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FEATURES OF THE SHIN RHEOGRAM VALUES IN VOLLEYBALL PLAYERS

Abstract. *The paper presents the features of the time, amplitude and derived values in the shin rheovasogram of young volleyball players. We found out that volleyball players have higher values of the arterial tone, time of ascending part of the rheovasogram and slow blood supply and lower values of dicrotic index, duration of the cardiac cycle and the time of the descending part of the rheovasogram compared to those in non-athletes.*

Key words. *Shin rheovasogram, volleyball players, adolescence.*

Introduction. Nowadays one of the main links in athletes' achieving a high level of skill is to maximize their adaptation, including cardiovascular system, to different exercises. The fact is that as a result of constant, intense exercise, the circulatory system undergoes some changes[1]. Diseases of the cardiovascular system has long been a main target for studying. Despite medical advances and scientific discoveries, diseases of the cardiovascular system in athletes are not fully understood and have a lot of unsolved issues. Particular attention is drawn to the early diagnosis, easy availability, high sensitivity of the examination of an athlete that provides a unified approach to the prevention of overtraining state and to a detection of early pathological changes that occur in people who are professionally involved in sports. Studying peripheral hemodynamics is required for the formation of scientific and methodological recommendations for monitoring, optimizing and maximizing circulation system in terms of training and competitive activities [2].

Rheovasography as relatively fast, affordable and non-invasive method for diagnosing peripheral circulation is very important in the implementation of the diagnosis of peripheral arteries and veins, accompanied by partial narrowing or complete obturation of blood vessels, which in turn causes some changes in blood flow to the studied areas of the body [3]. That is why in the US, Japan and most European countries rheovasography is a part of the screening recommendations on cardiovascular disease for professional athletes [4].

Objective: To establish the changes of time, amplitude and derivatives of these parameters in rheovasogram of the shin in young volleyball players.

Materials and methods. The study involved 133 young boys (from 17 to 21). The control group consisted of 74 young men who were not involved in sports and were virtually healthy at the time of the survey. The main group consisted of 59 highly qualified volleyball players (from the first adult category to the masters of sports). All the volleyball players had sports experience at least 3 years and at the time of the survey were in the preparatory period of the training cycle. Rheovasography parameters were determined by computer diagnostic complex that provides simultaneous registration of electrocardiogram, phonocardiogram, basic and differential tetrapolar rheogram and blood pressure. Assessments of quantitative parameters were conducted after the time, amplitude indicators and their derivatives by Ronkin and Ivanov technique [5]. Analysis of the results was performed using STATISTICA 5.5 (license № AXXR910A374605FA) using nonparametric methods. The reliability of the difference between the indices of quantitative values were determined using the U-Mann-Whitney test.

Results and discussion. After analyzing temporal parameters of the shin rheovasogram, we found out that volleyball players' cardiac cycle length was reliably shorter than in boys who are not involved in sports (Table. 1). The time of the rheovasogram ascending part, which is independent of heart rate and reflects the period

of full disclosure of the vessels and provides clear information on the state of the vascular wall [5], in volleyball players, in contrast, is reliably longer than that in the boys from the control group. We have found that volleyball players had two more statistically significant lower indices: the time of the descending part of the rheovasogram and rapid blood supply, and the duration of slow blood filling in them is reliably longer than in non-athletes (see Table. 1).

We found a slight increase ($p > 0.05$) of the values of base impedance in the volleyball players, which reflects the resistance of tissues, when weak electric current of high frequency passes through them. All other amplitude parameters have no reliable differences compared with non-athletes. (table 2). We found out that the dicrotic index in volleyball players was significantly lower than in the control group (Table. 3), since this figure mainly reflects the tone of the arterioles

Table 1**Features of time parameters (c) of the shin rheogram in volleyball players ($M \pm \sigma$)**

Value	Volleyball players	Control	p
Duration of the cardiac cycle	0,921 \pm 0,127	0,995 \pm 0,162	$p < 0,01$
Time of the ascending part	0,150 \pm 0,024	0,146 \pm 0,038	$p < 0,01$
Time of the descending part	0,771 \pm 0,122	0,846 \pm 0,151	$p < 0,001$
Time of the rapid blood supply	0,060 \pm 0,023	0,062 \pm 0,037	$p > 0,05$
Time of the slow blood supply	0,090 \pm 0,012	0,085 \pm 0,011	$p < 0,05$

Table 2**Features of amplitude values (Ohm) of the shin rheogram in volleyball players ($M \pm \sigma$)**

Value	volleyball players	Control	p
The base impedance	69,03 \pm 9,902	66,97 \pm 10,62	$p > 0,05$
Amplitude of the systolic wave	0,055 \pm 0,014	0,053 \pm 0,015	$p > 0,05$
Amplitude of incisure	0,018 \pm 0,007	0,020 \pm 0,010	$p > 0,05$
Diastolic wave amplitude	0,021 \pm 0,006	0,023 \pm 0,009	$p > 0,05$
Amplitude of the rapid blood supply	0,023 \pm 0,006	0,022 \pm 0,005	$p > 0,05$

Table 3**Features of performance of ratios of amplitude and time parameters in the rheogram of the shin in volleyball players ($M \pm \sigma$).**

Value	volleyball players	Control	p
Dicrotic index (%)	32,34 \pm 13,36	37,85 \pm 17,06	$p < 0,05$
Diastolic index(%)	38,43 \pm 8,350	42,66 \pm 11,28	$p > 0,05$
The average speed of rapid blood supply (Ohm/s)	0,416 \pm 0,129	0,414 \pm 0,149	$p > 0,05$
The average speed of slow blood supply (Ohm/s)	0,348 \pm 0,097	0,375 \pm 0,118	$p > 0,05$
Indicator of the tone of arteries (%)	16,07 \pm 2,880	14,45 \pm 3,404	$p < 0,001$
Indicators of the tone of large diameter arteries (%)	6,135 \pm 2,491	5,669 \pm 2,766	$p < 0,05$
Indicators of the tone of arteries of medium and small diameter (%)	9,449 \pm 1,613	8,324 \pm 2,059	$p < 0,001$
Ratio of arterial tone (%)	69,08 \pm 30,93	74,91 \pm 45,39	$p > 0,05$

and depends on the peripheral vascular resistance [6]. Its reduction can be considered as an example of rational adaptation of the cardiovascular system in volleyball players for regular physical activity. The difference between the diastolic

index values of athletes and young men who are not involved in sports, is not reliable, but we observed a slight decrease in this value in volleyball players. Average speeds of rapid and slow blood supply have no significant differences

between comparison groups. The increase in the tone of the arteries which was found in a group of volleyball players is noteworthy. Compared with the control group they had reliably higher value in the tone of arteries and arterial tone indices of large, medium and small diameters (see Table 3). Playing volleyball has a significant impact on the development of skeletal muscles of the lower extremities, as evidenced by the increase in their circle size of femur and tibia [7]. It is the development of skeletal muscles that causes the increase in vascular tone of the shin in volleyball players.

Indicators of the arterial tone affect the time values of the rheovasogram particularly on the slow blood supply, as its value is mainly due to tonic properties of the vascular wall of small and medium-sized arteries [5].

Conclusions. 1. Compared to non-athletes, volleyball players have reliably higher values of overall tone of arteries and arteries of different diameter, time of ascending part of the rheovasogram and slow blood supply.

2. The dicrotic index, duration of the cardiac cycle, time of the descending part of the rheovasogram are reliably smaller in volleyball players than in non-athletes.

Prospects for further research. The results of this study might be used when evaluating prognostic parameters of the shin rheovasogram in volleyball players to achieve their results.

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MORPHOGENESIS OF STRUCTURES IN HIP JOINT REGION DURING EMBRYONIC AND PREFETAL PERIODS OF HUMAN ONTOGENESIS

Abstract. *On 45 series of histological sections of embryos and prefetuses and 30 prefetuses the hip joint has been studied by means of the morphological methods: histological, plastic and graphic reconstruction, ordinary and fine dissection under control of microscope «Olimpus BX-2" digital camera and software packages for digital morphometry "Video Test 5.0" "Video size 5.0".*

Key words: *hip joint, embryotopography, embryo, prefetus, human.*

Introduction. The literature data on patterns of embryonic development of the hip joint are controversial [1-10]. Based on this, we consider it appropriate to conduct a comprehensive study of the characteristics and formation of structures that form the hip joint region during embryonic and prefetal periods of human ontogenesis.

Objective: to study the morphogenesis and peculiarities of topography of structures of the hip joint area during embryonic and prefetal periods of human ontogenesis, with the definition of critical periods, morphologic variants and possible development of congenital defects.

Materials and methods. The study was conducted through a set of morphological methods: making and microscopy of 45 series of consecutive histological and 20 topographoanatomic microscopic sections, macroscopy, standard and fine dissection of 30 prefetus cadavers, under control of «Olimpus BX-2" microscope, making and studying of graphic and plastic reconstruction models, stereoscopic photography, statistical digital data processing.

Results and discussion. The lower limbs buds are still absent in 4.0 mm embryos of parietal-coccygeal length (PCL). The limbs' buds in the form of short projections on the lateral aspects of the body, are noticeable in embryos of 5.0 mm PCL. Initially, these germs are formed by accumulation of mesenchymal cells coated with a single layer of epithelium. However, the latter quickly becomes multilayered. At the distal end of the limb bud, due to proliferation of the basal layer cells, this epithelium forms a bulge - "ectodermal ridge".

Lower limb of embryos with 7.0 mm PCL has the shape of an elongated ridge with a constriction at the base, without distinction between its parts. However, even at this stage a little bend, facing its bulge is laterally seen.

In 8.0 mm PCL embryos, a concentration of mesenchymal cells towards the nerve trunks in the center of extremity is clearly distinguished. Nerves have a coarse-grained structure, and their diameters are: femoral 41.5 ± 2 mcm, obturator 41.5 ± 2.1 mcm, sciatic 48.5 ± 1.7 mcm. Ectodermal ridge in limbs' buds is more clearly defined in comparison with the embryos of 7.0 mm PCL.

Lower limbs of 9.0 mm PCL embryos look like short and flat outgrowth that end as a flat "spatula" with rounded smooth edges. However, signs of the formation of the fingers are still missing. Nerve trunks grow into the buds of the lower extremities earlier than the rudiments of the muscles appear. In 9.0 mm PCL embryos the prechondral clusters of skeletogenous mesenchyme are observed.

In prefetuses of 14,0-15,0 mm PCL, lower limb is situated almost at a ventrally open right angle to the axis of the body, pressed to the body side and elongated in the anteroposterior direction. In the limb anlage we distinguish proximal and distal parts (future thigh and foot) and a slight gap occupies the middle section (future crural region). If we consider the entire length of the lower extremity is 100%, then 37% would stay for the hips, 22% for legs, 41% for the foot.

During the investigated period of ontogenesis the germs of hip bones and femur are formed of

immature prechondral tissue. Germ of iliac wing is located at an angle of $20-23^\circ$ to the horizontal plane and hangs above the acetabulum. The latter doesn't have clearly defined contours. Its diameter is 460 ± 12 mcm, maximum depth – 90 ± 10 mcm. The plane of acetabular input lies under the angle of 10° to the sagittal and 17° - to the frontal plane. The germ of femoral head has an irregular spheroid shape and is directly continues with the body of the bone. Greater trochanter and other anatomical details are not yet defined. Inclination angle is $145-150^\circ$, and the declination angle is negative ($10-15^\circ$).

The first signs of differentiation of lower extremity bud manifests as condensation of mesenchymal cells in areas of relevant bones. The germ of future hip joint for the first time determines in prefetuses 14.0 mm TKD with the appearance of contours of mesenchymal condensation of femur and hip bone. The gap between the future articular surfaces of the adjacent bones is filled with mesenchymal cells (interzone of the joint). Hip joint is on the stage of continuous joint (synarthrosis) (Fig. 1).

Hipbone germ is built with prechondral tissue in prefetuses of 16,0-19,5 mm (7 weeks). Iliac wing retains its oval shape, elongated in dorso-ventral direction. At this stage a bend in pubic and sciatic bones germs is formed, but obturator's foramen is not formed yet. Acetabulum is well defined: its diameter is 710 ± 10 mcm, its deepest part – 110 ± 5 mcm, corresponding to its posterior-superior quadrant.

In prefetuses of 19,0-20,0 mm PCL, femoral head has spheroid shape, slightly elongated in

cranio-caudal direction. Its diameter is 705 ± 5 mcm. At this time, the formation of the femoral neck and greater trochanter germ begins (Fig.2.). Cervical-diaphyseal angle is $135-145^\circ$, declinational angle is still negative and equals to -7° . The maturity level of prechondral tissue in different parts of the femur varies, most differentiated it is within the central area. In prefetuses of 19,0-20,0 mm PCL (6th week of development) in the center of the intermediate zone of the hip joint, the cavity formation starts (Fig. 3, Fig. 4). Thus we have not observed cases of fusion and degeneration of cells, described in the literature. At the 7th week, the dilution of intermediate zone of the hip joint germ continues. In the center of germ an articular fissure is seen with unclearly marked borders, its width is 27 ± 3 mcm. At this stage the formation of the femoral

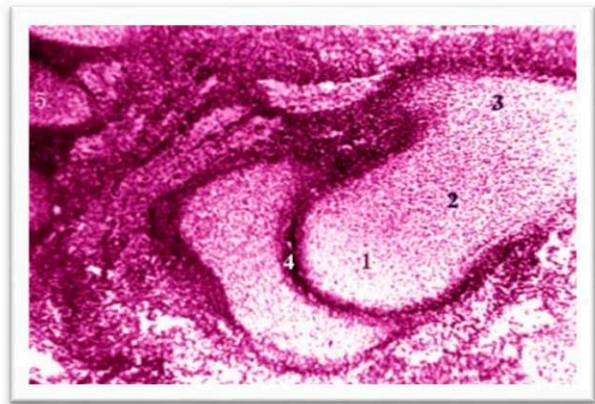


Fig.2. Frontal cut of hip joint of a prefetus of 19,0 mm PCL. Stained with hematoxylin and eosin.

Microphotography. Lens $\times 8,0$. Oc. $\times 7,0$. 1 – head of femur; 2 – neck of femur ; 3 – greater trochanter; 4 – acetabulum; 5 – lumbar vertebra.

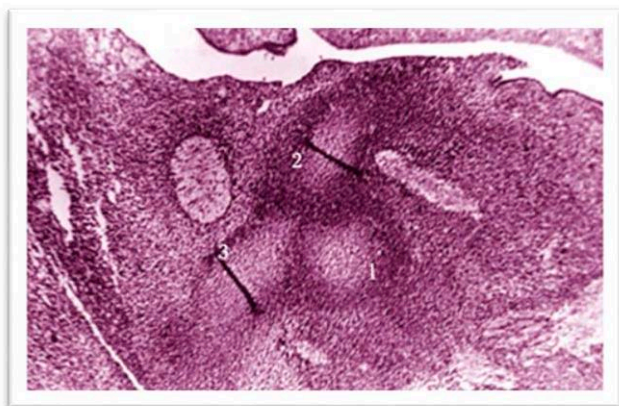


Fig.1. Sagittal cut of a prefetus of 15,0 mm PCL.

Stained with hematoxylin and eosin.

Microphotography. Lens $\times 8,0$. Oc. $\times 7,0$. 1 - head of the femur; 2 – of ilium; 3 - germ of ischium.

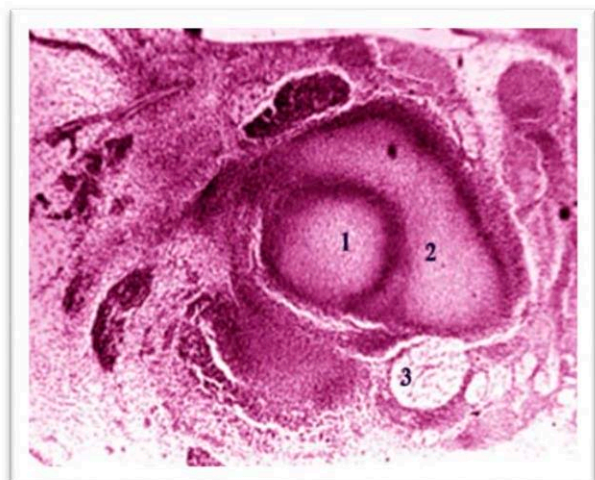


Fig. 3. Frontal cut of hip joint of a prefetus of 21,0 mm PCL. Stained with hematoxylin and eosin.

Microphotography. Lens. $\times 8,0$. Oc. $\times 7,0$. 1 – head of femur; 2 – acetabulum; 3 – sciatic nerve.



Fig. 4. Frontal cut of hip joint of a fetus of 21,0 mm PCL. Stained with hematoxylin and eosin. Microphotography. Lens. x8,0. Oc. x 7,0. 1 – head of femur; 2 – acetabulum; 3 – sciatic nerve.

head ligament is outlined. It is represented by an accumulation of intermediate zone cells, located in the center of joints germ, and has a cone shape with the base on top of the femoral head. The ligaments length is 30 ± 3 mcm, diameter of its base - 50 ± 2 mm. The germ of the capsule of the joint is seen as a thickening of mesenchymal cells, with the width of $18 \pm 1,2$ mcm, which distinguishes intermediate zone from surrounding regions.

The most intensive process of formation of the joint cavity is observed in the end of 7th and the beginning of 8th week of intrauterine development (prefetuses 23,0-27,0 mm PCL). In prefetuses with 23.0 mm PCL, the contours of articular fissure are clearly outlines are separated unclearly (Figure 5.). Articular surface of the

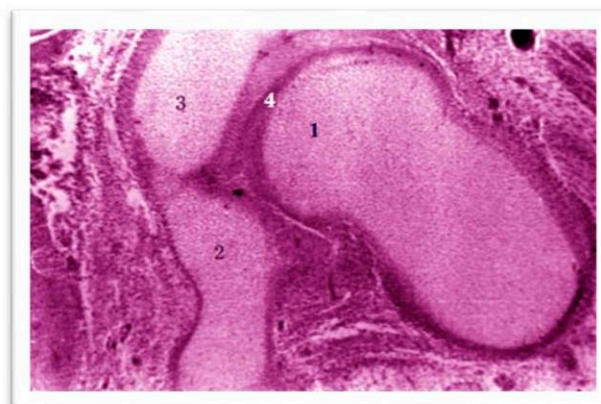


Fig.5. Frontal cut of pelvis of a fetus of 23,0 mm PCL. Van Gieson's stain. Microphotography. Lens x8,0. Oc. x 7,0. 1 – head of femur; 2 – pubic bone germ; 3 – iliac bone germ; 4 – ligament of the head of the femur.

acetabulum and the head of femur are uneven and are presented by accumulation of cells with large, round nuclei. In the lumen of the articular fissure, the cells sized from 4 to 8 mcm with round nuclei are often found. The maximum width of the joint fissure is 30 ± 2 mcm, minimum – 10-16 mcm. The germ of the ligament of femoral head occupies considerable space of the joint cavity, which is being formed. At the top of the femoral head and the base of acetabulum, the ligament is seen as an accumulation of mesenchymal cells.

In prefetuses of 23.0-27.0 mm the ligament of the head of the femur is expanded at the base of the acetabulum and the top of head of femur. Width of the base of the ligament is 120 ± 5 mcm, central part - 100 ± 7 mcm. Significant changes occur in the structure of the joint capsule. In almost all areas of the separation into two layers starts. The outer layer is more denses and consists mainly of fibroblast accumulation and collagen fibers, and the inner layer is lined with flat cells.

Conclusions. 1. On the early stages of embryogenesis the connection of bones germs, which form hip joint is continuous. In the region of the future joint a layer of undifferentiated mesenchymal cells - interzone of the joint is situated. Homogeneous interzona works as an obstacle to the extensive growth of neighboring cartilaginous elements and thus fulfills the role of mechanical blocking factor of further growth, and assists in modeling the shapes of articular surfaces. 2. In the region of the future hip joint, the thickness of mesenchymal layer between the future articular surfaces is being reduced, it becomes less dense and probably forms articular cartilage. Loosening of mesenchyme occurs due to an increase of intercellular substance, where the beginning of fibrous structures – intracapsular ligaments of the hip joint - formation is observed.

