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## PECULIARITIES OF PREGNANCY PROGRESS IN WOMEN WITH CORRECTED ISTHMIC-CERVICAL INCOMPETENCE

**Abstract.** *The article deals with the results of the study of peculiarities of pregnancy progress and its outcome among women with isthmic-cervical incompetence corrected by means of different methods. The conducted analysis demonstrated the lack of statistically significant difference between the results of applied methods of ICI correction, which requires more deliberate approach to use surgical correction of this pathology and detection of accurate indications for its application.*

**Key words:** *miscarriage, isthmic-cervical incompetence, pessary, suture on the uterine cervix.*

**Introduction.** Miscarriage is one of the topical issues of contemporary obstetrics caused by a high frequency and lack of tendencies to reduce this pathology. Isthmic-cervical incompetence (ICI) is a common cause of habitual non-carrying of pregnancy involving from 14,5% to 65% of late miscarriages and preterm labour.

ICI progress can be under the impact of organic, functional and congenital factors promoting the development of the following types of the pathology: anatomical (traumatic, organic), functional and congenital. Organic ICI occurs in case of traumatic damages of the uterine cervix due to huge fetus delivery, precipitated labour, as well as delivery by means of obstetric forceps, induced abortion, diathermocoagulation and other manipulations when instrumental dilation of the uterine cervix is used [1]. Due to the above mentioned the connective tissue is formed in the area of the isthmic portion of the uterus. This tissue is a morphological substrate of ICI. Functional ICI develops during pregnancy and can be stipulated by both hormonal disorders (ovarian hypofunction, hyperandrogenesis) and changes of uterine response to neurohumoral stimuli [4].

Premature labour in case of ICI is caused by several mechanisms [1, 5]. Incompletely closed cervical canal promotes ascending spread of the vaginal microflora to the uterine cavity resulting in infection of the fetal membranes. Due to inflammatory process metabolites are formed producing cytotoxic action on trophoblast and causing chorion detachment. In the II half of pregnancy they increase uterine irritability initiating the onset of uterine contractions and preterm labour (PL) [6]. On the other side, due to gradual shortening of the vaginal part of the uterine cervix and dilation of the cervical canal the ovum loses its support and descends in the caudal direction, the fetal membranes penetrate into the

dilated cervical canal and open. Biometrium contractility occurs and the ovum is extruded.

Nowadays both conservative and surgical methods of correction of ICI are applied. All of them are principally directed to prevent dilation of the uterine cervix as a factor of ICI. Conservative methods of treatment are: keeping to bed regimen, application of obstetric pessary, hormonal or tocolytic therapy. It should be noted that all pharmacological agents indicated to prevent PL in case of ICI block the final stage of their progress – biometrium contraction. Therefore, their administration cannot be considered sufficient. It is these causes that might affect considerable prolongation of pregnancy [7].

Scientists do not share the same views concerning application of obstetric pessary: some of them consider its use to be rather effective [8, 9], others [10] are more restrained. Therefore, application and comparison of the results of different methods to correct ICI remain rather topical.

**Objective** of the investigation was to study the progress of pregnancy and its outcome in women with isthmic-cervical incompetence corrected by various methods.

**Materials and methods.** A retrospective analysis of the progress and outcome of single pregnancy in 84 patients with corrected ICI has been performed. Depending on the methods of correction the women were distributed into three groups. The first group included 25 women who underwent the procedure of applying circular sutures on the uterine cervix. The second group included 34 women who were treated by means of the obstetric discharging pessary of "Arabin" type. The third group comprised 25 women with a combined correction of ICI (circular sutures on the uterine cervix followed by insertion of the obstetric discharging pessary). Women with

multiple pregnancy were not included into the study. The diagnosis of ICI was made on the basis of obstetric-gynecological examination and transvaginal ultrasonic cervicometry.

The groups were statistically similar. The mean age of the patients was  $28,7 \pm 4,2$ . There were 7 (28%) primigravid women in the 1<sup>st</sup> group, 14 (41,2%) – in the 2<sup>nd</sup> group, and 5 (20%) – in the 3<sup>rd</sup> group. Occurrence of abortions and voluntary miscarriages in secondary pregnant women concerning the groups was 32%, 29,4% and 36% respectively. Habitual miscarriage was found in 10% of the examined women from all the three groups.

Complicated gynecological anamnesis was found in 69 women (82,1%). The most frequent complications included chronic adnexitis, endometriosis, uterine myoma, ovarian cystic disease, urinary infections and endometrium polyps.

The findings were statistically processed by means of the applied computer program Statistica 10.0. Significant difference was considered to be reliable with  $p < 0,05$ .

**Results and discussion.** Pregnancy of the examined women was clinically complicated with a pronounced threat of miscarriage. All the pregnant women before correction of ICI were at least once hospitalized for threat of miscarriage. After ICI correction pregnancy was not complicated in 19 (22,6%) women. Others had different complications both on the maternal and fetal side. Preterm effusion of amniotic fluid was registered according to the groups in 16%, 14,7% and 12% cases. Placental dysfunction occurred in 24%, 8,8% and 16% of patients respectively.

Efficacy of all the three types of ICI correction was rather high. Thus, the number of preterm labour in the 1<sup>st</sup> group was 8%, in the 2<sup>nd</sup> – 11,8%, and in the 3<sup>rd</sup> – 12%, without reliable difference between the groups ( $p > 0,05$ ).

Delivery through the physiological maternal passages was more frequently registered among the women from the 1<sup>st</sup> group, and cesarean section was performed in more than 30% of pregnant women from the 2<sup>nd</sup> and 3<sup>rd</sup> groups, including 37,8% – due to urgent indications.

In all the examined groups there was rather high (27,4%) rate of babies transferred to the second stage of general medical care or those who required resuscitation and intensive care. It was indicative of the fact that perinatal complications were found more often in pregnant women with ICI.

**Conclusion.** The conducted analysis

demonstrated the lack of statistically significant difference between the results of applied methods of ICI correction. The use of aggressive methods of correction (applying sutures of the uterine cervix) should be administered for those patients with contraindications to alternative methods of treatment of this pathology.

**Prospects of further studies.** A comprehensive investigation of the issue of miscarriage in women with isthmio-cervical incompetence and its differentiation correction should be of practical value considering the elaboration of comprehensive methods of treatment of this group of pregnant women and prevention of perinatal complications.

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## STRUCTURAL ORGANIZATION OF THE CEREBELLUM OF 17-18 WEEK HUMAN FETUSES DURING INTRAUTERINE DEVELOPMENT

**Abstract.** *The study established micrometrical parameters of the cerebellar hemispheres and the brain worm in 17-18-week human fetuses, as well as structural organization, morphometric parameters of the cerebellum and morphology of the radial glia.*

**Key words:** *cerebellar hemispheres, the brain worm, morphometric parameters, fetal development, radial glia.*

**Introduction.** The study is conducted within the frame of the scientific-research work on the topic: "Detection of regularities of the organ- and histogenesis and topography of the internal thoracic and abdominal organs, the structures of the central nervous system in human fetuses (macroscopic, histological, immunohistochemical, and US-examination). Comparison of the findings obtained with the similar ones of fetuses with congenital developmental defects", State Registration № 0113U005070.

The functional system is evaluated as a unit of anatomical-physiological integration in every certain case combining various nervous systems and dynamics of nerve processes into one adjustment reaction. For example, the fetus is characterized by acceleration and selective development of those structures of the central nervous system and their functions essential for a newborn to perform various kinds of vital activity [4].

The cerebellum plays an important role in adaptation and setup of motor programs to make movements accurate by means of trial-and-error method (for example, learn to play baseball and other games requiring body movements). Although the cerebellum is more often considered from the point of view of its control over movements, it is also involved into certain cognitive functions, such as language. These functions of the cerebellum are not still studied so

well that they can be described in details. The recent years has been marked by an increasing interest of researchers to investigation of the central nervous system (CNS) of the fetus, and it is not accidentally, as now morbidity and mortality rates due to congenital cerebral defects occupies one of the leading positions among all other developmental defects in childhood. To our mind, one of the main reasons of such situation is untimely detection and difficulty in accurate differential diagnostics of a number of nosological forms of congenital cerebral defects of the fetus [1].

Therefore, in many countries of the world timely diagnostics (especially prenatal one), prevention and prognosis of this pathology are of a great priority. Within the span of human life the cerebellar structure undergoes qualitative and quantitative changes having a certain interest not only from the point of theoretical and practical aspects of medicine. They are important factors to understand age neuromorphology and changes in pathological conditions [1].

Vimentin has been found to be detected in embryogenesis in the cells of radial glia (neural stem cells) which are precursors of neuron, glioblasts, expressed during differentiation of neuroblasts [2].

In the germinal layer the cells are differentiated into neuroblasts and glioblasts and migrate into a reverse direction. The movement of cells through the layer of Purkinje cells is directed by radial

(Bergmann's) glia [8].

Due to this fact investigation of age and individual changeability of the cerebellar structure in prenatal human ontogenesis is of a considerable importance both for practical activity and theoretical design, because in spite of all the studies conducted rather many gaps remain unsolved.

**Objective:** to determine macrometric parameters of the cerebellar hemispheres and brain worm, as well as cytoarchitectonics and morphometric parameters of the cerebellar structures of human fetuses of 17-18 weeks of the intrauterine development.

#### Materials and methods.

Anatomical-histological, immunohistochemical and morphometric examinations of the cerebellar hemispheres and brain worm of 15 human fetuses with gestation period (GP) of 17-18 weeks have been conducted. The fetuses were obtained during late abortion at the Regional Pathological-Anatomical Bureau in Vinnytsia. Congenital defects of the CNS were not found. Parietal-coccygeal length (PCL) was  $-136,0 \pm 6,7$  mm, mass  $-230,0 \pm 10,1$  g (Fig.1). Sizes of the head:

transverse  $-53,0 \pm 2,7$  mm, longitudinal  $-57,0 \pm 2,9$  mm, height  $-56,0 \pm 2,9$  mm. Sizes of the frontal sinciput: longitudinal  $-22,0 \pm 1,0$  mm, transverse  $-33,0 \pm 1,5$  mm. Sizes of the parietal sinciput: longitudinal  $-16,0 \pm 0,8$  mm, transverse  $-14,0 \pm 0,8$  mm. The material obtained was fixed in 10% neutral formaldehyde solution, then the cerebellum was filled in paraffin and celloidin blocks. After series of cerebellar sections 10-12 mm thick were made, the specimens were stained with hematoxylin and eosin, toluidine blue and by Van Gieson's stain. During immunohistochemical examination diagnostic monoclonal antibodies were used manufactured by "DacoCytomation": vimentin, Ki-67 and synaptophysin.

To conduct morphometric examination the microscopes SIGETA and M5C-10 were used. Photofixation and morphometry of the sections obtained was made by means of the camera ETREK Ucmos and computer program ToupViem (computed histometry).

Macrometric parameters of the cerebellar hemispheres and brain worm were detected by means of our own methods developed [3].

The digital data obtained were statistically processed by means of the standard program package "Statistica 6.0" by the firm Statsoft.

**Results and discussion.** In the process of the study we have obtained the following macrometric parameters of the cerebellar hemispheres and brain worm: transverse size of the cerebellum  $-18,0 \pm 0,7$  mm, left hemisphere: longitudinal size  $-11,0 \pm 0,7$  mm, height  $-7,0 \pm 0,4$  mm; transverse size  $-7,0 \pm 0,4$  mm; right hemisphere: longitudinal size  $-11,0 \pm 0,7$  mm; height  $-7,0 \pm 0,4$  mm; transverse size  $-7,0 \pm 0,4$  mm. Transverse size of the brain worm  $-4,0 \pm 0,2$  mm; longitudinal size of the brain worm  $-7,0 \pm 0,4$  mm; height of the brain worm  $-6,0 \pm 0,5$  mm; cerebellum mass  $-700,0 \pm 35,7$  mg. Transverse fissures are found on the surfaces of the cerebellar hemispheres and brain worms forming the layers of the cerebellum. A deep horizontal fissure is also found. It begins in the point where the middle peduncle enters the cerebellum (Fig. 1). The left and right cerebellar hemispheres and the brain worm are clearly visualized. Liu F. (2011) found that the primary cerebellar fissure of the human fetus is detected on the 14<sup>th</sup> week. Since



Fig. 1. Human fetus of 17-18 weeks of intrauterine development. PCL  $-136,0$  mm. A-general view. B-cerebellum (upper surface): 1-horizontal fissure.



the 16<sup>th</sup> week the secondary fissure and dentate nucleus can be identified [6].

Yamaguchi K. (1997) states that after the 22<sup>nd</sup> week of the intrauterine development primary curves or fissures are found on the lateral surface of the cerebellar hemispheres. At the same time, curves are formed on all the surfaces since the 28-29<sup>th</sup> weeks [9].

Rakic P. (2004) characterized the layers of the cerebellum in the period from the 7<sup>th</sup> to 40<sup>th</sup> week of gestation. Till the 10<sup>th</sup> week proliferation of cells was limited by the ventricular zone. External granular layer is isolated separately in the 10-11<sup>th</sup> week, and Purkinje cells appear till the 13<sup>th</sup> week. In the 20-21<sup>st</sup> week they cross intermediate layer (future molecular layer). The 5<sup>th</sup> layer appears since the 32<sup>nd</sup> week. During examination of the histocytoarchitectonics of the cerebellar hemispheres and brain worm in this gestation term the following layers are clearly visualized: ventricular, intermediate and cerebellar cortex. Rakic P. (2004) differentiates the similar cerebellar layers [8].

Rakic P. (2004) describes that the cerebellum is formed at the expense of overgrowth of the dorsal-lateral wall of the neural tube in the area of the hindbrain. In the first weeks of the human development neuroblast migration of the matrix zone results in anlage of the nuclei and Purkinje cells. In the 9-11<sup>th</sup> weeks matrix stem cells are isolated from the ependymal layer and migrate (primary migration) on the surface of the cerebellum germ. They form external germinal layer there (till the 21<sup>st</sup> week of development its thickness is 6-9 cellular layers).

The study detected that histocytoarchitectonics of the cerebellar hemispheres in this gestation term is clearly visualized. On the horizontal section of the cerebellum the dentate nucleus is of a thin concave tape shape turned laterally and dorsally by its concave part. In the medial direction the outlines of the dentate nucleus are not closed. This place is termed the gate of the dentate nucleus. The three layers have been found: ventricular zone, intermediate zone, cortical zone, which in its turn is divided into the internal granular, intermediate, external granular layers (Fig. 2).

General thickness of all the cerebellar layers in the right and left hemispheres varies. Thus,

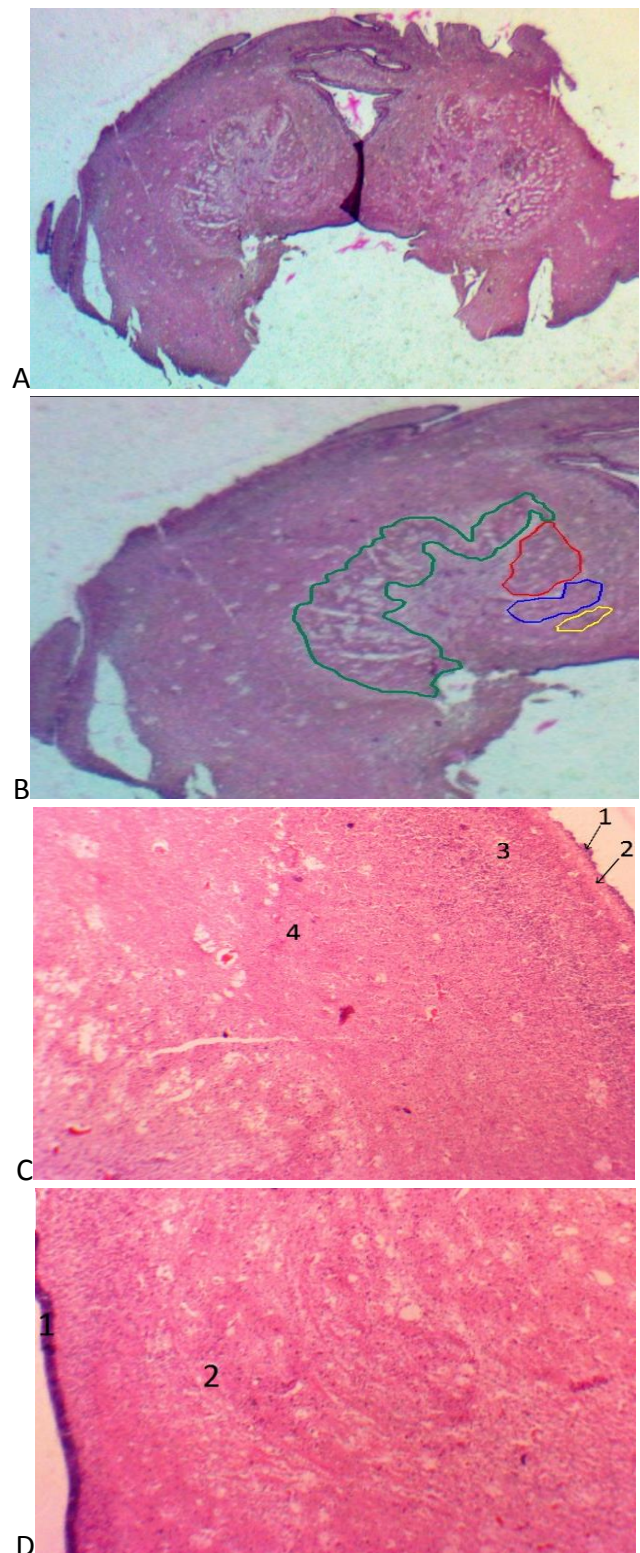


Fig. 2. Cerebellum of the human fetus 17-18 week of gestation. A – horizontal section of the cerebellum.

Hematoxylin-eosin;  $\times 6$ . B – nuclei of the right cerebellar hemisphere: dentate nucleus (green), crustate nucleus (red), spherical nucleus (blue), topocal nucleus (yellow). Hematoxylin-eosin;  $\times 6$ . C – the right hemisphere: 1-external granular zone, 2-molecular zone, 3-internal granular zone, 4-intermediate zone. Hematoxylin-eosin;  $\times 40$ . D – the right hemisphere: 1-ventricular zone, 2-intermediate zone. Hematoxylin-eosin;  $\times 40$ .

general thickness of all the layers of the right hemisphere is  $4189,7 \pm 234,6$  mcm, general thickness of the gray matter of the right cerebellar hemisphere –  $447,3 \pm 21,9$  mcm, external granular –  $28,3 \pm 1,3$  mcm, molecular –  $56,0 \pm 2,7$  mcm, internal granular –  $363,0 \pm 19,2$  mcm, intermediate zone –  $3711,0 \pm 144,7$  mcm, ventricular zone –  $31,4 \pm 1,8$  mcm. General thickness of all the layers of the left cerebellar hemisphere is  $4056,2 \pm 229,4$  mcm, general thickness of the gray matter of the left cerebellar hemisphere –  $441,1 \pm 20,8$  mcm, external granular –  $27,2 \pm 1,2$  mcm, molecular –  $55,4 \pm 2,6$  mcm, internal granular –  $358,5 \pm 18,7$  mcm, intermediate zone –  $3584,0 \pm 193,5$  mcm, ventricular zone –  $31,1 \pm 1,8$  mcm. General square of the right dentate nucleus was  $0,25 \pm 0,01$  mm<sup>2</sup>, general square of the left dentate nucleus was –  $0,26 \pm 0,01$  mm<sup>2</sup>. General square of the right crustate nucleus was  $0,05 \pm 0,002$  mm<sup>2</sup>, the left one –  $0,05 \pm 0,002$  mm<sup>2</sup>. General square of the right spherical nucleus was  $0,03 \pm 0,001$  mm<sup>2</sup>, the left one –  $0,03 \pm 0,001$  mm<sup>2</sup>. General square of the topical right nucleus was  $7875,3 \pm 417,4$  mcm<sup>2</sup>, the left one –  $8291,8 \pm 406,3$  mcm<sup>2</sup>.

The highest density of the neutral stem cells (NSC) was detected in the ventricular zone of all the structures of both hemispheres and it was  $18,3 \pm 8,4$  cells per 0,01 mm<sup>2</sup>. In the external granular layer (neurons and glial cells) –  $14,0 \pm 0,5$  cells per 0,01 mm<sup>2</sup>. In the intermediate zone –  $6,3 \pm 0,2$  cells per 0,01 mm<sup>2</sup>. In the internal granular layer –  $9,0 \pm 0,3$  cells per 0,01 mm<sup>2</sup>. The least density of cells was visualized in the molecular zone –  $3,7 \pm 0,1$  cells per 0,01 mm<sup>2</sup>.

Therefore, to our mind, investigation of the cellular growth in the cerebellum of human embryos and fetuses is of a great importance as it can be used for evaluation of the cortical growth and appearance of the cerebellar nuclei in the white matter of the cerebellum, non-invasive studies and improve the analysis of embryonic disorders of the cerebellum.

During the use of proliferation protein Ki-67 more intensive proliferation of cells in the ventricular zone of the cerebellum and less intensive in the white matter were found (Fig. 3). Acton A. (2012) describes that in the studies performed by means of immunocytochemical marker of the proliferative protein Ki-67 in the

cerebellum of the human fetus in the term of gestation of 17-21 weeks more intensive proliferation of cells was found in the ventricular zone and external granular layer [5].

During the use of radial glia marker we have found that fibers of the radial glia begin from the ventricular zone, penetrate all the zones of the cerebellum in the radial direction and finish in the external granular layer. Vimentin expression in the fibers of radial glia was found to be relatively moderate in the external granular and intermediate zones, and relatively strong in the ventricular and internal granular zones. An average length of the short radial glia fibers was  $179,5 \pm 8,4$  mcm, and the long ones –  $284,3 \pm 13,1$  mcm (Fig. 3).

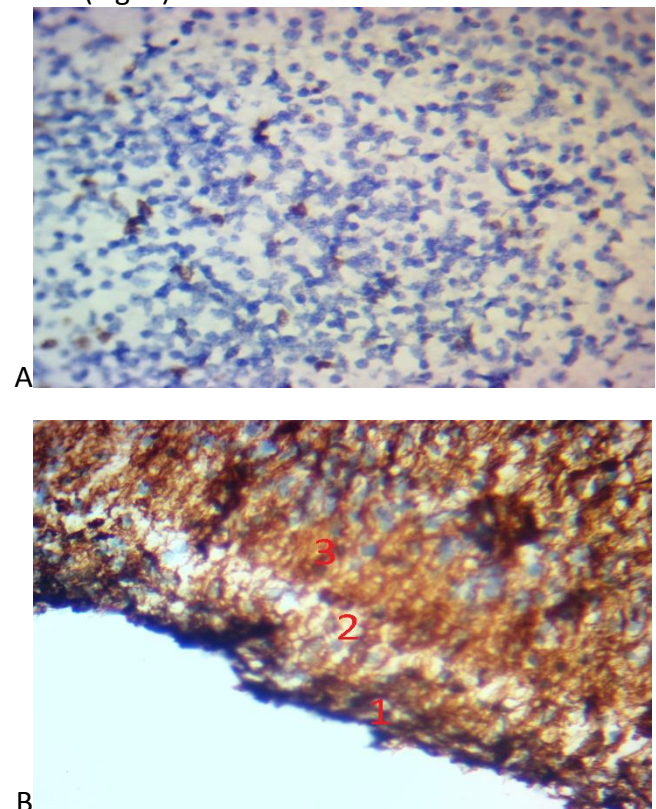


Fig. 3. A – proliferation of glioblasts in the cerebellar hemispheres (brown) Ki-67;  $\times 400$ . B – cerebellar hemisphere. 1-external granular zone, 2-molecular zone, 3-intermediate zone. Vimentin;  $\times 400$

While examining expression of synaptophysin the expression of the cells was found in all the layers of the cerebellum at this age (Fig. 4). Our studies correspond to the investigations conducted by Nag T.C. (2001). The author indicates that expression of synaptophysin cells was found in all the zones of the cerebellum since the 16<sup>th</sup> week of the intrauterine development [7].



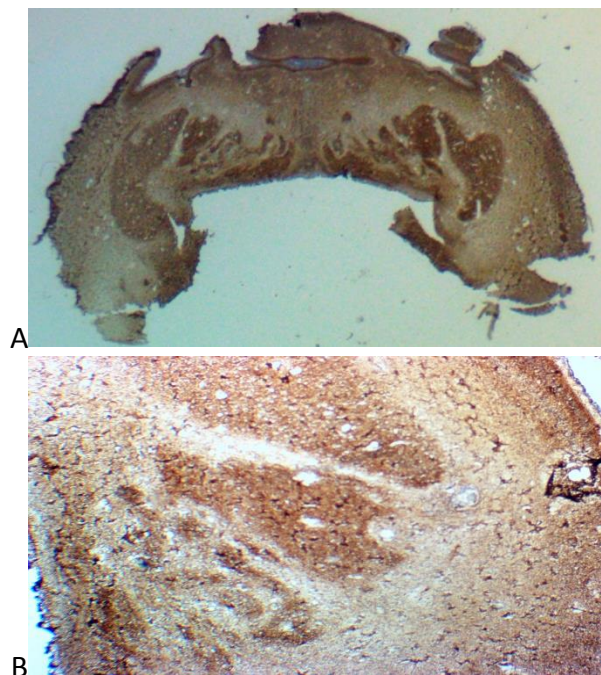


Fig. 4. A – cerebellar hemisphere. Synaptophysin;  $\times 6$ .  
B - Synaptophysin;  $\times 100$ .

Therefore, in the process of investigation we have detected macrometric parameters of the cerebellar hemispheres, peculiarities of cytoarchitectonics and morphometric parameters of the cerebellar hemisphere structures of the human fetuses in the 17-18<sup>th</sup> weeks of intrauterine development.

### Conclusions.

1. In the 17-18<sup>th</sup> weeks on the upper and lower surfaces of the cerebellar hemispheres and brain worm transverse fissures are found passing through the hemispheres and worm forming the layers of the cerebellum. A deep horizontal fissure is formed.