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MORPHOMETRIC PARAMETERS OF THE STRUCTURES OF THE MEDULLA OBLONGATA OF HUMAN FETUSES WITH SACROCOCCYGEAL TERATOMA AT 17-18 WEEKS OF PRENATAL DEVELOPMENT

Abstract. *The results of the study of morphometric parameters and structure of medulla oblongata in human fetuses at 17-18 weeks of prenatal development with sacrococcygeal teratoma are presented. The dimensions of nuclei of medulla oblongata, shapes and the degree of differentiation of neurons have been measured.*

Keywords: *teratoma, morphometric parameters, medulla oblongata, nuclei of medulla oblongata.*

Introduction. Teratomas are considered as tumors that develop from pluripotent cells and are represented by a wide range of tissues, which are not specific to the organ or body part [4].

The tumor is formed at the early stages of embryogenesis as a result of chromosomal abnormalities when the cells of the germ layers migrate to an area, which is atypical for normal development.

The most common teratomas in fetuses and newborns are the ones in the area of coccygeal and sacral bones. These tumors are 40% of all diagnosed tumors. Teratomas in the neck, in the ovaries or testes, in the brain, mediastinum and retroperitoneal space are less common. The incidence of sacrococcygeal teratomas (SCT) is 1 case per 40,000 births. The incidence of the tumors in girls is in 4 times higher than the one in boys [14]. In 5-26% of cases teratomas are combined with other malformations. Thus, SCT growth and its immersion between the layers of cloacal membrane can lead to the formation of anorectal malformations in the form of urinary rectal fistulas and cause division of the scrotum and hypospadias. Front location of the tumor promotes the atresia of the anal canal and rectum [10]. In addition, teratomas are combined with the spinal dysraphia, agenesis of the sacral bone, meningocele [9]. Malformations of the spine were found in 80% of 45 patients with benign SCT. In isolated cases there are malformations of the heart in the form of the interventricular septum defect and malformations of the digestive tube [6]. Structural organization of the white and gray matter of the segments of the spinal cord in

fetuses with teratoma is described in detail in the works of V.S. Shkolnikov [3].

There are no data on the structure of the brain in fetuses with sacrococcygeal teratomas in the available scientific literature. Therefore, this problem requires more in-depth and detailed study of morphometric parameters of parts and structures of the brain in fetuses with this malformation.

Objective: to study morphometric parameters of medulla oblongata in human fetuses at 17-18 weeks of prenatal development, measuring the sizes and areas of nuclei of cranial nerves and neurons forming nuclei of medulla oblongata.

Materials and methods. The anatomical and histological study of the medulla oblongata of 2 female human fetuses with sacrococcygeal teratoma at 17-18 weeks of prenatal development has been performed. The crown-rump length was $165,0 \pm 2,3$ mm, the weight was $385,8 \pm 9,4$ g (Fig. 1).

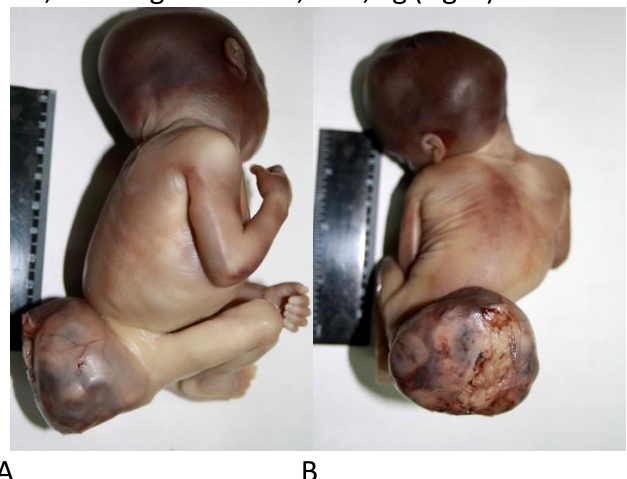


Fig. 1. General view of human fetus with the teratoma of the sacrococcygeal spine. Gestational age (GA) – 17-18 weeks. A – side view. B – back view

Material for the study was obtained as a result of late abortions in the Vinnytsya Regional Pathoanatomical Office with the following fixing in 10% neutral formalin solution. From the celloidin and paraffin blocks serial horizontal sections of the medulla oblongata of 10-15 microns thick were performed. The samples were stained with hematoxylin-eosin, toluidine blue and by van Ghisoni, also silver impregnation was performed by Bilshovskiy.

Obtained samples were studied visually using microscopes Unico G380, MBS-9, the video capture was performed by camera Trek. For morphometric study computer histometry (ToupView) was used. Digital data were processed statistically.

Materials of the study do not contravene the fundamental bioethical norms of WMA Declaration of Helsinki adopted by the 59th World Medical Association in 2008.

Results and discussion. The primary olivary nuclei have the form of winding toothed plate (Fig. 2). The area of the right primary olivary nucleus in fetuses with teratoma is $2,04 \pm 0,05 \text{ mm}^2$, of the left – $2,22 \pm 0,05 \text{ mm}^2$. Area of the right medial accessory olivary nucleus is $0,12 \pm 0,003 \text{ mm}^2$, of the left one – $0,14 \pm 0,003 \text{ mm}^2$. The area of the dorsal right accessory olivary nucleus is $0,14 \pm 0,003 \text{ mm}^2$, and of the left one – $0,16 \pm 0,003 \text{ mm}^2$.

Neurons of the inferior olive are of oval or spherical shape with homogeneous eosinophilic cytoplasm and rounded basophilic nucleus (Fig. 3A). The average values of the areas and sizes of all the olivary neurons (main, medial and dorsal) are the same and are equal to $47,8 \pm 1,7 \mu\text{m}^2$ and $8,6 \pm 0,3 \times 7,8 \pm 0,2 \mu\text{m}$ accordingly. The area of the nucleus of the neuron is $27,5 \pm 0,9 \mu\text{m}^2$ and its dimensions are $6,2 \pm 0,2 \times 5,2 \pm 0,1 \mu\text{m}$.

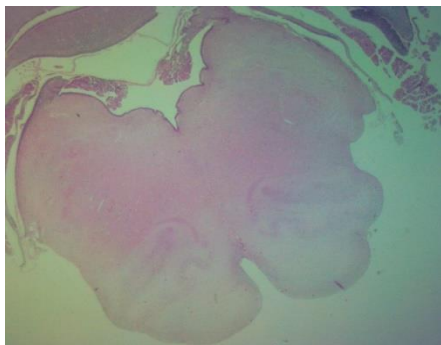


Fig. 2. The horizontal section of the medulla oblongata at the middle of the olive of the human fetus with teratoma. GA 17-18 weeks. Stained with hematoxylin-eosin. Magnification $\times 10$

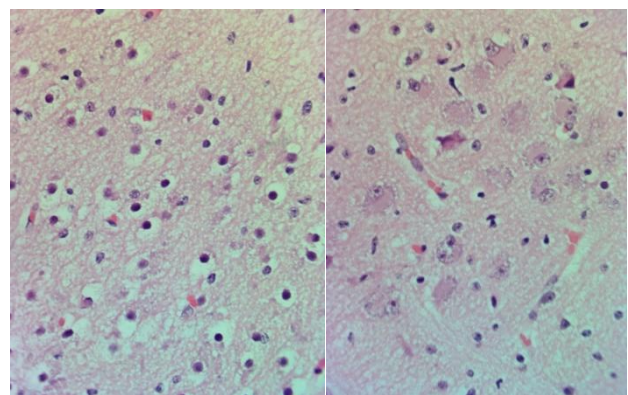
The process of differentiation of neurons during the ontogenetic development from the early stages of the prenatal ontogenesis to the definitive age is accompanied by an increase in their size, formation of axon and mediators, development of interneuron communications and other structural and functional changes [1, 5].

Studies by L.D. Starlychanova [2] performed on the brains of 32 human fetuses and the ones by B. Narasinga Rao [12] performed on the brains of 25 fetuses of different gestational age, have found that the nucleus of inferior olive in fetuses of up to 20 weeks gestation are presented by poorly differentiated neurons of rounded and oval shapes, which is reaffirmed by our research.

Dual nucleus in fetuses with teratoma is located in a typical place of the medulla oblongata, which is more dorsally from the accessory dorsal olivary nucleus, or has an irregular oval shape. Its right area is $0,06 \pm 0,002 \text{ mm}^2$, the left one is $0,04 \pm 0,001 \text{ mm}^2$.

The nerve cells of the dual nucleus have irregular oval shape (Fig. 3B). The average area of a neuron is $301,2 \pm 9,8 \mu\text{m}^2$, its dimensions are $20,2 \pm 0,6 \times 18,1 \pm 0,5 \mu\text{m}$. In the neurons of the dual nucleus the nucleus with basophilic nucleolus and heterogeneous patches of chromatin is visualized. The area of the nucleus of a neuron is $80,14 \pm 2,2 \mu\text{m}^2$ and its dimensions are $10,0 \pm 0,3 \times 9,5 \pm 0,3 \mu\text{m}$.

The nucleus of the hypoglossal nerve in fetuses with teratoma of 17-18 weeks of prenatal development is located in the medulla oblongata slightly posterior the midline at the bottom of the IV ventricle. It has no clear contours and is

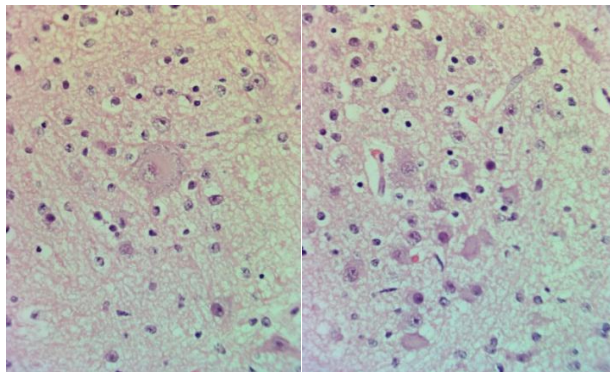


A.

B.

Fig. 3. Neurons and glial cells in human fetus with teratoma. GA 17-18 weeks. A. Cells of the olivary nucleus. B. Cells of the dual nucleus. Stained with hematoxylin-eosin. Magnification $\times 400$

presented by 2-6 neurons of various sizes (Fig. 4A). Thus, the area of a neuron is from $205.2 \mu\text{m}^2$ to $1021.4 \mu\text{m}^2$, the area of a neuron nucleus is from $30.2 \mu\text{m}^2$ to $158.2 \mu\text{m}^2$. The average area of a



A.

B.

Fig. 4. Neurons and glial cells in human fetus with teratoma. GA 17-18 weeks. A. Cells of the nucleus of the hypoglossal nerve. B. Cells of the dorsal nucleus of the vagus nerve. Stained with hematoxylin-eosin. Magnification×400

neuron is $612.7 \pm 18.1 \mu\text{m}^2$, its dimensions are $30.72 \pm 0.9 \times 25.32 \pm 0.7 \mu\text{m}$. The area of a neuron nucleus is $85.4 \pm 1.6 \mu\text{m}^2$, and its dimensions are $10.1 \pm 0.2 \times 9.3 \pm 0.2 \mu\text{m}$.

The main structural organization of the motor nuclei of the medulla oblongata is set in fetuses of 8-9 weeks of prenatal development. The cells with characteristics of mature neurons appear in the motor nuclei in 9-weeks fetuses, with the following gradual increase in their number and formation of an integral nucleus with differentiated nerve cells. The dual nucleus obtains its final organization and localization on the 12th week, and the hypoglossal nerve nucleus – on the 13th week of gestation [7, 13]. Therefore, the arrangement of the motor nuclei in the medulla oblongata in fetuses of 17-18 weeks is the same to the one in adult and the motor nuclei is presented by differentiated neurons, which also confirmed by our research. Significantly different sizes of neurons of nuclei of hypoglossal nerve in fetuses of 17-18 weeks of prenatal development are not described in the available scientific literature. Also there are no data on this fact in fetuses with sacrococcygeal teratoma.

The dorsal nucleus of the vagus nerve is located near the bottom of IV ventricle of the caudal medulla oblongata some dorsally and laterally than the nucleus of the hypoglossal nerve, and in the medial medulla oblongata it is located more

laterally than the nucleus of the hypoglossal nerve. The right and left dorsal nuclei of the vagus nerve in fetuses of 17-18 weeks teratoma have irregular oval shape and fuzzy contours, they consist of two additional nuclei (dorsal, ventral). The right area of the nucleus is $0.11 \pm 0.003 \text{ mm}^2$, and the left area is $0.07 \pm 0.003 \text{ mm}^2$. The dorsal nucleus of the vagus nerve is formed by the nerve cells that are irregular pear-shaped or oval-shaped (Fig. 4B). The average area of the neuron is $282.3 \pm 8.4 \mu\text{m}^2$, its dimensions are $18.7 \pm 0.5 \times 16.4 \pm 0.4 \mu\text{m}$. The average area of the nucleus of the neuron is $64.01 \pm 1.8 \mu\text{m}^2$, its dimensions are $9.8 \pm 0.2 \times 8.5 \pm 0.2 \mu\text{m}$.

Structural changes in the localization of dorsal nucleus of the vagus nerve starts on the 13th week. In this gestational age the nucleus is represented by two accessory nuclei. Three accessory nuclei (caudal, dorsal, ventral) are clearly visible starting from 15th week of prenatal development. Major structural changes in the dorsal nucleus of the vagus nerve are completed to the 21th week, although the morphological differentiation of neurons lasts throughout all the period of fetal development [11, 8]. In our study, the dorsal nucleus of the vagus nerve is represented by two instead of three accessory nuclei, which contradicts the results of known scientific research.

Arcuate nucleus at the intersection of pyramids is located in front of and more laterally to the pyramids, at the lower edge of the olive it is located in front of the pyramids, at the middle of the olive - in front of and more medially to the pyramids. It has a shape elongated plate. The right area of the nucleus is $0.31 \pm 0.009 \text{ mm}^2$, and the left one is $0.29 \pm 0.008 \text{ mm}^2$. The nucleus is represented by small spherical-shaped neurons (Fig. 5A). The average area of the neuron is $21.2 \pm 0.6 \mu\text{m}^2$, and its dimensions are $4.7 \pm 0.1 \times 5.2 \pm 0.1 \mu\text{m}$.

The raphe nuclei in fetuses with sacrococcygeal teratoma are located in the typical location of the medulla oblongata. The area of the nucleus raphe obscurus is $0.4 \pm 0.01 \text{ mm}^2$, the one of the nucleus raphe pallidus is $0.1 \pm 0.003 \text{ mm}^2$. These nuclei are represented by rounded-shaped neurons (Fig. 5B). The average area of the neuron is $58.3 \pm 1.7 \mu\text{m}^2$, and its dimensions are $9.2 \pm 0.2 \times 8.7 \pm 0.2 \mu\text{m}$.

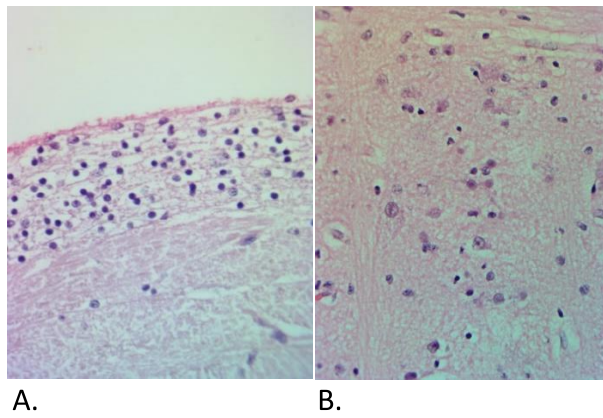


Fig. 5. Neurons and glial cells in human fetus with teratoma. GA 17-18 weeks. A. Cells of the arcuate nucleus. B. Cells of the raphe nuclei. Stained with hematoxylin-eosin. Magnification×400

Arcuate nuclei and raphe nuclei belong to the caudal serotonergic system. Serotonergic neurons appear in 5-7-week embryo. On the 7th week the neurons form two discs on both sides of the midline with the following development of the nucleus raphes obscurus. Up to 20th week of pregnancy the nuclei of the caudal serotonergic system have their typical location in the medulla oblongata. In fetuses starting from the 20th week and in newborns the number of spherical neurons decreases and the content of spindle neurons increases, also the processes of their differentiation occur [15].

The nuclei of the caudal serotonergic system in our study in fetuses of 17-18 weeks of prenatal development with sacrococcygeal teratoma are located in their typical places in the medulla oblongata and are presented by spherical undifferentiated nerve cells.

The solitary nucleus and spinal nucleus of the trigeminal nerve have not clear contours. These nucleus are presented by spherical and spindle single neurons. The average area of the neuron of the solitary nucleus is $59,7 \pm 1,5 \mu\text{m}^2$, its dimensions are $7,9 \pm 0,1 \times 7,3 \pm 0,1 \mu\text{m}$. The area of the nucleus of the neuron is $21,1 \pm 0,6 \mu\text{m}^2$, its dimensions are $5,1 \pm 0,1 \times 4,2 \pm 0,1 \mu\text{m}$. The average area of the neuron of the spinal nucleus is $86,2 \pm 2,2 \mu\text{m}^2$, its dimensions are $10,1 \pm 0,2 \times 8,7 \pm 0,2 \mu\text{m}$.

The solitary nucleus and spinal nucleus of the trigeminal nerve start to form on the 13th week of the prenatal development. Major structural changes and increase in the number of nerve cells in the nucleus of solitary tract occur from 21st to

25th weeks of gestation. [7] In our study the solitary nucleus has no clear contours and is presented by poorly differentiated neurons.

The neuroepithelial layer is formed by the neural stem cells (NSC) of spherical and ellipsoidal shape, which are located on the basal membrane (Fig. 6). The average area and dimensions of NSC of ellipsoidal shape are equal to $41,5 \pm 1,6 \mu\text{m}^2$ and $10,7 \pm 0,4 \times 5,1 \pm 0,1 \mu\text{m}$ accordingly. The average area and dimensions of NSC of spherical shape are equal to $32,6 \pm 1,1 \mu\text{m}^2$ and $7,3 \pm 0,2 \times 6,7 \pm 0,3 \mu\text{m}$ accordingly.

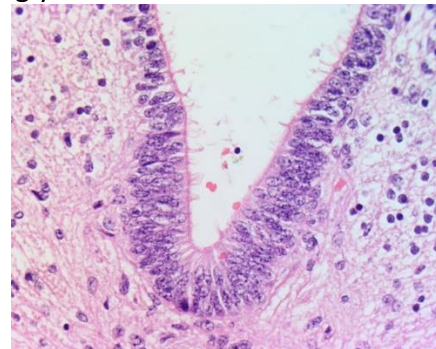


Fig. 6. NSC of the neuroepithelial layer in human fetus with teratoma. GA 17-18 weeks. Stained with hematoxylin-eosin. Magnification×400

The density of NSC in the ventral neuroepithelium is considerably larger than the one in the lateral and dorsal parts. In addition, the highest frequency of ellipsoidal NSC is in the ventral part, and the highest frequency of spherical NSC is in the lateral and dorsal parts. The thickness of the neuroepithelium in the ventral, lateral and dorsal parts is nearly the same and in average is equal to $39,7 \pm 2,1 \mu\text{m}$.

Conclusions. 1. In the samples of the medulla oblongata of human fetuses at 17-18 weeks of prenatal development with sacrococcygeal teratoma all the neural systems are clearly visualized and identified.

2. The group of motor neurons has the largest area. There are heterogeneous by size neurons in the neural systems that form the nucleus of hypoglossal nerve.

3. The dorsal nucleus of the vagus nerve is represented by two accessory nuclei which is not typical for this gestational age.

4. The neuron systems forming the inferior olive, sensitive nuclei of cranial nerves and nuclei of serotonergic system of medulla oblongata are presented by poorly differentiated neurons.

5. The highest density of neural stem cells is in the ventral part of the neuroepithelium. It was established that the ventral neural epithelium is

mainly represented by ellipsoidal NSC, and the lateral and dorsal ones – by NSC spherical.