2. Three layers are clearly visualized in the cerebellar hemispheres: ventricular layer, intermediate layer and cortical layer. The highest density of the neutral stem cells was found in the ventricular zone –  $18,3 \pm 8,4$  cells per  $0,01\text{mm}^2$ . The least density of cells was found in the molecular zone –  $3,7 \pm 0,1$  cells per  $0,01\text{mm}^2$ . The highest thickness was found in the intermediate zone –  $3711,0 \pm 144,7\text{mcm}$ , the least thickness was found in the external granular layer  $28,3 \pm 1,3\text{mcm}$ .

3. The biggest proliferation of cells was found in the ventricular cerebellar zone, the least intensive proliferation was detected in the intermediate zone. Expression of synaptophysin was found in all the layers of the cerebellum.

4. The fibers of the radial glia begin from the

ventricular zone and finish in the external granular layer. Vimentin expression in the fibers of radial glia was found to be relatively moderate in the external granular and intermediate zones, and relatively strong in the ventricular and subventricular zones. An average length of the short radial glia fibers was  $179,5 \pm 8,4\text{mcm}$ , and the long ones –  $284,3 \pm 13,1\text{mcm}$ .

**Prospects of further studies.** Further studies suggest detection of regularities of the location of the white and gray matter of the human cerebellum in the prenatal period using immunohistochemical methods.

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## TOPOGRAPHIC-ANATOMICAL PECULIARITIES OF BLOOD SUPPLY AND INNERVATION OF THE MEDIASTINUM IN HUMAN FETUSES

**Abstract.** Macroscopic examination of the variants of blood supply and innervation of the mediastinum was carried out on 17 specimens of 6-7-month human fetuses. Certain topographic-anatomical peculiarities of the mediastinal-diaphragmatic arteries were found. Asymmetric location of the vascular-nervous bundle of the mediastinum was described. The right mediastinal-diaphragmatic artery and the right diaphragmatic nerve have a winding passage and greater number of branching. It should be noted that diaphragmatic nerves form nerve plexuses innervating anterior-lateral parts of the mediastinum and participate in the formation of paravascular plexuses of the internal thoracic artery.

**Key words:** mediastinum, mediastinal-diaphragmatic vessels, internal thoracic vessels, diaphragmatic nerve, fetus.

**Introduction.** Due to an increased rate of cardio-vascular diseases and congenital heart defects investigation of the problems of formation and development of blood supply to the heart and mediastinum during the prenatal period of human ontogenesis has become rather topical. Modern scientific literature contains information concerning additional sources of blood supply in case of disorders of the coronary circulation paying attention to the topography of the mediastinal vessels [1, 4]. Vascular network of the mediastinum connects the myocardial vessels with the vessels of the organs of the anterior and posterior mediastinum, diaphragm, bronchial and esophageal vessels [3, 5]. Rapid development of perinatal medicine and neonatology requires a detailed study of interrelations of the heart vessels with surrounding structures to perform more accurate surgery [5, 6]. Investigation of innervation of the mediastinal organs through the adjacent location of vessels and nerves deserves no less attention [2]. Although, the sources of blood supply and innervation of certain parts of the mediastinum during the fetal development of human ontogenesis are not examined sufficiently.

**Objective:** to find the sources of blood supply and innervation of the mediastinal parts in 6-7-

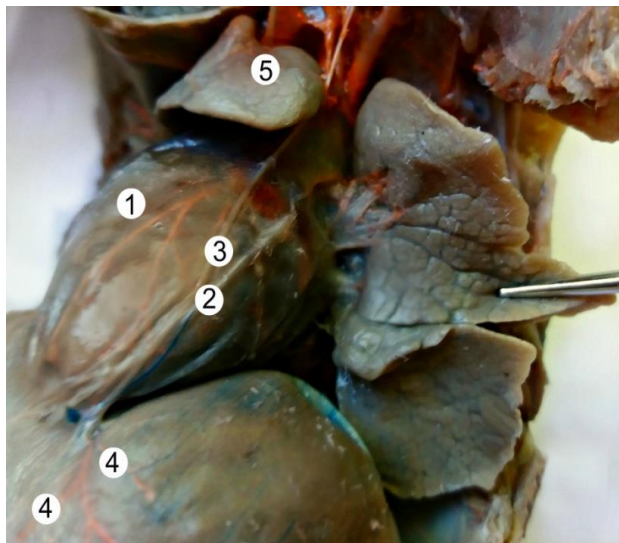
month fetuses.

**Materials and methods.** Macroscopic examination of typical and variant anatomy of vessels and nerves of the mediastinum has been carried out on 17 specimens of human fetuses 186,0-270,0 mm of the parietal-coccygeal length (PCL) by means of the methods of anatomical dissection and vascular injection.

**Results of the study and their discussion.** The mediastinum is known to have the anterior – sternal-costal, two lateral – the right and left mediastinal, and inferior – diaphragmatic parts (walls). According to the data presented by I.M. Shvetsov [7] while lining horizontally on the level of the inferior border of the lung root, the anterior and anterior-lateral parts of the mediastinum are divided into two portions: upper and lower. Due to this fact 6 segments are differentiated in the sternal-costal part of the mediastinum: 2 anterior and 4 anterior-lateral. Examination of fetuses found mediastinal-diaphragmatic vessels accompanied by diaphragmatic nerve passing both on the right and on the left between the mediastinum and mediastinal part of the deciduous pleura. Location of the right and left vascular-nervous bundles of the mediastinum is asymmetrical. The right vascular-nervous bundle

of the mediastinum is shorter. Thoracic portion of the diaphragmatic nerve is located asymmetrically on the right and on the left. The right diaphragmatic nerve passes to the mediastinum joining the wall of the upper hollow vein (vena cava), and on the very mediastinum the nerve is covered with the deciduous pleura. In the area of the mediastinum the right diaphragmatic nerve is located anteriorly, or sometimes (5 cases) directly near the root of the right lung. Inferior thoracic part of the right diaphragmatic nerve passes along the inferior hollow vein (vena cava), along its lateral surface. The left diaphragmatic nerve passes to the mediastinum along the lateral surface of the hemiazygos vein, and then it is located anteriorly from the root of the left lung. At the same time, mediastinal portion of the left diaphragmatic nerve is longer than that of the right one (Fig. 1).

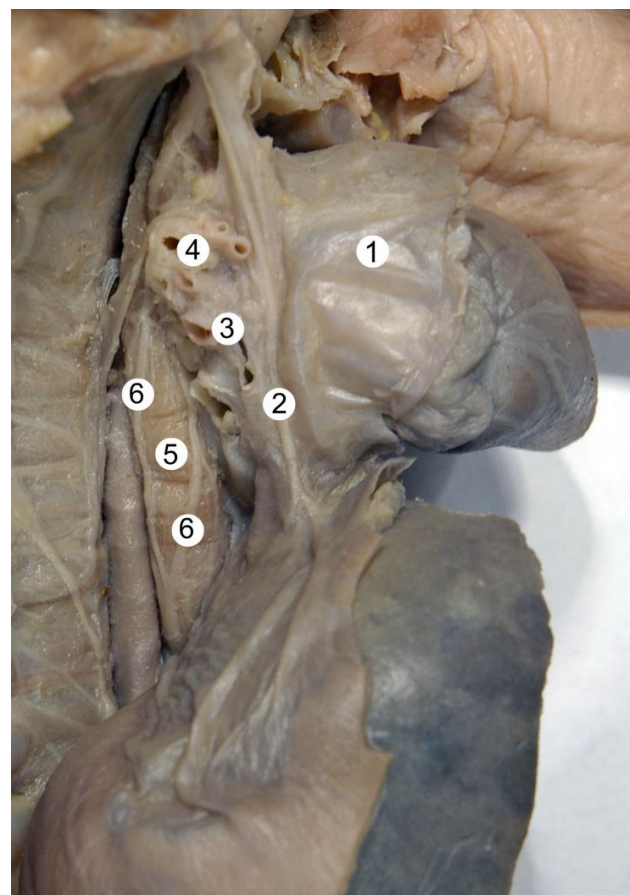
Since the right and left diaphragmatic nerves are topographically located anteriorly from the root of an appropriate lung, vagus nerves pass posteriorly from the lung root (Fig. 2). The right and left diaphragmatic nerves participate in the formation of nerve plexuses of the mediastinum, and together with branches of vagus nerves and sympathetic trunks form paravascular plexuses of the internal thoracic artery. Diaphragmatic nerves innervate anterior-lateral portions of the mediastinum.



**Fig. 1.** Organs and structures of the thoracic cavity of the fetus with 230,0 mm PCL. Macrospecimen. Anterior-left view. Magnification 2,5<sup>x</sup>: 1 – heart covered with mediastinum; 2 – left mediastinal-diaphragmatic vessels; 3 – left diaphragmatic nerve; 4 – branches of the muscular-diaphragmatic artery; 5 – retrosternal gland.

The mediastinal-diaphragmatic artery passes from the internal thoracic artery on the level of I rib, and together with the diaphragmatic nerve runs to the caudal direction. In the anterior part of the mediastinum 3 branches pass from the mediastinal-diaphragmatic artery, mainly from the left one: superior, anterior and inferior supplying lateral surfaces of the mediastinum, mediastinal part of the deciduous pleura and diaphragm. At the same time, the areas of blood supply of the left mediastinal-diaphragmatic artery are bigger than those of the similar right artery. The right mediastinal-diaphragmatic artery and the right diaphragmatic nerve have winding passages and a greater number of branching. The number of branches of the right mediastinal-diaphragmatic artery is usually 4-6 (Fig. 3).

The superior part of the anterior portion of the mediastinum is supplied with blood by means of the branches of the retrosternal gland, and venous outflow is carried along the retrosternal



**Fig. 2.** Organs and structures of the mediastinum of the fetus with 215,0 mm of PCL. Macrospecimen. Right view. Magnification 3,2<sup>x</sup>: 1 – right atrium covered with mediastinum; 2 – mediastinal-diaphragmatic vessels and diaphragmatic nerve; 3 – right pulmonary veins; 4 – root of the right lung; 5 – esophagus; 6 – branches of the right vagus nerve.



vein into the system of the internal thoracic vein. The inferior part of the anterior portion of the mediastinum is supplied with blood by means of the mediastinal branches of the internal thoracic artery and anterior branch of the mediastinal-diaphragmatic artery. The outflow of venous blood is carried along the similar vessels into the internal thoracic vein.

The superior part of the anterior-lateral portion of the mediastinum in the right and left is supplied with blood by means of the superior branch of an appropriate mediastinal-diaphragmatic artery. The outflow of the venous blood is carried through the similar vein into the brachial-cephalic vein, sometimes – into the internal thoracic vein. It should be noted that two left internal thoracic veins (middle and lateral) were found on 9

specimens out from 17 examined fetuses, and two right ones – only in 6 fetuses; and the internal thoracic artery is located between the same veins. Fusion of the left middle and lateral internal thoracic veins occurs, as a rule, in the 2-3 intercostal space (7 cases out of 9), and the right similar veins – in 3-4 intercostal space (4 cases out of 6). One internal thoracic vein along the whole length of the similar artery was found in the left in 8 fetuses, and in the right – in 11 examined fetuses. Arcuate anastomosis between the right and left middle internal thoracic veins was found anteriorly from the inferior third of the sternal body in 4 cases.

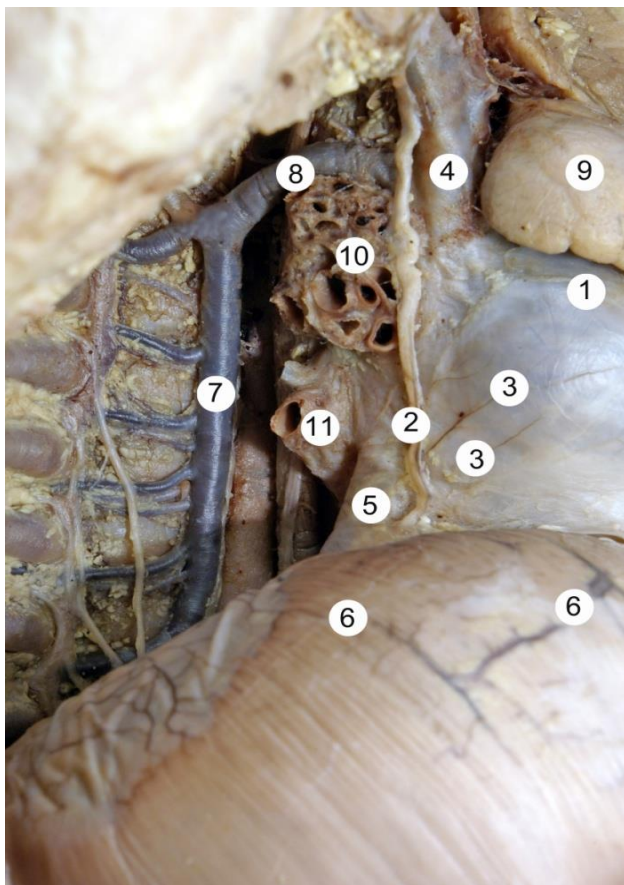
The inferior part of the anterior-lateral portion of the mediastinum is supplied with blood by means of the inferior branch of the mediastinal-diaphragmatic artery and bronchial branches. Venous outflow is carried into the inferior diaphragmatic vein. The diaphragmatic part of the mediastinum is supplied with blood by means of the branches of the superior and inferior diaphragmatic arteries, and venous outflow – into the similar veins. The posterior wall of the mediastinum is supplied with blood by means of the bronchial branches, and venous outflow is carried into the azygos and left brachial-cephalic veins. The posterior part of the mediastinum is supplied with blood by means of the bronchial and esophageal branches. In fetuses due to a weak development of the cellular tissue of the mediastinum the posterior wall adjoins the esophagus, trachea, bronchi, aorta, vagus nerves and pleura.

**Conclusions:** 1. The major vessels ensuring blood supply of the anterior-lateral parts of the mediastinum are mediastinal-diaphragmatic arteries. The latter together with diaphragmatic nerves form vascular-nervous bundle of the mediastinum. Location of the right and left vascular-nervous bundles of the mediastinum is asymmetrical, and the right vascular-nervous bundle of the mediastinum is shorter.

2. The areas of the blood supply of the left mediastinal-diaphragmatic artery are bigger than those of the similar right artery.

3. The right mediastinal-diaphragmatic artery and right diaphragmatic nerve have a winding passage and greater number of branching.

4. the right and left diaphragmatic nerves



*Fig. 3. Organs and vessels of the superior and middle mediastinum of the fetus with 270,0 mm of PCL. Macrospecimen. Right view. Magnification 3,7 $\times$ : 1 – right atrium covered with the mediastinum; 2 – mediastinal-diaphragmatic vessels and diaphragmatic nerve; 3 – branches of the mediastinal-diaphragmatic artery; 4 – superior vena cava; 5 – inferior vena cava; 6 – muscular-diaphragmatic vessels; 7 – azygos vein; 8 – arch of the azygos vein; 9 – right lobe of the retrosternal gland; 10 – root of the right lung; 11 – right pulmonary veins.*

participate in the formation of nervous plexuses of the mediastinum, and together with branches of the vagus nerves and sympathetic trunks form the paravascular plexuses of the internal thoracic artery. Diaphragmatic nerves innervate anterior-lateral portions of the mediastinum.

**Prospects of further studies.** The investigation is indicative of the necessity to conduct further study of the variant anatomy of blood supply and innervation of the mediastinum in human fetuses of various age groups.

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## CLINICAL-MORPHOLOGICAL PROGNOSTIC CHARACTERISTICS OF PROSTATE CANCER

**Abstract.** Among diagnostic clinical-morphological signs of prostate cancer (PC) the most significant ones are the level of prostate specific agent (PSA) of the blood, Gleason's pattern, and stage of the disease according to TNM (tumor, nodus, metastasis) system. Registration of these indices is essential for prognosis of the disease and choosing therapeutic tactics. Certain relations have been observed concerning an increased PSA level and T stage as Gleason's pattern increases ( $p < 0,0001$  and  $p < 0,0001$  respectively), as well as a tendency to higher Gleason's pattern among older people. Distribution of PC into the three groups of a low, intermediate and high risk considering PSA level, Gleason's pattern and invasive degree has shown the ratio 18,7%, 25,0% and 56,3% respectively. Risk groups were predominantly formed at the expense of extension of tumor process (T stage) and PSA level in the least.  
**Key words:** prostate cancer, Gleason's pattern, T stage, PSA level, disease prognosis.

**Introduction.** The study is a fragment of the scientific-research work of Kharkiv Medical Academy of Post-Graduate Education, the Ministry of Public Health of Ukraine "Nanotechnologies in Chemotherapy of Malignant Tumors in Adults and Children", 0113U000972 (2013–2017).

According to official statistical data in Ukraine [1] prostate cancer (PC) occupies the second position in the structure of oncological diseases among manhood and the first one among men over 75. Annual 5,3 % increase of its sickness rate is registered [1]. The choice of therapeutic tactics of patients is based on consideration of prognostic criteria of the disease including the most significant ones: Gleason's pattern, tumor extension according to TNM classification, PSA level of the blood [2, 3]. According to the information of the European Association of Urology (EAU) [4] the issue of a prognostic value of certain clinical-morphological criteria remains unsolved, including lack of recommendations to apply immune-histochemical markers to prognosticate and manage PC patients. The objective of the study is to investigate the major prognostic PC signs and detect their interrelations with clinical-morphological characteristics and risk of recurrent disease.

**Materials and methods.** 886 patients diagnosed with PC were operated on at V.I. Shapovalov Kharkiv Regional Clinical Centre of Urology and Nephrology during the period of five

years: from 2011 to 2015. In 280 cases open retropubic radical prostatectomy was performed. 168 patients were dropped out from the study due to incomplete data available, lack of microslides and paraffin blocks, or their low quality. Therefore, 112 cases of PC served as the material of the study.

PSA level of the blood, age of patients, Gleason's pattern according to the latest WHO classification [1], invasive degree according to TNM system [2] have been examined. In certain cases immune-histochemical examination to find basal cells markers – p63 and high molecular weight keratin (HMW) – was performed to confirm the diagnosis of PC.

The results of the study were statistically processed by means of the package «Statistica 6.0». The correlation between signs was evaluated according to non-parametric Pearson  $\chi^2$  criterion. The results were considered reliable with  $p < 0,05$ .

**Results and discussion.** An average age of PC patients was  $69,5 \pm 7,9$ . The peak of morbidity was marked at the age of 60-79 with practically equal number of patients at the age of 60-69 and 70-79 (48 patients at the age of 60-69 and 46 at the age of 70-79, average 42,8% and 41,8% respectively).

PSA level in PC patients was  $19,1 \pm 28,2$  and ranged from 0 to 210 ng/ml. The most relative number of patients was with PSA level of 4-10 (34,8%) and 10-20 (25,0%). As it is evidenced from Table 1, PSA level under 4 ng/ml is not specific for

PC, although this PSA level could not be a criterion to exclude cancer as well as 0 PSA level which was found in 2 patients.

In PC group 18,7% of tumors were characterized by invasive growth within the borders of a half of the prostate one lobe, that is it corresponded to T1-2a stage according to the latest TNM system [5]. Those were tumors rarely bigger than 1 cm in size. Extension of PC more than a half of one lobe (T2b) and involving two lobes (T2c) was detected in 26,7% and 16,1% respectively. Among those tumors there were cases when several tumor nodes were found. Prostate capsule invasion was found in 38,4% (43 cases) including 16 ones with invasion into the seminal vesicles, and 3 with invasion into the muscular tissue and adjacent organs.

In general the data obtained correspond to those found in scientific literature. Thus, in 22-50% of patients with localized PC tumor process extended beyond the organ, and recurrent disease developed approximately in 15-44% of patients [6, 7]. Nowadays oncologists are facing the task to detect risk factors promoting relapse and progression of the disease enabling to prevent the onset of clinical signs of a local relapse or remote metastasis. A number of studies appear dealing with new prognostic factors of relapse in PC patients after prostatectomy, which would enable in clinical practice to isolate a high risk group of patients more accurately. Nowadays the most reliable independent prognostic system of PC is Gleason's pattern, which application is essential for choosing therapeutic tactics of patients [8].

In our material average Gleason's pattern was  $6,8 \pm 1,35$ . The biggest group of PC was with Gleason's pattern 2-6 – 36,6% (41/112). According to the latest principles of PC gradation according to Gleason's pattern dated 2014 a great number of PC with Gleason's pattern  $\leq 6$  were classified into PC with Gleason's pattern 7, and all the forms of PC  $\leq 6$  were considered the least aggressive [9]. This group includes PC with microscopic manifestation in the form of dominated close adjacent glands located separately one from another, small and medium in their size, often branching and regular round shape. With the purpose to make highly specific differentiative diagnostics of PC with atrophic, hyperplastic processes, prostate intraepithelial neoplasm

(PIN), and atypical adenosis immune-histochemical examination to find the markers of basal cells p63 and high molecular weight keratin (HMW) was carried out. Complete lack of basal cells was a criterion of cancer available. According to the latest changes of Gleason's pattern cribriform structures should be referred to 4 degree, although single cribriform glands available are allowed in case of 3 degree [8]. According to the modified system 4 degree according to Gleason's pattern is characterized by fusion or cribriform, or poorly formed glands, or glomerular structures [WHO, 2016].

In our material a prevailing number of cases – 65 (58,0%) were PC 4 degree according to Gleason's pattern. 5 degree is characterized by isolation of cancer cells, their solid location with possible unclear microacinar structure, formation of cords and rarely found glands, availability of comedonecrosis in solid nests and cribriform structures [9]. According to the latest recommendations of WHO and European Association of Urology [4, 8] PC should be distributed into groups with Gleason's pattern 2-6, 7 (3+4), 7 (4+3), 8, 9-10. It is that distribution into 5 groups with integration of PC with Gleason's pattern 2-4 and 4-6 into one group, and separation of PC with Gleason's pattern 7 into two groups which is of the greatest prognostic value. Thus, according to a mass-scale investigation involving 20 845 cases of PC after radical prostatectomy, 5-year relapse-free course of the disease was according to the distribution of PC into 5 groups – in 96%, 88%, 63%, 48% and 26% [10]. In our material PC with Gleason's pattern 2-6 constituted 36,6%, 7 (3+4) – 17,8%, 7 (4+3) – 13,4%, 8 – 16,9%, 9-10 – 15,1%. Scientific literature presents controversial information concerning the relation of patient's age and Gleason's pattern [11, 12]. In our study, as it is seen from Table 1, patients older than 70 were found more often among those with higher Gleason's pattern (8-10) than among the cases with Gleason's pattern 7 and less. All the patients with Gleason's pattern 9-10 were older than 60 ( $\chi^2=1,9$ ,  $p=0,1$ ), and the age group of 50-59 included the biggest number (60%) of patients with Gleason's pattern  $\leq 6$  ( $\chi^2=2,5$ ,  $p=0,1$ ). Therefore, higher Gleason's pattern was found among older patients. PSA level is one of the most



Table 1

Relation of age and PSA level of PC patients

Index	Gleason's pattern					Reliability, criterion $\chi^2$
	$\leq 6$ n (%)	7 (3+4) n (%)	7 (4+3) n (%)	8 n (%)	9-10 n (%)	
Age						
50-59, n=10	6 (15)	2 (10)	0	2 (10)	0	$\chi^2=7,6$ , $p=0,8$
60-69, n=48	19 (46)	8 (40)	8 (53)	6 (32)	7 (41)	
70-79, n=46	14 (34)	9 (45)	6 (40)	9 (47)	8 (47)	
80-89, n=8	2 (5)	1 (5)	1 (6)	2 (10)	2 (12)	
PSA level						
0-4,0 (n=15)	7 (17)	4 (20)	3 (20)	1 (5)	0	$\chi^2=30,1$ , $p<0,03$
4,1-10,0 (n=39)	19 (46)	8 (40)	4 (26)	5 (26)	3 (17)	
10,1-20,0 (n=28)	12 (29)	5 (25)	4 (26)	3 (15)	4 (23)	
20,1-40,0 (n=17)	2 (4)	1 (5)	2 (13)	5 (26)	7 (41)	
>40,1 (n=13)	1 (2)	2 (10)	2 (13)	5 (26)	3 (17)	
Total	41	20	15	19	17	

required prognostic criteria, although with Gleason's pattern less than 6 this index is not of a prognostic value [13]. The experts from the College of American Pathologists suggest that PSA level should be referred only to the third prognostic category due to controversial data [14].

Comparing PSA level with Gleason's pattern statistically significant dependence was found in the form of increased PSA level as Gleason's pattern increases ( $\chi^2=75,0$ ,  $p<0,0001$ ). As Table 2 presents PSA level of PC with Gleason's pattern  $\leq 6$  and 7 was predominantly 4-10 ng/ml, a high relative number of cases among them was with PSA level lower 4 and 10-20. PC with Gleason's pattern  $\leq 6$  is not characterized by PSA level of 20-40 ( $\chi^2=5,3$ ,  $p<0,03$ ) and more than 40 ( $\chi^2=5,2$ ,  $p<0,03$ ). PC with Gleason's pattern 8 and more demonstrated an opposite dependence: there was none of the case with PSA level lower than 4 among PC with Gleason's pattern 9-10, the biggest relative number of cases was with PSA level 20-40 and a great relative number of cases with PSA level >40. PC with Gleason's pattern 8 was found to be associated with PSA level > 40,1 ( $\chi^2=4,8$ ,  $p<0,03$ ), and PC with Gleason's pattern 9-10 — with PSA level 20,1-40,0 ( $\chi^2=10,5$ ,  $p<0,003$ ).

The dependence between Gleason's pattern and degree of PC invasion was found in the form of Gleason's pattern increase as the indices of pathomorphological stage T ( $\chi^2=72,1$ ,  $p<0,0001$ )

increase as well. Among PC with Gleason's pattern  $\leq 6$  the most relative number of tumors were localized in one lobe (41%) or its half (39%), there were no cases with invasion into the seminal vesicles and adjacent organs. In its turn, among PC with Gleason's pattern 8 and 9-10 there were none case of tumors localized in the half of one lobe, and they included all the three cases of PC of T4 stage. PC of the groups 7 (3+4) and 7 (4+3) were rather close by the level of invasion, although among PC with Gleason's pattern 7 (4+3) less relative number of tumors localized in the half of one lobe was found (6,6% and 20% respectively). Apparently, in case a dominating by its volume part of tumor is of a lower differentiation, such kind of cancer is more invasive (Table 2).

Considering association of PC in every group with T stages it was found that PC with Gleason's pattern  $\leq 6$  was characterized by its localization within the borders of a half of one lobe, that is T1-2a stage, ( $\chi^2=17,4$ ,  $p<0,0001$ ) and the whole lobe, T2b stage ( $\chi^2=7,4$ ,  $p<0,01$ ). It is not characterized by invasion of prostate capsule, T3a stage ( $\chi^2=13,8$ ,  $p<0,0003$ ) and invasion into the seminal vesicles, T3b stage ( $\chi^2=10,7$ ,  $p<0,003$ ). PC with Gleason's pattern 7 (3+4) and 7 (4+3) was characterized by lack of dependence considering the level of invasion of the process. PC with Gleason's pattern 8 was associated with T3a stage, that is, it was characterized by invasion of



Table 2

Age	T stage and Gleason's pattern of PC					Reliability, criterion $\chi^2$
	≤6 n (%)	7 (3+4) n (%)	7 (4+3) n (%)	8 n (%)	9-10 n (%)	
T1-2a	16 (39)	4 (20)	1 (6,6)	0	0	$\chi^2=72,1, p<0,0001$
T2b	17 (41)	4 (20)	4 (26,6)	4 (21)	1 (6)	
T2c	7 (17)	4 (20)	4 (26,6)	1 (5)	2 (12)	
T3a	1 (2,4)	5 (25)	3 (20)	11 (58)	4 (23)	
T3b	0	3 (15)	3 (20)	2 (10)	8 (47)	
T4	0	0	0	1 (5)	2 (12)	
Total	41	20	15	19	17	

the organ capsule into the paraprostate cellular tissue ( $\chi^2=18,0, p<0,0001$ ). It was not characterized by its localization within the borders of one half of prostate lobe ( $\chi^2=5,2, p<0,03$ ). PC with Gleason's pattern 9-10 was associated with T3b and T4 stages, that is, it was characterized by pronounced extra-organic invasion with infiltration of the seminal ( $\chi^2=17,5, p<0,0001$ ) and adjacent organs ( $\chi^2=6,4, p<0,03$ ). At the same time, PC with Gleason's pattern 9-10 is not characterized by localization within the half ( $\chi^2=4,6, p<0,05$ ) and one prostate lobe ( $\chi^2=4,4, p<0,05$ ).

According to the recommendations of the WHO and EAU [4, 8] to prognosticate the risk of relapse, repeated therapy and lethal outcome, PC should be divided into three groups considering PSA level, T stages and Gleason's pattern.

High risk group included 56,3% (63/112) of tumors including 96,8% (61/63) of cases with T2c-T4 stages, two more cases were on T2b stage of tumor process; 57,1% (36/63) PC from the high risk group was characterized by Gleason's pattern 8-10, other 27 cases were characterized by Gleason's pattern 7 — in 36,5% (23/63) and Gleason's pattern ≤6 — in 6,3 % (4/63). PSA level

more than 20 ng/ml was found only in 47,6% (30/63) of cases, other PC cases from this group were with PSA level of 0-4 ng/ml — in 1,5% (1/63), 4-10ng/ml — in 22,2% (14/63) and 10-20 ng/ml — in 28,5% (18/63) (Table 3).

Distribution of PC into low and intermediate risk groups constituted 18,7% (21/112) and 25% (28/112) respectively. All 28 PC cases from the intermediate risk group were in T2b stage and with Gleason's pattern 7 in 42,8% (12/28) and Gleason's pattern ≤6 in 57,1% (16/28); PSA level 10-20 was found in 35,7% (10/28) of cases, 4-10 — in 46,4% (13/28), 0-4 — in 17,8% (5/28). All 21 cases of PC from the low risk group were localized within the borders of the half of the prostate lobe, with Gleason's pattern 2-6 and PSA level up to 10 ng/ml (0-4 ng/ml — in 42,8% (9/21), 4-10 ng/ml — in 57,1% (12/21)).

**Conclusions:** 1. An average age of PC patients was  $69,5 \pm 7,9$ . The peak of morbidity was marked at the age of 60-79 with practically equal number of patients at the age of 60-69 and 70-79 (42,8% and 41,8% respectively). An average PSA level was  $19,1 \pm 28,2$  and ranged from 0 to 210 ng/ml.

2. The comparison of patients' age, PSA level, T stage of tumor process with Gleason's pattern has

Table 3

Risk groups of PC			
	I (low risk group)	II (intermediate risk group)	III (high risk group)
Definition	PSA up to 10 ng/ml, T1-2a stages, Gleason's pattern 2-6.	PSA 10-20 ng/ml, or T2b stage, or Gleason's pattern 7.	PSA more than 20, or T2c stage, or Gleason's pattern 8-10.
Number of cases (%)	21 (18,7%)	28 (25,0%)	63 (56,3%)

found dependence between increased PSA level and T stage as Gleason's pattern increases ( $p < 0,0001$  and  $p < 0,0001$  respectively). Patients of older age had a tendency to higher Gleason's pattern.

3. PC with Gleason's pattern  $\leq 6$  was associated with its localization of tumor process within the borders of a half of one lobe (T1-2a and T2b stages), ( $p < 0,0001$ ). It is not characterized by PSA level more than 20 ( $p < 0,03$ ), invasion of prostate capsule (T3a stage) ( $p < 0,0003$ ), and invasion into the seminal vesicles (T3b stage) ( $p < 0,003$ ). PC with Gleason's pattern 8 was associated with PSA level  $> 40$  ( $p < 0,03$ ), invasion of the organ capsule (T3a stage) ( $p < 0,0001$ ), localization within the borders of the half of the prostate gland (T1-2a stage) ( $p < 0,03$ ). PC with Gleason's pattern 9-10 was associated with PSA level 20-40 ( $p < 0,003$ ), invasion of the seminal vesicles (T3b stage) ( $p < 0,0001$ ) and adjacent organs (T4 stage) ( $p < 0,03$ ), but it is not characterized by localization within one prostate lobe (T1-2b stage) ( $p < 0,05$ ).

4. Distribution of PC into the three groups of a low, intermediate and high risk considering PSA level, Gleason's pattern and degree of invasion has found the ratio of 18,7%, 25,0% and 56,3% respectively. Risk groups were mainly formed at the expense of extension of tumor process (T stage) and at the expense of PSA level at the least.

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## PSYCHOHYGIENIC ASPECTS OF TRAINING OF DISABLED ADOLESCENTS WITH PATHOLOGY OF THE VISION (literature review)

**Abstract.** *The objective of this article is to summarize information about some psycho-hygienic aspects of teaching the blind and visually impaired adolescents, including features of communication, learning environment, psycho-emotional stress in specialized educational institutions, as well as individual psychological characteristics of personality, emotional and volitional state of visually impaired.*

**Key words:** *psychohygiene, the blind and visually impaired, psychoprophylaxis, education, visual disturbances, prenosological state.*

One of the most urgent problems of today is the health of children and adolescents as well as reducing the number of healthy children. Increasing the proportion of children with a chronic diseases and people with disabilities greatly reduces the potential for development of the country. In the last decade throughout the world, including Ukraine, a lot of attention is paid to the occurrence of child disability. The growth of the total number of children with disabilities and a high level of primary disability of the child population, define the necessity of the state level measures for the correction of social policy for children with disabilities, the basic directions of that should be the prevention of disability, medical and pedagogical rehabilitation of children with disabilities, social adaptation, conducting primary preventive measures aimed at improving the stability of mental health, resilience of the psyche of children - disabled to the influence of various environmental factors that would entail the prevention of severe secondary somatic and neuropsychiatric consequences already at the initial stage of their manifestations without severe socially significant violations.

Throughout last few years were adopted and actively implemented national programs to preserve and improve the health of the most vulnerable groups, namely children and adolescents with disabilities, namely "Children of Ukraine" (1996), the Concept of Health Development of Ukraine (2000), the Interdepartmental complex program "Health of the nation" (2002-2011), and currently developed nationwide program "Health 2020: Ukrainian dimension".

According to the World Health Organization

(WHO) today there are 40 million blind people in the world, 1.5 million of them - are children. As for Ukraine, 40 thousand people are suffering from true blindness, visually impaired people are five times more [19]. And every year this number is increasing.

It is known that one of the most common causes of disability is blindness. Today, a variety of visual disturbances are extremely common worldwide. In recent years there has been tendency to growth of severe and disabling diseases that lead to loss of vision. Apart the causes, heredity, injury, complications at birth, infectious diseases, and common to all human diseases - environmental degradation, canned excess, etc. Important role played the tendency of civilization progress: the dominant role of vision, as a means of receiving and processing information. Each year, the flow of information increases, the visual system adapts to such loads much slower.

According to the current classification blind persons whose visual acuity is in the range from 0% to 0,04%. Thus, contingent includes people fully devoid of vision (totally blind) and with residual vision (visual acuity from light perception to 0,04%). Children with visual acuity from 0,05% to 0,2% are in the category of visually impaired, and may have to work with the help of sight under certain hygienic requirements [4].

One of the priorities of the existence and development of the prosperous state is to take care about getting all the representatives of the younger generation high-quality and high-grade education, as stipulated in the Law of Ukraine "Higher Education", which is associated with the creation the necessary conditions for quality

education of persons with disabilities including the blind and visually impaired. Totally blind children use touch and hearing to obtain educational information. Blind children with residual vision also obtain core training information through the sense of touch and hearing because if there is such a profound defeat of vision use for a long time entails a negative impact on its further development. However, in the process of training and education residual vision is not ignored because it gives children more information about the environment. For a student with a visual disturbance is important even before the start of classes to learn the movement and orientation in classrooms. It is necessary to maintain a constant placement of furniture and equipment in the classroom, and inform the visually impaired student about any changes in the room. Foreign methodologists prefer horseshoe seating arrangement of students when the teacher is in an open part of the "horseshoe" for easy access of all trainees to teacher. It is necessary to allow the student to sit where he is better sees the board, but not separately from other students. In the room is necessary to provide modifiable lighting conditions; because students may have different visual impairment, requirements to lighting are different for each student, in particular, require adjustable lighting in different parts of the class, to create different lighting conditions to meet the individual needs of students; local illumination, where it necessary; natural lighting and blinds to limit natural light and glare if it necessary. The classroom should be with perfect acoustics, because the sound is very important for a blind student. It is also necessary to minimize the extraneous sounds. Special coating of the walls and floor soften the sound and improve the learning environment, and conversely uncovered floor can create an echo and distort intonation [6, 18].

Visually impaired and disabled - is a special case, since 80% of the information people receive through the visual analyzer [5]. With a sharp decrease of vision, it interferes with the normal ability to self-care, movement in space, and also severely limits the possibility of learning and social interaction.

For a clearer perception of the problems of children with disabilities should be highlighted two groups of factors: the objective, depending on surrounding reality and subjective, depending

directly on the person, that can lead to mental health problems.

The objective factors include: a negative public perception of the disabled; low levels of social support, protection and assistance to persons with disabilities; not well-appointed accommodation and public areas for use by people with disabilities; low level of social status.

Subjective factors include: life position, consisting in passive and not an effort to feel like a full member of society; psychological self-awareness, underestimation of their capabilities, hidden personal potential; lack of life objectives, settings; rejection by society (isolation, aggression); the desire to learn, to work, to live [1].

It is known that all training programs must be aimed at solving the triune task: training and strengthening of health of students with regard to special schools for pupils with eye pathology, the additional challenges facing them both, because they need to focus on medical-social and psycho-hygiene aspects of training.

For medical and social rehabilitation of students, adolescents with disabilities, with the pathology of vision it is necessary to develop a methodological program for the study of the functional state and health of disabled adolescents due to ophthalmic pathology, which includes adequate, well proven in the currently researching methods, as well as the adaptation of special methods to study the functionality of people with ophthalmologic diseases.

According to many scientists one of the most important factors influencing the functional state of the organism, its adaptation possibilities, level of health (both mental and physical), is a psychoemotional stress. Depending on the causes and conditions conducive to appearance of stress, available different stressful situations that early detection and elimination of risk factors of their occurrence can prevent the development of pathological processes [3].

Overcoming of borderline conditions helps the applying of adaptogenic measures. They are aimed at training the organism functions contained in the reactions of individual adaptation practices and maintaining constitutional evolutionarily conditioned defense mechanisms. In the period of adaptation and a compensatory stress depending on it severity adaptogenic activities should be preserving, correcting, and in the stage of adaptation "collapse" - with reducing



character. Measures for the correction should be based on the objectification of evaluation of the organism functional state at the level of prenosological - premorbid state, as a result of mismatch the organism capabilities and environmental requirements arise predictors of pathological process [14].

One of the main tasks of the modern psychohygiene - providing mental health of individuals and the population as a whole. Not less important task psychohygiene - implementation of measures of primary psychoprophylaxis aimed at improving the mental health to resistance to the influence of various environmental hazards [7]. A subject of direct study of psychohygiene presented by such common mental conditions such as personality accentuation, which under certain conditions can be transformed into the corresponding psychopathy - condition of the morbid character; various types of deviant behavior that bring personal and social danger; a wide range of borderline mental states that accompany the situation and risk periods and has neurotic character [14].

Prenosological states arise from dysfunction of the adaptive systems, which are currently intended to ensure stable functioning of the organism, and therefore the preclinical diagnosis is based on the definition of qualitative and quantitative indicators of the adaptation process, measured, and (or) calculated as a result of prophylactic examinations. With the use of monitoring observation of the state health of students in special educational institutions for the blind and visually impaired in the complex of hygienic diagnostic measures, resolve the significantly extend our views on the formation of prenosological states among students and accordingly propose a system of preventive measures for the correction of the functional state of the organism [8, 14 12, 13].

Based on the direct and reverse incremental regression analysis are developed statistical models allowing to predict the degree of probability of prenosological shifts in mental health, taking into account characteristics of the living and social conditions, the mode of the day and training adaptation, characteristics of the psycho-physiological functions development of the body and the personality traits [2, 17].

Introduction into the research activity of the borderline states involves the creation of well-structured system of diagnostic and corrective

measures, enabling consistently meet the challenges of population health assessment, sanitary and preclinical diagnosing and hygienic correction of the functional state of the organism, whose ultimate goal is the preservation of the individual, population and public health [11].

However, is necessary to emphasize that the current system of primary prevention, actually deprived of an extremely important element, which consists of objectification of evaluation of the functional state of the organism at prenosological state level, in circumstances where as a result of non-compliance, conformity of the organism capacity to environmental requirements and social conditions arise prerequisites for the formation of the pathological process [15].

Basic hygienic measures in special schools for children with pathology of the organ of vision is a prenosological hygienic diagnostics of the health state of students. It involves a detailed study of the whole complex of educational and domestic factors in connection with their targeted influence on child and adolescent organism. In addition, the development of methods for the detection and measurement of individual psychological characteristics of personality [9]. The objective of these programs is to establish qualitative and quantitative characteristics to an external influence. During experimental work on studying the modes of learning for the blind and visually impaired in specialized educational institutions one of actual tasks is to establish a thin line separates the normal reaction to external environmental impacts of pathological manifestations.

Thus, the basis of our research is a natural experiment that allows, based on studies using modern adapted techniques to develop a set of effective measures psychohygienic correction of the functional state of students, as well as to justify scientifically prognostic criteria for assessing social adaptation of the under study contingent. The search criteria for assessing the level of health is important to make timely and adequate organizational, medical and social measures for the correction of premorbid states [16, 10].

**Conclusions.** Thus, analysis of foreign and native literature on sociocultural rehabilitation of people with special needs, gives grounds to say that undoubtedly the development of the sphere of social protection and support to developing pretty rapidly in almost all countries of the world,



but I can't mention the lack of study of the combined effect of educational and household activities on the functional state and the state of mental health the adolescents with disabilities of organ vision, which belong to the "group of risk" of prenosological deviations in neuro-psychic sphere. Before issues of development of special needs children were solved mainly in way of defect correction and compensation. At today's level at the top of the issue should be clearly set the task of studying and managing the development of child personality with special needs with a view to its fulfillment in the world of sighted people. For the organization of competent pedagogical work must take into account not only the age, but also the individual characteristics of children, due to their personal psycho-emotional qualities, as well as differentiated features associated with the diagnosis of eye diseases, the degree of visual impairment and their health.

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## **DEVELOPMENT OF PARAMESONEPHRIC DUCTS AND THEIR DERIVATIVES AT THE END OF EMBRYONIC PERIOD OF HUMAN ONTOGENESIS**

**Abstract:** *The process of formation of paramesonephric ducts at the end of embryonic period of human ontogenesis is closely associated with the development of sexual glands, mid-kidney (archinephron or mesonephros) and hind-kidney (metanephros).*

**Key words:** *paramesonephric ducts, development, embryo, human.*

**Introduction.** Investigation of the derivatives of the paramesonephric ducts is not sufficient, although they are of great theoretical and practical value. They are especially important for learning the development and formation of topography of the uterine tubes, uterus and vagina [1-8].

**Objective:** to find out further development of mesonephric and paramesonephric ducts at the end of embryonic period of human ontogenesis.

**Materials and methods.** The study was conducted on 9 human embryos. Morphological and histological methods were used.

**Results.** An intensive growth of mid-kidneys is observed in embryos of 9,0-10,0 mm PCL accompanied by an increasing number of mesonephric bodies. An intensive growth of the sexual gland germs occurs. Cranial portions of the mesonephroses (archinephrons) are located dorsally and laterally from the lung germs. Mesonephric ducts are located on the lateral surfaces of the mid-kidneys, their lumen increases. Lateral longitudinal fissures become more visible. Medial longitudinal fissures are formed in this period. Not deep fissure appears between the sexual glands and mesonephric part of the sexual crest in embryos 9,5 mm PCL.

In embryos 10,0-11,0 mm PCL the borders of the longitudinal fissures come closer, and due to this fact paramesonephric ducts (Muller ducts) are formed. They look like tubes located in the parenchyma of the mid-kidney (mesonephros). Appearance of germs of the paramesonephric ducts activates the growth of gonad germs. Mesenchymal taeniae extend between the upper poles of the mid-kidneys and pleuroperitoneal

folds – diaphragmatic ligaments of mesonephroses. Cranial portions of paramesonephric ducts are located posteriorly and laterally, their external diameter ranges from 20,0 to 22,0 mcm. A characteristic feature of embryos 11,0 mm PCL is the onset of reduction of the mid-kidneys occurring in the cranial-caudal direction. It plays a crucial role in the formation of future male or female sex. This stage of human embryogenesis can be considered as one of the critical periods in development.

Mesonephros inflection is seen in embryos 11,5-12,0 mm PCL which is connected with occurrence of natural inflection of the embryo. Gonad germs are located on the anterior-medial surface of the mid-kidneys in the form of longitudinal crests. Densely spaced mesenchymal cells of the gonads transform into mesenchymal taeniae. The length of gonads is  $1,2 \pm 0,1$  mm, the thickness –  $220 \pm 10$  mcm. Lateral and medial fissures become deeper. Coelomic epithelium transforms into the external layer of the mid-kidneys, mesonephric and paramesonephric ducts.

In embryos 12,0 mm PCL the germs of paramesonephric ducts have inconsiderable lumen. The length of paramesonephric ducts is  $660 \pm 10$  mcm, their lumen is  $4 \pm 0,2$  mcm. Intensive formation of paramesonephric ducts is indicative of one of the critical periods in the development of embryos 11,5-12,0 mm PCL. Caudal-mesenchymal taeniae pass from the caudal portions of the gonads and mid-kidneys. Hind-kidneys (metanephroses) are dislocated upwards coming closer to the inferior poles of the mid-kidneys. The umbilical arteries are located

laterally from the hind-kidneys. Upper borders of the left sexual gland are located on the level of X thoracic rib, and the superior pole of the right sexual gland – on the level of the inferior border of the same vertebra. The inferior extremities of the sexual glands correspond to the level of II lumbar vertebra, and the inferior extremity of the left sexual gland is located higher than that of the right one. A vertical size of the left sexual gland is  $1,4 \pm 0,01$  mm, a transverse size of the right sexual gland is  $1,3 \pm 0,1$  mm. The transverse size in the medial portion is  $460 \pm 20$  mcm.

Embryos 13,5 mm PCL have certain peculiarities in anatomical interrelations between the constituents of the urogenital complexes: mid-kidneys occupy a central position, they considerably protrude into the coelomic cavity gradually separating from the posterior wall of the trunk. Paramesonephric ducts grow in the caudal direction, their length is  $1,2 \pm 0,01$  mm, width –  $120 \pm 4$  mcm. Sizes of the hind-kidneys increase. Urogenital complexes are separated by the dorsal mesentery. Pleuroperitoneal fold is connected with the cranial pole of the mid-kidney by means of diaphragmatic ligament of the mesonephros. Taeniae extend downwards from the caudal portions of the mid-kidneys and sexual glands. They are further transformed into appropriate habenulae of the sexual glands. The length of the right mid-kidney is  $2,8 \pm 0,02$  mm, and the length of the right sexual gland is  $1,2 \pm 0,01$  mm. The length of the left mid-kidney is  $2,9 \pm 0,01$  mm, and the left sexual gland –  $1,3 \pm 0,01$  mm.

In embryos 14,0-14,5 mm PCL the lumen of paramesonephric ducts near the urogenital sinus is practically absent, which should be considered as a stage of physiological atresia. The diameter of the lumen of paramesonephric ducts on the level of the upper third of the mid-kidneys is  $4 \pm 0,1$  mcm, and on the caudal level from this position –  $2 \pm 0,05$  mcm. Retention or absence of recanalization of ducts can cause their retardation or absence which is one of the critical periods in the development of these structures. Sexual glands and mid-kidneys present a single complex of an elongated oval shape. The size of sexual gland increases and they begin isolate themselves from the mid-kidneys. Longitudinal depressions are formed between them and mid-kidneys in the form of lateral and medial fissures. The germ of

the hind-kidney is located medially concerning gonadomesonephric complex. The size of the mid-kidneys grows considerably. A vertical size of the left kidney is  $2,6 \pm 0,2$  mm, the right one –  $2,4 \pm 0,1$  mm. The cranial extremity of the left mid-kidney corresponds to the level of I thoracic segment, and the cranial extremity of the right mid-kidney – to the level of II thoracic segment. Lower extremities of the mid-kidneys are located on the level of I sacral segment. Mid-kidneys are characterized by appearance of larger mesonephric bodies and tubules in the caudal portion. 24 pairs of arterial vessels from the dorsal aorta pass to the mid-kidneys. Habenula of the sexual gland is clearly seen. The hind-kidney is located between the posterior wall of the coelom and caudal portion of the mid-kidney. The diameter of the lumen of mesonephric ducts is  $8 \pm 0,2$  mcm, and paramesonephric ducts –  $10 \pm 0,2$  mcm. The cranial portions of the urogenital complexes are located inferior from the pleuroperitoneal folds. The caudal portions of the above mentioned complexes reach the pelvic portion of the coelom. In the cranial portions germs of the gonads are located on the anterior surfaces of the mid-kidneys. At the same time the process of reduction of the mid-kidneys is initiated. It occurs in the cranial-caudal direction.

In embryos 15,0 mm PCL urogenital taeniae including mesonephric and paramesonephric ducts protrude over the internal surface of the coelom. The process of their separation begins. Habenula of the sexual gland becomes  $420 \pm 6$  mcm long. The caudal extremities of the paramesonephric ducts are detected on the border between the medial and inferior thirds of the mid-kidneys. Enlargement of the size of the adrenal glands results in dislocation of the urogenital complexes laterally.

**Conclusions.** 1. Embryos 13,0-14,0 mm PCL have certain peculiarities in anatomical interrelations between the constituents of the urogenital complexes: mid-kidneys occupy a central position, they considerably protrude into the coelomic cavity gradually separating from the posterior wall of the trunk, and are characterized by appearance of larger mesonephric bodies and tubules in the caudal portion.

2. At the end of the embryonic period formation of paramesonephric ducts occurs in

close morphological connection with the development of sexual glands, mid-kidneys and hind-kidneys.

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## HETEROGENEITY OF ESOPHAGITIS IN SCHOOLCHILDREN

**Abstract.** We observed 60 8-18 years old children who could have suspected features of esophagitis. Endoscopy of the esophagus was performed to all the children, during which the biopsy samples were taken. The children were divided into 3 groups: the main group №1 - 20 children with gastroesophageal reflux, who had some signs of food allergy at that time or in the past, they had standard antisecretory therapy and elimination or hypoallergenic diet, levocetirizine, probiotic bacteria *Lactobacillus reuteri*; the main group №2 - 20 children with gastroesophageal reflux who had pronounced manifestations of autonomic dysfunction who received standard antisecretory therapy and Phenibut; control group - 20 children with gastroesophageal reflux, who received standard antisecretory therapy. After 1 month of starting treatment an evaluation of its efficacy was conducted. Modification of GERD treatment in children with manifestations of food allergy and autonomic dysfunction promotes more rapid positive dynamics of the disease and better treatment results.

**Key words:** GERD, autonomic dysfunction, food allergies, schoolchildren

**Introduction.** Pathology of the digestive organs occupies a considerable position in the structure of pediatric somatic sickness in the whole world including highly developed countries. Its current occurrence in Ukraine is 148,41 per 1000 children and it has a tendency to grow. In the structure of gastroenterological diseases among children of different ages diseases of the upper portions of the alimentary canal occupy the first position. Nowadays they constitute 49,1% of all the pathology of the digestive organs [1].

Esophageal lesions occur more and more frequently among children of different ages in a wide spectrum of chronic inflammatory diseases of the digestive tract. Since recently pathology of the esophagus has included mainly developmental abnormalities and defects, injuries of the mucous membrane due to thermal or chemical lesions or remote consequences of these lesions, today inflammatory changes of the mucous membrane occur more frequently [2].

The findings of modern epidemiological studies are indicative of an increasing occurrence of esophageal diseases, and first of all gastroesophageal reflux disease (GERD). According to literary evidence this tendency is found in all the countries of the world and involves different age periods [3, 4, 5, 6, 7, 8]. There are certain evidences

concerning an increasing sickness rate for GERD among children, although, in spite of a growing interest of pediatric gastroenterologists to this pathology, the results of investigations do not enable to estimate a real spread of this disease [4-6, 8-10].