Perspectives of further investigations. In prospect it is planned to determine the topography of neurons and glia cells of the medulla oblongata in fetuses with teratoma by expression of immuno-histochemical markers and to compare the results with those in fetuses without malformations.

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STRUCTURAL ORGANIZATION OF BLADDER MUCOSA IN WOMEN WITH EARLY AND LATE MENOPAUSE WITH OVERACTIVE BLADDER SYNDROME

Abstract. *The article describes the results of histological study of structural components of bladder mucosa in women with menopause. The morphological changes in the bladder mucosa in 48 women with different menopause have been studied. It has been revealed that in group of women with "early menopausal bladder" inflammatory and degenerative changes, combined with hemodynamic disorders prevail. In mucosal biopsies of women with late menopause degenerative, metaplastic and sclerotic manifestations prevail.*

Key words: *mucosa, bladder, menopause, overactive bladder*

Introduction. According to the World Assembly on Ageing, the percentage of older women is higher than the percentage of older men, and in older age groups this trend is even clearer. The implementation of measures aimed at improving the health of older women should be a priority strategy area in all countries [1, 7, 8].

In recent years problems associated with urogenital aging begun to prevail in the symptomatology of menopausal disorders, due to their pronounced negative effect on quality of life in a postmenopausal woman. Diagnosis of imperative urinary incontinence, which is typical for overactive bladder is the greatest and not fully studied problem in this aspect. The latter is found in 50-60% of patients. It is proved that incidence of urinary incontinence in postmenopausal women increases by 30% for every 5 years [1-4].

Despite the significant amount of studies many key aspects of morphogenesis and pathogenesis of the disease, which are associated with regional microcirculation features and the nature of cellular and intracellular changes in the bladder mucosa, are still unclear [6]. This prevents the formation of a rational strategy for therapeutic measures [5]. The removal of structural and functional abnormalities that promote development of pathological process may be one of its main areas.

Objective: to study the structural changes, dynamics and degree of their severity in the bladder mucosa of women with various menopause.

Materials and methods. In order to study morphological features of menopausal bladder

the biopsy of its wall mucosa in 48 women aged 35-74 years was performed. The women were divided into groups due to the common classification of menopause: 45-51 years - premenopause, 51-52 years - menopause, over 52 years - postmenopause.

Thus, the women with premenopause and menopause were in the group of patients with early menopause of 20 people. 28 patients (over 52 years) were in group with late menopause. The control group consisted of 14 women of reproductive age (35-42 years). The criteria for the inclusion in the study were the following: female gender, age over 35 years, informed consent of the patient.

The bladder examination was carried out with cystoscope Richard Wolf with tube 19,5F and telescope with refraction angle of 30° and 70°. The biopsy sampling was performed with a stiff bent spoon biopsy forceps from the left side wall and triangle. In order to detect the overall structure of histopathological changes and topographical relationships between the stroma and parenchyma, and elements of ICR, the histological sections were stained with hematoxylin and eosin by the Van Gieson's method.

The histological samples required for demonstration were photographed. The image on the computer screen was taken out of the microscope Olympus CX22 using the camcorder VISION Color CCD Camera and software Inter Video Win DVR.

Results and discussions. The characteristic features, which are constantly met in all cases, are

hyperemia of venules and veins, stasis of erythrocytes in precapillaries, hemorrhagic impregnation, thrombosis of small veins, inflammatory infiltration preferentially localized in the lamina propria of the mucosa, inflammatory, degenerative and hyperplastic changes of epithelium.

Mucosa of women in the control group have a normal structure and consists of the transitional epithelium and own layer formed by fibrous unformed connective tissue.

Histological changes of the mucosal epithelium in studied group 1 in different areas of the bladder are different. In 7 cases (35%) structural organization of the mucosa structure differs little from the structure of normal mucosa.

The difference is in hemocirculatory disorders accompanied by edema and lymphohistiocytic infiltration of varying intensity. The areas of the surface epithelial desquamation are detected rarely.

In most cases transitional epithelium is sharply thinned to the formation of a single layer of flattened cells or the desquamated on the surface layer with small or deep erosion, which is more often.

Lamina propria of the mucosa is thickened due to the edema, there is a lymphohistiocytic inflammatory infiltrate of varying intensity with impurities of plasma cells, neutrophilic and eosinophilic leukocytes and fibroblasts, with inflammation spreading to the epithelium and submucosa.

Quite often there are focal and diffuse hemorrhage. There is an edema of the lamina propria and submucosa. The microcirculation have the following changes: spasm of the arterioles and the venous dilatation with signs of hemodynamic - stasis, sludge and parietal aggregation of the erythrocytes.

In 5 cases there are areas of squamous metaplasia. In biopsies taken from the nearby cells of squamous metaplasia, there is an urothelium with proliferative changes in the form of simple hyperplasia with increased number of layers in the transitional epithelium, with areas of the urothelium invagination in the lamina propria of the mucosa (Brunn's nests) or separated from the epithelial layer urothelium as a groups of cells located within the lamina propria of the mucosa (Fig. 1). In 2 cases there is a glandular metaplasia – the transitional epithelium is substituted by the prismatic epithelium with formation of glands.

These changes are accompanied by the distinct inflammatory cell infiltration, which is localized not only in the lamina propria, but is also extended to the submucosa and penetrated into the epithelial layer. These changes are combined with the proliferation of the collagen fibers in the lamina propria.

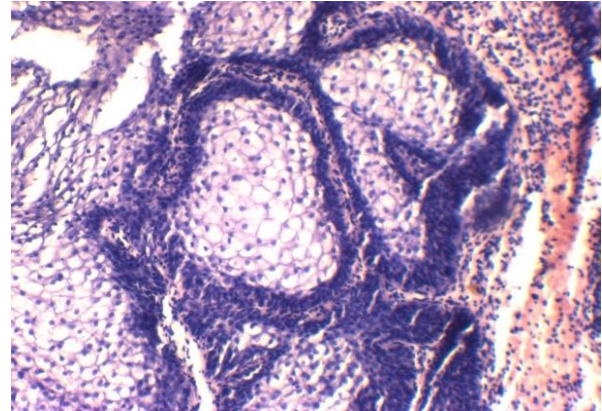


Fig. 1. Squamous metaplasia of the urothelium with the formation of Brunn's nests. Stained with hematoxylin and eosin. × 200

In one case in a patient with a long history of dysuric disorders there are histological characteristics, which are typical for leukoplakia, that is parakeratosis, acanthosis and squamous metaplasia.

In biopsies of the bladder mucosa in the women of the studied group 2 - with late menopause - there are similar structural changes, which are typical for all cases. However, the frequency of these changes is another. Minimal changes of the structure of the mucosa compared with the intact one are just in 3 cases (10.7%).

Along with the changes described above, there are degenerative changes in the cells in all layers of the transition epithelium, preferably in the form of balloon degeneration. The frequency of destructive changes of the epithelial cover increases. In some cases there are the cell necrobiosis and necrosis of the urothelium cells. Expressed microcirculatory disorders are observed with the prevailed hyperemia of the varicose veins. Arterioles have thick walls that visually reduces their lumens. Quite often there are hemorrhages of varying length.

In 9 cases (32.1%) the signs of squamous metaplasia are detected. At the simplest form of leukoplakia in the women with the disease duration up to 2 years the acanthotic bands are uniform and located in one direction. In this case the parakeratosis centers on the epithelium surface are represented by several rows of keratinized cells located in the form of a dense plate.

At verrucous leukoplakia (history of 3-6 years) the Malpighian layer has a considerable thickness. Epithelial bands of varying thickness and length are located in different directions. Parakeratotic epithelial cells form thickenings of various shapes, towering above the epithelial lining.

In all the studied cases there is an increased formation of collagen both in the lamina propria of the mucosa and in the underlying tissues. It should be noted that quantitative changes depends directly on the duration of the disease.

In 5 study cases (17.8%) of leukoplakia morphological changes in the bladder mucosa, which are characteristic for squamous metaplasia with leukokeratosis, have been revealed. All the changes are focal and characterized by mainly hyperplastic processes in the transitional epithelium. Actually the hyperplastic changes of the urothelium are manifested in the form of simple hyperplasia with increased number of the cell layers, invagination of the transitional epithelium in the lamina propria of the mucosa, formation of the Brunn's nests, cystic or glandular transformation (Figure 2).

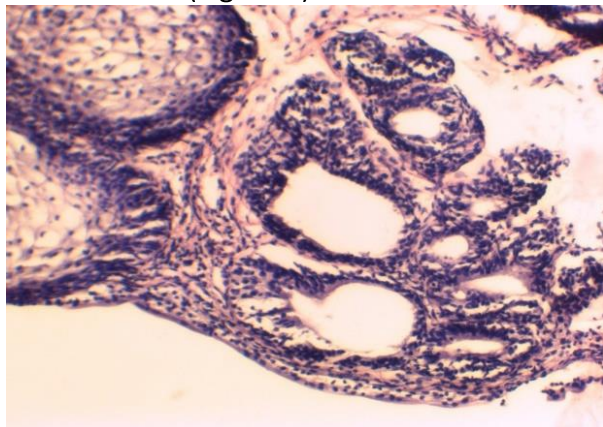


Fig. 2. Glandular and cystic transformation of the urothelium in a patient with leukoplakia of the transitional epithelium. Stained with hematoxylin and eosin. $\times 200$

Conclusions. Histological study of biopsies of bladder mucosa has revealed the full range of its structural changes. It should be emphasized that while the heterogeneity of histology in each case, these changes are generally stereotyped and vary by frequency of their detection and depth of

destruction. In women with "early menopausal bladder" inflammatory and degenerative changes, combined with hemodynamic disorders prevail. In mucosal biopsies of late menopausal women degenerative, metaplastic and sclerotic manifestations prevail.

Outlooks are the study of changes in the structural components of the bladder wall in women with early and late menopause at the submicroscopic level.

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EFFECTIVENESS OF CORRECTION OF METABOLIC DISORDERS WITHIN MYOCARDIUM TISSUE OF RATS WITH HYPOTHYROIDISM ON THE BACKGROUND OF COMBINED IODINE AND COPPER DEFICIT

Abstract. *In experiments on rats with hypothyroidism on the background of combined iodine and copper deficit (HTG_{I+Cu}) the changes of oxygen dependent processes and activity of NO-synthases in myocardium were studied and effectiveness of correction of found changes by microelements, antioxidants and donators of nitric oxide (NO) was ascertained. It was found that HTG_{I+Cu} lead to excessive peroxidation and enhancement of NO-synthases activity (mainly by inducible – iNOS) in myocardial tissue to analogical indexes in animals with isolated iodine deficit. The introduction of Potassium iodide to experimental animals stabilizes the passing of metabolic processes. The carrying out complex correction by microelements, antioxidants and donators of NO is accompanied by more significant positive therapeutic dynamics.*

Key words: *hypothyroidism, iodine deficit, copper deficit, peroxide processes, NO-synthases, correction of metabolic disorders.*

Introduction. One of the leading nexus of disorders of heart operant behavior is deemed to be changes of metabolic processes in it, first of all – activation of peroxide destruction of proteins and lipids on the background of hypoactivity of antioxidant defense system of organism [8]. Disorder of pro-antioxidant homeostasis is possible upon conditions of hypothyroidism (HTG). It is common that combined deficit of microelements, in particular of iodine and copper, is capable to potentiate the influence of actual factors on an organism. Wherein deceleration of copper content in myocardium may be negatively reflected on energy metabolism of heart and acted as risk factor of progression of cardiological pathology [1]. Nitric oxide (NO) may decelerate the reaction behavior of peroxidation. Such a peculiar anti-oxidative effect of NO may be biologically important way of detoxication of potentially dangerous reactive oxygen intermediates [19]. Taking into consideration the role of NO in neurohumoral regulation of physiological functions of cardiovascular system, figuring out of changes of indices of NO-synthases system upon conditions of microelementosis is of some interest.

Objective: to assess the history of oxygen dependent reactions and activity of NO-synthases in myocardium of rats with HTG on the background of combined iodine and copper deficit

and to figure out effectiveness of correction of detected changes caused by microelements, antioxidants and donators of NO.

Materials and methods. Researches were carried out on more than 180 white non-pedigree male rats of about 150-180 g. weight each. Animals were allocated on five experimental groups: rats with HTG on the background of iodine deficit (HTG I, 1st group, 30 animals), rats with HTG on the background of combined iodine and copper deficit (HTG_{I+Cu}, 2nd group, 30 animals), upon conditions of HTG_{I+Cu} correction by: potassium iodide (3rd group, 30 animals), potassium iodide and copper sulfate (4th group, 30 animals), potassium iodide, copper sulfate, α -tocopherol acetate and L-arginine hydrochloride (5th group, 30 animals). Reference group consisted of 30 intact rats. Animals from experimental groups were being on iodine deficiency diet [15] during 45 days. Copper deficit was modeled by addition of chelate of D-penicillamine (cuprenil, „Polfa” Kutno Pharmaceutical Company, Poland, 100mg/100g of body weight) to the drinking water from 25 to 45 day of research [14]. HTG_{I+Cu} correction was being carried out by potassium iodide (iodide-100, Nycomed Merck KGaA, Denmark, 50 mcg of iodide preorally daily during 30 days) [2], copper sulfate (0,09 mg/100g of body weight preorally daily during 30 days) [5]. α -tocopherol acetate was

utilized as anti-oxidant (Kyiv Vitamin Factory, Ukraine, 20mg/kg of body weight preorally daily during 30 days) [12]. Donator of NO L-arginine hydrochloride (tivortin-aspartate, "Yuria-Pharm", Ukraine, 2.5g/day) was provided for the animals preorally daily during last 21 days of research [10]. Keeping, feeding and euthanasia of rats were being complied with regulations of current international requirements regarding humane treatment of animals.

Content of products of protein peroxidation (PP) and lipid peroxidation (LP) was being determined within homogenate of myocardium. The level of oxidative protein modifications (OPM) was being detected resting on the quantity of their products via spectrophotometry when longitude of wave (356, 370, 430, 530) nm [6]. The state of LP was being assessed resting on accumulation of diethenoid conjugates (DC) of polyunsaturated fatty acids [3] and active products that respond to thiobarbituric acid – TBA-AP [7]. For characterization of NO synthesis system within myocardium homogenate NO-synthases activity was being determined: neuronal (nNOS), inducible (iNOS), constitutive (cNOS) [11].

Statistical processing of results was being carried out resting on statistical software package Statistica 7.0.

Results and discussion. Research outcomes showed (see table), that progression of $\text{HTG}_{\text{I}+\text{Cu}}$ caused activation of processes of peroxidation of proteins and lipids. Thus within myocardium of 2nd experimental group of animals the increase of OPM was detected (E_{430} - 2,6 times, $p<0,001$), content of DC – by 48,2% ($p<0,02$) to data of intact animals. Amplifying of PP and LP processes may act as risk factor of ischemic heart injury. It ought to be emphasized that the level of E_{430} OPM in animals with combined microelementosis was 2,2 times ($p<0,001$) higher than in animals with HTG_{I} . Because of OPM products are more stable than metabolites of lipid peroxidation, the level of protein destruction may act as marker of oxidative damages of myocardium when HTG. Upon such conditions NOS activity increased by 25,5% ($p_{1-2}<0,001$) to the analogical indice of animals from the 1st experimental group, generally by means of iNOS, which activity increased by 51,8% ($p_{1-2}<0,05$) to the analogical indices in animals with HTG_{I} . It is noteworthy that increase of expression and activity of exactly iNOS appears due to myocardial infraction, hypertension, angor pectoris, cardiomyopathy, cardiac distress and

other pathological processes [4].

Conducting of correction of microelement imbalance caused inhibition of peroxidation processes within the tissue of myocardium (see table). Thus introducing of potassium iodide into animals caused to decrease of peroxide destruction of proteins predominantly, that characterized decrease of content of OPM products of $E_{356, 370, 430}$ fractions by 92,0-94,9% ($p_{2-3}<0,001$), and also of TBA-AP – by 68,6% ($p_{2-3}<0,001$) to the analogical indices in animals before correction. Increase of cNOS activity by 91,5% ($p_{2-3}<0,001$) to data of animals from the 2nd experimental group attracts attention. Wherein protecting abilities of NO (vasodilation, inhibition of aggregation processes, opening of $\text{K}^+(\text{ATF})$ -channels, control of coronary circulation and heart beats) [9] are connected with cNOS.

In animals from the 4th experimental group was being observed predominant decrease of PP content (level of $E_{356-430}$ fractions decreased by 65,1-79,5 %, $p_{2-4}<0,001$) and LP (DC content decreased by 56,0 %, $p_{2-4}<0,001$) to the analogical indices in animals from the 2nd experimental group (see table). In animals was detected the decrease of activity of iNOS by 45,7 % ($p_{2-4}<0,01$) on the background of increase of NOS activity by 37,1 % ($p_{2-4}<0,01$) and cNOS activity – by 2,8 times ($p_{2-4}<0,01$) to the analogical indices in animals with microelementosis. Dynamics of such the changes shows the weakening of absolute risk of accompanying heart pathology development upon conditions of correction of thyroid homeostasis by microelements.

Carrying out of complex correction caused more evident changes of processes of free-radical oxidation of proteins and lipids within the myocardium tissue. Thus, level of OPM $E_{356, E_{370}}$ and E_{430} fractions in myocardium decreased by 59,0-82,6 % ($p_{2-5}<0,01$), content of DC and TBA-AP – by 85,0% and 73,4% ($p_{2-5}<0,001$) respectively to the analogical data in animals from the 2nd experimental group. Upon such conditions cNOS activity in rats from the 5th experimental group was less by 51,8 % ($p_{3-5}<0,01$) to the analogical data in rats with $\text{HTG}_{\text{I}+\text{Cu}}$ that were receiving potassium iodide.

Conclusions. Progression of $\text{HTG}_{\text{I}+\text{Cu}}$ is accompanied by activation of PP, LP processes within myocardium on the background of increase of NOS activity, generally by means of iNOS. Conducting of correction of detected changes by the potassium iodide caused to inhibition of free-radical processes on the background of particular increase of activity of protector cNOS.

Table
Indices of peroxidation of proteins and lipids, NO-synthases activity in myocardium of rats with hypothyroidism on the background of iodine deficit, combined iodine and copper deficit and upon conditions of correction by potassium iodide, copper sulfate, α -tocopherol acetate and L-arginine hydrochloride.

Indices	Reference group (n=30)	1 st experimental group (animals with iodine monodeficit, n=30)	2 nd experimental group (animals with combined iodine and copper deficit, n=30)	3 rd experimental group (correction of microelementosis by potassium iodide, n=30)	4 th experimental group (correction of microelementosis by potassium iodide and copper sulfate, n=30)	5 th experimental group (correction of microelementosis by potassium iodide and copper sulfate, α -tocopherol acetate, L-arginine hydrochloride n=30)
OPM, E ₃₅₆ , c.u.	1,66±0,13	1,83±0,02	1,95±0,08	0,15 ± 0,02 ^{##} p ₂₋₃ < 0,001	0,68 ± 0,27 ^{**} p ₂₋₄ < 0,01	0,80 ± 0,31 [*] p ₂₋₅ < 0,01
OPM, E ₃₇₀ , c.u.	1,74±0,13	1,89±0,02	2,01±0,11	0,16 ± 0,01 ^{##} p ₂₋₃ < 0,001	0,57 ± 0,32 [#] p ₂₋₄ < 0,01	0,67 ± 0,42 [#] p ₂₋₅ < 0,02
OPM, E ₄₃₀ , c.u.	0,74±0,12	0,88±0,04	1,95±0,11 ^{##} p ₁₋₂ < 0,001	0,10 ± 0,01 ^{##} p ₂₋₃ < 0,001	0,40 ± 0,25 p ₂₋₄ < 0,001	0,34 ± 0,09 [#] p ₂₋₅ < 0,001 p ₃₋₅ < 0,05
OPM, E ₅₃₀ , c.u.	0,06±0,08	-	-	0,03 ± 0,008	-	-
DC, c.u./ml	1,35±0,17	1,70±0,06	2,00±0,13 ^{**}	4,75 ± 2,67	0,88 ± 0,11 [#] p ₂₋₄ < 0,001	0,30 ± 0,09 p ₂₋₅ < 0,001 p ₄₋₅ < 0,01
TBA-AP, nM/ml	3,70±0,26	3,79±0,13	3,98±0,19	1,25 ± 0,3 ^{##} p ₂₋₃ < 0,001	2,1 ± 1,16	1,78 ± 0,07 [*] p ₂₋₅ < 0,05
NOS (nM/min×mg)	16,57±1,11	13,44±0,48 [*]	16,86±0,36 p ₁₋₂ < 0,001	18,78 ± 2,94	5,73 ± 0,82 ^{**} p ₂₋₄ < 0,001 p ₃₋₄ < 0,01	15,29 ± 0,93 [#] p ₄₋₅ < 0,01
iNOS (nM/min×mg)	11,96±1,65	7,05±1,21 [*]	10,70±0,63 p ₁₋₂ < 0,05	14,74±0,56 [#]	15,87 ± 2,07 ^{**}	12,75 ± 1,74 [#]
cNOS (nM/min×mg)	4,55±0,61	5,43±0,78	4,11±0,66	11,7±0,83 ^{##} p ₂₋₃ < 0,001	17,24 ± 2,94 ^{**} p ₂₋₄ < 0,01	5,64 ± 1,07 p ₃₋₅ < 0,01 p ₄₋₅ < 0,001

Engaging to the scheme of microelement and anti-oxidative complexes contributed enhancing of therapy efficiency and more evident stabilization of pro-oxidative and anti-oxidative balance of myocardium.