Practically all chronic esophagitis (CE) in children are considered to be a consequence of pathological gastroesophageal reflux, that is a sign of GERD. Actually, GERD is not rare in pediatric practical work, it occupies a dominating position in the structure of CE. Other possible mechanisms of its development should not be neglected.

During the recent decades a number of allergic diseases has been increasing constantly associated with lesions of the gastro-intestinal tract (GIT). The manifestations of GIT allergy are various, therefore formation of chronic esophagitis is not an exception [11].

Insufficient functional activity of the lower esophageal sphincter plays an important role in the development and progression of GERD. Its relaxation is found to be innervated by the nervus vagus through the preganglionic cholinergic fibers and postganglionic non-cholinergic and non-adrenergic nerve fibers. Therefore, investigation of the state of the vegetative nervous system in case of GERD in children promotes specification of



pathogenic mechanisms causing development and progression of the disease [12].

**Objective:** to detect peculiarities of esophagitis in schoolchildren against the ground of food allergy and vegetative dysfunction in order to improve the therapeutic tactics for gastroesophageal reflux disease.

**Materials and methods.** 60 children aged from 8 to 18 were under our observation including 23 boys and 37 girls, who were treated at the Municipal Pediatric Clinical Hospital in Lviv with suspected esophagitis. Endoscopy of the esophagus was performed to all the children, during which the biopsy samples were taken for further verification of the diagnosis.

The children were distributed into 3 groups. The main group №1 included 20 children (7 boys and 13 girls), an average age was  $14,0 \pm 2,4$ , with the diagnosis of gastroesophageal reflux disease (GERD), with the signs of food allergy in anamnesis or at the moment of examination; the main group №2 included 20 children (10 boys and 10 girls), an average age was  $14,7 \pm 1,81$ , with the diagnosis of GERD, 3 who had the signs of vegetative dysfunction; and the control group included 20 children (6 boys and 14 girls), an average age was  $15,1 \pm 1,83$  with the diagnosis of gastroesophageal reflux disease. The main group №1 received standard anti-reflux therapy and elimination or hypoallergenic diet (depending on the results of food allergy tests), levocetirizine in the dose of 5 mg once a day in the morning on empty stomach, probiotic bacteria *Lactobacillus reuteri* in the dose of  $10^8$  vital bacteria once a day irrespective of taking meals. The main group №2 received standard anti-reflux therapy and Phenibut (Noophen®, Olain Farma, Latvia) in the dose of 250 mg twice a day during 21 days. The control group received standard anti-reflux therapy according to the Order of the Ministry of Public Health of Ukraine №59 dated 29.01.2013 «Unified Clinical Protocols of Medical Aid for Children with Digestive Diseases».

The role of food allergy and causative food allergens were detected by means of skin allergy tests (prick-tests).

To evaluate vegetative changes of the nervous system Wien's questionnaire (1998) and Kerdo or vegetative index (KI) were applied.

The patients were examined twice to detect the

dynamics of GERD signs, during the primary examination and 4 weeks later after the beginning of treatment.

**Results and discussion.** According to our findings clinical signs of esophagitis in children were not specific. The main complaints during the primary examination were pain the epigastric region of various intensity (100% of children from the three groups), low appetite (75% children of the main group №1, 80% children of the main group №2 and 75% children from the control group), heartburn (65%, 70% and 60% children respectively), periodical regurgitation (50%, 50% and 45% children respectively), nausea (25%, 35% and 30% children respectively), vomiting (10%, 10% and 15% children respectively) and dysphagia (10% of the main group №1 and 5% children from the control group).

Objective examination found pain with palpation of the epigastric region of various intensity in all the children.

The skin prick-tests made in the main group №1 presented the following results: most frequently positive tests were found for yolk and egg-white of chickens (85% and 80% respectively), cow milk casein (75%), hake and pollack (65%), soya beans, chicken, oranges, tangerines (60%), less often – lemons (55%), carp and cocoa (45%), raspberries (35%), tomatoes (30%), rarely – beef, pork, carrot (20%), grapes and water-melon (15%), beets, bananas, oatmeal (10%). 4 children (20%) from the main group had negative food allergy tests.

According to the results obtained after Wien's questionnaire an average score in the main group №2 was  $24,55 \pm 3,30$ , and in the control group –  $23,9 \pm 1,94$ . In addition we have found: inclination to flush (when excited) in 35% children of the main group №2 and 40% of the control group; paleness – in 5% children of the main group №2; numbness or cool sensations of finger and toes – in 45% children of the main group №2 and 40% children of the control group; the whole hands and feet – in 5% children from both groups; colour changes (paleness, cyanosis, redness) of finger and toes – in 30% and 35% children respectively; colour changes of the whole hands and feet – in 5% of the control group; heartbeat, sensations of a sinking heart or cardiac arrest – in 50% children of the main group №2 and 45% children of the control group; excessive perspiration – in 60% and 65% children

respectively; sensations of difficult breathing (lack of air, desire to take a deep breath, shortness of breath) – in 30% and 25% children respectively; functional disorders of the alimentary canal (inclination to constipation, diarrhea, abdominal bloating, stomach ache) – in 90% and 85% children respectively; cases of unconsciousness – in 15% and 10% children respectively; attacks of headache – in 25% and 20% children respectively; low ability to work, quick fatigue – in 60% children of both groups; sleep disorders (difficulty in falling asleep; troubled sleep; sleepy sensations; feeling of tiredness in the morning after waking up) – in 25% children of the main group №2 and 20% children of the control group.

At the beginning of the study KI was  $14,7 \pm 12,3$  in the main group №2 and  $14,4 \pm 11,2$  – in the control group.

Endoscopic examination found macroscopic changes of the mucous membrane of the esophagus in 100% of all the examined children and teens.

Moreover, endoscopic examination found focal or diffuse erythema and mucous membrane swelling, multiple white coating in 100% children of the main group and 60% of the control group, erosive changes in 15% children of the main group №1, 70% children of the main group №2 and in 35% children of the control group (Fig.1).

Morphological examination of tissue sampling (material taken for biopsy from the mucous membrane of the esophagus) found the following changes: dystrophy of epithelial cells - in 90%

children of the main group №1, in 75% children of the main group №2 and 65% children of the control group; destruction of keratohyalin granules - in 60%, 40% and 50% children respectively; vascular hyperemia in microcirculation - in 90%, 90% and 85% children respectively; hemorrhages of a diapedetic character – in 65%, 50% and 65% children respectively; perivascular polymorphocellular infiltration – in 35% children of the main group №2 and 5% children of the control group; focal intraepithelial hemorrhages – in 25% and 5% children respectively; swelling of the stroma – in 10% children of the main group №2 (Fig.2).

After the course of treatment a positive dynamics was observed in children from all the groups, although its rate was different. Complaints of pain in the epigastric region remained in 10% children of the main group №1, 20% children of the main group №2 and in 25% children of the control group; low appetite - in 25%, 40% and 45% children respectively; heartburn - in 10%, 30% and 30% children respectively; periodical regurgitation - in 5%, 10% and 15% children respectively; nausea - in 5% children of the main group №2 and in 5% children of the control group. There were no complaints of vomiting and dysphagia in all the groups (Table 1).

Objective examination found pain retention during palpation in the epigastric region although of less intensity in 10% children of the main group №1, 25% children of the main group №2 and 25% children of the control group.

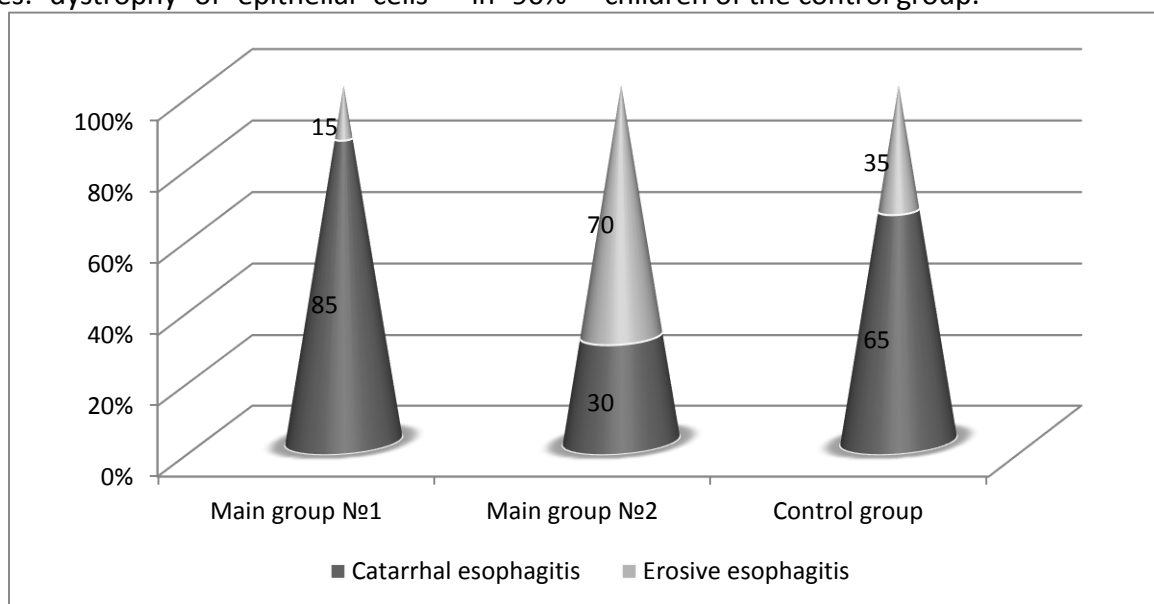


Fig. 1. Structure of endoscopic changes of the esophageal mucous membrane in schoolchildren with gastroesophageal reflux disease.

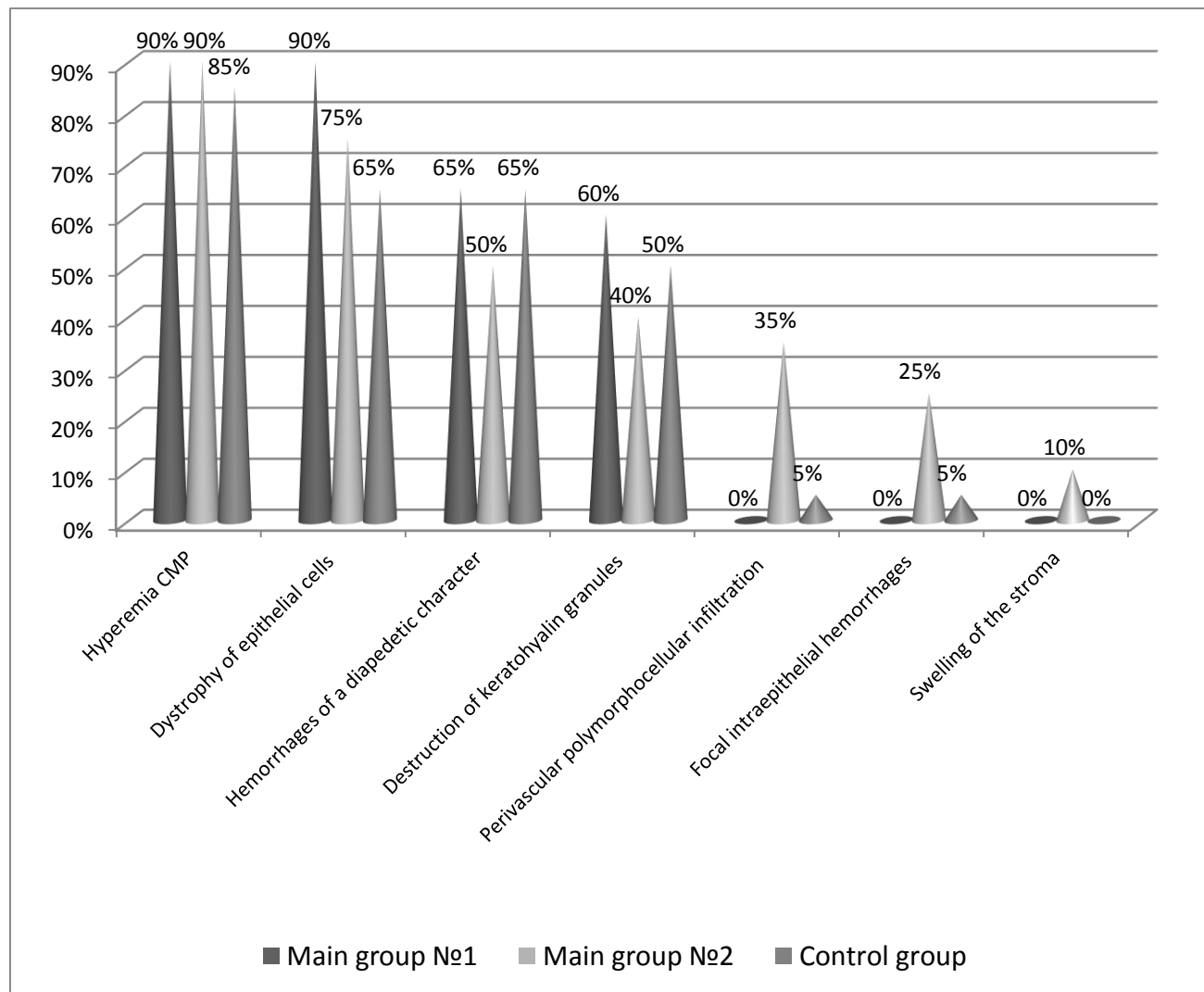


Fig.2. Results of morphological examination of tissue sampling of the esophageal mucous membrane of schoolchildren with GERD.

Table 1

**Dynamics of complaints in children with gastroesophageal reflux disease**

Indices	Main group №1		Main group №2		Control group	
	Before therapy	After therapy	Before therapy	After therapy	Before therapy	After therapy
Pain in epigastric region	100%	10%	100%	20%	100%	25%
Low appetite	75%	25%	80%	40%	75%	45%
Heartburn	65%	10%	70%	30%	60%	30%
Periodical regurgitation	50%	5%	50%	10%	45%	15%
Nausea	25%	0%	35%	5%	30%	5%
Vomiting	10%	0%	10%	0%	15%	0%
Dysphagia	10%	0%	0%	0%	5%	0%

A positive dynamics of vegetative imbalance signs was found in children of the control and main group №2, although in children of the main group №2 it was more pronounced (Fig.3). Thus,

vegetative KI that at the beginning of the study was  $14,7 \pm 12,3$  in the main group №2, became  $5,9 \pm 7,4$  ( $p < 0,01$ ), and in the control group it became also lower from  $14,4 \pm 11,2$  to  $11,0 \pm 9,0$  (Table 2)

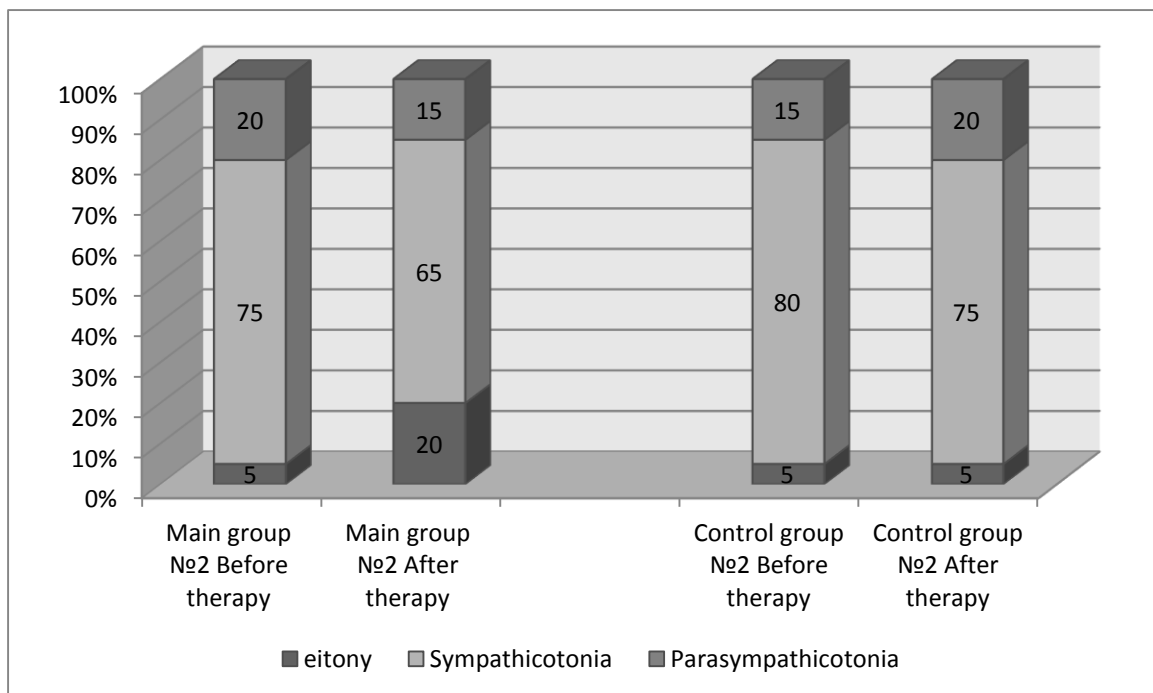


Fig 3. Distribution of children of the main group №2 and the control group according to vegetative Kerdo index before and after therapy.

Table 2

Dynamics of Kerdo index before and after treatment in two examined groups

N	Main group №2 (n=20)		Control group (n=20)	
	Before therapy	After therapy	Before therapy	After therapy
1	-1,4	0	14,6	16,7
2	14,5	12	27,1	22,2
3	16,7	8,7	-2,6	0
4	7,9	5,4	23,1	14,6
5	-2,9	1,3	18,5	22,2
6	28,6	18,6	0	-1,4
7	10,3	0	-5,3	-2,6
8	20,7	14,6	16,7	14,6
9	22,2	12,8	24,4	16,7
10	16,7	11,1	8,5	10,7
11	16,7	-2,6	-2,6	-1,4
12	36,2	14,6	22,2	10,7
13	10,3	-1,4	24,4	14,6
14	28,6	12,5	8,5	-2,6
15	-2,9	-5,3	12,5	7
16	20,0	10,3	18,6	10,7
17	-4,5	-4,2	10,7	10,3
18	0	0	8,5	8,5
19	27,8	10,3	36,2	27,8
20	28,6	0	23,9	20,5
M±δ	14,7±12,3	5,9±7,4*	14,4± 11,2	11,0±9,0

Note: \*  $p \leq 0,01$  – reliable difference

**Conclusions.** Gastroesophageal reflux disease occupies a dominating position in the structure of chronic esophagitis in schoolchildren. Symptomatology is not specific in children with

GERD against the ground of food allergy and vegetative dysfunction, therefore, the diagnostic complex should include allergy tests to detect causative allergens (in children with complicated



allergic anamnesis) and tests to find the parameters of vegetative balance.

Modification of GERD treatment in children against the ground of food allergy with obligatory introduction of elimination diet, antihistamines and probiotics, as well as GERD against the ground of vegetative dysfunction with the use of vegetostabilizing agents promote quicker positive dynamics of the course of the disease and better results of treatment.

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## AGE FEATURES OF CERVICAL ARCH AND HEIGHT OF HUMAN RENAL CALYCES IN MATURE AND ELDERLY AGES

**Abstract.** *The material of the study are 175 corrosive preparations of pyelocaliceal complex mature and elderly humans. We studied linear parameters of human renal calyces and their changes depending on age. As a result of the study we found that height of human renal calyces ( $h_c$ ) significantly changes in different age groups ( $t>2$ ) and diameters of calyceal arch ( $d_c$ ) and calyceal cervix ( $c_c$ ) didn't change significantly. These data can be used in urological clinics in nephrourological operations (extracorporeal lithotripsy, percutaneous puncture, etc).*

**Key words:** kidney, pyelocalyceal complex, renal calyx.

**Introduction.** In connection with the introduction into surgical practice of organ-preserving operations (percutaneous puncture of renal calyces, extracorporeal lithotripsy) and the use of noninvasive diagnostics (ultrasound, NMR and computed tomography) in modern nephrourology, a detailed study of morphometric parameters of initial department of the extrarenal urinary tract (kidney calyces) and their age characteristics.

**Aim of study.** To study the age-related changes in morphometric characteristics of human renal calyces.

**Material and methods.** The material of the study included 175 human kidneys (88 of men and 87 of women), obtained from corpses of mature and elderly people who lived in Ukraine in Kharkiv and Kharkiv region and died as a result of accidents or died of diseases not associated with renal disease. We obtained pyelocalyceal complexes with corrosive method and measured their linear parameters: diameter of calyceal arch ( $d_c$ ), calyceal height ( $h_c$ ), and diameter of calyceal cervix ( $c_c$ ) and performed statistical analysis of data by methods of linear regression, informational-entropic analysis variational method, etc.

**Results and discussion.** Diameters of calyceal arches ( $d_c$ ) are variable in different age groups (Table 1) and vary between  $11,5\pm 5,7$  mm (upper

renal calyx) and  $5,6\pm 1,3$  mm (lower renal calyx). Difference in average sizes between the biggest (upper) and the smallest (lower) renal calyces is highly significant ( $t>3$ ). Arches of all renal calyces don't significantly change in different age groups (except lower one,  $t>2$ ). Height of renal calyces  $h_c$  (Table 2) significantly ( $t>2$ ) changes in different age groups:  $S$  - decreases by 2.5-3 times,  $P_2$  - decreases by 1.5-1.7,  $I$  - increases by 2 times. Height of other renal calyces  $A_1$ ,  $A_2$ ,  $A_3$ ,  $P_3$ ,  $P_1$ ) doesn't significantly change in different age groups. Upper renal calyx has maximal number of variants of height individual changes, especially in age  $57,3\pm 3,0$  years.

The range of values of calyceal cervix diameter  $c_c$  (Table 3) in different age groups doesn't differ significantly and is within  $4,6\pm 7,9$  mm. This fact demonstrates sufficiently stable morphometric value of index (both in types of renal calyces and in age aspect).

**Conclusions.** Studying age and morphological characteristics of renal calyces in order to properly orient of nephrostome canal during its passage through the renal parenchyma and the vault of the renal calyx enables us to avoid complications such as perforation of the renal calyx followed by the formation of urinary fistula, as well as damage of renal vessels that lead to bleeding and infarction of kidney.

Table 1

**Diameters of calyceal arches of mature and elderly humans (in age aspect)**

Name and designation of renal calyces		Number of organs	Age groups	$d_c \pm \delta$ (mm)
Upper	S	7	<29 years	9,9±2,9
		28	30-39 years	11,4±3,9
		42	40-49 years	11,5±5,7
		57	50-59 years	11,5±5,0
		41	>60 years	11,0±4,0
Upper anterior	A <sub>3</sub>	7	<29 years	7,0±1,1
		28	30-39 years	7,0±2,8
		42	40-49 years	7,1±1,8
		57	50-59 years	6,7±2,4
		41	>60 years	6,7±1,9
Upper middle	A <sub>2</sub>	7	<29 years	7,2±1,5
		28	30-39 years	7,5±1,9
		42	40-49 years	7,1±1,8
		57	50-59 years	7,6±2,1
		41	>60 years	7,4±2,2
Lower anterior	A <sub>1</sub>	7	<29 years	7,8±2,6
		28	30-39 years	7,8±3,3
		42	40-49 years	7,4±1,9
		57	50-59 years	7,1±2,0
		41	>60 years	6,9±2,0
Upper posterior	P <sub>3</sub>	7	<29 years	8,9±2,7
		28	30-39 years	8,0±3,3
		42	40-49 years	8,5±3,2
		57	50-59 years	8,9±2,9
		41	>60 years	7,8±2,7
Middle posterior	P <sub>2</sub>	7	<29 years	9,0±3,0
		28	30-39 years	8,4±3,5
		42	40-49 years	8,2±2,1
		57	50-59 years	7,7±2,0
		41	>60 years	7,2±2,0
Lower posterior	P <sub>1</sub>	7	<29 years	8,2±3,9
		28	30-39 years	7,3±2,3
		42	40-49 years	7,0±2,1
		57	50-59 years	7,3±2,4
		41	>60 years	7,2±1,9
Lower	I	7	<29 years	6,4±1,3
		28	30-39 years	8,9±3,9
		42	40-49 years	7,2±2,2
		57	50-59 years	7,2±1,7
		41	>60 years	7,2±1,9

$d_c$  – average diameter of calyceal arch  
 $\delta$  – standard deviation

Table 2

**Height of calyces of mature and elderly humans (in age aspect)**

Name and designation of renal calyces		Number of organs	Age groups	$h_c \pm \delta$ (mm)
Upper	S	7	<29 years	32.8±5.1
		28	30-39 years	17.4±9.1
		42	40-49 years	12.7±7.9
		57	50-59 years	14.4±9.5
		41	>60 years	12.9±6.4
Upper anterior	A <sub>3</sub>	7	<29 years	7.1±2.3
		28	30-39 years	6.7±3.3
		42	40-49 years	7.0±2.8
		57	50-59 years	7.4±3.3
		41	>60 years	7.7±2.9
Upper middle	A <sub>2</sub>	7	<29 years	11.7±2.6
		28	30-39 years	10.0±4.8
		42	40-49 years	9.9±4.7
		57	50-59 years	11.5±5.6
		41	>60 years	11.2±5.4
Lower anterior	A <sub>1</sub>	7	<29 years	10.0±4.0
		28	30-39 years	7.8±3.2
		42	40-49 years	8.9±4.8
		57	50-59 years	9.8±4.9
		41	>60 years	9.2±4.4
Upper posterior	P <sub>3</sub>	7	<29 years	11.4±5.6
		28	30-39 years	8.7±4.8
		42	40-49 years	8.3±4.3
		57	50-59 years	8.5±4.8
		41	>60 years	8.4±3.8
Middle posterior	P <sub>2</sub>	7	<29 years	17.0±5.8
		28	30-39 years	11.7±5.4
		42	40-49 years	9.8±4.5
		57	50-59 years	10.2±4.4
		41	>60 years	10.4±5.4
Lower posterior	P <sub>1</sub>	7	<29 years	6.0±0.9
		28	30-39 years	7.3±4.4
		42	40-49 years	6.6±3.0
		57	50-59 years	6.0±2.5
		41	>60 years	8.7±4.2
Lower	I	7	<29 years	5.1±1.6
		28	30-39 years	10.2±3.1
		42	40-49 years	9.1±5.4
		57	50-59 years	8.0±3.9
		41	>60 years	8.6±4.3

$d_{n4}$  – average height of human calyx  
 $\delta$  – standard deviation

**Table 3**  
**Diameter of calyceal cervix of mature and elderly humans (in age aspect)**

Name and designation of renal calyces		Number of organs	Age groups	$c_{\text{нч}} \pm \delta$ (mm)
Upper	S	7	<29 years	$7.0 \pm 2.6$
		28	30-39 years	$6.7 \pm 1.7$
		42	40-49 years	$7.9 \pm 2.2$
		57	50-59 years	$7.3 \pm 2.6$
		41	>60 years	$7.0 \pm 2.3$
Upper anterior	A <sub>3</sub>	7	<29 years	$5.1 \pm 1.4$
		28	30-39 years	$5.3 \pm 1.4$
		42	40-49 years	$5.3 \pm 1.4$
		57	50-59 years	$5.0 \pm 1.6$
		41	>60 years	$4.2 \pm 1.7$
Upper middle	A <sub>2</sub>	7	<29 years	$4.8 \pm 0.8$
		28	30-39 years	$5.2 \pm 1.6$
		42	40-49 years	$5.0 \pm 1.6$
		57	50-59 years	$4.5 \pm 1.6$
		41	>60 years	$4.9 \pm 1.8$
Lower anterior	A <sub>1</sub>	7	<29 years	$4.5 \pm 1.5$
		28	30-39 years	$5.2 \pm 2.2$
		42	40-49 years	$4.6 \pm 1.5$
		57	50-59 years	$4.9 \pm 1.9$
		41	>60 years	$4.5 \pm 1.8$
Upper posterior	P <sub>3</sub>	7	<29 years	$6.7 \pm 2.5$
		28	30-39 years	$5.9 \pm 1.9$
		42	40-49 years	$5.7 \pm 2.0$
		57	50-59 years	$6.1 \pm 2.1$
		41	>60 years	$5.1 \pm 2.1$
Middle posterior	P <sub>2</sub>	7	<29 years	$6.0 \pm 2.1$
		28	30-39 years	$4.9 \pm 1.9$
		42	40-49 years	$5.5 \pm 2.2$
		57	50-59 years	$5.2 \pm 1.8$
		41	>60 years	$4.7 \pm 1.5$
Lower posterior	P <sub>1</sub>	7	<29 years	$5.4 \pm 0.7$
		28	30-39 years	$4.5 \pm 1.7$
		42	40-49 years	$5.5 \pm 2.5$
		57	50-59 years	$6.0 \pm 2.4$
		41	>60 years	$5.0 \pm 2.2$
Lower	I	7	<29 years	$5.4 \pm 1.7$
		28	30-39 years	$6.2 \pm 2.5$
		42	40-49 years	$4.9 \pm 1.7$
		57	50-59 years	$5.3 \pm 1.8$
		41	>60 years	$5.3 \pm 2.6$

$c_{\text{нч}}$  – average diameter of calyceal cervix

$\delta$  – standard deviation

**Perspectives of further studies.** Increasing number of cases of urolithiasis and their "rejuvenation" requires morphologists to study in detail the morphometric characteristics of renal calyces and to change them in various aspects (age, sex, etc.).