Perspectives of further investigations.

Determination of microelement balance within organism with the aim of research of aetiopathogenesis of comorbide pathology on the background of HTG; finding out of opportunities of engaging of microelements, anti-oxidants and donators of NO to the scheme of treatment of metabolic abnormalities of myocardium with the aim of complex treatment and early detection of cardiological pathology upon conditions of thyroid dysfunction.

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ECOLOGICAL ANALYSIS OF THE DIVERSITY IN THE ELEMENTS OF MELANIZED PICTURE IN THE INTEGUMENT OF A RED SOLDIER BUG (PYRRHOCORIS APTERUS L.) IN THE URBANIZED ECOSYSTEM OF TERNOPIL

Abstract. *The paper analyzes the phenotypic diversity of red soldier bug larvae in the population of the urbanized ecosystem of Ternopil in terms of its role in entomo-bioindication of its ecological condition. The study was conducted by analyzing four signs of the melanized picture in the integument of a red soldier bug larvae.*

Key words: *red soldier bug, larva, entomo-bioindication, phenotypic diversity.*

Introduction. Monitoring the ecological state of the environment has a pronounced regional character and reflects the individual characteristics of the analyzed biota. Such studies help identify disturbances in ecosystems caused by the transforming influence of anthropogenic factors at early stages of their occurrence.

Actually, entomo-bioindication belongs to such research methods and it is carried out using the incidence of different phenes of melanized picture in the integument of a red soldier bug.

Objective: to study phenotype diversity of red soldier bug larvae in the population of the urbanized ecosystem of Ternopil.

Materials and methods. Population insects sampling was performed in their natural habitat. We selected the species with varying degrees of anthropogenic load. The sample consisted of 28 specimens of red soldier bug larvae.





Collection of materials included the following steps: collection of larvae by hand and their fixing in 70% ethanol solution; sorting and drying insects; registration of individuals in the diary and their description.

When registering a population sample each larva was given its own serial number. The description of specimens was performed by the method of E.P. Klymets [3] namely: examined the melanized picture on the insects' body; conducted the selection of forms that differed by one or more elements; painted these forms on the cards; systematized and made a phenotypic line of variability; revealed discrete variations (of phenes).

To study the intrapopulation diversity of groups of red soldier bugs 4 main signs are usually used: polymorphism of the picture of the pronotum "P"; polymorphism of elytra buds "A"

Table 1





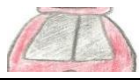








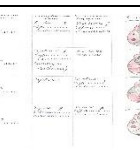
Variants of melanized picture of the red soldier bug larvae pronotum

Variants	Picture	Number	Description of the variant
P1		18	The upper and lower melanized bands are closely adjacent to each other.
P2		2	There are no melanized bands on the pronotum.
P3		5	The upper and lower melanized bands are closely adjacent to each other and are oval in shape.
P4		3	The upper and lower melanized bands are closely adjacent to each other but they are divided into two rectangular elements.

Next sign "A" in the catalogue relates to the figure of elytra of signs "B" and "C" - the picture on the insect abdomen (Table 2).

Table 2

Catalogue of variants of the melanized picture elements on the red soldier bug larvae

Variant	Number	Picture	Description of the variant
Wing shape			
A1	19		Rounded buds of wings without membrane.
A2	3		Rectangular buds of wings completely separated.
A3	2		Deformed round buds of wings.
A4	2		Buds of wings are rounded and the membrane goes along the full length
A5	1		Buds of wings are rectangular with the membrane along the full length
A6	1		Buds of wings are rounded and completely separated.
Number of spots on the abdomen			
B1	3		No spots on the abdomen.
B2	2		The abdomen has two round spots of the same shape.
B3	13		The abdomen has three round spots of the same shape.
B4	3		The abdomen has three oval spots.
B5	6		The abdomen has four round spots.
B6	1		The abdomen has four oval spots increasing in size gradually.
Striae on the body			
C1	25		No striae on the body.
C2	3		The abdomen is striated with approximately even lines.

and the figure (the number, shape of spots and striae) on the dorsal side of the red soldier bug abdomen "B", "C" [1].

It should be noted that in the phenetical analysis of the bilateral signs presented on the left and right side of the body (for red soldier bug it is the element "A"), we followed the rule: one sign – two phenes.

During the processing of the collected material we made up a catalogue of signs for regional fauna

of red soldier bug larvae (Table 1, 2). Mathematical processing of the material that characterizes the phenetical population structure was performed by the Zhyvotovskyi L.A. technique [2]. The paper analyzed the incidence of the phene (P_m), studied the intrapopulation diversity of the phenes (μ) for each sign. To determine the reliability of the obtained findings, we calculated the error of the phenotype diversity (S_μ). We also found the ratio of scanty phenes for each sign (h).

Results and discussion. The results of phenetical analysis of red soldier bug urbanized populations in the urbanized ecosystem of Ternopil showed the presence of four elements of melanized picture on the integument of insect larvae. The largest number of phenes (6) was found in the "A" elements (shape of wings) and "B" (the number of spots on the abdomen). Somewhat fewer morphs were observed for sign "P" (picture of the pronotum) - 4 phenes, and the smallest number of species (2 phenes) is characteristic for sign "C" (Table 3).

Table 3

Phenetical analysis of the red soldier bug population by some signs

Sign	N	m	$\mu \pm S_{\mu}$	$h \pm S_h$
P	28	4	$3,312 \pm 0,285$	$0,142 \pm 0,071$
A	56	6	$2,217 \pm 0,387$	$0,63 \pm 0,063$
B	28	6	$4,999 \pm 0,423$	$0,139 \pm 0,063$
C	28	2	$1,623 \pm 0,148$	$0,153 \pm 0,071$

The highest values of intrapopulation phenetical diversity is characteristic for signs "B" ($\mu = 4,999$) and "P" ($\mu = 3,312$), the element "A" is the second with the value of the intrapopulation diversity ($\mu = 2,217$), while the element "C" is characterized by the lowest value of this sign ($\mu = 1,623$). The differences are reliable, as the reliability index (t) ranges from 2,3 to 4,62, $0,1 < p < 0,02$).

Correlation of the distribution of the scanty phenes ratio with the sign of intrapopulation diversity was not found. At the same time the incidence of rare forms among the studied signs tends to decrease ($0,1 < p < 0,01$): «A» ($h = 0,63$), «C» ($h = 0,188$), «P» ($h = 0,172$), «B» ($h = 0,167$).

Conclusions. The results, which were obtained, allow to suggest that the high rate of intrapopulation diversity (μ) and the presence of rare larvae phenes (h) in the population of red

soldier bug may be the result of unfavorable ecological state of urban ecosystem in the region, accompanied by a change in the typical environmental parameters associated with increasing anthropogenic or any other effect on insects.

The identified abnormalities in the structure of certain morphological structures of the body is an important indicator of disorders in population homeostasis [4]. Since these changes also characterize the level of stability of individual development of an organism, it is interesting to repeat such studies on the example of adult red soldier bugs, try to specify the list of factors that derange the state of regional ecosystem and to propose means of overcoming their influence.

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MORPHOLOGICAL CHANGES OF KIDNEY TISSUE WHEN USING GLUTATHIONE AT RHABDOMYOLYTIC ACUTE KIDNEY INJURY

Abstract. *Morphological study of rats kidneys after the simulation of rhabdomyolytic acute kidney injury by the single injection of 50% glycerol revealed the morphological changes in the renal cortex and medulla, which were manifested by the luminal obstruction of the cortical and medullary tubules with myoglobin casts, epithelial dystrophy and signs of coagulative necrosis. Use of glutathione improved the renal histology significantly, which was confirmed by restriction of dystrophy and necrotic processes, indicating its nephroprotective activity.*

Keywords: *rhabdomyolytic acute kidney injury, glutathione, morphological changes.*

Introduction. Acute kidney injury (AKI) is a polyetiological syndrome, which is characterized by violation of filtration and concentration, excretory and incretory functions of the kidneys caused by rapid multiple changes of major kidney functions due to intrarenal blood flow disorder and occurrence of acute tubular necrosis [4, 6, 10–12]. This sudden renal damage is caused by prerenal, renal and/or subrenal influences of etiological factor. Myorenal syndrome and pigment myoglobinurial nephrosis caused by massive rhabdomyolysis are the most common causes of renal AKI. Rhabdomyolysis is a syndrome of skeletal muscle damage leading to lysis of myocytes, resulting in excretion of intracellular contents, including myoglobin (MG) and creatine kinase (CK) into blood plasma. Along with traumatic rhabdomyolysis (crush syndrome, cramps, excessive exercise) nontraumatic rhabdomyolysis often develops as a result of various toxic and physical actions (poisoning with heavy metal compounds, drugs, medicines), muscle ischemia, infections etc. Normally MG freely bounds to plasma globulin and just a small its amount gets into urine. But at its mass excretion plasma cannot bind all MG in the bloodstream. As a result, it is filtered through the glomerular filter and gets into the tubules of the kidneys, which can cause obstruction of the tubules and the consequent decrease in glomerular filtration rate (GFR) and renal function violation [1, 5, 7]. Besides, MG is characterized by direct nephrotoxic effect [1]. Because of necrotic

or degenerative changes in renal tubular epithelial cells, which develop due to the action of MG, obstruction of tubular cell with detritus and reverse movement of the tubular content with regurgitation of primary urine in the blood and lymph occur. Today cases of rhabdomyolytic kidney injury are 5-15% of total AKI cases, and the mortality rate is 8% [7]. In view of the relevance of AKI, pharmacological correction of this syndrome is still an important task of medicine and necessitates search for new approaches to its treatment or prevention.

At rhabdomyolysis glutathione (G) as an antioxidant plays an important role in protecting cellular structures from oxidative stress, acting as donor of electrolytes for peroxidase, which prevents the development of free-radical processes [9]. Another important function of G is the formation of mixed disulfides with proteins, which can be an additional element in the regulation of biological processes [8]. Glutathione can exist in oxidized (G-S—S-G) and restored (G-SH) forms. Restored form of G protects SH-groups of proteins from oxidation by various free radicals. The mechanism of protection is the oxidation of SH-groups of the G with the formation of its oxidized form and preservation of SH-groups of proteins in the active reduced form.

Therefore for confirmation of nephroprotective influence of glutathione at rhabdomyolytic AKI, we have studied the morphological changes in kidney tissues of laboratory rats in experimental model of rhabdomyolytic AKI [3]. Thus, the

experiment proved that glutathione improves functional activity of kidneys at rhabdomyolytic AKI, which was manifested by an increase in urine output, a corresponding increase in GFR, a decrease in creatinine content in blood plasma and a decrease in proteinuria parameters.

Also, when using the drug positive changes in the prooxidant-antioxidant balance in the kidneys and blood plasma of animals were observed: the content of TBA-active products and oxide-modified proteins decreased, while indicators of activity of glutathione peroxidase and ceruloplasmin, and content of SH-groups increased significantly [3].

Objective: to study of morphological changes of kidney tissues at the correction with glutathione at the experimental model of rhabdomyolytic AKI.

Materials and methods. Experiments were performed on 28 white outbred rats (weighing 140-200 g). AKI was caused by intramuscular injection of 50% glycerin solution in amount of 10 mg/kg. Glutathione (TAD 600 "Biomedica Foscam", Italy) was injected at a dose of 40 mg/kg once intraperitoneally in 40 min after injection of glycerol. In 24 hours after simulation of AKI the blood sampling and the kidney tissues sampling were performed after decapitation of animals under ether anesthesia in strict accordance with the requirements of the "European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1986).

Kidney tissues for histological study were fixed in 10% solution of neutral buffered formalin for 48 hours, dehydrated in alcohols of ascending concentrations, embedded in paraffin at 64°C with the following obtaining of histological sections of 5 microns thick, stained with hematoxylin and eosin. For objectification and improving reproducibility of the results of quantitative research computerized morphometry of objects in histological samples was carried out. For this digital copies of optical image of areas of microscopic samples were obtained with a digital camera Olympus (model C740UZ) and microscope LYUMAM-P8 with the following creation of a bank of digital micrographs, which were further analyzed by the software "VideoTest - Size 5.0" ("VideoTest", Russia).

Results and discussion. Study of the

morphological structure of kidney tissues of animals revealed that in intact animals the vessels are moderately blood-filled, hemorrhages are absent, the tubular epithelium is not changed, the tubular lumen is easily visible, the glomeruli are not changed (Figs. 1, 2).

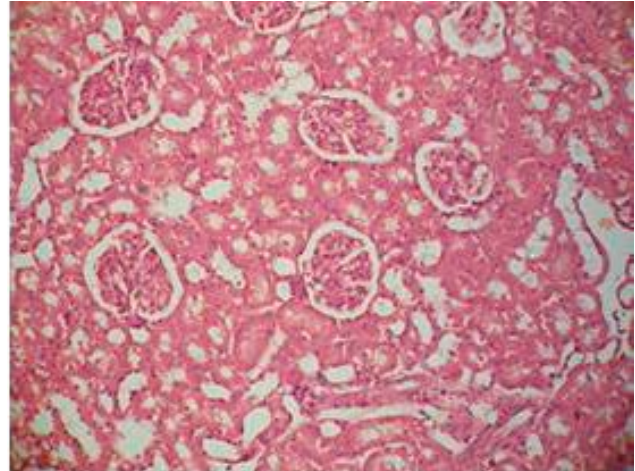


Fig. 1. The kidney sample (the cortical substance) of an intact rat. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

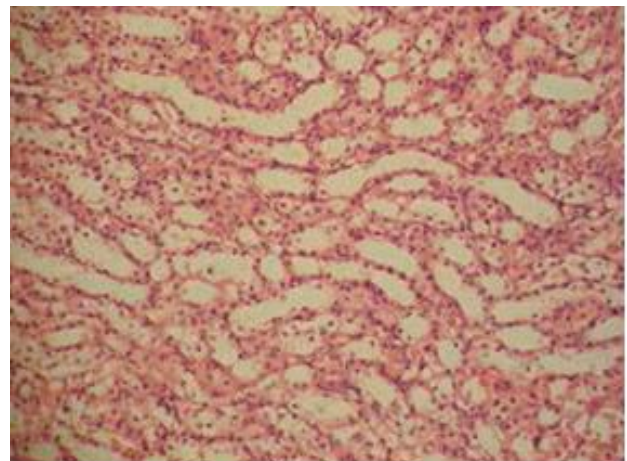


Fig. 2. The kidney sample (the medullary substance) of an intact rat. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

In contrast to the intact animals, in the animals with simulation of rhabdomyolytic AKI significant changes in the kidney histostructure are observed (Figs. 3, 4).

Thus there is an obstruction with myoglobin casts of lumens of $28 \pm 0,8\%$ of convoluted tubules of cortical substance (Fig. 3) and $61 \pm 1,2\%$ of excretory tubules of medullary substance (Fig. 4). Myoglobin casts in most cases expand the lumens in the field of their localization strongly. The nuclei of the epithelium are not seen clearly, the lumen is almost absent. In the convoluted tubules $94 \pm 1,0\%$ of epithelial cells have signs of granular and hydropic dystrophy, and $2 \pm 0,1\%$ of epithelial

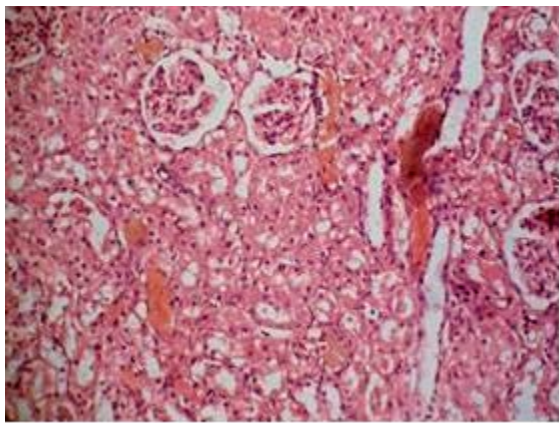


Fig. 3. The kidney sample (3 – the cortical substance) of a rat with rhabdomyolytic AKI. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

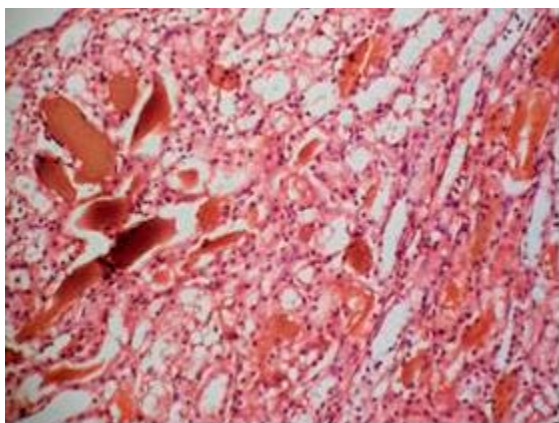


Fig. 4. The kidney sample (4 – the medullary substance) of a rat with rhabdomyolytic AKI. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

cells are in a state of coagulation necrosis, which is manifested by the cytoplasm induration and karyopyknosis (Fig. 3). In the excretory tubules of the medullary substance $37 \pm 1,4\%$ of epithelial cells are affected by hydropic dystrophy, which is the reverse process (Fig. 4).

At the correction of rhabdomyolytic AKI with glutathione on the 24th hour of the experiment the morphological picture of kidneys improves slightly (Figs. 5, 6), but there is still an obstruction of the lumens of the tubules of the cortical substance with myoglobin casts, covering $6 \pm 0,4\%$, and $11 \pm 0,9\%$ of the excretory tubules of the medullary substance. Myoglobin casts have varying degrees of staining, that is they are of varying density and slightly expand diameters of tubules in the places of their localization. In the convoluted tubules $82 \pm 1,3\%$ of the epithelial cells have signs of granular and hydropic dystrophy. Dystrophic process in the form of granular dystrophy in the excretory tubules of the medullary substance covers $69 \pm$

$0,9\%$, and $2,0 \pm 0,3\%$ of epithelial cells are in a state of coagulation necrosis with the cytoplasm induration and karyopyknosis.