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## CHARACTERISTIC OF ALUMINUM SALTS INFLUENCE ON INDEXES OF ION REGULATIVE RENAL FUNCTION IN MATURE AND IMMATURE RATS AGAINST THE BACKGROUND OF THE PINEAL GLAND HYPERFUNCTION

**Abstract.** *It is known that reabsorption of sodium ions is one of the most energy-dependent kidney process, which is the basis for providing homeostatic functions, especially ion regulatory, acid regulatory and excretory, which differ in mature and immature rats. These differences are often conditioned by insufficient maturity of nephron tubules, juxtaglomerular and regulatory mechanism in immature rats. In order to assess the impact of nephrotoxic action of aluminum salts in the ion regulatory function of the kidney and under the conditions of hyperpituitarism of the pineal gland, we studied the effect of 14-day action of aluminum chloride compounds on the ion regulatory function in 24 white male rats. It was found that the environmental stress of aluminum salts is accompanied by a nephrotoxic effect, which is characterized by the development of the loss of sodium ions with urine due to a damage of the nephron tubular portion. Hyperfunction of the pineal gland causes a nephrotoxic effect of aluminum salts in mature rats with a more significant manifestation of the syndrome of loss of sodium ions in the urine, which is probably conditioned by high level of melatonin.*

**Key words:** kidney, aluminum chloride, pineal gland.

**Introduction.** Nowadays, the increase of xenobiotics action is beyond the scope of biological adaptability of ecosystem and can cause changing environmental habitat, create straight threat to life and health of population. The intake and accumulation of aluminum salts in organs and tissues of human body have a nephrotoxic action, which is conditioned by disorders of metabolic processes and development of different pathologies [1, 2, 7, 9]. Complexes with phytoestrogens polyphenols, drinking water, food, cosmetics, pharmaceuticals and vaccines are sources of intake aluminum in vitro [3, 4, 6]. Despite the prevalence of aluminum compounds, the question about the impact of aluminum salts on the ion regulatory function of the kidney has not been studied sufficiently under the condition of hyperfunction of the pineal gland in mature rats [5, 8, 10].

**Objective:** to study the influence of toxic effects of aluminum chloride on the ion regulatory function in mature and immature rats and under the conditions of hyperfunction of the pineal gland.

**Materials and methods.** The experiments involved 24 mature and immature nonlinear male albino rats weighing 0,06-0,10 kg and 0,14-0,20 kg respectively. We studied a nephrotoxic effect of aluminum salts on ion regulatory renal function. Aluminum chloride in a dose of 200 mg/kg was administered chloride intragastrically daily within 14 days of the experiment at 8.00 a.m. and 8.00 p.m. with the 1% starch slurry. Hyperthyroidism of the pineal gland was simulated by keeping the animals in conditions of constant illumination (24.00L:00D) for 7 days. The ion regulatory function was assessed in terms of excretion of sodium ions and their concentrations in the urine,

absolute and relative cation reabsorption, filtration charge and sodium ions clearance, sodium-potassium ions in the urine factor, concentration index of sodium ions, the values of the proximal and distal transport.

**Results and discussion.** The assessment of the ion regulatory renal function in intact immature rats which were administered aluminum salts (Table 1.) showed that the concentration of sodium ions in the urine increased. The excretion of sodium ions tended to increase. The filtration fraction of sodium ions in the conditions of administering aluminum salts in immature rats was characterized by a downward trend compared to the control. The clearance of water free of sodium ions tended to reduce in the conditions of administering aluminum salts in immature rats.

The concentration index of sodium ions increased reliably. The distal reabsorption of sodium ions tended to reduce due to the administration of aluminum salts in immature rats. An analysis of ion regulatory renal function

values in mature intact rats after introduction aluminum salts (Table 2.) showed that the concentration of sodium in the urine increased. Filtration fraction of sodium ions in case of introducing aluminum salts in mature rats was characterized by a downward trend compared to the control. The trend toward the growth was recorded for the excretion of sodium ions, standardized by the glomerular filtrate speed. The clearance of sodium was growing. The clearance index of sodium ions increased reliably.

An analysis of the values of the ion regulatory renal function in mature and immature rats after introducing aluminum salts against the background of the pineal gland hyperfunction (Table 3.) showed that the concentration of sodium in the urine was higher in mature rats. We established a similar pattern regarding the excretion of sodium ions, standardized by the glomerular filtrate rate. The distal reabsorption of

**Table 2.**

**Values of the ion regulatory function of the kidney in intact mature rats under the influence of aluminum salts ( $\bar{x} \pm S_{\bar{x}}$ )**

Values	Mature rats (Al) (n=6)	Control (n=6)
1	2	3
The concentration of sodium ions in the urine mmol / l	1,90±0,15	0,70±0,03 p<0,001
The excretion of sodium in urine mmol / 2h 100 g	3,23±0,56	1,96±0,26
The excretion of sodium, umol / min 100 g	3,46±0,43	2,17±0,17 p<0,02
The excretion of sodium, mg / 100 ml Ccr	0,03±0,01	0,01±0,006
Clearance of sodium-free water, ml / 2h·100 g	1,95±0,31	3,19±0,08 p<0,01
Clearance of sodium ions ml / 2h 100 g	0,03±0,004	0,01±0,0002 p<0,05
Concentration index of sodium, stand units.	0,01±0,001	0,005±0,0002 p<0,001

**Table 1.**

**Values of the ion regulatory function of the kidney in intact immature rats under the influence of aluminum salts ( $\bar{x} \pm S_{\bar{x}}$ )**

Values	Immature rats (Al) (n=6)	Control(n=6)
1	2	3
The concentration of sodium ions in the urine mmol / l	1,50±0,29	0,50±0,05 p<0,01
The excretion of sodium in urine mmol / 2h 100g	2,43±0,76	0,99±0,23
Filtration fraction of sodium ions, umol / min 100 g	17,50±5,44	25,51±5,32
The excretion of sodium, umol / min 100 g	2,54±0,72	1,08±0,19
The excretion of sodium ions, mg / 100 ml Ccr	0,03±0,01	0,009±0,0004
Concentration index of sodium, stand units	0,01±0,002	0,003±0,0003 p<0,01

Table 3.

**Values of ion regulatory function of the kidney in mature and immature rats under the influence of aluminum salts against the background of the pineal gland hyperfunction ( $\bar{x} \pm S_x$ )**

Values	Mature rats(Al) (n=6)	Immature rats(Al) (n=6)
1	2	3
The concentration of sodium ions in the urine mmol / l	1,03±0,25	0,75±0,02
The excretion of sodium in urine mmol / 2h 100 g	2,38±0,85	1,15±0,19
The excretion of sodium, umol / min 100 g	2,63±0,72	1,29±0,13
Clearance of sodium-free water ml / 2h 100 g	2,73±0,28	1,84±0,23 p<0,05
Clearance of sodium ions ml / 2h 100 g	0,01±0,006	0,009±0,001
Concentration index of sodium, stand units.	0,008±0,001	1,84±0,23 p<0,001
Distal reabsorption of sodium ions, micromoles / 2h 100g	349,10±41,60	229,50±28,60 p<0,05
Distal reabsorption of sodium ions, micromoles / 100ml Ccr	1,31±0,09	0,85±0,03 p<0,001

sodium ions after introducing aluminum salts in mature rats tended to decrease. The proximal reabsorption in the comparison group was higher in mature rats.

**Conclusions.** The analysis of aluminum salts influence on the ion regulatory renal function in mature and immature rats showed that studied environmental stress is accompanied by a nephrotoxic effect, which is characterized by the development of the loss of sodium through urine nephron tubular damage. Hyperfunction of the pineal gland causes nephrotoxic effect of aluminum

salts in mature rats with a significant manifestation of the syndrome of loss of sodium in the urine, which is conditioned by high level of melatonin.

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## **CHRONOREGULATING AND RHYTHM-STABILIZING ROLE OF MELATONIN IN SEASONAL STRUCTURE OF CIRCADIAN RHYTHMS OF NON-SPECIFIC IMMUNITY INDICES WITH AGING**

**Abstract.** *The effect of melatonin, the pineal gland hormone, on a seasonal structure of non-specific immunity circadian rhythms with aging has been examined. Multidirectional biorhythmic changes of humoral and cellular indices of the non-specific defense have been found. It ensures the most valuable adjustment of the body to cyclic environmental changes. The pineal gland effect is characterized by age features and preserved to extreme old age. The studies with modified lighting are indicative of the possibility to stimulate melatonin-producing function of the pineal gland by means of prolongation of a dark period and intensification of activity of the non-specific immunity system at the elderly age.*

**Key words:** *chronoregulation, melatonin, pineal gland, density, mineral content, dynamics.*

**Introduction.** In man and other mammals the pineal gland (PG) or epiphysis plays an important role in synchronization of circadian endocrine activity. The role of PG in neuroendocrine regulation of the body [2] and its direct participation in the development of general adaptation syndrome [1] is also known. The pineal gland is one of the main oscillator to regulate chronobiological processes of the body [3].

In the process of aging circadian and seasonal oscillations of the body vital signs are gradually fading [4], production and secretion of melatonin by the epiphysis decrease, daily oscillations of melatonin level in the blood plasma reduce [9], resulting in the development of various pathological conditions due to increased reactivity of the sympathoadrenal, hypophysial-adrenal and cardio-vascular systems. Restoration of melatonin concentration increases resistance of the cardio-vascular and other systems of the body to the impact of stress factors [5, 10].

A positive effect of the hormone melatonin on the neuroendocrine regulation and its antioxidant action have been described as well [8, 11]. Melatonin reduces activity of the hypothalamic-hypophysial and sympathoadrenal systems, decreases the initial stage of stress development – the anxiety stage, and therefore, preventing development of general adaptation syndrome.

Recent studies are indicative of the role of PG as a constituent of the central biological clock with aging [7], and administration of melatonin in pharmacological doses can prevent development of aging signs [6]. A stimulating action of melatonin on immunostructural homeostasis is evidenced [9]. Seasonal oscillations of certain signs of non-specific immunity are studied [3].

**Objective:** to investigate the role of melatonin, a hormone of the pineal gland, in alternations of circadian rhythms seasonal structure of non-specific immunity signs with aging, its controlling and rhythm-stabilizing action.

**Materials and methods.** Our studies were conducted on 160 albino laboratory male rats of two age groups: mature – at the age of 12-15 months and body weight 140-180 g and old ones at the age of 24 months and older with their body weight of 200 g and more. The rats were kept in vivarium at a stable room temperature and artificial light. The light regimen was the following: 12 hours – light and 12 hours darkness. Pseudo-operated rats were also used in the experiment. Together with intact animals they constituted the control group contrary to those animal with epiphysectomy performed on the 15-20th days after PG removal. With the purpose to study circadian rhythms of non-specific immune signs of the body the experiments were conducted on



mature and old male rats. A light period of the day was from 8 a.m. to 8 p.m., and the period of darkness – from 8 p.m. to 6 in the morning. The blood was taken every 6 hours: at 9 a.m., 3 p.m., 9 p.m. and 3 in the morning. To examine seasonal rhythms the experiments were conducted during 2 years in spring (April, May), in summer (July, August), Autumn (October, November), and winter (January, February).

The indices of non-specific immunity were studied in the experiment: activity of the serum complement, concentration of the serum lysozyme, total leukocyte amount, HCT-test, myeloperoxidase activity of neutrophils, glycogen level, phagocytic activity and phagocytic index of polymorphonuclear leukocytes.

**Results and discussion.** The results of the study are indicative of the complement system rhythm availability and decrease of its level due to epiphysectomy. Circadian rhythm of the serum complement activity depend not only on age and PG available, but the time of the year, especially in spring and summer. The content of serum lysozyme in mature rats decreased after pinealectomy, and in old rats circadian rhythm was leveled. Seasonal rhythm after removal of PG changed: in old rats miniphase was shifted to autumn. Administration of melatonin was associated with growth of lysozyme content in the control groups of mature and old rats, and in mature animals after epiphysectomy – a reduced level of this index.

A considerable role of lysozyme should be mentioned here. Its content increased with aging which is a compensatory mechanism directed to activation of the phagocyte enzymatic activity, first of all lysosomal enzymes, and muromidase in particular, that breaks bacterial walls.

Leukopenia was found both in mature and old rats due to pinealectomy. The staging of circadian rhythm reduced, acrophase and miniphase were shifted. The index of leukocyte amount was not informative concerning the effect of melatonin and changed lightening, although its dynamics and rhythmstasis changed.

HCT-test remained unchanged considerably when animals were kept under conditions of long darkness. Melatonin effect was not found in this case. This index characterizes activation of neutrophil metabolism, first of all, the function of

hexosomonophosphate shunt and free radical synthesis associated with it which is essential for successful implementation of phagocytosis. In our experiments we have found a tendency to alternation of this index with age and disorders of circadian rhythms.

Circadian rhythms of glycogen content in neutrophils of mature rats after epiphysectomy did not differ considerably, and in old ones – they decreased reliably, and acrophase and bathyphase amplitudes leveled. Similar changes were registered in animals with removed PG. Melatonin administration was accompanied by increasing content of glycogen in the mature and old rats after pinealectomy. A low level of glycogen in experimental animals is indicative of insufficient energy supply of neutrophils as the main chain in functioning of the non-specific immune adaptation system to possible oscillations in the activity of non-specific protective system. These findings clearly characterize the processes of body aging.

Myeloperoxidase activity of neutrophils in the peripheral blood provides their bactericidal properties and destruction of hydrogen peroxide. Circadian rhythm of myeloperoxidase activity was characterized by miniphase in the morning in all the three groups of old rats. Low activity of myeloperoxidase was normalized under the influence of melatonin under conditions of usual photoperiod, long darkness and in case of continuous lightening.

The results obtained due to our experimental studies are indicative of the fact that after pinealectomy the indices of glycogen content, level of HCT-test and myeloperoxidase activity change, which is a direct evidence of alternations of phagocytic activity of segmented neutrophilic leukocytes under these conditions. Phagocytic activity in old animals reduced reliably, and removal of PG resulted in disorders of staging of a daily curve, the levels of indices decreased reliably at any period of time. Melatonin administration made reduced indices of phagocytic activity normal both in mature and old rats, and with the gland available the hormone did not affect this index in case of usual photoperiod. In case of PG inhibition under continuous lightening melatonin administration stimulated phagocytic activity both in mature and old control animals. Similar

changes were found in both groups of rats after epiphysectomy. Therefore, in case PG is removed melatonin effects do not depend on photoperiod.

Phagocytic index in mature rats after removal of PG was characterized by disorders of staging of circadian rhythm, shifting of acrophase to morning hours. Reduced rhythmic oscillations were registered as well as reliable decrease of the index in old rats after epiphysectomy. Exogenous melatonin made the level of phagocytic index normal, as it was reduced due to removal of PG and after the impact of continuous lightening. Together with absent effect of continuous darkness and melatonin on the dynamics and rhythmstasis of phagocytic index in all the groups of mature rats, the index increased in the control group of old animals.

**Conclusions.** Therefore, different directions of biorhythmic changes of the humoral and cellular indices of non-specific immunity found provides the most substantial adaptation of the body to cyclic environmental changes. PG in mammals is directly associated with regulation of circadian rhythms of the non-specific adaptation system of the body. This effect possesses age peculiarities and is kept till old age. A regulating action of the pineal gland on the immunostructural homeostasis is provided by melatonin and other biologically active substances produced by this organ. The studies with changed lightening are indicative of existence of principal possibility to stimulate melatonin-producing function of PG by means of elongation of light period, and as a result, intensification of the activity of the non-specific immune protection system of the body, which is especially important in gerontology and geriatrics, prevention of age changes in old age.

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## CHARACTERISTICS OF CONGENITAL PATHOLOGY WITH INHERITED AND MULTIFACTORIAL NATURE IN CHILDREN OF KYIV REGION

**Abstract.** *In the process of conducting epidemiological studies congenital pathology with inherited and multifactorial nature of children in Kiev region, 2010-2015, was characterized. The cases of diagnosis of newborns and individuals whose pathology was found for the first time beyond the neonatal period are reviewed.*

**Key words:** *congenital developmental defects; hereditary pathology; primary prophylaxis.*

**Introduction.** Among newborns in Ukraine a certain fluctuation range of genetic diseases is found that can be associated with various causes, and the following ones may occupy not the last position among them: availability of medical-genetic aid, quality and fullness of diagnostics, accurate registration of pathology, effect of primary and secondary prevention measures [1].

Therefore, the **objective** of the study was assessment of congenital pathology among newborns and individuals whose pathology was first found beyond the neonatal period.

**Materials and methods.** The objects of the study were cases of congenital and inherited pathology in newborns, in patients with the diagnosis first made among the individuals older than one year. To characterize congenital pathology in newborns (507 cases) and beyond the neonatal period (953 cases), the data of hospital registers of Kyiv region from the establishment "Kyiv Regional Center of Health Care of Mother and Child" during 2010-2015 were used. Methods of investigation: epidemiological, statistical.

**Results.** First, congenital pathology among newborns have been characterized. Its structure during 2009-2015 is indicative of prevailing congenital developmental defects (CDD) of the circulatory system (Q 20-28), who constituted one third of the registered CDD (30,18±2,04 %). The second position belonged to CDD of the osseous-muscular system (Q 65-79) - (24,85±1,92 %), and

the third one – CDD of the gonads (Q 50-56), (17,75±1,70 %).

Every fifteenth defect was cleft lip or palate (Q 35-37) (6,51±1,10 %), practically every twelfth CDD referred to the category of "CDD of the digestive organs Q 38-45" (3,75±0,84 %) or "chromosome abnormalities not classified in other groups Q 90-99" (4,14±0,88 %), every thirtieth multifactorial CDD (MCDD) including defects of several classes (3,16±0,78 %), CDD of the urinary system, Q 60-64 (2,96±0,75 %) and CDD included into other CDD, Q 80-89 (2,96±0,75 %). Specific gravity of CDD of the nervous system (Q 00-07), CDD of the eye, ear, face (Q 10-18) and respiratory CDD (Q 30-34) was 1,78±0,59 %, 1,58±0,55 % and 0,39±0,28 % respectively.

To characterize congenital pathology among newborns several groups of analysis were considered to be reasonable to differentiate:

- I – newborns whose parents were born in the region of residing;
- II – newborns whose parents were born in different districts of Kyiv region;
- III – newborns whose parents were born above the borders of the region.

The structure of congenital pathology among newborns whose parents were born and resided within the borders of one district of Kyiv region is indicative of prevailing CDD of the circulatory system (Q 20-28), constituting one fifth and one seventh part of all the registered CDD (18,34±1,72 % - for mothers and 13,21±1,50 % - for fathers).

CDD and deformities of the osseous-muscular system (Q 65-79) were on the second position – every seventh defect ( $14,20 \pm 1,55$  % and  $13,61 \pm 1,52$  % respectively), CDD of the gonads – on the third position (Q 50-56), ( $9,47 \pm 1,30$  % and  $9,47 \pm 1,30$  % respectively).

Every twentieth and thirtieth defect was cleft lip or palate (Q 35-37) ( $4,73 \pm 0,94$  % - for mothers and  $2,76 \pm 0,73$  % - for fathers), practically every forty-second and every fiftieth CDD referred to the category «CDD of the digestive organs Q 38-45» ( $2,37 \pm 0,68$  % and  $1,97 \pm 0,62$  % respectively) or every fiftieth or forty-ninth CDD referred to «chromosome abnormalities not classified in other groups Q 90-99» ( $1,78 \pm 0,59$  % and  $2,56 \pm 0,70$  % respectively). Specific gravity of the rest CDD was not considerable (up to 2 %).

The structure of CDD among newborns included II group of the analysis is indicative of prevailing CDD of the circulatory system (Q 20-28), constituting the thirtieth and twentieth part of all the registered CDD ( $2,76 \pm 0,73$  % - for mothers and  $4,93 \pm 0,96$  % - for fathers). The second position was occupied by CDD of the gonads (Q 50-56) and CDD and deformities of the osseous-muscular system (Q 65-79) – where every fiftieth defect ( $2,17 \pm 0,65$  % and  $2,37 \pm 0,68$  %;  $1,97 \pm 0,62$  % and  $2,17 \pm 0,65$  % respectively), the third one – by MCDD, - practically every hundredth defect among newborns ( $0,59 \pm 0,34$  % and  $0,79 \pm 0,39$  % respectively). The rest of CDD were less than 1%, and minimal specific gravity was found among respiratory CDD (0,00 % both for mothers and fathers).

The structure of congenital pathology among newborns of III group is indicative of prevailing CDD of the circulatory system (Q 20-28), constituting the thirteenth part of all the registered CDD ( $7,50 \pm 1,17$  % among mothers). CDD and deformities of the osseous-muscular system (Q 65-79) were on the second position – every fourteenth defect ( $7,10 \pm 1,14$  %), on the third position – CDD of the gonads (Q 50-56), - practically every twentieth defect among newborns ( $5,13 \pm 0,98$  %). The rest of CDD were less than 1%, and minimal specific gravity was found among CDD of the eye, ear, face and neck (0,00 %).

The structure of congenital pathology among newborns of III group of the study is indicative of

prevailing CDD of the circulatory system (Q 20-28), constituting the thirteenth part of all the registered CDD ( $7,69 \pm 1,18$  % among fathers). The second position is occupied by CDD and deformities of the osseous-muscular system (Q 65-79) – every fourteenth defect ( $6,71 \pm 1,11$  %), the third one – CDD of the gonads (Q 50-56), - practically every twenty-fifth defect among newborns ( $3,94 \pm 0,86$  %). Minimal specific gravity was found among respiratory CDD (0,20 %), and specific gravity of the rest CDD was less than 1%.

While characterizing individuals whose pathology was found beyond the neonatal period it was found that the structure of congenital pathology among those children during 2010-2015 was prevailing CDD included into the group “other CDD” (Q 80-89), constituting one third of all the registered CDD ( $30,85 \pm 1,50$  %). The second position is occupied by CDD and deformities of the osseous-muscular system (Q 65-79) – every fourth defect ( $26,97 \pm 1,44$  %), the third position – chromosome abnormalities not classified in other groups (Q 90-99), practically every seventh defect among newborns ( $14,48 \pm 1,14$  %).

Every eleventh defect was MCDD (including CDD of several classes) ( $8,60 \pm 0,91$  %), practically every thirteenth CDD referred to the category «CDD of the nervous system Q 00-07» ( $7,66 \pm 0,86$  %), every fortieth – CDD of the eye, ear, face, neck (Q 10-18) ( $2,52 \pm 0,51$  %), every fiftieth – phenylketonuria (FKU, E 70.0) ( $2,20 \pm 0,48$  %), CDD of the circulatory system, Q 20-28 ( $2,10 \pm 0,46$  %) and CDD of the gonads, Q 50-56 ( $1,89 \pm 0,44$  %). Specific gravity of hypothyroidism (E 03.1), CDD of the digestive organs (Q 38-45), CDD of the urinary system (Q 60-64) and cleft lip and palate (Q 35-37) were  $1,15 \pm 0,35$  %,  $0,73 \pm 0,28$  %,  $0,52 \pm 0,23$  % and  $0,31 \pm 0,18$  % respectively.

Concerning the characteristics of a middle age as to the making diagnosis of patients (Table), syndrome diagnosis were found to be made at the latest stages (other CDD, Q 80-89) ( $14,69 \pm 0,58$  years). Hypothyroidism was on the second position, E 03.1 ( $12,84 \pm 3,27$  years), on the third one – CDD of the eye, ear, face and neck Q 10-18 ( $11,54 \pm 2,02$  years).

Manifestation of a number of CDD occurs beyond the neonatal period. As it is evidenced by previously conducted studies and proved by present findings, special attention should be paid



**Table**  
**An average age to make the diagnosis of**  
**patients according to the classes of diseases**  
**(ICD -10), Kyiv region, 2010-2015.**

Classification according to ICD-10	Average age according to nosology, years	Minimal value of age of making diagnosis, years	Maximal value of age of making diagnosis, years
Q 00-07	7,13±0,87	1,00	31,00
Q 10-18	11,54±2,02	1,00	40,00
Q 20-28	10,79±1,11	1,42	17,00
Q 35-37	10,67±2,96	5,00	15,00
Q 38-45	9,86±0,94	7,00	13,00
Q 50-56	5,94±1,21	1,00	14,00
Q 60-64	6,05±1,58	2,25	11,00
Q 65-79	9,12±0,44	1,00	44,00
Q 80-89	14,69±0,58	1,00	44,00
Q 90-99	9,37±0,61	1,00	30,00
E 03.1 (hypothyroidism)	12,84±3,27	1,08	34,00
E 70.0 (FKU)	10,58±1,71	1,00	28,00
MCDD	9,47±0,95	1,00	48,00
All CDD	10,85±0,28	1,00	48,00

to FKU and hypothyroidism. Their timely detection will enable to indicate the essential course of treatment, since children with such diagnoses made after one year of their life, are subjected to irreversible disability.

**Conclusions.** Analysis of the hospital register of patients with the first made diagnosis of congenital pathology beyond the neonatal period during 2010-2015 was indicative of prevailing CDD

included into the group "other CDD" (Q 80-89), constituting one third of all the registered CDD (30,85±1,50 %). The second position belonged to CDD and deformities of the osseous-muscular system (Q 65-79) – every fourth defect (26,97±1,44 %), the third position – chromosome abnormalities not classified in other groups (Q 90-99) – (14,48±1,14%).

An average age of making the diagnosis of patients according to the classes of diseases is indicative of inefficacy of the screening system of FKU and hypothyroidism. Thus, the diagnosis of FKU was first made even at the age of 28 (a mean value – 10,58±1,71), hypothyroidism – at 34 (a means value – 12,84±3,27). Syndrome diagnoses were made at the latest period of life (at 14,69±0,58), the diagnoses of congenital defects of the eye, ear, face (11,54±2,02), congenital developmental defects of the circulatory system (10,79±1,11), and cleft lip or palate (10,67±2,96).

**Prospects of further studies.** The studies conducted enable to improve the system of prevention of congenital pathology at an individual level when a family doctor is performing his professional duties, and in case of specification of preventive measures; to reduce social and economic consequences.

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*Higher State Educational Establishment of Ukraine "Bukovinian State Medical University", Chernivtsi, Ukraine***METABOLIC DISORDERS IN WOMEN DEPENDING ON MENOPAUSE DURATION**

**Abstract.** Menopausal period constitutes practically one third of a woman's life. Due to this fact not only woman's health, but her ability-to-work, ability to perform various social functions depend on the character and course of this period. One of the complications of post-menopausal period is metabolic disorders. With the aim to investigate the degree of metabolic disorders depending on the menopause duration 75 women were examined. Investigation of genealogical anamnesis enabled to find the main clinical signs, pathognomonic for metabolic syndrome (type 2 diabetes mellitus in 32% of cases, arterial hypertension – in 52%, early ischemic heart disease – in 36% of parents and close relatives). The longer the menopause duration is, the more pronounced the signs of obesity, lipid and carbohydrate metabolic disorders are (increased levels of cholesterol, triglycerides, low density lipoproteins, decreased levels of high density lipoproteins, insulin resistance development). Increased level of C-reactive protein ( $4,3 \pm 0,6$  mg/L) was found among women with menopause more than 5-7 years, which is a risk factor promoting the development of vascular diseases. 32% of patients with menopause duration longer than 7 years were diagnosed with such pronounced metabolic disorders as type 2 diabetes mellitus, and in 48% of cases hypertensive disorders were diagnosed. Therefore, timely diagnostics and correction of metabolic disorders will promote a reduced risk of occurrence of cardio-vascular diseases and diabetes mellitus among women in the period of menopause, as well as improvement of their quality of life.

**Key words:** post-menopause, metabolic disorders, lipid metabolism, insulin resistance.

**Introduction.** In recent years more attention has been paid to women's health during menopause period as this period constitutes practically one third of a woman's life. Due to this fact not only woman's health, but her ability-to-work, ability to perform various social functions depend on the character and course of this period [7, 8]. Estrogen deficiency results in the development of various complications. Therefore, it is important to predict probability of functional disorders of different organs and systems during menopause, and to make timely diagnostics and treatment [5, 7, 8, 9].

Metabolic disorders are one of the menopausal complications. Metabolic syndrome (MS) is a complex of interrelated disorders of carbohydrate and lipid metabolism, as well as mechanisms of regulation of arterial blood pressure (BP) and endothelial function, stipulated by a lowered susceptibility of the body tissues to insulin – insulin resistance (IR) [1, 2, 6]. An increased synthesis of free fatty acids in the liver and hepatocyte IR are proved to result in an intensified synthesis of triglycerides (TG) and very low density lipoproteins (VLDLP). In case of insulin resistance

lipoprotein lipase activity decreases which is under insulin control. A characteristic type of dyslipidemia occurs associated with visceral obesity: increased concentrations of VLDLP and TG, decreased concentration of high density lipoproteins (HDLP), and an increased number of minor compact cholesterol particles of low density lipoproteins (LDLP). Therefore, obesity and IR promote the development of lipid profile disorders, and together with hyperglycemia and hypertension they result in early and quick development of atherosclerosis in patients with carbohydrate metabolic disorders and visceral obesity [2, 4, 6, 10].

The efficacy of treatment of metabolic syndrome is known to depend on duration of its development. The best results can be obtained at the very beginning of pathology development, when excess weight should not be considered as an esthetic problem only, but as a signal to initiate certain actions [1, 3, 7, 10]. Therefore, timely diagnostics and correction of metabolic disorders will promote prevention of the development of cardio-vascular diseases and diabetes mellitus.

**Objective:** to study the degree of metabolic

disorders signs among women depending on menopause duration.

**Materials and methods.** 75 women aged from 45 to 60 have been examined. Groups were distributed depending on menopause duration. The first group included 25 patients with menopause duration up to 2 years, the second group – 25 patients with menopause duration from 2 to 7 years, the third group – 25 women with menopause more than 7 years. The control group included 20 women during menopausal period without signs of metabolic disorders. None of the women received hormonal replacement therapy.

Obstetrical-gynecological and genealogical anamnesis, the term of menopause beginning, its duration and course have been studied in all the patients. By means of anthropometric method the following parameters were estimated: body mass index (BMI), waist circumference (WC), the ratio of WC to hip circumference (WC/HC). The state of lipid metabolism was evaluated on the basis of biochemical examination of general cholesterol (GC), TG, HDLP, LDLP, VLDLP. Insulin resistance was estimated by means of HOMA index in the blood serum (HOMA-IR – Homeostasis Model Assessment of Insulin Resistance) – ratio of glucose and insulin levels. The index is considered to be normal in case it is not 2,7 times higher than that of boundary value [4, 6, 7].

In addition, the level of C-reactive protein in the blood serum was evaluated as well. Arterial blood pressure was monitored, and electrocardiogram (ECG) findings were registered.

**Results and discussion.** The groups being examined did not differ statistically by their age, beginning of menstrual period, number of labours and abortions ( $p>0,05$ ).

Examination of genealogical anamnesis enabled to find the main clinical signs, pathognomonic for metabolic syndrome in parents and close relatives (type 2 diabetes mellitus in 32% of cases, arterial hypertension – in 52%, early ischemic heart disease – in 36%) corresponding to the data presented by other authors [2, 3, 6]. In the control group only in 1 case (5%) arterial hypertension was found.

The main complaints presented by the examined women were quick weight gain after menopause beginning, hair growth in unusual

places, increased arterial pressure. Coarse brown skin on the elbows, under mammary glands, in the armpits (so-called acantosis nigricans) were found in 2 patients (8%) of II group, in 10 patients (40%) – of III group, and in I and control groups it was not diagnosed.

In women of I group an average body mass became 2,8 kg larger, in II group – 3,6 kg more during the first two years of post-menopause. In seven years of menopause weight gain in the III group was 7,6 kg. The adipose tissue is mainly distributed in the waist area. In the control group the body mass became in an average 2,2 kg bigger during 7 years of menopause. In patients from I group during two years of menopause WC increased in an average by 5,6 cm, in five years (II group) – by 7,8 cm, in seven years (III group) – by 9,2 cm. WC/HC index increased to 0,95 in 27 (36%) of the examined women, in 34 (45,32%) patients it was 1,01. At the same time, 60 (80%) women in the reproductive age had a proportional figure according to a female type and they did not suffer from excessive weight.

During examination of patients, considerable changes of lipid spectrum in the blood plasma were found characterized by increased general cholesterol, TG, LDLP, VLDLP, and decreased HDLP. In 66,7% of the examined patients reduced level of HDLP lower than 1,29 mmol/L and TG level higher than 1,69 mmol/L were found. These changes were more pronounced in the patients from III group, while in I group these values ranged on the upper border of the norm ( $p>0,05$ ). Thus, general cholesterol level increased with menopause duration: I group –  $4,7\pm0,5$  mmol/L, II group –  $6,2\pm0,5$  mmol/L, III group –  $7,2\pm0,2$  mmol/L. Triglyceride levels increased with menopause duration as well: I group –  $1,7\pm0,2$  mmol/L, II group –  $3,1\pm0,3$  mmol/L, III group –  $3,5\pm0,2$  mmol/L.

Excessive synthesis of triglycerides is indicative of carbohydrate metabolic disorders, as together with gluconeogenesis this process is the method of bioutilization of free fatty acids [2, 3, 5]. The majority of scientists consider that the most typical sign of dyslipidemia associated with IR is increased TG and decreased HDLP, and these changes are suggested to be used as markers. Principally important pathogenic mechanism of IR is a disorder of lipid metabolism regulation by

means of increased release of free fatty acids in the adipose tissue [2, 3, 10].

IR in this category of women was evidenced by the values of HOMA index (Table).

Table

**HOMA index depending on menopause duration**

Examined groups	n	HOMA index
Control group	20	$2,6 \pm 0,2$
Group I	25	$2,7 \pm 0,2$
Group II	25	$3,4 \pm 0,5^*$
Group III	25	$3,8 \pm 0,5^*$

\* – reliable difference concerning the control group, ( $p < 0,05$ )

During examination of 8 (32%) patients of III group an increased basal level of C-reactive protein was found ( $4,3 \pm 0,6$  mg/L), which is a risk factor of vascular complications: acute myocardial infarction and stroke [2,3,9]. This index was higher in 4 (16%) women of II group and in 1 (2,5%) – I group ( $p < 0,05$ ). An increased level of C-reactive protein was found in 80% of women with obesity. It is indicative of the availability of a direct correlation between obesity factor and an increased level of C-reactive protein.

In addition, after the examination type 2 diabetes mellitus was found in 8 (32%) patients from III group. Glucose level on empty stomach was on the upper border of the norm among the patients from II and I groups. After glucose loading test in 3 (12%) patients of II group the glucose level was higher than that of the norm.

Arterial hypertension was found in 24% women of II group and 48% – III group. ECG findings were indicative of characteristic signs of hypertrophy of the left heart cavities.

**Conclusion.** 1. Heredity plays a certain role in the development of metabolic disorders.

2. The longer the menopause duration is, the more pronounced the signs of metabolic disorders are: obesity, increased levels of GC, TG, LDLP and VLDLP, decreased levels of HDLP, insulin resistance development.

3. Obesity is a factor promoting an increased level of C-reactive protein, development of

vascular complications, diabetes mellitus.

**Prospects of further studies.** Timely diagnostics and correction of metabolic disorders will promote a reduced risk of occurrence of cardio-vascular disorders and diabetes mellitus among women during post-menopause, and improvement of their quality of life.

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## PECULIARITIES OF ADMINISTRATION OF ANTISEPTIC DRUGS IN CHILDREN SUFFERING FROM CHRONIC CATARRHAL GINGIVITIS UNDER CONDITIONS OF DIABETES MELLITUS

**Abstract.** *The analysis of the sensitivity of the microflora of the oral cavity of children with chronic catarrhal gingivitis under conditions of diabetes reflects the high efficiency of bactericidal action of surface-active preservatives in a wide range of opportunistic pathogens. Intermediate sensitivity of bacterial strains research to action "Dekasan" in terms of in vitro  $17,13 \pm 4,01$  mg/ml. In the presence of "Chlorhexidine bihlyukonatu" should be 2 times higher concentration.*

**Keywords:** *children, gingivitis, diabetes, "Dekasan" "Chlorhexidine bihlyukonat".*

**Introduction.** Diseases of the periodontal tissues among children population is an important and complicated issue in dentistry. Scientific literature presents certain evidence of the main causes of gingivitis development, a leading role among which belongs to disorders of microbiocenosis in the oral cavity [2, 6].

The transmission from a healthy condition to the development of diseases of the periodontal tissues is accompanied by a successive change of microflora: from facultative and gram-positive kinds of bacteria to anaerobic and proteolytic gram-negative bacteria [1, 8]. In the result of active secretion of various enzymes microorganisms promoting the development of microcirculatory disorders of the periodontal tissues trigger a number of inflammatory reactions, cause depolymerization of glycosaminoglycans, proteins of the periodontal tissues, initiate hypoxia of the tissues [6, 7, 9]. At the same time, severity of the inflammatory process and its clinical-morphological peculiarities determine the patient's organism reactivity. The qualitative and quantitative content of the oral microflora are altered against the ground of comorbid somatic pathology complicating the course of periodontal tissue diseases [2, 10].

Due to variability of representatives of the oral microbiocenosis various antiseptic means of a wide spectrum of action, enzymes, fungicides, anti-protozoal drugs and antibiotics are administered for the treatment of gingivitis [1, 3, 4].

The most effective antiseptic means are superficially active substances. Their mechanisms of action are based on diphylic structure of the molecule and ability to a destructive effect on the prokaryote membrane. The drugs of this class are of a wide spectrum of antimicrobial action involving gram-positive and gram-negative bacteria, fungi-dermatophytes, yeast-like fungi, protozoa, chlamydia, and even complicated viruses (causative agents of hepatitis, HIV) [1, 4]. Resistance of microorganisms to these drugs is formed slowly. They possess a property to increase susceptibility of microorganisms to other antimicrobial means in sub-bacteriostatic concentrations [3]. From the mentioned group of drugs the pharmaceutical market presents the solution "Chlorhexidine gluconate" 0,05 % and «Decasan» — 0,02 % solution of decamethoxin isotoned by sodium chloride [3, 5]. Therefore, investigation of susceptibility of the oral microflora to the action of widely spread antiseptics is a topical issue.

**Objective:** to determine susceptibility of the oral microflora in children suffering from chronic catarrhal gingivitis (CCG) under conditions of diabetes mellitus (DM) to the action of antiseptic drugs "Decasan" and "Chlorhexidine gluconate" in the experiment.

**Materials and methods.** The serial industrial samples of medical means «Decasan» 0,02 % solution and "Chlorhexidine gluconate" 0,05 % solution were used in the study. Susceptibility of

the isolated strains of microorganisms from the oral cavity of children suffering from CCG under conditions of DM (284 strains) to the action of the examined drug – decamethoxin and antiseptic compound – chlorhexidine bigluconate was investigated by means of two-phase serial dilution in liquid nutrient media optimal for the growth of the examined test-cultures under conditions in vitro.

The results obtained were statistically processed by means of the licensed program «Statistika 6.0». The mean value (M), mean accuracy (m), reliability of statistical indices (p)

were estimated.

**Results and discussion.** The level of bactericidal concentration reflects the susceptibility of microorganism strains isolated from children suffering from CCG and DM to the main active substance of antiseptic preparations under conditions in vitro.

The Table presents the results of detection the susceptibility of microorganism strains isolated from children suffering from CCG under conditions of DM to “Decasan” and “Cholrhexidine bigluconate”.

**Table**

**Susceptibility of the oral microflora in children suffering from CCG under conditions of DM to the action of antiseptics**

№	Test-cultures of microorganisms	Number of examined strains of microorganisms	Antiseptic compound			
			«Decasan»		«Cholrhexidine bigluconate»	
			Bacteriostatic (BSC) and bactericidal (BCC) concentrations, mkg/ml			
			BSC	BCC	BSC	BCC
1.	Streptococcus pyogenes	20	1,06 ±0,32	2,12 ±0,74	1,52 ±0,48	3,03 ±0,34
2.	Streptococcus faecalis	6	19,53 ±3,46	39,06 ±7,81	23,43 ±7,81	46,87 ±15,62
3.	Streptococcus anginosus	4	1,11 ±0,37	1,22 ±0,74	1,4 ±0,48	2,92 ±0,97
4.	Streptococcus salivarius	18	1,06 ±0,15	2,12 ±0,37	1,53 ±0,19	3,06 ±0,39
5.	Staphylococcus aureus	22	0,88 ±0,19	1,96 ±0,38	1,65 ±0,14	3,31 ±0,29
6.	Staphylococcus epidermidis	10	0,17 ±0,03	0,34 ±0,07	0,22 ±0,02	0,45 ±0,03
7.	Escherichia coli	30	17,8 ±3,27	35,8 ±6,53	26,44 ±2,68	52,88 ±4,16
8.	Neisseria oralis	6	0,65 ±0,16	1,3 ±0,33	1,31 ±0,16	1,62 ±0,32
9.	Neisseria elongata	4	1,47 ±0,49	2,93 ±0,98	1,72 ±0,17	3,55 ±0,35
10.	Proteus mirabilis	3	46,4 ±15,7	93,8 ±31,3	62,5 ±10,41	137,0 ±12,5
11.	Proteus zettgeri	2	15,6 ±5,75	31,25 ±10,25	31,25 ±15,62	62,5 ±10,41
12.	Pseudomonas aeruginosa	6	20,85 ±5,2	41,7 ±10,4	26,04 ±5,21	52,08 ±10,41
13.	Candida albicans	19	1,19 ±0,19	2,39 ±0,38	1,75 ±0,16	3,41 ±0,32
14.	Candida tropicalis	12	0,82 ±0,15	1,94 ±0,37	1,56 ±0,24	3,12 ±0,47
15.	Candida krusei	2	0,87 ±0,15	1,95 ±0,37	1,95 ±0,37	3,9 ±0,53
16.	An average level of susceptibility	164	8,63 ±1,98	17,13 ±4,01	12,21 ±1,14	25,51 ±2,24

Among the representatives of the genus streptococci the most tolerant to the action of antiseptics was *Str. faecalis*, the bactericidal action of «Decasan» for it was  $39,06 \pm 7,81$  mkg/ml, and «Chlorhexidine bigluconate» —  $46,87 \pm 15,62$  mkg/ml. *Str. anginosus* manifested the highest susceptibility to «Decasan» ( $1,22 \pm 0,74$  mkg/ml), twice as low — to «Chlorhexidine bigluconate» ( $2,92 \pm 0,97$  mkg/ml). *Str. salivarius* and *Str. pyogenes* manifested a high susceptibility to «Decasan» —  $2,12 \pm 0,37$  mkg/ml and  $2,12 \pm 0,74$  mkg/ml, but susceptibility to «Chlorhexidine bigluconate» was also rather high —  $3,06 \pm 0,39$  and  $3,03 \pm 0,34$  mkg/ml. The data obtained enable to consider these antiseptics highly effective concerning the examined microorganisms.

*Staphylococcus aureus* presented the highest susceptibility to «Decasan» and died at the presence of 1,96 mkg/ml of decamethoxin. To kill this kind of microorganisms twice as much concentration of «Chlorhexidine bigluconate» is necessary. The susceptibility of epidermal staphylococci to «Decasan» and «Chlorhexidine bigluconate» did not differ reliably. Therefore, concerning this genus of microorganisms «Decasan» appeared to be practically in 3,5 times more active than «Chlorhexidine bigluconate».

Gram-negative opportunistic microorganisms of the enteral bacteria genus presented less susceptibility to the examined drugs than staphylococci. Thus, *Escherichia coli* died at the presence of  $35,8 \pm 6,53$  mkg/ml of decamethoxin, chlorhexidine —  $52,88 \pm 4,16$  mkg/ml.

Similar tendency was observed for *Proteus* as well. Bactericidal concentration of «Decasan» for *P. mirabilis* and *P. zettgeri* was  $93,8 \pm 31,25$  and  $31,25$  mkg/ml. These microorganisms died at the presence of chlorhexidin of a twice higher concentration.

Staphylococci and enteral bacteria play a leading role in the development of inflammatory diseases of the periodontal tissues, and therefore the efficacy of antimicrobial means is first of all evaluated by the influence on the representatives of these groups of microorganisms.

In recent years the representatives of the genus *Pseudomonas* are the most spread and highly resistant to antimicrobial means. The examined strains *Pseudomonas aeruginosa* appeared to be more tolerant to the action of

antiseptics than staphylococci and enteral bacteria. BCC of «Chlorhexidine bigluconate» for them was  $52,08 \pm 10,41$  mkg/ml. The representatives of this genus presented the highest susceptibility to «Decasan» (BCC —  $41,7 \pm 10,4$  mkg/ml).

The medical forms of «Decasan» (0,02% solution or 200 mkg/ml) and «Chlorhexidine bigluconate» (0,05% solution or 500 mkg/ml) even within the limits of standard deviations contain sufficient concentration of the main active substance to ensure a destructive action on the isolated strains of any representative of *pseudomonas*.

Yeast-like fungi of the genus *Candida* are an integral constituent of opportunistic oral microflora of a healthy individual. Among the drugs examined the lowest BCC for *Candida* was for «Decasan» (*C. albicans* —  $2,39 \pm 0,38$  mkg/ml, *C. tropicalis* —  $1,94 \pm 0,37$  mkg/ml, *C. krusei* —  $1,95$  mkg/ml). To kill yeast-like fungi twice as much concentration of «Chlorhexidine bigluconate» is required. It should be noted that concentrations of antiseptics in all the examined medicinal forms were considerably higher than the indices of susceptibility of the examined fungal strains considering individual strain deviations.

The conducted analysis of susceptibility of the oral microflora of children suffering from CCG under conditions of DM reflects a high efficacy of bactericidal action of the superficially active antiseptics of a wide spectrum on opportunistic microorganisms. An average level of susceptibility of the examined bacterial strains to the action of «Decasan» under conditions in vitro is  $17,13 \pm 4,01$  mkg/ml. With «Chlorhexidine bigluconate» twice as much concentration is required.

Choosing an antimicrobial compound in the content of a ready medicinal form BCC of the main active substance should be considered for every specific clinical strain of microorganisms. Under clinical conditions activity of an antiseptic compound decreases due to the impact of biological fluids, sorption properties of the body tissues and other factors requiring a considerable safety factor in the concentration of a substance in a ready medicinal form as compared to the bactericidal concentration.

**Conclusion.** A high efficacy of administration of the antiseptic «Decasan» is proved in the

treatment of CCG in children against the ground of DM. BCC of the antiseptic preparation for any of the examined microbial strains was less than the content of the main acting substance in ready medicinal forms, although the level of susceptibility of separate kinds differed considerably.

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## TOPOGRAPHIC PECULIARITIES OF THE ANTERIOR CEREBRAL VESICLE ON THE 4<sup>TH</sup> WEEK OF THE EMBRYONIC PERIOD

**Abstract.** *In the article a conducted embryological investigations is described with the aim to understand and clarify causes and time of possible occurrence of congenital diseases, variants and abnormalities in the development of organs and structures of the body. We have figured out that by the end of the first month of the intrauterine development the brain is represented by the three cephalic vesicles: anterior, middle and rhomboid (prosencephalon, mesencephalon and rhombencephalon). We consider that at this period the ventricular system is visible as the cavity of these vesicles, and the lateral and third ventricles in particular as a part of the cavity of the anterior cephalic vesicle.*

**Key words:** *cerebral vesicle, embryonic period, human.*

**Introduction:** the necessity to conduct embryological investigations for correct understanding and clarification of causes and time of possible occurrence of congenital diseases, variants and abnormalities in the development of organs and structures of the body is universally recognized and promotes detection of real directions concerning the processes of organogenesis.

According to the WHO data 3-4 million out of 140 million newborns born annually have serious abnormalities, a part of which belongs to defects of the nervous system [1, 2, 3]. Congenital developmental abnormalities in Ukraine according to the data of the state reports occupy the second position among the causes of death of newborns.

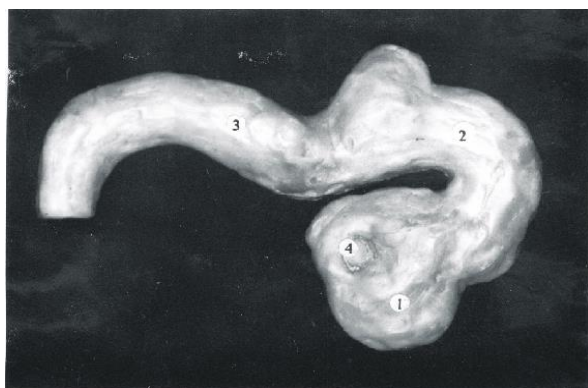
Introduction of artificial fertilization, grafting of embryos, screening of the embryonic material, ultrasound examination of the fetal development, prenatal diagnostics of defects from the normal human ontogenesis into the world laboratories [4]

and other modern methods of examination of medical embryology enable to conduct antenatal prevention of disorders of normal development [5] and surgical correction of certain defects of the human fetus during intrauterine development [6, 7, 8].