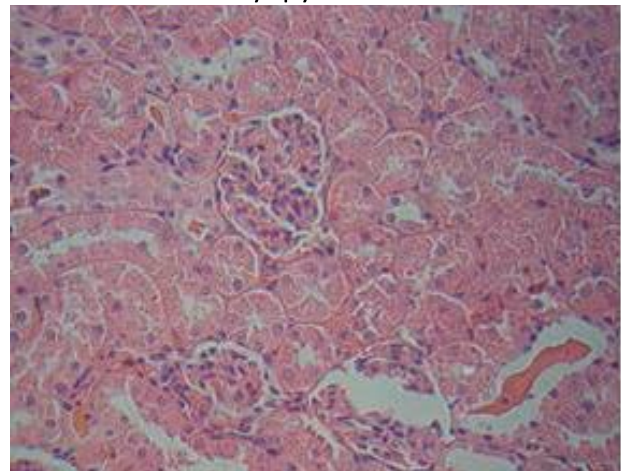


Fig. 5. The kidney sample (5 – the cortical substance, 6 – the medullary substance) of a rat with rhabdomyolytic AKI after glutathione injection. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

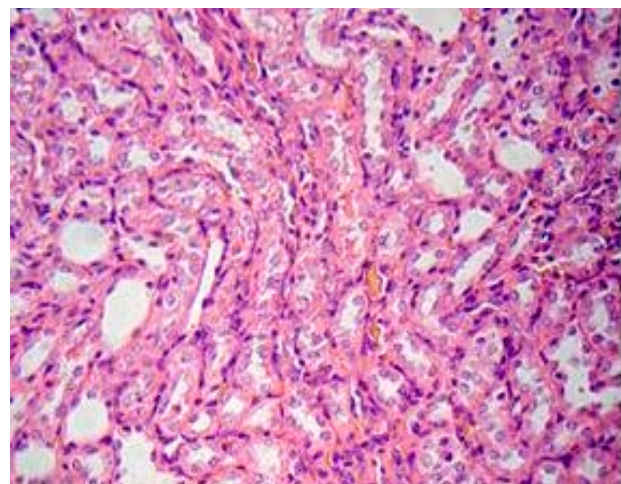


Fig. 6. The kidney sample (6 – the medullary substance) of a rat with rhabdomyolytic AKI after glutathione injection. Stained with hematoxylin and eosin. Magnification: eyelens×40, objective ×10.

Conclusion. 1. Rhabdomyolytic AKI leads to significant dystrophic and necrotic changes both in the cortical and medullary substances of the kidneys.

2. The use of glutathione reduces incidence of dystrophic and necrotic processes in the kidneys, confirming the nephroprotective effectiveness of glutathione.

Prospects for further research. The use of glutathione at rhabdomyolytic kidney damage makes it possible to reduce the damaging effect of myoglobin on renal tubules due to its powerful antioxidant effect, which, in turn, is the prospect for the use of this tool for correction of AKI.

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REMOTE RESULTS OF OBSERVATION OVER THE PATIENTS WITH RHEUMATOID ARTHRITIS WITH COMORBID INTESTINAL DISBACTERIOSIS

Abstract. Remote results of a comprehensive treatment of patients with rheumatoid arthritis with comorbid intestinal disbacteriosis after additional administration of Quercetin, Bifilact extra and Enterosgel to the standard therapy were analyzed. It was found that after administration of a comprehensive therapy including the above mentioned medicines the course of the disease of patients with RA and their general condition improved, the period of remission became longer, the necessity of repeated admissions to the hospital decreased.

Key words: rheumatoid arthritis, intestinal disbacteriosis, Quercetin, Enterosgel, Bifilact extra.

Introduction. Rheumatoid arthritis (RA) is a disease of a great medical-social importance [2, 12]. Patients with RA have 3-7 years reduced life expectancy as compared with the general population [1, 4, 5]. This disease results in quick disability which in case of absent active therapy can occur in the first 5 years since the onset of the disease [9, 13].

The main sign of the therapeutic efficacy is remote results and their correct evaluation. Remote results enable to examine the dynamics of the therapeutic effect found while studying direct results, to determine its duration and stability.

Objective: to study remote results of a comprehensive treatment with administration of Quercetin, Bifilact extra and Enterosgel in patients with rheumatoid arthritis and comorbid intestinal disbacteriosis (ID).

Materials and methods. The observation was conducted during 1 year among 18 patients (the main group receiving a comprehensive therapy (CT)) and 23 patients (the comparison group receiving a standard therapy (ST)). The study was carried out keeping to the main regulations of GCP ICH and Helsinki Declaration on Biomedical Studies. The diagnosis was verified according the criteria suggested by ARA/EULAR (1987/2010) [8, 10], the Order of the Ministry of Public Health of Ukraine №263 dated 11.04.2014. An average age

of patients was $44,7 \pm 9,4$. Disease remoteness ranged from 1 to 12 years. women prevailed among the examined patients – 34 (82,93%), the majority of individuals were seropositive by rheumatoid factor – 26 (63,41%). Practically all the patients had polyarteritis form of the disease – 40 (97,56%). RA activity was estimated by disease activity status of 28 joints (DAS28) [6]. In 24 (58,54%) of them was the I degree of activity, in 17 (41,46%) – the II one. Half of the patients had radiological changes in joints: I stage – in 16 (39,02%) individuals, II – in 20 (48,78%), II-III degree – in 5 (12,2%) patients. Functional ability of the patients and disability index were determined by the Health Assessment Questionnaire (HAQ) [11]. The I (19 (46,34%)) and II (22 (53,66%)) classes of functional disorders of joints prevailed.

By the results of clinical examinations indices were detected (painful, articulate, inflammatory), the time of morning joint stiffness was considered. The quality of life of patients and joint functional condition were analyzed on the base of Stanford Health Assessment Questionnaire (HAQ) [7]. Pain assessment was conducted by the visual analogue scale (VAS).

During out-patient-polyclinic stage the patients from the main group additionally to a standard complex of treatment in order to consolidate achieved results were indicated to: Quercetin 1

packet twice a day up to 1 month in case of the I degree of activity; up to 1,5 month – with the II degree of activity; as well as Bifilact extra in the similar time regimen, but per 1 capsule twice a day, Enterosgel per 1,5 table-spoon after dinner for two weeks – in case of the I degree of activity, up to three weeks – in case of the II degree of activity. Conditional criteria of these indications were clinical signs of RA (concerning Quercetin) and the need in periodical intake of NSAIDs by patients due to articulate pain syndrome and their known negative effect on the intestinal microbiota, acquired comorbid digestive disorders promoting an increased susceptibility to relapses of ID as a trigger factor of a torpid course of RA and activation of rheumatoid process. The group of comparison received basic (standard) treatment according to the Order of the Ministry of Public Health of Ukraine №263 dated

11.04.2014. The results of treatment were controlled in 1, 6 and 12 months by means of questionnaire and objective examination considering the dynamics of the course of the disease, the necessity and volume of the complex of therapeutic agents, duration of their use.

Arithmetic mean and its error were calculated. Comparison between the groups of the study was conducted by means of nonparametric Mann-Whitney criterion in the computer program medium PAST [3]. The results were considered reliable with the significance level $p < 0,05$. For statistical estimation of remote results of the study the method of odds ratio detection was used. To check the statistical hypothesis concerning the equality of the unit odds ratio ($\omega=1$) the criterion χ was applied.

Results and discussion. The findings of the dynamics of remote results are presented in the

Table

Effect of a comprehensive treatment on the functional parameters in patients with RA of the I degree of activity in dynamics ($\bar{x} \pm Sx$)

Index	Group	Before treatment	After treatment	In 1 month	In 6 months	In 12 months
Stanford Health Assessment Questionnaire, score	ST (n=13)	1,58 \pm 0,13	1,32 \pm 0,087 $p < 0,05$	1,30 \pm 0,045 $p < 0,001$	1,33 \pm 0,098 $p < 0,001$	1,53 \pm 0,78
	CT (n=11)	1,61 \pm 0,54	1,04 \pm 0,096 $p < 0,05$	1,08 \pm 0,035 $p < 0,001$ $p_1 < 0,001$	0,98 \pm 0,058 $p < 0,001$ $p_1 < 0,001$	0,92 \pm 0,023 $p < 0,001$ $p_1 < 0,001$
Morning stiffness, min	ST (n=13)	65,72 \pm 3,67	48,43 \pm 4,5 $p < 0,05$	60,41 \pm 4,12 $p < 0,05$ $p < 0,001$	63,12 \pm 4,31	63,85 \pm 3,64
	CT (n=11)	67,12 \pm 4,78	32,32 \pm 3,7 $p < 0,05$ $p_1 < 0,001$	27,48 \pm 1,94 $p < 0,001$ $p_1 < 0,001$	24,15 \pm 1,12 $p < 0,001$ $p_1 < 0,001$	25,45 \pm 1,84 $p < 0,001$ $p_1 < 0,001$
Painful index by Ritchie, points	ST (n=13)	2,38 \pm 0,073	1,83 \pm 0,12 $p < 0,05$	1,75 \pm 0,35 $p < 0,001$	1,99 \pm 0,28 $p < 0,001$	2,23 \pm 0,17
	CT (n=11)	2,46 \pm 0,089	1,4 \pm 0,132 $p < 0,05$	0,84 \pm 0,05 $p_1 < 0,001$	0,65 \pm 0,12 $p_1 < 0,001$	0,61 \pm 0,03 $p_1 < 0,001$
Articulate index by Ritchie, points	ST (n=13)	2,76 \pm 0,193	1,78 \pm 0,16 $p < 0,05$	1,98 \pm 0,18 $p < 0,001$	2,08 \pm 0,09	2,22 \pm 0,16
	CT (n=11)	2,82 \pm 0,097	1,77 \pm 0,097 $p < 0,05$	1,34 \pm 0,04 $p_1 < 0,001$	0,82 \pm 0,05 $p_1 < 0,001$	0,68 \pm 0,03 $p_1 < 0,001$
Inflammatory index by Ritchie, points	ST (n=13)	2,32 \pm 0,159	1,66 \pm 0,097 $p < 0,05$	1,75 \pm 0,15 $p < 0,001$	1,98 \pm 0,1 $p < 0,001$	2,17 \pm 0,24
	CT (n=11)	2,34 \pm 0,167	1,2 \pm 0,086 $p < 0,05$	0,78 \pm 0,05 $p < 0,001$ $p_1 < 0,001$	0,55 \pm 0,04 $p < 0,001$ $p_1 < 0,001$	0,52 \pm 0,04 $p < 0,001$ $p_1 < 0,001$

Notes. p – in comparison of indices concerning the initial data, p_1 – significance level of indices difference with basic and comprehensive treatment; ST – standard therapy, CT – comprehensive therapy.

table. It was found that under the influence of a comprehensive therapy the indices of Stanford Health Assessment Questionnaire in patients with RA of the I degree of activity in 1, 6 and 12 months did not differ much from those fixed in 1 month, they were 1,7 times less as much in the group of comparison. The time of morning stiffness in patients with a comprehensive treatment was no longer than 27,15 min, while in case of a basic treatment it lasted for about an hour. At the same time a negative dynamic was found with painful, articular and inflammatory indices, the number of points gradually increased and in a year it was by 1,2, 1,2 and 1,3 times more respectively and was close to the initial level. The difference between the groups in this period was 72,6 %, 69,4% and 76,0 % in favour of the patients from the main group.

In patients with RA of the II degree of activity the analogical dynamics was observed.

At the same time it was found that in 11 patients with RA with the I degree of activity the period of remission was (103,4±12,3) days against (47,12±14,1) days in the group of comparison, the frequency of relapses was (1,18±0,43) cases against (2,65±0,62) cases in the group of comparison. There was no need for repeated admissions, while there was 1-2 admissions in the group of comparison. In 7 patients with RA of the II degree of activity the period of remission was (82,4±10,43) days against (47,12±15,5) days in the group of comparison, relapse frequency was (1,83±0,83) cases against (2,78±0,62) in the group of comparison, 1-2 times a year repeated admission to the hospital was required, 2-3 admissions in the group of comparison.

Therefore, with indication of a comprehensive therapy including Quercetin, Enterosgel and Bifilact extra patients with RA admitted improved course of the disease, general condition, the periods of remission became longer, the necessity in repeated admissions to the hospital decreased. A considerable difference of the examined indices in the dynamics between the groups was indicative of certain advantages of the improved comprehensive treatment.

Conclusions. 1. A combined administration of Quercetin, Enterosgel and Bifilact extra in a comprehensive treatment of patients with rheumatoid arthritis with comorbid intestinal

disbacteriosis improves direct and remote results of treatment. 2. Additional use of these medicines in a comprehensive therapy of such patients is safe and promotes reduced needs in repeated admission to the hospital and relapse frequency, longer remission period.

The prospects of future studies include further examination of Quercetin effect on the signs of the cardio-vascular system in patients with rheumatoid arthritis as one of the most frequent causes of death in case of rheumatoid arthritis.

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TEACHING MEDICAL STUDENTS ON THE BASE OF A COMPETENCE APPROACH

Abstract. *The article gives an example of the definition of the notion “competence”. Training a medical student is not possible without considering the grounds of the competences approach. The combination of theoretical and practical tasks of the teacher in the work with students provides a multistep system of the quality of mastering knowledge and skills, and promotes stage-by-stage formation of professional competence. An example of the competence approach is brainstorming method applied in teaching the students of the Stomatological Faculty.*

Key words: *competence approach, brainstorming, medical student.*

Topicality of the study and problem statement. Joining the European space by Ukraine requires all the educational branch to think over the questions of educational quality and search of new conceptions of education reflecting contemporary changes in the society and directed to making up of personality of the XXI century. One of the approaches directed to the improvement of professional education is a competence approach. It is a substantiated and objective phenomenon in modern education, as accelerated rate of social development, transition to information technologies, new requirements to specialists and development of informatization processes promoted reorientation of the educational conception from getting knowledge to a competence one.

Analysis of the studies and publications. One of the priority tendencies to improve professional education is a competence approach. The problem of a competence approach in the systems of higher and general secondary education is studied in the works of domestic scientists – I. Drach, I. Babyn, P. Bachynskyi, N. Bibik, G. Gavryshchak, I. Gudzyk, N. Dvornikova, Y. Kodliuk, O. Lokshyna, S. Nikolayenko, O. Ovcharuk, L. Pylgun, O. Pometun, I. Rodygina, K. Savchenko, O. Sadivnyk, L. Sen, S. Sysoyeva, O. Sytnyk, T. Smagina, G. Tereshchuk, S. Trubachova, N. Fomenko etc.

Although, the analysis of literary sources is

indicative of the fact that there is no a coordinated view concerning the list of professional competences of a medical student that should be formed after graduation from a higher educational establishment.

Task statement. Analysis of the main items of the competence approach and its application to the teaching process for medical students.

Brief description of the main material. Designing of educational programs on the base of a competence approach (general European project TUNING (“Establishing Educational Structures”)) means: reflection of educational results in the systemic and integral aspects; formation of educational results at the Higher Educational Establishment as a characteristic of a student’s/graduate’s ability to demonstrate appropriate knowledge, skills and values; definition of the structure of competences that should be acquired and demonstrated by learners [1]. As a result, a competence list of a specialist in different branches was designed containing 31 positions (for example, ability to communicate in another language, ability to apply knowledge in practical situations, ability to make a substantiated decision, ability to abstract thinking, analysis and synthesis, ability to a team work etc.). The project «TUNING MEDICINE» for medical branch includes over 50 competences (both general and special without clear systematization and differentiation) [8].

Considering this fact a question arises as to the instruments of formation of medical student's competences.

«Competence education», as a notion, appeared at the end of the 80-s beginning of the 90-s XX century in the USA. The basis for it was the requirements to business and entrepreneurship of the graduates of higher educational establishments, who have certain difficulties in the application of knowledge and make decisions in real situations due to the lack of experience and uncertainty [5].

Since 1986 in Great Britain the competence-oriented conception was taken as a basis of the national system of qualification standards and received an official support of the leaders. In 1997 within the framework of the Federal Statistical Department of Switzerland and the National Center of Educational Statistics of the USA and Canada the program "Detection and Selection of Competences: Theoretical and Conceptual Bases" (DeSeCo) was initiated [4].

The competence approach intensifies a practical orientation of education, ensures the ability of a personality to meet new requirements of the labour market, to have appropriate potential for practical solution of professional tasks. This approach accentuates on the ability to apply acquired knowledge, to use the experience of successful actions in the situations of educational and professional work, but at the same time it does not deny the value of knowledge. According to the competence approach the first place is occupied by the ability to solve problems occurring in various professional situations, but not by the students being informed [2].

Availability of the competence approach in education is in the ability of a graduate to future professional activity. This approach is oriented to getting practical results, experience of the personality and its activity stipulating principle changes in the organization of education. Improvement of the educational process considering the competence approach is in the teaching students to apply acquired knowledge and skills effectively in certain situations [2].

While preparing for practical classes on the base of the competence approach, first of all, one should be definite with the list of competences,

pedagogical methods of teaching and learning, formulation of the kinds of work of students and estimation criteria of the results of education, as well as detection of the level of their competences [7].

Conditions to provide an integral approach is the combination of traditional and contemporary forms, methods and technologies of teaching students, motivation of students' activity and their interaction, discussion, application of standardized patients, clinical rounds etc.

In higher medical education today there are pedagogical methods ensuring interaction of students. Application of such methods by teachers promotes the formation of professional competences [3].

One of the most effective methods, especially during the introductory part, is "brainstorming" [6]. Brainstorming method was suggested by Alex Osborn (USA) in the 40-s of the XX century. Alex Osborn paid attention to the fact in certain situations some people begin to generate a number of ideas, while others, according to the peculiarities of their thinking, are more inclined to the analysis and critical estimation of other people ideas and their development. Brainstorming is the method to stimulate creative activity and productivity to solve problems. Brainstorming is the method to solve urgent tasks in very limited time. The sense of the method is in the necessity to express the biggest number of ideas for a short period of time, discuss them and make a right choice. This method is used for the development of creative abilities or for the solution of complicated problems. Brainstorming method can be used in various forms of activity: in the work with small groups, teams, big groups (game with the audience). The most optimal groups are considered those containing from 3 to 12 persons (the number of participants should be divided into three).

Brainstorming method is widely used at the Department of Propedeutics of Internal Diseases during practical classes. The teacher begins the class with the statement of a clearly formulated problematic question before the students. It enables to suggest a number of versions for answer and invites students to express their ideas and comments. While "ideas are suggested" none of them cannot be ignored. All the students

should be encouraged to suggest their ideas. In case during brainstorming the teacher fails to get many variants it is indicative of the fact that students are not sure in their suggestions. Combination or changes of the ideas suggested before frequently leads to the appearance of new ones which can be better than the previous ones.

Conclusions. While training a medical student the main issues of the competence approach should be considered, it promotes the quality of education and the use of effective pedagogical technologies. Creation of conditions to form necessary competences promotes productivity and competitiveness of a specialist on the labour market.

Prospects of further studies: to work on the improvement of a competence model in teaching medical students for the formation of professional competence.

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EFFECT OF THYROID GLAND FUNCTIONAL STATE ON THE FUNCTIONING OF HOMOCYSTEINE REMETHYLATION CYCLE IN RAT ORGANS

Abstract. *L-thyroxine and Mercazolil were used for the modeling of hyper- and hypothyroidism, which were confirmed by the content of fT_3 , fT_4 and TSH. The decrease of the S-adenosylmethionine synthetase, S-adenosylhomocysteine hydrolase and betaine-homocysteine methyltransferase activities in the liver and kidneys of animals with hypothyroidism were observed. At the same time, injection of L-thyroxine increased the activity of these enzymes in the liver and kidney tissues. Hyperthyroidism caused the decrease of homocysteine concentration in blood whereas hypothyroidism increased the level of this amino acid. It has been concluded that the affection of cardiovascular system in hypothyroidism could be due to the disorders of remethylation processes in organs and tissues.*

Keywords: *thyroid hormones, remethylation cycle, homocysteine.*

Introduction. Sulphur-containing amino acids (methionine, cysteine, homocysteine and taurine) ensure the vital processes of cells, maintain redox potential and integration of cellular systems, incapacitate delirants and free radicals, support methylation processes. Disorders of metabolism of sulphur-containing amino acids due to genetic or acquired defects of enzymes which regulate their metabolism are associated with progression of variety of pathologies including Alzheimer disease, malignant tumors, neural tube defects, kidney decease. Disorder of homocysteine (HC) metabolism is particularly topical. Increase of HC stream is a serious risk factor of progression of cardiovascular deceases such as atherosclerosis, hypertension, venous thrombosis. Blood HC level directly lines up with thickness of coronary paries and contrary lines up with endothelial-dependent blood flow within coronary arteries [6].