**Objective:** the topicality of the study is explained by the necessity to conduct a comprehensive investigation of the peculiarities of morphological regularities in the prenatal period of human ontogenesis, formation of its organs and systems for correct understanding of the essence of processes occurring in the period of intrauterine life, investigation of peculiarities of different periods of the embryonic development that can be used to find out etiology, pathogenesis, to carry out antenatal prevention in order to substantiate radical methods of treatment of various diseases after childbirth.

**Materials and methods:** the study was conducted on 15 dead human embryos by means of histological examination, dissection and morphometry.

**Results of the study and their discussion:** the central nervous system including its cephalic portion is known to look like a tubular formation at the initial stages of development. Therefore, all further stages of development are associated with changes of the shape and differentiation of the wall of this formation into the portions, are accompanied by delimitation and further division of the lumen into the cavities of various sizes (ventricles, canals). The brain develops from the anterior, major end of the neural tube. This portion growth considerably and at the beginning of the 4<sup>th</sup> week of the intrauterine life it is divided into the three convex dilations – cephalic vesicles – anterior (prosencephalon), middle (mesencephalon) and rhomboid (rhombencephalon). Due to uneven growth of separate parts of the neural tube its head end, that was previously practically straight, forms a number of flexures. The border between these portions is caused by irregular rates of growth and availability of flexures: cervical and mesencephalic occurring first of all. It is turned with its convexity outside, its apex forms parietal tuber well seen from the dorsal side. Due to the formation of flexures the prosencephalon or forebrain is located at an angle to the rhomboid one. At the same time, on the border between the spinal cord and brain the cervical flexure is formed. Simultaneously the cervical tuber occurs, well seen in the embryos of the early period of development. Later the pontine flexure appears directed ventrally. This flexure divides the posterior cephalic vesicle into the proper posterior cephalic vesicle (myelencephalon) – posterior portion and the germ of the pons and cerebellum (metencephalon) – the anterior portion (Fig. 1).



*Fig. 1 Plastic reconstruction of the embryonic brain 5,0 mm PCL. 1 – anterior cephalic vesicle; 2 – middle cephalic vesicle; 3 – posterior cephalic vesicle; 4 – eyecup; 5 – ventral cephalic fold*

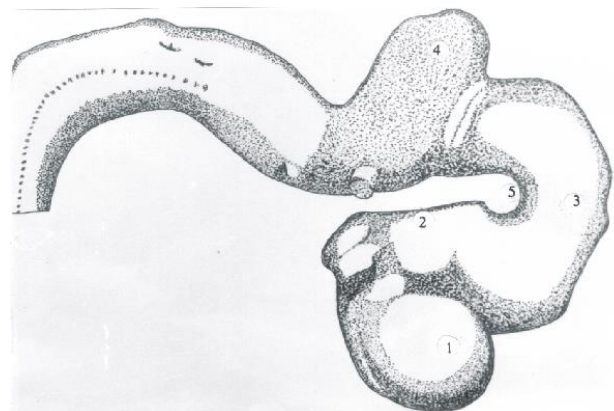
Investigation of a number of histological sections is indicative of the fact that at the end of the 4<sup>th</sup> week of the embryonic development (in embryos of 5,00 mm PCL) the brain consists of three cephalic vesicles forming an arch embracing the oral part of the embryo. The anterior cephalic vesicle is located on the level of the heart germ.

This period is the beginning of formation of the ventricular system in the form of cavities connected together. The junction between the future third and lateral ventricles is practically solid, therefore at this stage it can be considered as one cavity. This formation is dilated on the sides, anteriorly and inferiorly it is closed with the thin final plate formed due to the closure of the anterior neuropore.

Two layers are differentiated in the embryos of the 4<sup>th</sup> week of development in the cephalic tube. The first of them, internal, is wide. It is also termed ependymal. The second one, external, or nuclear is rather narrow. The cells of this layer are closely adjusted to each other. The ventral wall of the cephalic vesicles is marked better than the dorsal one. The dorsal wall for a long time remains thin and consists of only 1-2 layers of cells.

Due to intensive growth of the ventral wall of the cephalic vesicles the ventral cephalic fold is formed (Fig. 2). This fold is short and passes practically horizontally between the rhomboid and anterior cephalic vesicles. The isthmus between these cephalic vesicles is relatively wide. Thus, the forebrain is rather lowered.

**Conclusions:** therefore, at the end of the first month of the intrauterine development the brain is represented by the three cephalic vesicles: anterior, middle and rhomboid (prosencephalon, mesencephalon and rhombencephalon). We



*Fig. 2 Graphic reconstruction of the brain of the embryo 5,0 mm PCL. 1, 2 – anterior cephalic vesicle; 3 – middle cephalic vesicle; 4 – posterior cephalic vesicle; 5 – ventral cephalic fold.*

consider that at this period the ventricular system is available as the cavity of these vesicles, and the lateral and third ventricles in particular as a part of the cavity of the anterior cephalic vesicle.

**Prospects of further studies:** further investigations should focus their attention on the development of the cephalic cavities at the following terms to find critical periods, possible developmental defects and elaboration of new methods of the study.

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## PECULIARITIES OF MORPHOLOGICAL MANIFESTATION OF THE PERIODONTAL TISSUE IN EXPERIMENTAL ANIMALS AGAINST THE GROUND OF A SHORT-TERM EFFECT OF OPIOID ANALGESIC

**Abstract.** *Pathomorphological changes in the periodontal tissues on early terms of opioid effect in experiment have been studied. 16 mature outbred male rats with the body weight of 200 g and age of 4,5 months were used as the material of the study. The animals were subjected to opioid analgesic injections i/m every day once a day during 14 days. The initial dose of Nalbuphine was 0,212 mg/kg during the first week and 0,225 mg/kg during the second week. Thus, conditions of chronic opioid effect were created. Amputated upper and exarticulated lower jaws were used for microstructural examination. Histological specimens were prepared with preliminary made decalcination using hematoxylin, eosin and azan by Heidenhain's method. The results of the study obtained were indicative of changes available possessing an inflammatory character and present in all the soft periodontal tissues, although within the borders of the hard tissues those changes were not considerable without visible signs of pathologic lesion.*

**Key words:** *periodontium, opioid, microscopic examination, rats.*

**Introduction.** A long-term and not always controlled administration of psychotropic drugs, opioid analgesics, tranquilizers, certain stimulators and pain relieving medicines caused a problem of pharmacological addiction similar to that of drug addiction [18]. According to the results of the studies opioid-addicted individuals in addition to severe changes of the internal organs present considerable lesions of the dentoalveolar system, which complicates to make differential diagnostics and treatment of oral pathology including diseases of the periodontium. Therefore this problem is not only of a medical but social importance as well [2-4, 6-8, 11, 13, 16, 19]. Dental pathology in drug addicted persons is not studied considerably on clinical material, and thus it requires special scientific studies including experimental ones [4, 10].

The published literary sources present data concerning experimental reproduction of pathological changes in the periodontal tissues of laboratory rats with modeling acute and chronic morphine intoxication using high doses of morphine hydrochloride – from 10 to 30 mg/kg of the body weight [1, 4]. There are also findings concerning general influence of drug pathology in rats with modeling of morphine intoxication injecting maximal doses from 5 to 70 mg/kg of the

body weight [5, 12, 17].

Although, the literary sources available do not present data concerning peculiarities of morphological periodontal changes in experimental animals against the ground of a gradual increase of small doses of an opioid analgesic.

**Objective:** to study the dynamics of morphological changes in the periodontal tissues on early terms of opioid effect.

**Materials and methods.** 16 mature outbred male rats with the body weight of 200 g and age of 4,5 months were used as the material of the study. The animals were subjected to opioid analgesic injections i/m every day once a day at the same period of time (10-11 a.m.) during 14 days. The initial dose of Nalbuphine was 0,212 mg/kg during the first week and 0,225 mg/kg during the second week. Thus, conditions of chronic opioid effect were created [14].

The animals were distributed into two groups. The 1<sup>st</sup> group of animals received Nalbuphine during 14 days with the following material sampling (the end of the 2<sup>nd</sup> week of experimental opioid effect); the 2<sup>nd</sup> group, as the control one, received injections of physiological solution i/m at the same period of time (10-11 a.m.) during 14 days. All the animals were kept under conditions



of vivarium, and the work concerned the issues of their keeping, care, labeling and other manipulations were conducted according to the regulations of "European Convention for the Protection of Animals used for Experimental and Other Scientific Purposes" [Strasbourg, 1985], "General Ethical Principles of Experiments on Animals" approved by the First National Congress in Bioethics [Kyiv, 2001], the Law of Ukraine № 3447 – IV «On Protection of Animals against Cruel Treatment». The Bioethics Committee of Danylo Halytskyi Lviv National Medical University found that conducted scientific studies correspond to ethical requirements according to the Order of the Ministry of Public Health of Ukraine № 231 dated 01. 11. 2000 (minutes № 10 dated 26.12.2011), (minutes №2 dated 20.02.2012). Before the material was taken for biopsy examination the animals were put to sleep by means of intra-abdominal injection of thiopental (25 mg/1 kg). Amputated upper and exarticulated lower jaws were used for microstructural examination considering further preservation of topographic ratio of the dental organ making histological sections 5-7 mcm thick. Histological specimens were prepared according to common method with preliminary made decalcination [15] using hematoxylin, eosin and azan by Heidenhain's method [9]. Microscopic examinations and photos of specimens were made by means of the microscope Meiji MT4300 LED and digital camera Canon EOS 550D.

**Results and discussion.** Morphological changes found at the end of the 2<sup>nd</sup> week of the experiment appeared to be moderately pronounced in the soft tissues and practically absent in the hard tissues of the periodontal tissues. The changes found were of inflammatory character peculiar for catarrhal gingivitis. Inflammatory signs were found in the layer of the gingival epithelium manifested by hyperkeratosis of the stratified squamous keratinous epithelium of the oral portion of the free gingival part. Epithelial buds are of mainly common size, a round shape with signs of inconsiderable acanthosis, manifested by proliferation of the epithelial layer into the depth of the connective tissue of its proper plate presented on Fig. 1, 2.

There are signs of a moderate swelling and inconsiderable polymorphic-cellular infiltrate in the proper plate of the mucous membrane illustrated on Fig. 1, 2, 3, 4. Small aggregations of lymphocytes and single neutrophils, numerous

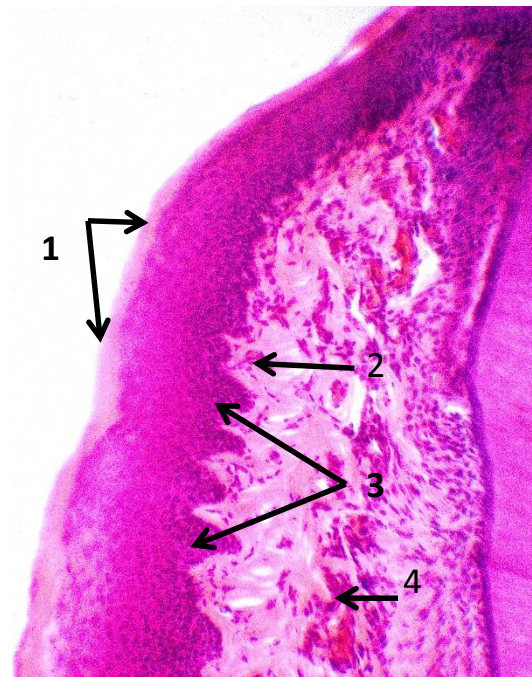


Fig. 1. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x 200). 1 – hyperkeratosis of the epithelium in the free gingival part; 2 – swelling of the proper plate of the gingival mucosa with moderately pronounced polymorphic-cellular infiltrate; 3 – inconsiderable acanthosis of the epithelium; 4 – blood filling of hemomicrocirculatory flow.

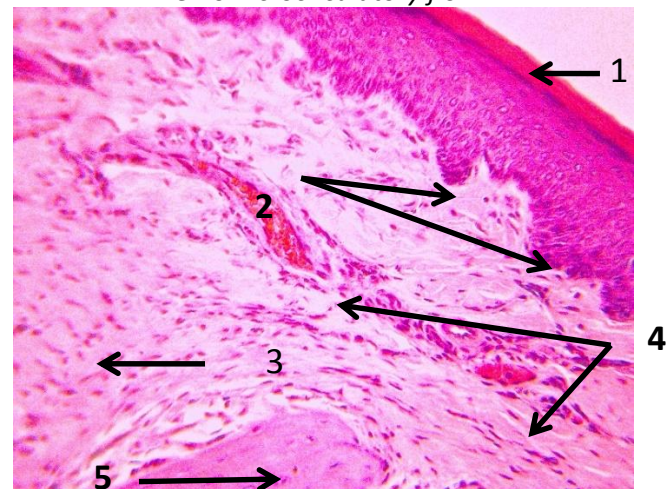


Fig. 2. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x 400). 1 – hyperkeratosis of the stratified squamous keratinous epithelium; 2 – round epithelial buds; 3 – moderate swelling of the gingival mucosa proper plate; 4 – vessels of the hemomicrocirculatory flow filled with blood; 5 – signs of mineralization disorders in the apical place of intercellular septum

fibroblasts and fibrocytes are visualized as it is presented on Fig. 5.

Granulation tissue appears in the gingival tissue from the vestibular site at the end of the 2<sup>nd</sup> week of opioid effect as it is seen on Fig. 4. The vessels of the hmeomicrocirculatory flow were filled with blood, which resulted from hypoxia.



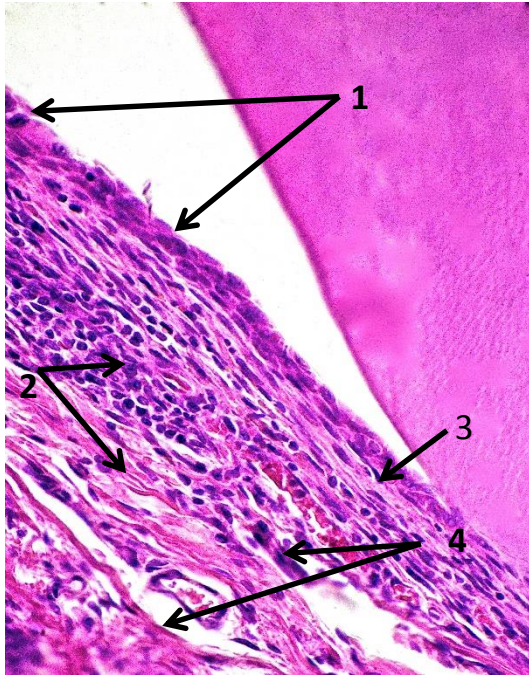


Fig. 3. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x400). 1 – thinning of the stratified squamous keratinous epithelium of the dentogingival furrow; 2 – moderate swelling with signs of polymorphic-cellular infiltration; 3 – preserved intact epithelial attachment; 4 – hyperemia of the hemomicrocirculatory flow.

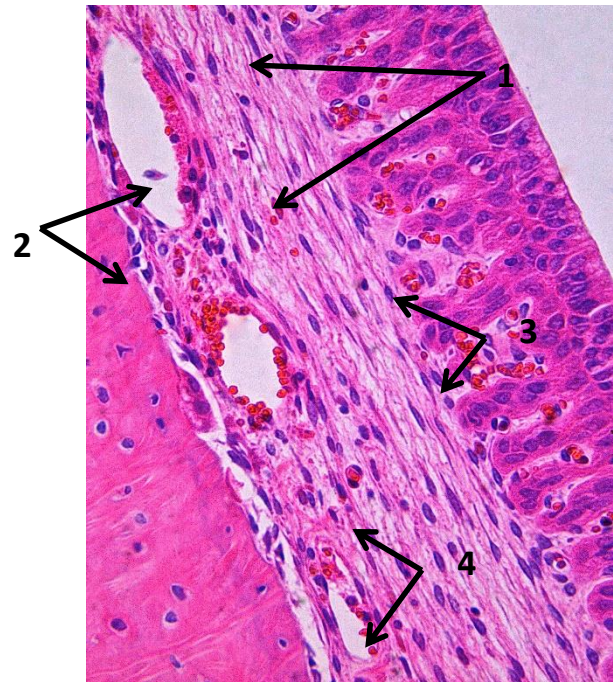


Fig. 5. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x 400). 1 – acanthotic teniae of the epithelium on the dentogingival furrow; 2 – inconsiderable aggregations of lymphocytes and single neutrophils in the proper plate of the mucous membrane; 3 – hyperemia signs in the links of hemomicrocirculatory flow in the place of the dentogingival furrow; 4 – numerous fibroblasts and fibrocytes.

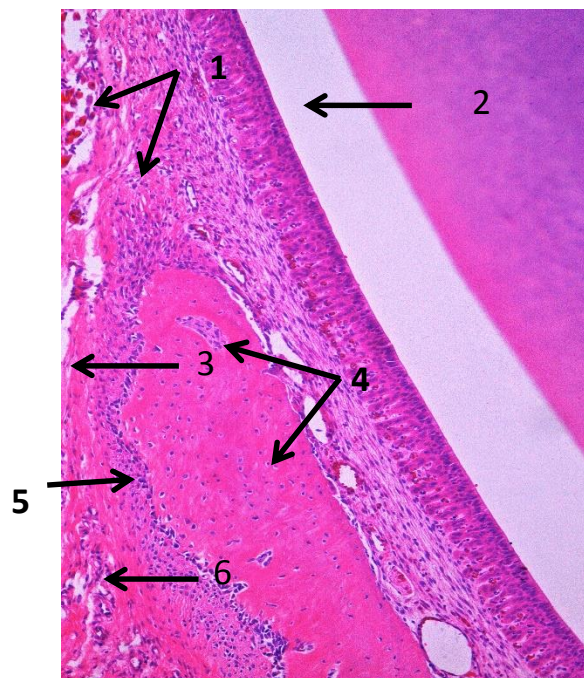


Fig. 4. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x 200). 1 – moderate swelling of the proper plate of the gingival mucosa; 2 – dentogingival furrow; 3 – granulation tissue in the gums from the vestibular site; 4 – numerous lymphoangiectasias of the proper plate of the gingival mucosa; 5 – apex of the cellular process of the jaw without changes; 6 – pronounced proliferation of osteoblasts.

Moreover, numerous lymphoangiectasias were found as it is illustrated on Fig. 1, 2, 3, 4, 5.

The lumen of the dentogingival furrow is clearly visualized as it is seen on Fig.3 and 4. A characteristic feature for the experimental animals of this group was thinning of the stratified squamous keratinous epithelium and regular outlines of the epithelial attachment with preserved integrity in the place of the dentogingival furrow as it is illustrated on Fig.3. In half of the cases the place of epithelial attachment coincides with the level of the enamel-cement border (within the norm in 75% higher than this level). The signs of hyperemia were found in the portions of hemomicrocirculatory flow, between acanthotic teniae of the stratified squamous keratinous epithelium of the dentogingival furrow as it is illustrated on Fig.4 and 5.

Epithelial buds in the area of the furrow are rather high with signs of pronounced acanthosis, which is atypical for this area, since within the norm bud are absolutely absent or considerably lower than in other areas of the gums. These changes are characteristic signs of primary inflammatory-destructive signs occurring in the



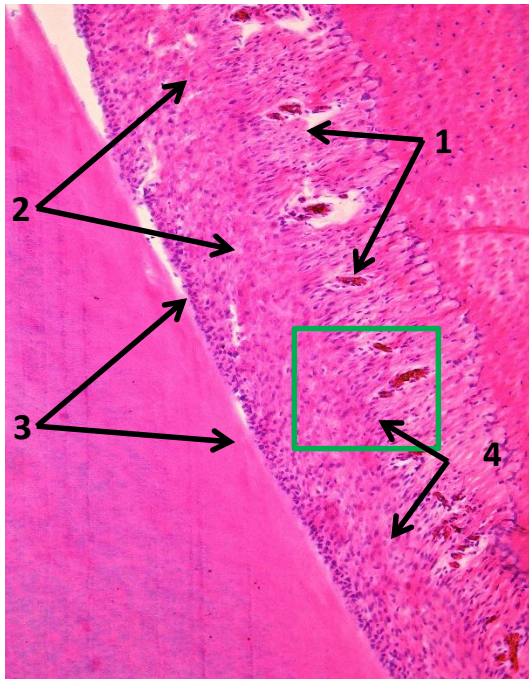


Fig. 6. 2<sup>nd</sup> week, the 1<sup>st</sup> group (hematoxylin and eosin, x 200). 1 – area of fixation of the collagen fibers of the periosteal layer into the compact plate of the cellular process of the jaw; 2 – angiomatosis with signs of erythrocyte aggregation; 3 – signs of fibroblast cytotaxis and swelling of fibers of the periradical periodontal layer; 4 – hyperemia of the links of hemomicrocirculatory flow of the periodontium.

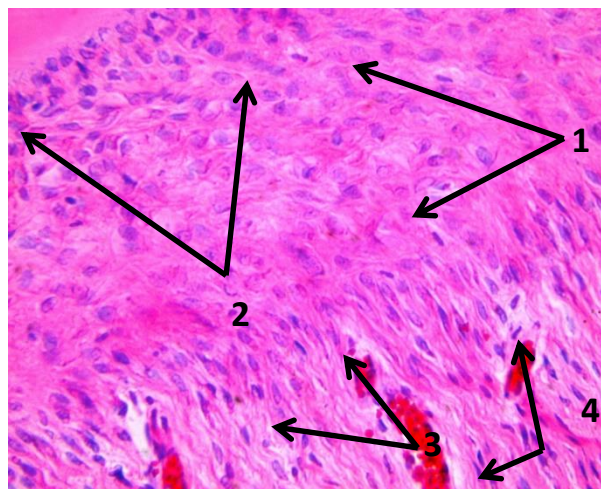


Fig. 7. Fragment of Fig. 6. 2<sup>nd</sup> week (hematoxylin and eosin, x400) 1 – more “cytosoled” periradical periodontal layer at the expense of fibroblasts; 2 – mitosis in fibroblasts; 3 – more fibrous periosteal periodontal layer at the expense of fibrocytes and collagen fibers; 4 – hyperemia with aggregation of erythrocytes in hemomicrocirculatory flow of the periodontium.

soft periodontal tissues under the action of small doses of opioid analgesic as it is illustrated on Fig. 4 and 5. The periodontal tissue at this term of opioid effect was characterized by available

longitudinal and transverse oriented fibers of the connective tissue. Thus, the fibers of the periosteal layer were transverse, the fiber of the periradical layer – longitudinal. At the same time, the periosteal periodontal layer was more fibrous and presented by fibrocytes and collagen fibers of I type. In its turn, the periradical layer was more “cytosoled” at the expense of fibroblast mitosis as it is seen on Fig. 6 and 7.

Collagen fibers of the periosteal periodontal layer are atypically combined with the compact plate of the cellular process of the jaw in the form of “cellular line” as it is demonstrated on Fig. 6 and 7. Within the borders of loose sufficiently vascularized connective periodontal tissue hyperemic vessels were found with erythrocyte aggregation, which was indicative of exertion of the links of the hemomicrocirculatory flow as it is seen on Fig. 6 and 7. The osseous tissue of the cellular process of the jaw was evenly mineralized as it is shown on Fig. 4, 5 and 6, with available single areas with signs of mild mineralization. It was mainly found in the area of the apical intercellular septum as it is illustrated on Fig. 2.

**Conclusions.** Pathomorphological changes found at the end of the 2<sup>nd</sup> week of the experiment in case of a short-term effect of opioid appeared to be inflammatory and moderately pronounced in the soft tissues and practically absent in the hard tissues of the periodontal tissues.

**Prospects of further studies.** The conducted studies concerning opioid effect during 14 days will enable to observe gradually the appearance of pathomorphological changes in the dynamics and their growth at later terms. In the long term possessing the clinical manifestation and growth of pathomorphological changes in the periodontal tissues will enable to determine correcting effect at early and late terms of opioid impact.

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## RENAL TISSUE FIBRINOLYSIS AGAINST THE GROUND OF STRESS AND XENOBIOTICS

**Abstract.** *The article presents the results of experimental studies concerning the investigation of a combined impact of stress and metal chloride compounds – of lead and aluminum on the renal tissue fibrinolysis of albino rats. The dependence of the process intensity of the renal tissue fibrinolysis of animals under the effect of stress and metal salts on the stages of daily period was found.*

**Key words:** *chronobiology, tissue fibrinolysis, intoxication, stress, metal salts.*

**Introduction.** Diagnostics of early signs of nephropathy caused by stress and metal salts does not always enable to evaluate the degree of severity and dynamics of structural-functional changes of the biological systems timely [1, 5]. To detect reorganization of the renal functions in case of exogenous intoxications application of chronorhythmological methods with the aim of early diagnostics, prevention and treatment of renal pathology is essential [2, 3].

Development of pathological conditions promotes changes of biological rhythmicity of the body and its functions. The study of these phenomena is the basis of chronopathology. The subject of this study is analysis of the ways and mechanisms of deviation occurrence in biological rhythms from their normal course and the role of these disorders in pathogenesis of diseases [1, 4].

The pineal gland was found to participate in the processes of adaptive self-regulation of the body in case of exogenous intoxications. Although, the regularities of chronobiological regulation of the renal function according to the changes of the daily cycle remain insufficiently investigated. Clarification of this issue is of an important theoretical and practical value, as it will enable to improve the methods of diagnostics, prevention and treatment of renal pathology considering dependence of its peculiarities of occurrence and course on daily phases.

**Objective:** to detect circadian peculiarities of the renal tissue fibrinolysis within the norm and in case of the impact of stress and aluminum and lead chlorides on the body.

**Materials and methods.** The experiments were conducted on mature male albino rats in three series. In the first series the daily rhythmical organization of the renal tissue fibrinolysis was

studied when a negative exogenous effect was absent (the control group).

In the second series a pathogenic effect of metal salts on the chronorhythmical order of the renal tissue fibrinolytic condition of the albino rats was studied. During 14 days the rats were given minimal doses (DLmin) of aluminum chloride compounds (AlCl<sub>3</sub>) – 200 mg/kg and lead (PbCl<sub>2</sub>) – 50 mg/kg every day intragastrically [6, 7].

In the third series the peculiarities of fibrinolytic changes in the renal tissue were investigated under conditions of stress and combined action of the metal salts.