Metabolism regulation of sulphur-containing amino acids is carried out on the different levels including by endocrine system. Thyroid hormones are one of the key hormones which regulate all the types of metabolism in organism. It was found that in patients with hypothyroidism increase of HC content occurred, and substitutive therapy by thyroxin improved actual indicator up to the level of healthy individuals [3]. K.M. Colleran and others, 2005 [7] showed that subclinical

hyperthyroidism, evoked by introduction of methimazole, causes to decrease of blood HC level. However specific molecular mechanisms of impact of thyroid hormones on increase or decrease of blood homocysteine level remain unknown. In particular the issue of impact of thyroid gland hormones on functional state of enzymes which ensure remethylation processes in organism, from which blood HC concentration directly depends on, are uninvestigated.

Objective: experimentally investigate the impact of functional state of thyroid gland on the strength of enzymes of HC remethylation cycle within liver and kidneys and blood HC level.

Materials and methods. For the purpose of investigations 40 outbred male rats of 150-180g weight each which were being kept on the standard diet were involved. All the animals were divided into 5 groups: the 1st – control group (intact rats). This group of animals was intragastrically injected 1% starch solution; the 2nd – animals in which hyperthyroidism was provoked (daily during 14 days intragastrically L-thyroxine on the 1% starch solution by 200 mcg/day per 1 kg of body weight was injected); the 3rd – animals in which hyperthyroidism was provoked (daily during 21 days intragastrically L-thyroxine on the 1% starch solution by 200 mcg/day per 1 kg of body weight was injected); the 4th – animals in

which hypothyroidism was provoked (daily during 14 days intragastrically mercazolil on the 1% starch solution by 10 mcg/day per 1 kg of body weight was injected); the 5th – animals in which hypothyroidism was provoked (daily during 21 days intragastrically mercazolil on the 1% starch solution by 10 mcg/day per 1 kg of body weight was injected); on the 14th and 21st day animals were sacrificed by the method of cervical dislocation. For the purpose of investigations blood plasma, liver and kidney tissues were used. Investigation was being carried out in accordance with common ethical principles of experiments on animals, approved by the First National Ukrainian congress on bioethics (Kyiv, 2001), “European Convention for the protection of vertebrate animals used for experimental and other scientific purposes” (Strasbourg, 1986), other international agreements and national legislation in this field.

Liver and kidneys were perfused by cold 1,15% potassium chloride solution and homogenized upon 3000rpm within 1,15% potassium chloride environment (1:3 ratio). Homogenates were centrifuging during 30 minutes upon 1500g and +4°C and derived post-nuclear fraction was being used for detection of enzymes strength that ensured the remethylation processes in organism – S-adenosylmethionine synthetase (S-AMS), S-adenosylhomocysteine hydrolase (S-AHH), betaine-homocysteine methyltransferase (BHMT). Total HC content was being detected within blood serum.

S-AMS strength was being detected by evaluation of increase of inorganic phosphate that was originated when hydrolytic cleavage of ATP when interreacting with methionine [1], S-AHH strength was being detected by evaluation of increase of sulfhydryl groups in hydrolysis reaction of S-adenosylhomocysteine [5], BHMT strength – by evaluation of increase of sulfhydryl groups in homocysteine-betaine reaction [2].

For demonstration of hyper- and hypothyroidism states within the blood serum the content of free thyroxine (FT4), free triiodothyronine (FT3) and thyroid-stimulating hormone (TSH) were being detected by immunoenzyme method with a use of kits of “Diagnostic Systems” Company (Russia Federation) in accordance to the user tips of the manufacturing company.

Within blood serum the total HC content was being detected by immunoenzyme method with a use of kit of «Axis-Shield» Company (Great Britain).

The results were expressed as average±SEM among 8 experiments. Variations $P<0,05$ were considered as statistically-valid. Statistical analysis was being carried out using standard statistical software and Student's t-test.

Results and discussion. Daily injection to the animals of 200mcg/kg of L-thyroxine during 14 and 21 days caused the state of chronic hyperthyroidism that was being evidenced by increase of blood FT4 concentration in rats from the 2nd and 3rd groups by 83% (from $11,07\pm0,47$ to $20,23\pm2,10$ pmol/l) and by 136% (from $11,07\pm0,47$ to $26,12\pm1,85$ pmol/l) respectively. Wherein the TSH concentration was adequately being decreased (on the 14th day by 56% (from $0,34\pm0,03$ to $0,15\pm0,02$ mmol/L), on the 21st day by 76% (from $0,34\pm0,03$ to $0,08\pm0,01$ mmol/L). FT3 concentration when L-thyroxine injection had only increasing tendency after both periods of experiment, however when statistical analysis variances were uncertain.

Merkazolil medication (1-methyl-2-mercaptoimidazole), that blocked peroxidase enzyme that was involved in thyronine iodation within thyroid gland to triiodo- and tetraiodothyronine and decreased thyroxine increment, was used for inhibition of end-products of thyroid hormones. Daily injection of 10mg/kg of mercazolil in the animals during 14 days caused to decrease of FT4 content in blood serum by 38% (from $11,07\pm0,47$ to $6,84\pm0,27$ pmol/l), medication administration during 21 day caused to almost three times of FT4 decrease (from $11,07\pm0,47$ to $4,25\pm0,42$ pmol/l). Daily injection of 10mg/kg of mercazolil in the animals during 14 and 21 days caused to adequate increase of TSH level by 59% (from $0,34\pm0,03$ to $0,54\pm0,05$ mmol/L) and by 550% (from $0,34\pm0,03$ to $2,21\pm0,16$ mmol/L). At the same time blood serum FT3 level decreased by 66% on the 14th day (from $2,58\pm0,24$ to $0,87\pm0,06$ pmol/l) and by 74% on the 21st day (from $2,58\pm0,24$ to $0,67\pm0,04$ pmol/l). All the data listed above shows that with a help of L-thyroxine the condition that equal to hyperthyroidism was modeled, and evident hypothyroidism was being progressed in rats in

which mercazolil was injected.

HC is metabolized through one of two ways – though remethylation or transsulfuration. In normal range HC is remethylated to methionine by two ways. The first reaction is catalyzed by B12-dependent methionine synthase enzyme for which N-5-methyltetrahydrofolate, building-up process of which is occurred in the active folate cycle, is the methyl group donor. Alternative reaction of building-up of methionine from HC is catalyzed by folate-independent BHMT enzyme that exists in liver and kidneys, for which betaine is the methyl group donor. In methylation reactions not methionine but its secondary – S-adenosylmethionine, that is built-up upon conditions of methionine-ATP interaction under the impact of S-AMS enzyme, is the direct methyl group donor. S-adenosylmethionine, losing methyl group, transforms into S-adenosylhomocysteine that under the impact of S-AHH enzyme is degraded into adenosine and HC [4].

We have determined that experimental hyperthyroidism was being accompanied by increase of enzymes capacity of remethylation cycle – BHMT, S-AMS and S-AHH. Under the impact of L-thyroxine BHMT strength was increasing within liver tissue in the both follow-up periods (from $8,65 \pm 0,50$ to $11,90 \pm 0,78$ nM/min*mg on the 14th day and up to $12,50 \pm 0,89$ nM/min*mg on the 21st day). Within kidney tissue the similar changes were observed - enzyme strength was adequately (by 35 and 47%) increasing (from $3,33 \pm 0,17$ to $4,48 \pm 0,21$ nM/min*mg of protein on the 14th day and up to $4,90 \pm 0,33$ nM/min*mg of protein on the 21st day). At the same time S-AMS strength was adequately increasing in the both organs only on the 21st day (within liver tissue from $5,84 \pm 0,43$ to $7,85 \pm 0,48$ nM/min*mg of protein, within kidney tissue from $3,04 \pm 0,27$ to $4,96 \pm 0,28$ nM/min*mg of protein). Also only on the 21st day of experiment the strength of the next remethylation cycle enzyme was adequately metamorphosing – S-AHH (within liver tissue by 35% - from $5,66 \pm 0,30$ to $7,66 \pm 0,53$ nM/min*mg of protein, within kidney tissue by 59% - from $3,83 \pm 0,36$ to $6,08 \pm 0,50$ nM/min*mg of protein).

At the same time, upon conditions of mercazolil administration, the capacity of

remethylation cycle enzymes as within liver as within kidneys was being varied backward. In particular within the liver tissue BHMT strength decreased after passing of both periods of investigation (on the 14th day of investigation by 35% (from $8,65 \pm 0,50$ to $5,60 \pm 0,43$ nM/min*mg of protein), on the 21st day – by 45% (to $4,95 \pm 0,27$ nM/min*mg of protein)). Within the kidney tissue under the impact of mercazolil BHMT strength decreased respectively by 25 and 47% (from $3,33 \pm 0,17$ to $2,15 \pm 0,19$ on the 14th day and up to $1,76 \pm 0,14$ nM/min*mg of protein on the 21st day of investigation).

Hypothyroidism modeling caused an inhibition of S-AMS capacity that adequately decreased within liver on the 14th day by 27% (from $5,84 \pm 0,43$ to $4,25 \pm 0,29$ nM/min*mg of protein) and on the 21st day by 31% (to $4,02 \pm 0,43$ nM/min*mg of protein). Mercazolil injection also caused to an inhibition of S-AMS strength within kidneys – by 33% on the 14th day (from $3,04 \pm 0,27$ to $2,03 \pm 0,14$ nM/min*mg of protein) and by 40% on the 21st day of investigation (to $1,82 \pm 0,26$ nM/min*mg of protein).

Only long-term mercazolil injection (during 21 days) was causing to adequate inhibition of S-AHH strength within liver tissue – by 24% (from $5,66 \pm 0,30$ to $4,28 \pm 0,32$ nM/min*mg of protein). At the same time within kidneys as on the 14th as on the 21st day of experiment the decrease of actual enzyme strength was observed (respectively by 39% (from $3,83 \pm 0,36$ to $2,32 \pm 0,17$ nM/min*mg of protein) and by 46% (to $2,08 \pm 0,18$ nM/min*mg of protein)).

Such course of changes in the strength of foregoing enzymes of remethylation cycle in a logical way has to cause to variations in HC content. As on the 14th, as on the 21st day after L-thyroxine injection blood serum HC level was decreasing – respectively by 19% (from $8,53 \pm 0,39$ to $6,88 \pm 0,37$ mcmmole/l) and 23% (to $6,53 \pm 0,45$ mcmmole/l) and, vice versa, when mercazolil administration during 14 days HC content was increasing by 98% (from $8,53 \pm 0,39$ to $16,91 \pm 1,12$ mcmmole/l), and during 21 days – by 160% (to $22,20 \pm 1,39$ mcmmole/l).

Conclusions. 1. Increase of blood thyroxine concentration amplifies the capacity of remethylation cycle enzymes within liver and kidneys and decreases the blood HC level, while

the strengths of BHMT, S-AMS and S-AHH in organs increase depending on the duration of hypertyrosinemia.

2. Hyperthyroidism state is accompanied with the decrease of enzymes strength, which is responsible for HC remethylation, within liver and kidneys. It causes to increase of blood HC level.

3. The mechanisms listed above apparently are one of the causes of abnormality of vascular tone and tendency to boosted thrombosis in patients with the hypothyroidism state.

4. In prospect it would be expedient to investigate the method of transsulfuration of the sulphur-containing amino acids when hyper- and hypothyroidism. It would empower more fundamentally understanding the molecular mechanisms which cause to metabolism disorders of sulphur-containing amino acids when thyroid gland abnormality.

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*Higher State Educational Institution of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine, voloshka3@mail.ru***EVALUATION OF QUALITY OF LIFE IN PATIENTS WITH OSTEOARTHRITIS**

Abstract. *Resume. In 268 patients with osteoarthritis of knees I-III radiological stages was assessed the degree of functional failure, disease severity and quality of life of patients, studied the influence of duration and severity of osteoarthritis on the quality of peoples' life in gender, age, professional and medical aspects. Established that the deteriorating quality of life in patients with progression of radiographic changes in the musculoskeletal system, and their numbers depend on gender, age and occupational characteristics of patients and severity of osteoarthritis.*

Key words: *osteoarthritis, quality of life, treatment.*

Introduction. Osteoarthritis (OA) is one of the most widespread disease that is associated with significant worsening of quality of life of patients and as consequence with a rise of costs for health care activities. The most meaningful clinical evidences and properly spent costs accrue to the last few decades of human's life. Increase of life expectancy and decrease of physical activity, almost naturally-determined increase of body weight are the most significant determinants of progression of OA. Taking into consideration this fact WHO and UN declared the first decade of the III millennium to be "Decade of bones and joints". In accordance with forecasts, by 2050 near half of population will be suffering from the difficulties of functioning of musculoskeletal system, which predictors are unhealthy diet, hypodynamia, overstrain of joints and inexpedient strain of bones. That is why development of new and more efficient ways of treatment is an important goal of future [1].

Evaluation of quality of life (QL) of patients with osteoarthritis is one of the assessment criteria of efficiency of different methods of their treatment [2, 3]. According to definition of WHO experts concept of quality of life is put across systemic medical and social characteristic that embraces physical and psychophysiological health of human, its spiritual and life values and also level of civilization of society and its economic status. In medical definition QL is an indicator of impact of primary disease and the results of its treatment for sweetness and light of the patient. In accordance to this the attention is paid at the personal definition by human of his/her own physical and psychoemotional health status. Using

actual approach, disorders of patient's health status may be precisely assessed, the essence of the clinical issue may be deeper understood and the most rational treatment regimen and program of re-education including forecast of expected treatment outcomes according to criteria that lays on the frontier of scientific approach of physicians and personal patient's point of view may be determined [2].

Assessment of QL in patients with OA often depends on age, sex, occupation and requires the differentiated approach to exploration of efficient treatment-and-prophylactic measures.

Objective: To evaluate the impact of duration and severity of osteoarthritis progression on indicators of quality of life of patients in respect of the gender-based, age-related, occupational and medical aspects.

Materials and methods. Investigation of 268 patients with osteoarthritis of the knees I-III stages aged from 40 to 76 years old of which 204 (76,12%) are female and 64 (23,88%) – male was carried out. Duration of disease of examined patients fluctuated in the range of 4-19 years. Verification of OA diagnosis was carried out in line with recommendations of EULAR (2010) according to clinical, index and laboratorial methods of investigation. Evaluation of quality of life in patients with osteoarthritis was carried out with the help of Ukrainian version of well-known enquirer Medikal Outcomes Study Short Form 36 (MOS SF-36) that patients had filled up by themselves. Data of enquirer was evaluated in scores of eight scales and two categories: somatic (SHC) and psychic health components (PHC); indicators of each scale fluctuate in the range

from 1 to 100 being 100 reflects perfect health status. Control group included 25 apparently healthy individuals of alike in age and sex.

Statistical analysis of collected data was being carried out with a use of PC software PaST Version 2.05. Analysis of filled data of enquirer SF-36 was being carried out with the technical tips regarding evaluation and estimation of data of actual enquirer.

Results and discussion. Analysis of division of 268 examined patients with OA by social status criterion showed that 42 (15,67 %) individuals were predominantly the office employees which were performing the moderate physical work for a long time, 164 (61,19 %) – employees which were performing hard physical work during their lives, the rest 62 (23,13 %) individuals – unemployed which were engaging in sedentary lifestyle. Thus in view of occupational aspect, more than ¾ of examined cohort of patients with OA were individuals whose professional activities were linked with long-lasting physical work.

In accordance with OA radiological stage through Kellgren and Lawrence the I stage was diagnosed in 28 (10,45%) patients, the II stage was diagnosed in 202 (75,37 %) individuals and the III stage was diagnosed in 38 (14,18%) patients. The first, less frequently the second stage of radiological abnormality within joints were detected in individuals aged up to 50-55 with

incontinious (up to 5-7 years) OA anamnesis, moderate strain on joints, without signs of obesity. Predominantly second and third stages of such abnormalities were detected in patients over 55-60, often with accompanying signs of the obesity I-III degrees (in 132 individuals – 49,25%).

Estimated results of indicators of quality of life in patients with OA depending on the stage are provided in Table.

As the data of Table 1 shows, when the OA I stage the quality of life almost does not suffer except of emotional state: decrease of Role-Emotional indicator (RE) by 13,8%, ($p<0,05$). However in patients with OA II stage indicators of QL in all parameters including integral indicators of somatic and psychic components of health, are probably ($p<0,05 - 0,001$) reduced in comparison with indicators of individuals from the control group: physical functioning (PF) by 33,65%, Role-Physical (RP) by 40,88%, amount of pain (AP) by 45,5%, general state of health (GSH) by 49,94%, vitality by 28,54%, social functioning (SF) by 32,5%, RE (by 33,44%), mental health (MH) by 33,25%, PhCH (by 35,3%) and PsCH (by 23,8%).

At the same time the most essential changes of investigated indicators of QL were detected in patients with AO III stage in which their probable decrease as regarding QL parameters of individuals from control group as the patients with OA II stage in relation to following indicators

Table

**Indicators of quality of life of patients with OA depending on OA stage
($M \pm m$; n)**

Investigated indicators	Control group, n=25	Patients with OA depending on radiological stage, n=268		
		I stage, n=28	II stage, n=202	III stage, n=38
Physical functioning	96,0 \pm 1,42	91,1 \pm 2,56	63,7 \pm 2,12*	45,3 \pm 3,51*#
Role-Physical	91,0 \pm 3,76	84,3 \pm 3,25	53,8 \pm 3,86*	39,4 \pm 3,16*
Amount of pain	100	95,1 \pm 3,16	54,5 \pm 4,88*	32,4 \pm 3,84*
General state of health	87,4 \pm 3,44	76,2 \pm 3,54	52,4 \pm 4,66*	42,1 \pm 3,42*#
Vitality	76,4 \pm 2,54	70,5 \pm 2,66	54,6 \pm 4,24*	36,8 \pm 2,92*#
Social functioning	95,8 \pm 1,16	88,4 \pm 3,52	64,7 \pm 3,82*	41,6 \pm 3,14*#
Role-Emotional	81,3 \pm 2,52	70,8 \pm 2,14*	54,2 \pm 3,14*	41,4 \pm 2,58*#
Mental health	77,6 \pm 1,64	72,8 \pm 2,84	51,8 \pm 3,16*	39,2 \pm 2,93*#
Integral indicators of health				
Somatic component of health	61,2 \pm 0,52	54,6 \pm 2,84	39,6 \pm 3,26*	30 \pm 3,54*
Psychic component of health	51,3 \pm 0,53	48,4 \pm 1,22	39,1 \pm 1,14*	31,4 \pm 2,12*#

Notes: * - probability of data deviation in comparison with healthy individuals ($p<0,05 - 0,001$);

- probability of data deviation between groups of patients with OA the first and the third radiological stages ($p<0,05-0,001$).

– PF (decrease respectively by 52,82% and 29,9%), GSH (by 56,7% and 26,77%), AP (by 77,6% and 40,65%), vitality (by 51,8% and 29,7%), SF (by 56,6% and 25,7%), RE (by 49,1% and 23,6%), MH (by 49,5% and 24,3%), PhCH (by 50,5% and 20,7%) and PsCH (by 48,8% and 20,1%), which characterize predominantly Psychic component of health was figured out.

Collected indicators reflect only general characteristics of QL in patients with different OA stages, but assessment of QL indicators in respect of the gender aspect showed that QL indicators, especially of affection (SF, RE, MH, Vitality), in patients with OA of a high duration of disease, more severe progress, of female with OA II and III stages, occurrence of accompanying obesity are majorly decreased in comparison with indicators of individuals of the control group. Tendency to more significant changes of indicators also pertained to the physically working patients aged from 40 to 60, and also to patients of the both sexes aged above 60-70.

During two month period of conventional management of patients with OA I and II stages the fact of probable bettering of major indicators of QL (PF, AP, GSH, RE, MH, PhCH) was figured out, however they did not achieve the level of indicators of apparently healthy individuals' status and tended to their bettering only in patients with OA III stage.

Estimated indicators of somatic and psychic components of health of QL in patients with OA require the necessity of improvement of the program of treatment-and-prophylactic approaches for these patients and control of QL parameter variations during more long-lasting periods of monitoring.

Conclusions. 1. In patients with osteoarthritis of knees I-III stages the probable changes of indicators of quality of life, determined by using of enquirer SF-36, which depended on the stage of disease, gender-based, age-related, occupational aspects of patients were figured out.

2. Estimation of indicators of quality of life in patients with osteoarthritis of knees by using of enquirer SF-36 is an important aspect of evaluation of physical and mental health of patients, and also the fail-safe criteria of efficiency of their treatment.

Prospects for further research. The further improvements of the direct care, assessment of efficiency of comprehensive treatment of patients with osteoarthritis, especially directed on correction of integral indicators of health in respect of stage of disease, age of patients, their sex and severity of disease progress are prospective.

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*Higher State Educational Institution of Ukraine "Bukovinian State Medical University", Department of Obstetrics, Gynecology and Perinatology, Chernivtsi, Ukraine, yuzko_s@ukr.net***HORMONAL CHANGES OF FETOPLACENTAL COMPLEX IN PREGNANT WOMEN WHEN ABNORMAL PLACENTATION DURING EARLY GESTATION**

Abstract. *In the article the results of investigation of hormones of fetoplacental complex were provided, videlicet: estradiol, chorionic gonadotropin, progesterone and placental lactogen. Specific characteristics of changes of hormones of fetoplacental complex during early gestation in pregnant women with low positioning of chorion were investigated. Analysing the results of investigation the decrease of level of all hormones of fetoplacental complex in pregnant women with low placentation in comparison with control group was detected that could be considered as incipience of progression of primary placental dysfunction.*

Key words. *low placentation, the I trimester of gestation, hormones of fetoplacental complex.*

Introduction. Positioning of chorion and placenta within uterine cavity plays a special role in an elaboration of placental dysfunction. In accordance with literature data during I trimester of pregnancy abnormal placentation is occurred about 9-30% of the time, and prior to childbearing the frequency of low placentation fluctuates within limits of 9,1 % [1-3].

Thereafter hormonal function of chorion system and placental complex, which synthesize a variety of hormonal substances of as proteinous as steroidal origins, plays an important role in progression of pregnancy during the I trimester. Self-regulation in regard to maternal neuroendocrinal system [4] is specific characteristic of the functioning of an actual complex.

Abnormality of hormonal function of decidual and trophoblastic and also chorial and placental systems, which are assessed through changes of hormonal level that are produced by them, lies in the root of pathogenesis of different complications of pregnancy including progression of primary placental dysfunction [4].

Till now the search of new methods of early diagnostics and forecasting of primary placental dysfunction upon conditions of low placentation remains one of the prioritized directions of nowadays obstetrics. In this the assessment of hormonal catastasis of fetoplacental complex is extremely important during early gestation.

Objective: Investigation of engagement of hormonal function of placental system in pregnant women with low positioning of chorion during the first trimester of gestation.

Materials and methods. Index group was consisted of pregnant women with low

positioning of chorion (50 pregnant women). Control group included 50 pregnant women with normal positioning of chorion within the body and fundus of uterus. Investigation was being carried out during the periods of 5-8 and 9-12 weeks of gestation.

By us the content of the following hormones was detected: estradiol, progesterone, placental lactogen and chorionic gonadotropin within blood serum by immunoenzymometric method, chemical reagents of the firms "Alkor-Bio" (Russia) and DRG (Denmark) were utilized.

Statistical processing of collected indices was carried out by estimation of Student's t-tests.

Results and discussion. Collected data showed that already during the I trimester of pregnancy the significant difference of concentrations of investigated hormones between pregnant women with low positioning of chorion and pregnant women with positioning of chorion within the body and fundus of uterus had place.

By us were found out that concentration of estradiol within blood serum of pregnant women from the index group was mionectic during whole I trimester. In particular content of an actual hormone was lower in comparison with the control group by 7,2% during 5-8 weeks period ($p>0,05$) and by 23,93% during 9-12 weeks period of gestation ($p<0,05$).

Estrogens deficit during early gestation causes to slowdown of synthesis and decrease of activity of enzyme systems, and also to slowdown of energy metabolism, accumulation of glycogen and ATP in cells, increase of uterine activity.

Analyzing the hormonal state of pregnant women during the I trimester of gestation, we also found out that content of progesterone within

blood plasma of pregnant women with a low placentation was probably lower in comparison with the control group by 10,86% during 5-8 weeks period of pregnancy and by 20,98% during 9-12 weeks period ($p<0,05$). Such changes witness about impairment of hormonal function as corpus luteum as decidual and trophoblastic complex that forms. It is common that progesterone is hormone that ensures maintenance of pregnancy, contributes the hyperpolarization impact on membranes of myometrium cells, suspends the uterine muscles activity.

Among the hormones of protein origin of placenta we determined chorionic gonadotropin (CG) and placental lactogen (PL), which were produced since early pregnancy by the cells of syncytiotrophoblast. During early pregnancy steroid function of corpus luteum is maintained by placental hormones – CG and PL. Upon conditions of low placentation the process of synthesis and secretion of CG is frustrated, in consequence of which its blood content is decreased. CG level in pregnant women with low positioning of chorion was definitely lower, than in pregnant women with positioning of chorion within the body and fundus of uterus. The content of chorionic gonadotropin within the blood of women with low placentation during the I trimester was estimated $36990,0\pm210,0$ mg/l during 5-8 weeks of gestation, in the control group – $43270,0\pm226,0$ mg/l ($p>0,05$); during 9-12 weeks - $36194,0\pm395,0$ mg/l, in the control group - $53700,55\pm525,0$ mg/l ($p<0,05$). In our opinion, such changes are connected with the fact that upon condition of low positioning of chorion during early gestation the robust gestational reconfiguration of coiled artery of the uterus is absent; the acute rheological shifts in intervillous space appear; so-called afunctional areas and pseudo infarcts form. In its turn this causes to harsh luminal occlusion and their complete obliteration. In consequence of which hormone producing function of chorion and placenta suffers that causes decreasing of CG level within blood plasma of pregnant women.

Carried out investigations also showed that content of placental lactogen within blood plasma of pregnant women with abnormal positioning of chorion during 9-12 weeks of pregnancy was

probably lower in comparison to the control group respectively: $1,16\pm0,04$ mg/l and $1,38\pm0,024$ mg/l ($p<0,05$). During the first half-time of pregnancy placental lactogen is secreted predominantly within foetal blood flow that directly influences the growth rate of foetus during this time period [5].

Conclusions. Thus investigation of hormonal function of fetoplacental complex in pregnant women with low placentation will allow diagnosing the progression of placental dysfunction during early pregnancy. Detection of laws of hormone producing function of fetoplacental complex will provide opportunity of forecasting of progression of placental dysfunction that will allow conducting the preventive measures and treatment of actual abnormality on time.

Prospects for further research. To draw out the algorithm of comprehensive diagnostics of primary placental dysfunction in pregnant women with low placentation.

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MODERN LITERARY DATA OF DEVELOPMENT FEATURES CORONAL ARTERIES OF HEART (literature review)

Abstract. *Relevance and the social importance of studying development of coronary arteries of heart for the purpose of searches effective treatment and ways of prevention of cardiovascular diseases which are caused by prevalence of the diseases among adult population having the adverse forecast and high death rate. Results of literary search about features of development of coronary arteries of heart are presented in article.*

Key words: *development, heart, coronary arteries of heart.*

In the second half of XX and at the beginning of XXI century non-communicable diseases, primarily cardiovascular diseases which currently are the leading cause of disease incidence, disablement and mortality of adult population, predominantly jeopardize for the health of population and provide the challenge for health protection. Regardless of centuries-long history of heart study as the central organ of cardiovascular system, issues of coronal blood circulation abnormalities till now remain in the public eye of majority of investigators [4, 5, 14, 19], that is why studying of coronal arteries (CA) progression is an actual and expedient issue of nowadays.

Coronal arteries elaboration is the fundamental stage in heart development and includes the chain of consequent phases. Development of arteries of coronary vasculature is a form of vasculogenesis with further angiogenesis. This vasculature uses few unique development processes which are not observed during elaboration of other blood vessels [7, 27]. Distinctive features of this process are commitment of angioblastic cells, interaction between angioblastic cells and mesenchyme and also differences in arterial and venous structures [22, 26]. Considering the mechanisms of elaboration of CA divergency from heart, it is worth noting that the heart is originated as nonvascular structure and elements, which direct blood flow towards the myocardium, develop later – at the appropriate development stages [1, 17, 18].

Vasculogenesis process starts from the delivery of vasculogenic types of cells to the surface of heart after the beginning of cardiac beat. These cells settle across the whole heart, differentiate into endothelial cells, unstrained muscle cells, adventitial cells and fibro-blasts, later build up arteries, veins, capillary tubes and connect to aorta and coronal antrum [17, 22, 26]. Spreading of the cell pool that demands active cell fission, and also coordination of cell movements and acute delivery time, commitment and differentiation is crucially important for normal elaboration of vessels [2, 21].

For a long period of time an opinion existed that coronal arteries elaborated out of ecphyma of wall of aortic medulla. This opinion was contradicted at the end of 80th by the series of papers which determined that coronary plexus began elaborating within subepicardium and further infiltrating myocardium [10, 18]. CA develop in two phases: vascular plexus is elaborated and surrounds the heart, and then this plexus transforms into mature vasculature that is joined with aorta.

Inside of the mature heart, junctions that link the plexuses with aorta interpenetrate two hiatuses or orifices through which left and right CA connect to aorta [20, 23, 24]. Thus in early period (9-10 weeks) elements of coronary vasculature [6] are added to sinusoid type.

The next phase of development of coronary vasculature is linked with elaboration of new vessels, in particular, of capillarity from the

primary vascular plexus. Coronary plexus first is formed in the form of multiple primary endothelial locuses which spread from the venous antrum along the anterior ventricle wall in order to elaborate the whole plexus [23]. One of the most interesting aspects of development of coronal vessels is that the huge part of initial differentiation and structure formation occurs without blood flow. Endothelial plexuses are observed across the whole square of grown heart and across the whole wall of trabecular myocardium before connection to aorta [10, 21, 26]. So in the closing stages of vasculogenesis without blood flow, an overall scheme of coronary vasculature is determined, but significant transformation of large vessels and capillarity will occur after connection with aorta [26].

Joining of coronary vasculature to the allover blood-vascular system is complicated development process, and till this moment it is unclear whether it is the motion that is directed to chemotaxis or it is merely “the line of least resistance”. First CA cephalic ends migrate to the proximal aorta. The mockers of coronary vessels penetrate through the middle aortic wall, needle an endothelial lining and create integrity in lumina [25].

Few coronary vessels grow near left and right aortic antrums, but only one of these arteries creates a solid linkage with every antrum and becomes the right or left CA. It is interesting to understand the accuracy of CA linkage with aorta, because they are located in the center of aortic valve [16, 21, 25]. Positioning of every CA varies as throughout the height as along the aorta [9, 24]. Baseline entrances of right and left CA are usually situated at the level of brims of aortic valves, but level of outsets of coronary vessels in regard to half-moon-like valves is variable [16, 24]. Great transformations of coronary vasculature are continued after positioning of chaotically located vascular plexus of arteries, veins and capillary tubes exactly after linkage with aorta [26].

Hiatus of the left CA may be situated on the free edge level of half-moon-like valve (in majority of cases – 42,6%), higher or lower of its edge (in 28 and 29,4% respectively). Positioning of above of free edge of half-moon-like valve is the most often for an entrance of the right CA (51,3% of cases), on the free edge level (30%) or lower than

free edge (18,7%) [8, 9, 24].

Bifurcation is the general type of divergency of coronary arteries regardless their diameter. In this type of divergency every vessel (trunk) is divided on two ramuses, the length of each is equal to the distance along the trunk from a vertex of angle of previous divergency [12]. Left CA grows away from the left coronary antrum of aorta and is located between the beginning of pulmonary trunk and the left atrial auricle; it is divided on circumflex artery and ramus interventricularis anterior. Ramus of circumflex artery is directed under the left atrial auricle in coronary transverse on diaphragmatic (back) surface of heart. From the circumflex ramus in upward and descending directions atrial and ventricular ramuses grow away. From 1 to 8 ramuses, which in regard to their topography are divided on anterior, middle and posterior, and regarding length – on short and long, direct towards the atriums [9, 13, 20].

Ramus interventricularis anterior runs down across the sulcus interventricularis posterior to the cardiac apex, and spreads the following ramuses: ramus diagonalis (side ramus); left- and right-ventricular ramuses anterior; ramuses interventricular septal anterior; infundibular conus branch [9, 20]. Ramuses diagonalis (from 1 to 4), which take part in blood supply of lateral left ventricular wall and can anastomose with left ventricular circumflex branch, grow away from the ramus interventricularis anterior of the left CA [9, 11]. In particular cases ramus diagonalis is grown out more proximally, thus three vessels instead of two grow out from the left CA trunk. In this case extra artery grows out from the left chief artery, between ramus interventricularis anterior and circumflex artery, and is called ramus intermedius. This artery ensures blood supply to the anterior segments of free left ventricular wall [1, 13, 15].

From 6 to 10 septal branches, which provide blood supply to 2/3 of interventricular septum, grow out from the left CA. Properly ramus interventricularis anterior of left CA reaches cardiac apex and supplies it with blood, sometimes it is shifted to the diaphragmatic surface of heart, anastomosing with posterior interventricular artery of heart, ensuring collateral blood flow between left and right CA. Circumflex artery lies in left atrioventricular sulcus and has

one or more branches which reach blunt heart edge, that ensures blood supply of the lateral and posterior left ventricular wall. Moreover vital atrial arteries grow out from the circumflex ramus [9, 15].

Left CA in comparison with the right CA has shorter trunk that in majority of cases is situated behind the pulmonary trunk root. Right CA after going out of aorta circumvents the right atrial auricle, then goes across the coronary transverse to the right, then – back, reaches direct sulcus interventricularis posterior, along which it runs down to the cardiac apex and is called posterior interventricular artery [3]. Right CA releases atrial and ventricular branches, ensuring blood supply of right atrium, the part of anterior and whole posterior surface of the left ventricle, interatrial septum and rear third part of interventricular septum [1, 9, 24].

Approximately in 90% of cases artery of atrioventricular ganglion goes out of right CA and only in 10% – from the circumflex artery. In certain cases both arteries – right coronary and circumflex arteries take part in elaboration of descending CA posterior. Many academics including W. Fulton, D. Lewin, G. Gadinier maintain an opinion that ramus interventricularis anterior plays a key role, the circumflex ramus plays medium role and the right CA plays insignificant role in the myocardium vascularization. Because regardless the type of heart blood supply, three times more blood flows through the left CA than through the right CA [1, 9].

So the development of CA is the complicated complex of controllable processes, which induce dramatic implications in physiology of human organism.

As of today the prospect of investigation of CA development remains in the focus of attention, because issues of coronal blood flow abnormality are the leading causes of disease incidence, disablement and mortality of population.

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DEGREE OF ADAPTATIVE STRAIN AND CELLULAR RESPONSIVENESS OF ORGANISM IN PATIENTS WITH ACUTE SHIGELLOSIS

Abstract. In patients with acute shigellosis within peripheral blood the percentage of polymorphonuclear heterophilic leukocytes is increased, while absolute number of these immunocompetent cells is factually unchanged. The absolute number and the percentage of agranulocytes (lymphocytes and monocytes) are significantly decreased.

Shigellosis in the majority (85,94 %) of patients is accompanied by formation of stress in (50,0 %) patients and by the reflex on the training session (35,94%). In insignificant number of patients with shigellosis the level of adaptative strain is in the zone of balanced arousal (10,16 %) and in the zone of excessive arousal (3,9%).

Key words: shigellosis, immunocompetent cells, adaptation.

Introduction. Species resistance of human's organism is occurred by biological specialty of human's organism. It is nonspecific, sustainable, runs in the blood, related to specialties of individual's genotype and includes a lot of indicators [1, 2]. These indicators hold key positions in studying of anti-infective screening. The first phase of studying of indicators is determination of absolute number and percentage of leading immunocompetent cell pools basing on which other indicators of anti-infective screening are determined [3, 4].

Objective: to determine the level of adaptative strain and cellular responsiveness of organism in patients with acute shigellosis on the ground of indicators of absolute number and percentage of leading immunocompetent cell pools.

Materials and methods. Post-hoc test of 198 patient histories of patients with acute shigellosis, which were receiving medical treatment in infectious disease ward of regional clinical hospital in Chernovtsy during the period of 2011-2015 yrs., was carried out by us.

Results and discussions. The degrees of autotoxemia, cellular and immune responsiveness of organism are the leading factors which determine the progress and severity of virulent disease. Determination of these indicators is based on the detection of absolute number and percentage of leading immunocompetent cell

pools.

The research outcomes of absolute number and the percentage of leading immunocompetent cells within peripheral blood in patients with shigellosis are provided in Table 1.

In patients with shigellosis (the tendency) towards decrease of absolute number of leukocytes by 26,64 % is formed. Moreover, the percentage of heterophilic leukocytes, when insignificant (by 3,16 %) decrease of absolute number, increases significantly (by 22,88 %). Increase of the percentage of heterophilic leukocytes is explained by increase of the percentage of stab neutrophils by 2,97 times and segmentonuclear multiform neutrophilous leukocytes – by 12,73%. Absolute number of segmentonuclear neutrophils is insignificantly (by 12,12 %) decreased.

Significant decrease of absolute number (by 88,42 %) and percentage (by 50,13 %) of lymphocytes and absolute number (from 3,86) and percentage (by 2,99 times) of monocytes. So shigellosis in humans is accompanied by significant increase (by 22,66%) of granulocytes and decrease (by 69,62%) of agranulocytes. It is the evidence of increased activity of factors and mechanisms of nonspecific anti-infective screening at the start of the disease, and also formation of specific immune anti-infective screening in latent state - adaptive immunity.

Table 1

Absolute number and the percentage of leading immunocompetent cell pools within peripheral blood in patients with shigellosis

Indicators	Unit of measurement	Apparently healthy humans (70)	Patients with shigellosis (n=128)		
		M±m	M±m	The degree of immune abnormalities	P
Leukocytes	x10 ⁹ /l	6,37±0,51	5,03±0,47	-I	>0,05
Heterophilic leukocytes	%	61,53±1,87	75,61±1,97	+I	<0,01
	x10 ⁹ /l	3,92±0,78	3,80±0,62	-I	>0,05
Stab neutrophils	%	3,39±0,23	10,06±1,02	+III	<0,01
Segmentonuclear neutrophils	%	58,15±2,07	65,55±2,15	+I	<0,05
	x10 ⁹ /l	3,70±0,41	3,30±0,32	-I	>0,05
Acidophil leucocytes	%	1,83±0,12	2,11±0,14	+I	>0,05
Basophilic leukocytes	%	0	-	-	-
Lymphocytes	%	28,27±1,69	18,83±0,93	-II	<0,05
	x10 ⁹ /l	1,79±0,31	0,95±0,23	-II	<0,05
Monocytes	%	8,47±0,27	2,83±0,22	-III	<0,001
	x10 ⁹ /l	0,54±0,05	0,14±0,07	-III	<0,05
ESR	mm/year	4,43±0,31	24,11±0,31	+III	<0,001

Erythrocyte sedimentation rate (ESR) is also nonspecific shielding reflex that talks about an availability of pathologic process. ESR increases along with the shift of protein assay towards coarsely dispersed proteins (fibrinogens, Ehrlich's serum factors). There are links between increase of fractions of Ehrlich's serum factors and increase of ESR. Apparently healthy humans have normal type of ESR, and the patients with shigellosis - accelerated type, and indicator value is on the line between accelerated and rapid. ESR increase by 5,44 times may prove that progression of inflammatory processes of different nature - transmissible diseases, immune inflammation, aseptic inflammation, virus infections and parasitic diseases...

Thus, at the beginning of admission of patient with shigellosis, the percentage of polymorphonuclear heterophilic leukocytes due to the increase (by 2,97 times) of stab segmentonuclear neutrophils increases within peripheral blood. The percentage of acidophil

leucocytes increases insignificantly. Increase of percentage of granulocytes within peripheral blood of patients with shigellosis is accompanied by significant decrease of absolute number and the percentage of agranulocytes (lymphocytes and monocytes), that shows that at the beginning of infection process while admission to the hospital care, t-factors and mechanisms of nonspecific anti-infective screening in the organism of patient are activated and the latent phase of formation of humoral and cellular immune reflex comes. Accelerated type of ESR proves this thinking and evidences about the beginning of producing of M-class coarse-molecular Ehrlich's serum factors by B-lymphocytes (by plasmacytes).

One of the topical issues of the modern medicine is the challenge of individuation of adaptative (accommodative) reflex of organism to different stimulants, diseases, pathologic states, surgical measures and other manipulations. All told causes to development of adaptative

processes of different degree of strain, formation of stress that varies depending on different severity, with a different duration and opportunity of compensatory processes. That is why the determination of degree of adaptative strain of organism in patients with shigellosis is an

expedient goal.

The results of investigation of level of adaptative strain of organism in patients with shigellosis, when admissions to the hospital care, are provided in Table 2.

General (average) level of adaptative strain in

Table 2

The level of adaptative strain of organism in patients with shigellosis

Level of adaptative strain depending on zone	Patients with shigellosis (n=128) M±m	Apparently healthy individuals (n=70) M±m	Degree of abnormalities	P
General level	0,30±0,04	0,48±0,05	II	<0,05
Stress zone	64- 50,00%	0	-	-
Zone of reflex on training session	46 — 35,94%	14 — 19,72%	III	<0,05
Zone of balanced arousal	13 — 10,16%	26 — 36,62%	III	<0,05
Zone of excessive arousal	5 — 3,90%	31 — 43,66%	III	<0,05

patients with shigellosis is lower by 60% and is positioned on the line between stress (0,29) and the level of adaptative strain of the reflex on training session. Depending on the level of individual adaptative strain, the patients with shigellosis are divided on zones of adaptative arousal. The half of patients shows the stress of different severity (from 0,07 to 0,29), and kind of fewer patients are in the zone of the reflex on the training session, fewer patients are in the zone of balanced arousal, and little number of patients is in the zone of excessive arousal (including 2 patients in the non-arousal zone). The majority of patients with shigellosis when admissions to the hospital care are in the stress zone (50,5%) and in the zone of the reflex on the training session (35,94%).

Increased level of adaptative strain in patients with shigellosis requires the consultation of patient not only by infectious disease physician, but also by medical psychologist.

Cellular responsiveness of patient's organism plays crucial role in diagnostics, first of all in pathogenesis of development, in the progress of shigellosis, the treatment and forecast of disease. Evocation on the exo- and endo-intoxication is the reflection of the cellular responsiveness of organism. Shigella produce low concentrations of enterotoxin and during their destruction

shigellosis intracellular toxin is released. The level of cellular responsiveness of organism in patients with shigellosis was determined depending on leukocytal intoxication index of B.A. Reys and Ya.Ya. Kalf-Kalifa, depending on nuclear index of endotoxemia degree, hematological indicator of intoxication of V.S.Vasiliev. Investigated results of the cellular responsiveness of organism in patients with shigellosis are provided in Table 3. It was demonstrated that in patients with shigellosis leukocytal intoxication index of B.A. Reys was significantly (by 73,77%) increased. Also indicator of intoxication is increased by 9,04 times, leukocytal intoxication index of Ya.Ya. Kalf-Kalifa is increased by 2,03 times, nuclear index of endotoxemia degree is increased by 2,5 times and hematological indicators of intoxication of V.S. Vasiliev – by 7,74 times. Listed above prove the high degree (the III degree of immune abnormalities) of cellular responsiveness of organism in patients with shigellosis, that requires carrying out of efficient extracorporeal blood purification therapy and following application of sorbing agents.

Conclusions: 1. In patients with shigellosis the percentage of polymorphonuclear heterophilic leukocytes is increased, while absolute number of these immunocompetent cells is factually unchanged.

Table 3

Cellular responsiveness of organism in patients with shigellosis

Indicators	Units of measurement	Patients with shigellosis (n=128) M±m	Apparently healthy humans (70) M±m	Degree of immune abnormalities	P
Leukocytal intoxication index of B.A.Reys	c.u.	2,17±0,04	1,72±0,03	III	<0,01
Indicator of intoxication	c.u.	0,45±0,041	0,052±0,003	III	<0,01
Leukocytal intoxication index of Ya.Ya.Kalf-Kalifa	c.u.	3,53±0,04	1,25±0,02	III	<0,01
Nuclear index of endotoxemia degree	c.u.	0,14±0,02	0,06±0,01	III	<0,01
Hematological indicators of intoxication of V.S.Vasiliev	c.u.	1828,25±93,47	238,20±17,82	III	<0,01

2. Shigellosis in the majority (85,94 %) of patients is accompanied by formation of stress in (50,0 %) patients and by the reflex on the training session (35,94%). In insignificant number of patients with shigellosis the level of adaptative strain is in the zone of balanced arousal (10,16 %) and in the zone of excessive arousal (3,9%).

3. Development and progression of shigellosis occurs upon conditions of increased cellular responsiveness of patients' organism.

Prospects for further research. Collected results are the cause to their use in diagnostics and treatment tactics of patients with shigellosis.

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EFFECT OF DIFFERENT MATERIALS USED FOR DURAPLASTY ON CHANGES OF THE PERIPHERAL BLOOD VALUES

Abstract. We are doing this research study to find the changes in peripheral blood indices in experimental animals 2 weeks, 2 and 6 months after duraplasty. We used autologous fascia lata, a collagen based material and a chitin-chitosan film for duraplasty. Using allografts and materials of biological origin leads to a change of peripheral blood in the early postoperative period, indicating the development of general nonspecific reaction. 2 months after the operation all blood indices returned to the control ones. Using chitin-chitosan films does not lead to a significant decrease in hemoglobin and red blood cells and exhibits less pronounced inflammatory reactions.

Key words. Dura mater, duraplasty, blood indices, chitin-chitosan film.

Introduction. As for medical, social and economic losses TBI leads in the structure of morbidity and mortality from injuries and ranks third in the structure of injuries. 1,5 million people die and 2.4 million become disabled worldwide every year due to TBI [7]. About 30% of patients with TBI of varying severity die in the prehospital phase, from 20 to 30% among those hospitalized die in hospital, and another 10-20% become disabled. 50-60% of discharged patients recover completely or have minor neurological complications, sustained abnormal function occurs in 7.1% of patients with TBI [3, 9].

In penetrating TBI the integrity of dura mater of brain and arachnoid of brain gets broken. This group of injuries include penetrating injuries of the skull, open depressed fractures of the cranial vault and skull base fractures involving leakage of cerebrospinal fluid (CSF). Replacement of DMB defects is made using materials of biological and non-biological origin, organic and inorganic nature [2].

The classic method for duraplasty uses the patient's fascia lata of thigh. The advantage of this technique is the absence of an immune response to the material, an ease of operation and lack of the financial burden on the patient or clinic. However, an additional trauma and a likelihood of postoperative complications restrict the use of this technique [4]. Today numerous medical tools used for duraplasty and based on natural (collagen) and synthetic materials have been developed [1, 5].

Chitosan and its derivatives is one of the materials which can be the base for the development of biocompatible implants [6]. Chitosan is a natural polysaccharide, which is derived from the chiton. Chitosan has no allergenic properties, it is biocompatible, biodegradable, has antibacterial properties and is able to stimulate regeneration. An important advantage of this material is its relatively low cost. Unfortunately, there are only rare data on the development of materials for duraplasty based on chitosan. In our previous work we proved the benefits of using a material based on chitin and chitosan, which are in the lack of toxicity, positive impact on the regeneration and the absence of inflammation [8]. We also studied blood indices during the experiment, which can be used to assess the safety of using the material.

Objective: to trace the changes of peripheral blood indices in the early and late postoperative periods after duraplasty with experimental chitin / chitosan film, with a piece of fascia lata of thigh and an agent based on collagen.

Materials and methods. The material for duraplasty was obtained from 3% solution of chitosan (mol. mass 200 kDa, degree of deacetylation is 80-90%). To this effect, 10 ml of 3% solution of chitosan in 1% acetic acid was poured onto Teflon circular substrate (substrate diameter 8 cm, height of the solution layer was 5 mm), the solvent evaporated at room temperature for 48-72 hours. To improve the mechanical properties and to reduce the

degradation time of the film, chitin particles (1-2 mm) were added in the solution of chitosan. The ratio of chitosan and chitin was 50:50 and 80:20. Shaking homogeneously, we distributed particles in a viscous solution of chitosan to obtain a homogeneous suspension. The resulting film was treated with 5% NaOH solution for 2 hours, repeatedly washed with distilled water and treated with glycerin for 30 minutes to give it elasticity and softness.

Design of the experiment and surgery.

In order to compare the effectiveness of innovative implant we conducted a an experiment on 90 rabbits aged 3-4 months, which were divided into three series:

Series I (18 animals) – duraplasty was performed with the use of an autograft - the fascia lata.

Series II (36 animals) – duraplasty was performed with the use of collagen based material. The animals in this series were divided into 2 groups:

1st – plasty without fixing the material,

2nd – plasty with fixing the material using atraumatic suture.

Series III (36 animals) – duraplasty was performed with the use of membranes based on chitosan reinforced with chitin. The animals in this series were divided into 2 groups:

1st – plasty without fixing the material,

2nd – plasty with fixing the material using atraumatic suture.

After general anesthesia and peripheral vein catheterization, we shaved the head from the supraocular edge of the skull to the base of the ears. After treating the surgical field with a solution C-4, we performed a T-shaped incision, first in the frontal plane between the ears edges drawn before their foundation and then perpendicular to it in the sagittal plane from the line of the first cut on the middle line almost to the bridge of the nose. Triangular patches of skin were separated in different directions. The temporal muscle was disjointed by an arcuate cut and separated by means of a raspatory with the periosteum in the lateral direction but not more than required by future access for trepanation. Using a trepan and a sharp cutter 0.5 cm in diameter, two holes at 0.5-0.7 cm apart were made. The only trepanation access and aligning of

sharp edges was made by the diagonal pliers. The wound was cleaned from chips and debris and, if necessary, hemostasis with the diploe was carried out. The DMB was dissected crosswise.

The fascia lata was fixed to the DMB using noninvasive suture material. The collagen-based material and chitosan-based implants were fixed due to their adhesive properties. In order to compare the effectiveness of fixing the membranes in the second subgroup of series II and III, we used an additional fixation of the materials by means of atraumatic suture. The implant was pre-formed larger than the defect, it was placed between the intact DMB and the inner surface of the bone (Figure).

After the plasty, without covering the bone defect, we performed myorrhaphy and passed to the other side of the head where we performed duraplasty with the same stages. The operation was completed by stitching the skin and applying aseptic dressings.

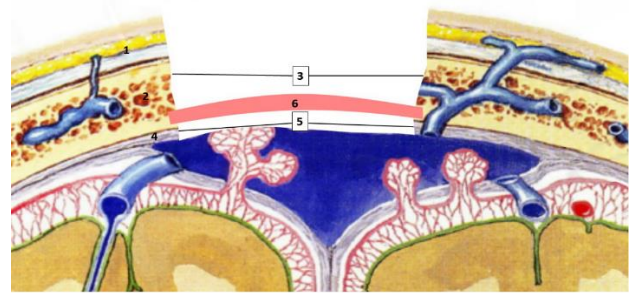


Figure. Scheme of duraplasty by using chitin-chitosan films: 1 – integument; 2 – skull; 3 – formed bone defect; 4 – dura mater; 5 – defect of the dura mater; 6 – material for plasty.

In order to assess the overall response of animals to the implant material the animals were taken 2 mL of venous blood before the surgery (control) and 2 weeks, 2 and 6 months after the plasty. We also tested the blood for hemoglobin, red blood cells, white blood cells and their populations and platelets.

All figures were recorded as mean value \pm error of the mean value ($M \pm m$). The reliability of the difference between the figures was calculated using Student t-test using the program SPSS-Statistic 21.0 (trial-version).

Results and discussions. In intact animals the content of blood cells and hemoglobin corresponds to the literature on blood parameters of rabbits. Duraplasty with the fascia lata leads to

a slight decrease in hemoglobin and erythrocyte count 2 weeks after the surgery, which may be the result of blood loss during the operation. (Table. 1).

However, after 2 and 6 months of observation the indices returned to the control level. The content of white blood cells increased after 2 weeks by 40.81% compared with the control and by 15.16% ($r \leq 0,05$) after 2 months and only after 6 months of observation they returned to the control level. The periods of 2 weeks and 2 months after the surgery are also characterized by an increased proportion of neutrophils, basophils and eosinophils (Table. 2). The percentage of lymphocytes, in contrast, decreased by 64.92% ($r \leq 0,05$) 2 weeks and by 36.85% ($r \leq 0,05$) – 2 months after the plasty. The level of platelets and monocyte percentage remained reliably constant throughout the observation period.

Using a collagen-based material leads to similar changes in the peripheral blood but there is a difference due to the method of fixing the material. For instance, the level of hemoglobin

and red blood cells reduced significantly after 2 weeks when using suture material for fixing artificial materials (Table. 3). With that, its recovery can only be observed at the last observation period, as opposed to a group of animals without fixation, in which hemoglobin and red blood cells indices return to that of the control as early as 2 months after the surgery.

The number of leukocytes increased by 36.44% 2 weeks after the surgery and does not depend on the method of fixing the material for duraplasty. Platelet count does not change during the experiment. Changes in the leukogram in case synthetic materials are used are less significant compared to the plasty with a piece of the fascia lata. For example, the percentage of neutrophils increased from 47.05% ($r \leq 0,05$) after 2 weeks in the absence of fixing material to 64.25% ($r \leq 0,05$) with the suture material. However, unlike the previous series, the parameters of leukogram do not differ from the controls after 2 months of observation (Table. 4).

Table 1

Hemoglobin and blood corpuscles at different time after duraplasty with a piece of the fascia lata.

	Hemoglobin	erythrocytes	leukocytes	Platelets
Control	103,6±7,3	4,32±0,67	6,86±1,3	256±34,5
2 weeks	91,6±3,5	3,98±0,39	9,66±0,85	297,6±51,3
2 months	100,2±1,8	4±1,2	7,9±0,65	279,2±25,8
6 months	105,6±4,7	4,3±0,92	6,96±1,03	286±40,3

Table 2

Wbc blood at different time after duraplasty using a piece of the fascia lata.

	neutrophils	basophils	eosinophils	lymphocytes	monocytes
Control	44,2±2,3	1±0,2	1,2±0,3	45,6±2,9	8,4±1,2
2 weeks	70,2±3,9	3,2±0,5	1,6±0,5	16±1,7	8,8±0,6
2 months	61,6±1,6	2,6±0,4	1,4±0,4	28,8±3,3	5,4±0,9
6 months	43,8±3,3	0,8±0,3	1,2±0,2	50±4,2	6,6±0,5

Table 3

Hemoglobin and blood corpuscle at different time after duraplasty based on collagen.

	Hemoglobin	Erythrocytes	Leukocytes	Platelets
control	103,6±5,8	4,32±1,1	6,86±0,4	256±34,5
2 weeks (without fixation)	95,6±4,8	3,96±0,7	9,08±1,1	246±84,6
2 weeks (with fixation)	90±9,2	3,74±0,5	9,36±0,8	290±44,3
2 months (without fixation)	105±3,7	4,28±0,6	7,22±0,92	274,2±29,5
2 months (with fixation)	95±5,1	3,94±0,2	7,48±0,5	348±60,0
6 months (without fixation)	103,2±4,3	4,3±0,8	6,66±1,4	290±45,2
6 months (with fixation)	105,6±8,2	4,22±0,5	6,32±0,7	278±33,7

Table 4

Wbc blood at different times after duraplasty using a collagen based material

	neutrophils	basophils	eosinophils	lymphocytes	monocytes
Control	44,2±2,3	1±0,3	1,2±0,5	45,6±3,2	8,4±0,9
2 weeks (without fixation)	65±5,2	0,6±0,2	3,2±0,3	23,8±1,8	5,4±0,4
2 weeks (with fixation)	72,6±3,1	1±0,4	3,8±0,0,4	19,6±1,3	5,2±0,7
2 months (without fixation)	45±4,0	1,2±0,5	5,4±0,2	35,8±2,7	8,6±0,5
2 months (with fixation)	49,6±2,7	1,6±0,5	3,8±0,6	33,8±4,1	10,6±1,3
6 months (without fixation)	41,4±1,2	1,2±0,3	1,4±0,2	48±3,3	8,4±0,9
6 months (with fixation)	45,4±4,6	0,6±0,2	1,2±0,4	41,4±3,8	11,4±0,6

Using chitin-chitosan films is accompanied by a slight decrease in hemoglobin and erythrocyte count 2 weeks after the surgery, perhaps due to hemostatic properties of chitosan, as evidenced by many authors [6]. 2 and 6 months after the operation the blood parameters returned to their control levels. The number of leukocytes grew by 18.2% ($r \leq 0,05$) after 2 weeks, whereas there was no significant difference between the group without the use of suture material, and a group of

graft fixation. Chitosan is known to have antibacterial properties and anti-inflammatory action, so a slight increase in inflammatory cells may be indicative of the monomer action of chitin-chitosan film during its degradation. Fluctuations of platelets level during the experiment was unreliable (table. 5).

The leukogram indices show a slight growth in overall reaction, especially in comparison with previous experimental animal groups. Neutrophil

Table 5

Hemoglobin and blood corpuscle at different time after duraplasty with chitin-chitosan film.

	Hemoglobin	Erythrocytes	Leukocytes	Platelets
control	103,6±7,4	4,32±0,4	6,86±0,2	256±33,2
2 weeks (without fixation)	98,4±4,2	3,92±0,5	8,18±0,25	274±41,4
2 weeks (with fixation)	98,2±2,9	3,84±0,2	7,98±0,3	293±53,4
2 months (without fixation)	105±5,4	4,38±0,67	6,46±0,7	280±27,8
2 months (with fixation)	103,8±4,6	4,26±0,7	6,14±0,3	189±21,9
6 months (without fixation)	104±6,2	4,26±0,4	6,54±0,5	272±56,2
6 months (with fixation)	102,6±5,9	4,38±0,6	6,68±0,7	254±41,1

Table 6

Wbc blood at different time after duraplasty with a collagen based material

	neutrophils	basophils	eosinophils	lymphocytes	monocytes
Control	44,2±1,3	1±0,2	1,2±0,3	45,6±2,33	8,4±1,1
2 weeks (without fixation)	56,6±2,3	1±0,5	1,8±0,4	32,8±2,8	7,8±0,6
2 weeks (with fixation)	60,6±1,9	1±0,1	1,4±0,2	30±1,8	7±0,3
2 months (without fixation)	49,6±2,8	0,6±0,2	0,8±0,3	40,2±3,1	8,8±0,7
2 months (with fixation)	43,2±1,9	0,8±0,3	0,8±0,1	46,6±2,4	8,6±0,5
6 months (without fixation)	48±3,2	1,2±0,2	1±0,4	41,4±1,8	8,4±1,4
6 months (with fixation)	42,4±4,1	1,2±0,4	0,8±0,4	47,6±2,5	8±0,7

percentage increased by 28.05% ($r \leq 0,05$) and 37.1% ($r \leq 0,05$) after 2 weeks in animals without using suture material and those with using it respectively. The percentage of eosinophils increased a little, lymphocytes decreased with a maximum of 28.1% ($r \leq 0,05$). After 2 months, all leukogram indices returned to those of controls. does not lead to a significant decrease in hemoglobin and red blood cells and demonstrates a less pronounced inflammatory response.

Prospects for further research. We are going to study the mechanisms of regeneration the defect of the dura mater using chitin-chitosan implants.

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- Conclusions.** Thus, using the allografts and biological transplants causes changes in peripheral blood indices in the early postoperative period, indicating the development of nonspecific general reactions. 2 months after the plasty all the studied parameters correspond to the control ones. Applying chitin-chitosan film as a transplant
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