The experimental studies and animal euthanasia were conducted according to the International Principles of the European Convention for the Protection of Animals Used for Experimental and Scientific Purposes (Strasbourg, 1986). The experiments were performed 14 days after introduction of aluminum and lead chlorides under condition of water induced diuresis at the following hours: 8 a.m., 2 p.m., 8 p.m. and 2 o'clock at night.

The condition of enzymatic and non-enzymatic fibrinolysis was evaluated according to azofibrinolysis ("Simko Ltd.", Lviv). The intensity of the renal tissue fibrinolysis was evaluated by the degree of staining of the solution in alkali medium. Due to azofibrinolysis with presence of  $\epsilon$ -aminocaproic acid as an inhibitor of enzymatic fibrinolysis non-enzymatic fibrinolysis is detected, and without it – total fibrinolytic activity (TFA). The difference between these indices reflects the condition of enzymatic fibrinolysis: TFA-NEA=EF (enzymatic fibrinolysis) [3]. The results of the study were statistically processed by means of "Cosinor-analysis" method and parametric methods of variation statistics.

**Results and discussion.** The results of chronobiological experiments found that fibrinolytic activity (FA) of the renal tissue by the kidney physiological activity depends on an accurate organization according to daily changes. The analysis of the mechanisms of enzymatic and biochemical reconstructions gives the evidence to suggest regulated chronorhythmic order of the renal functions.

The relation between the daily fluctuations of fibrinolytic activity with the adrenal cortex activity was found. The level of fibrinolytic activity of the renal tissue is connected with changes of light during 24 hours [1, 3].

Thus, in the 4 first series, synchronous daily variations of fibrinolysis activity in the renal cortex of albino rats is found in case of a combined impact of stress and metal salts. The indices of fibrinolysis changed at 2 p.m. and 8 p.m., and they increased at 2 o'clock at night. The mesor and amplitude of fibrinolysis rhythm in the cortical layer became 12% less. The above effects are caused by a number of adaptive-compensatory and decompensatory mechanisms of the renal function which are directly connected with the pineal gland.

Similar changes were found in the medullar layer of the kidney in case of aluminum-lead intoxication of the body. Chronorhythmic disorders of tissue fibrinolysis were registered that were reflected by a reliable shifting of the medullar tissue fibrinolysis at 8 p.m. The mesor and amplitude of fibrinolysis rhythm in the medullar layer became 29% less. It might be explained by the fact that adaptive-compensatory properties decrease during the light period of time and are renewed after dark at 2 o'clock at night.

In case of stress and a combined action of Al+Pb salts in experimental animals these indices of fibrinolytic activity in the papillar layer of the kidney changed more at 8 a.m. and 2 o'clock at night. The mesor and amplitude of rhythm became 30% less. Exogenous intoxication of the bodies with metal salts and effect of stress cause biochemical changes in the renal tissue, and fibrinolytic activity in particular, resulting in disorders of chronorhythmic organization of the renal function, that in its turn leads to deposits of fibrin in the renal structures with fibrinoid degeneration of tissues [3, 6].

Inhibition of the fibrinolytic system with the formation of tubular-interstitial syndrome is the most important on the level of the renal papilla and renal medullar substance, that can result in the development of thrombosis, urothrombosis followed by fibrin transformation into collagen [3].

**Conclusions.** The results of the studies presented have found a close relation between the daily changes of the parameters of the renal tissue fibrinolysis characterizing functional-biochemical condition of the kidneys stipulated by the term of photoperiod and the impact of stress and metal salts.

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## SPATIAL TOPOGRAPHY OF THE DIAPHRAGM IN THE SAGITTAL PLANE IN WOMEN

**Abstract.** Individual spatial topography of the patient diaphragm is of certain importance for diagnostic and therapeutic manipulations. The study to determine individual characteristics of the spatial topography of the human diaphragm in sagittal plane based on SCT-data considering sex, age and somatotype has been conducted. The material for the study was the data after examination of 75 patients with different diseases of the abdominal and thoracic cavities. Measuring of the diaphragm attachment angles in the sagittal plane was made on the vertebral, paravertebral, scapular and posterior axillary lines on both sides (front and back values). Statistical analysis of the measurements revealed little correlation between the age and angle of diaphragm attachment in female. Other parameters were not correlated with the studied values (sex and type of the body structure).

**Key words.** Individual spatial topography, attachment angle of the diaphragm.

**Introduction.** Individual spatial topography of the diaphragm is of a great importance for understanding the structural organization of this organ in every particular clinical case [1]. To conduct diagnostic and especially therapeutic manipulations the awareness of individual peculiarities of every patients is compulsory. This knowledge enables to avoid damage of the internal organs of the abdomen and thorax in case of their puncture (catheterization), to determine localization of a pathological process more precisely, and to choose the method of further surgery or conservative treatment [2, 3].

**Objective** of our study was to find individual peculiarities of the spatial topography of the human diaphragm in two vertical planes – sagittal and frontal on the bases of spiral computed tomography (SCT) examination considering sex, age and somatic type [4, 5].

On the basis of the results of the obtained findings availability (or absence) of relations between individual peculiarities of spatial topography and sex, age and somatic type has been planned to find. The data obtained were used to develop 3D program of an individual modeling of the human diaphragm [6, 7].

**Materials and methods.** The data of 75 patients examined during the last 2 years concerning various diseases of the abdominal and

thoracic organs were used in the investigation. There was no any diaphragmatic pathology found. The analysis and processing of the images obtained were conducted on the working station “HP-Z820” with application of the specialized program “Vitrea 2”.

There were 61 men and 14 women involved in the study. Their age ranged from 26 to 82. According to the body or somatic type the following proportions were found: male hypersthenic persons – 35%, normosthenic – 60%, asthenic – 15%; among women this proportion was the following: 30%, 50% and 20% respectively. The body constitutional type was determined according to Pinje index. Due to limited possibilities we will not present all the data obtained, but will show only minimal and maximal values. The article presents the findings obtained in the investigation of the attachment angles of the diaphragm to the sagittal pane in women. The data obtained will be presented in the following succession: the values of the angles of the diaphragm attachment to the vertebral line (vl), paravertebral line (pvl), scapular line (sl) and posterior axillary line (pal) in the left, and the same examinations (except vertebral line) in the right.

Figure presents the screenshot of the measurement of the human diaphragm

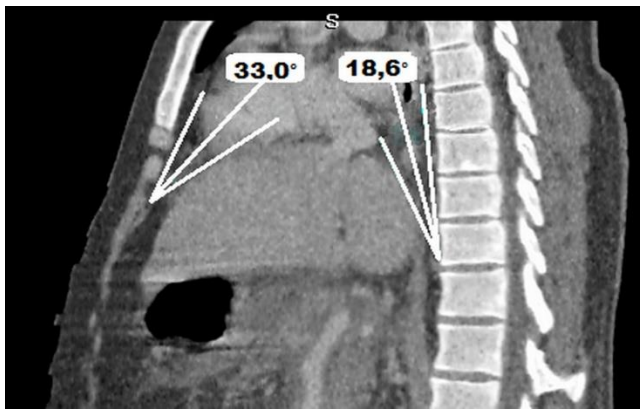


Figure. The angles of human diaphragm attachment along the vertebral line in the frontal plane.

attachment angles along the vertebral line in the frontal plane. The figure demonstrates that these investigations will present two values: the first value – the angle of the diaphragm attachment along the anterior surface (as – sternal line), and the second value – the angle of the diaphragm attachment along the posterior surface (ps – the vertebral line proper).

**Results and discussion.** The data characterizing minimal and maximal values of the diaphragm attachment in women are presented in Table 1. The biggest number of values of the diaphragm

**Table 1**

**Minimal and maximal values of the diaphragm attachment in women in the sagittal plane**

		asthenic		Normosthenic		hypersthenic	
		min	max	min	max	min	max
vl	as	26,4°	58,6°	33,6°	95,4°	29,6°	60,0°
	ps	5,2°	40,2°	10,0°	43,4°	9,2°	48,4°
Left pvl	as	35,7°	91,0°	27,7°	89,2°	15,0°	102,8°
	ps	20,5°	75,0°	23,3°	76,5°	17,1°	80,6°
Left sl	as	27,2°	83,5°	38,4°	106,0°	41,5°	101,8°
	ps	27,1°	75,6°	23,3°	66,1°	24,0°	69,1°
Left pal	as	27,2°	92,6°	38,4°	106,0°	41,5°	101,8°
	ps	24,0°	75,5°	16,1°	54,1°	23,1°	51,7°
Right pvl	as	32,6°	74,4°	16,1°	73,5°	42,4°	85,3°
	ps	32,9°	80,5°	24,1°	76,1°	17,5°	72,5°
Right sl	as	28,2°	66,0°	21,7°	65,2°	36,3°	75,7°
	ps	24,1°	69,7°	21,5°	70,4°	29,7°	74,5°
Right pal	as	22,1°	46,0°	16,6°	68,5°	19,5°	76,6°
	ps	20,4°	63,0°	21,5°	81,7°	24,8°	75,5°

attachment along the vertebral line (anterior surface) is found within the interval from 70° to 80°. There were 4 such cases (28,6%). 3 cases (21,4%) were found within the range from 50° to 60°. Therefore, 50,0% of cases were within the range from 50 to 60 and 70 – 80°.

The most frequent values of the diaphragm attachment along the vertebral line (posterior surface) in women were found within the range from 10° to 20° – 6 cases (42,9%) and within the range from 20° to 30° – 4 cases (28,6%). Therefore, within the range from 10° to 30° there were 71,5% of all cases found.

The angle of attachment along the posterior surface was not determined in all the cases. It is connected with individual peculiarities of the aorta location concerning the vertebral column.

The angles of the diaphragm attachment along

the left paravertebral line in the sagittal plane in women were measured anteriorly and posteriorly; the order of the data presented is: the first measurement – the angle of attachment along the anterior surface (parasternal line), the second measurement – along the posterior surface (paravertebral line).

The cases within the range from 60° to 70° (4 cases) were found most frequently (28,6%). 3 cases (21,4%) were found within the range from 70° to 90°. Therefore, 50,0% of cases were within the range from 60 to 90°. The rest of the measurements were not conducted due to individual peculiarities of the internal organs location.

The second value in women along the paravertebral line in the left looked like the following: the values within the range from 40° to



50° were found more frequently. There were 5 of them (35,7%). The rest of values were evenly distributed in all the intervals. It should be noted that all the values were not able to be obtained in the patients examined. It is associated with individual peculiarities of the aorta location concerning the vertebral column.

The first value of the angles of the diaphragm attachment along the scapular line in the left in women was the following: most frequent values were within the interval from 50° to 60°. There were 5 such cases (35,7%). Within the interval from 60° to 80° there were 42,8% of all the cases. Therefore, within the range from 50° to 80° there were 78,5% of all the cases.

The second value of the angles of the diaphragm attachment in women was the following: most frequent values were within the interval from 30° to 40° – 5 cases (35,7%). 3 more cases were found within the range from 40° to 50° (21,4%). Therefore, 57,1% of cases were found within the intervals from 30° to 50°.

The next line examined in the sagittal plane in the left is the posterior axillary line.

The first value (along the anterior surface) of the diaphragm attachment in women was the following: most frequent values were found within the interval from 30° to 40° – 6 cases (42,8%) and from 50° to 60° – 4 cases (28,8%). 2 more cases (14,3%) were within the range from 40° to 50°. Therefore, within the interval from 30° to 60° there were 85,9% of all cases.

The second value (posterior surface) of the diaphragm attachment along the posterior axillary line in women was the following: most frequent values were found within the interval from 30° to 40°. There were 6 such cases (42,8%). There were 5 values (35,7%) within the interval from 40° to 50°. Therefore, within the interval from 30° to 50° there were 11 cases (78,6%).

Then the angles of the diaphragm attachment in the sagittal plane in the right side of the thorax along the similar lines were studied.

In women the first value of the angles of the diaphragm attachment was the following: most frequent values were found within the interval from 50° to 60°. There were 5 values (35,7%). 3 more cases were found within the range from 40° to 50° (21,4%). Therefore, 57,1% of cases were within the range from 40° to 60°.

The second value (posterior surface) of the diaphragm attachment along the paravertebral line in the left in women was the following: most frequent values were found within the interval from 40° to 50°. There were 5 values (35,7%). 2 more cases (14,3%) were within the range from 30° to 40°. Therefore, 50% of all the cases were within these ranges.

The right scapular line was studied in the sagittal plane. In women the first value of the angles of the diaphragm attachment was the following: most frequent values were found within the interval from 50° to 60°. There were 4 such cases (28,5%). Within the ranges from 30° to 40° and from 60° to 70° there were 3 cases (21,4%). Therefore, within the interval from 30° to 70° there were 71,4% of all the cases.

The second value (posterior surface) of the diaphragm attachment along the scapular line in the right in women was the following: most frequent values were found within the interval from 30° to 40°. There were 6 such cases (42,8%). Within the interval from 40° to 50° there were 4 cases (28,5%). Therefore, within the interval from 30° to 50° there were 71,4% cases.

The measurement along the posterior axillary line in the right of the diaphragm attachment angle in the sagittal plane was the last.

In women the first value of the diaphragm attachment angles was the following: most frequent values were found within the interval from 30° to 40°. There were 5 of them (35,7%). 4 more cases were found within the range from 20° to 30° (28,5%). Therefore, within the range from 20° to 40° there were 64,3% of all cases.

The second value (posterior surface) of the diaphragm attachment along the posterior axillary line in the right in women was the following: most frequent values were found within the interval from 30° to 40° and from 40° to 50°. There were 5 and 4 such cases respectively, constituting 35,7% and 28,5% accordingly. Therefore, within the interval from 30° to 50° there were 64,3% of all the cases.

**Conclusions.** 1. Individual spatial topography of the diaphragm is very variable and practically does not depend on the sex, age and body constitution type. 2. In certain cases (16%) in individuals of both sexes the height of the location of the left cupola of diaphragm is longer in the left than in

the right, which is explained by a high position of the spleen. 3. The data obtained should be considered while interpreting X-ray images and performing thoracocentesis in the left.

**Prospects of further studies.** To advance knowledge concerning the spatial topography of the human diaphragm further studies in different planes and projections should be conducted considering the sex, age and somatic type.

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## EPIDEMIOLOGICAL ANALYSIS OF DENTAL DISEASES AMONG INDIVIDUALS EXPOSED TO UNFAVOURABLE PSYCHOEMOTIONAL SURROUNDINGS

**Abstract.** *The article highlights the evaluation of the convicts' quality of life. The indexes of the epidemiology of dental diseases are given. It is proved that prolonged stay in places of deprivation of liberty has an unfavorable psycho-emotional impact on convicts. It is established that dental pathology is widespread among prisoners. A conclusion is made about the need for further investigation of the problem.*

**Keywords:** *prisoner, epidemiology, dental pathology, an unfavorable psycho-emotional environment.*

**Introduction.** According to official statistics the population of Ukraine is 42388691 people on February 1, 2017. On the territory of the state there are 148 establishments and 589 units of the criminal-executive inspection where 60771 individuals were kept on September 1, 2016. There are approximately 143 prisoners per 100 000 of Ukrainian population including 1552 individuals who are sentenced to life imprisonment, 6800 sentences to the term of more than 10 years. Medical service for those who are sentenced and taken to prison is administered by 18 departmental hospitals (8 – TB hospitals, 9 – multi-profile, 1 – psychiatric clinic) and 114 medical departments in the establishments of execution of punishments and investigatory isolation wards. Medical care for the imprisoned individuals is given according to the orders and clinical protocols of the Ministry of Public Health of Ukraine without considering specific conditions of staying.

The review of popular scientific-medical periodical publications has found that the issues concerning the health of imprisoned, giving them medical aid, and dental service in particular, are not sufficiently reported. There is no scientifically substantiated approach as to the management of patients who are in places of confinement for a long period of time concerning a negative effect of social-psychological factors on their physical well-

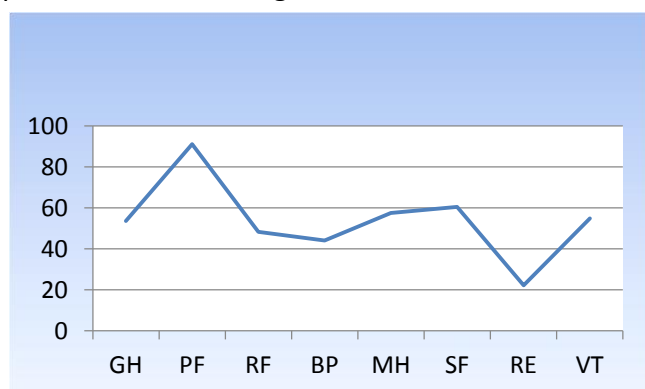
being.

**Objective:** to study the topicality of the issue to investigate dental mortality among prisoners concerning their long staying in unfavourable psycho-emotional surroundings.

**Materials and methods.** The group of the investigation included 31 male prisoners of the similar age category without comorbid somatic pathology who endure their punishment in a penal colony of Kherson region. An informed written consent was obtained from every individual who gave his permission to participate in the study and be additionally examined. To assess the quality of life of the prisoners we have used the international non-specific questionnaire sf-36v2 Health Status Survey. Epidemiology of dental diseases was assessed by four directions: diseases of teeth (CFE index), diseases of the gums (PMA index – Schour, Massler, 1948), condition of the periodontal tissue (CPITN index) and oral hygiene (Silness-Löe index, 1964).

**Results and discussion.** The questionnaire sf-36v2 Health Status Survey consists of 11 parts. According to the instruction as to the processing of the results obtained the data are interpreted in per cents by eight-point scale, each of them reflects a quantitative index of physical and psychic quality of life. General Health (GH) is an individual's assessment of his/her quality of life at the moment and prospects for treatment. Physical

Functioning (PF) is physical functioning, a degree when the level of health limits an individual in performing physical activity. Role-Physical (RP) a role physical functioning is the influence of physical condition on human functioning in everyday life. Bodily Pain (BP) – physical pain is the presence of pain and its effect on the ability to do everyday routine. Mental Health (MH) – psychic health is the assessment by an individual of his/her mood, depression, anxiety, positive or negative emotions available. Social Functioning (SF) – is a degree when physical or emotional condition limits social activity and communication. Role-Emotional (RE) – role-emotional functioning is the degree of effect of emotional condition on successful everyday activity. Vitality (VT) – a vital ability is a subjective assessment of an individual of his/her sensations to be full of life and energy or exhausted. Mean values concerning every out of eight indices are presented on the diagram:



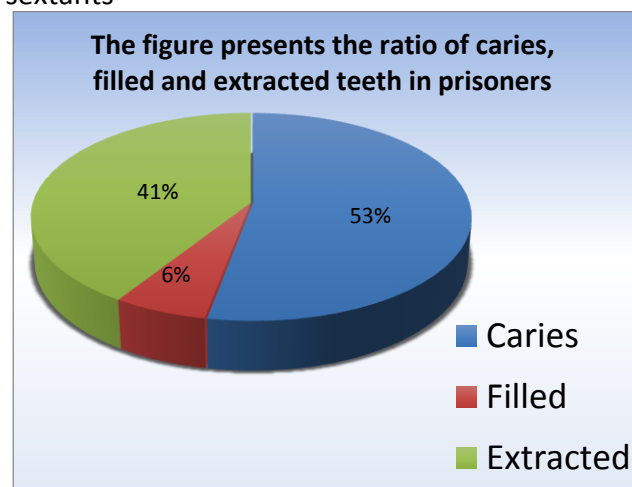
Prisoners mostly assess their lives to be within the scale from 40 to 60 per cent. Although, there are two clearly marked pick deviations: a sharp increase of PF scale (physical functioning) up to 91%, and a quick decrease of RE scale (role emotional functioning) up to 22%.

A mean value of CFE index in the examined patients was 14,81. The following ratio was found while analyzing the constituents of the parameter: teeth afflicted with caries – 7,84 (52,94 %), teeth being filled – 0,9 (6,1 %), teeth being extracted – 6,06 (40,96 %).

An average PMA index in sampling was 22,83 %, which is indicative of a considerable spread of gingivitis among the persons being imprisoned. 29,57 % of them presented inflammation of the interdental papilla, in 18,39 % inflammation involved the marginal edge of the gums, in 0,12 % it was spread onto the alveolar edge of the gums. The rest 51,93 % of the examined teeth possessed

intact gums.

While detecting CPITN index the dentition is divided into six sextants considering index teeth in every of them. Periodontal state of the index teeth was assessed in 186 sextants including 35 sextants



(18,82 %) with healthy periodontium (code 0), 87 sextants (46,77 %) with the signs of bleeding (code 1), 45 (24,19 %) with dental calculus or other factors promoting keeping of dental calculus (code 2), 7 sextants (3,76 %) had periodontal pockets up to 4-5 mm deep (code 3), 12 sextants (6,45 %) were not assessed due to inequality with requirements. In the course of examination of every sextant with the code of 4 periodontal pockets over 4-5 mm deep were not found.

Oral hygiene was assessed by means of Silness-Loe index detecting the thickness of dental plaque in the score determined while touching the edge of the teeth with a probe: 0 – no dental deposits, 1 – dental deposits are not visually detected, although they are seen on the tip of a probe, 2 – a moderate amount of dental deposits is seen with the naked eye, 3 – dental deposit covers a tooth considerably. The mean value of Silness-Loe index was 1,65.

**Conclusions.** The study was indicative of the fact that the prisoners assessed their quality of life as an average one. Although, in case of high physical functioning a pronounced negative effect of emotional condition is found on their active social position and motivation concerning everyday routine.

A wide occurrence of dental pathology is found among the prisoners, and it requires administration of an appropriate adequate therapy.

**Prospects of further studies.** The data obtained are rather perspective for further



examination and development of schemes to detect dental diseases among prisoners considering their staying under unfavourable psychoemotional surroundings.

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## PSYCHOLOGICAL ASPECTS OF PHYSICAL CULTURE AND SPORT

**Abstract. Abstract.** *This article describes the main psychological aspects of physical culture, these methods of psycho-diagnostics and psycho-prophylaxis in sport. The role of sports psychology.*

**Key words:** *sport, physical education, sports psychology, psychodiagnostics, psychological prophylaxis, hygiene.*

**Introduction.** Currently, the psychological aspects of physical education and training of athletes requires a search for ways, means and methods aimed at achieving the optimal state of the human organism, realization of its possibilities.

During the implementation of the training process it is necessary to consider that the persons engaged in sport activities often have problems of a psychological nature, since these individuals suffer not only physical but also psychological stress.

Various aspects of physical preparation and training athletes are reflected in the works of both foreign and domestic experts. So, G. D. Gorbunov noted that the concept of "psychological training" is the most common in sports psychology, but only a part of the professional support and identifies the following components: diagnostics, state management and behaviour of the individual in training and competitive conditions. And A. V. Rodionov in the process of psychological preparation includes complex of psychopedagogical and medico-biological influences, aimed at forming a high level of fitness, mental reliability and willingness to participate in responsible competitions. The works of scientists, which cover research on: - theory and methodology of physical education – L. Volkov, L. Dolzhenko, L. Matveev, V. Papusha; theory and methodology of training high-class athletes: G. Arzuov, A. Deminsky, N. Dutchak, V. Kashuba; training of specialists in physical education and sport - V. Hertsyk, O. Vatsaba, M. Isachenko, M. Pryymak, O. Tymoshenko deserve special attention [1-3].

But, the study of professional peculiarities of psychologists in sport shows, a complex and multifaceted activity of the psychologist in the field of sports, features of psychological readiness to professional activity are considered insufficient, which is reflected in the activities of

sports organizations in general.

Therefore, the relevance of the psychological aspects of training athletes has acquired a special significance.

**Objective:** the study of basic psychological aspects of sport, a review of the fitness psychological foundations.

**Materials and methods.** During the execution of the work the following research methods were used: comparative method, objective observation, introspection, and methods of psycho-diagnostics.

**Results and discussion.** The main objectives of sports psychology is the study of the athletes psychological patterns and teams, sportsmanship qualities necessary to compete and develop psychologically based methods of training and preparation for competitions (Millers), 1987) conservation, introspection and psychological diagnostics methods.

Achieving these goals involves the following specific tasks:

- psychodiagnostics;
- implementation of psycho-prophylaxis;
- solving the problems of mental health;
- implementation of psychotherapy.

Sports psychodiagnostics is the branch of sport psychology, where main task is the measurement and control of the mental athletes characteristics focused on problem solving. Practical use of psycho-diagnostics reduces the time and costs of training to enhance its effectiveness, reduces dropout of athletes to raise the level and stability of the results.

While solving psycho-diagnostics sports problems the central place belongs to the test – the specific measurement technique of individual psychological differences.

Psychological methods are divided into two large groups:

- 1- research;
- 2 – test

If the first task is to identify certain personality characteristics or interpersonal relationships, then the second goal is to provide answers to specific questions, to identify causes of specific psychological phenomena or disorders. At the same time diagnostics of the reasons is not for a psychologist in sport, an end in itself, it is always subordinated to the main task — the development of recommendations for the individual athlete mental development or correction of this development.

In sport there are three main areas of psychodiagnostic methods application: figuring out what sport is advisable to do for the beginner (child or teenager).

The formation of a sports team, competing in the competition as a whole (sports selection). Now most major League teams at the headquarters of the coaches have special scouts, who select the teams from other leagues of sportsmen, who, by their psychological, physiological and physical qualities apply for the role of the player (athlete) of the higher League.

The selection of athletes with the same high level of skills (picking teams) for inclusion in the national Olympic team.

Psychoprophylaxis is the branch of medical psychology, developing measures that prevent the emergence of mental illness.

Psychoprophylaxis in sport aimed at timely warning of deviations in the development of the athlete's personality and interpersonal relationships in sport groups, the prevention of conflicts between athletes and coaches.

Great attention should be paid to prevention of complications associated with a change of a sports team or group, and when changing coach in a sports team.

As modern sport imposes very high demands to the psyche of the athlete, he must possess certain psychological qualities: stress resistance, psychological stability, mental and physical stress, anxiety, excitement and so on.

Therefore psychologist should develop and consolidate these positive qualities of the athletes in the individual and group psychoprophylaxis.

The directions of psycho-prophylactic work in the sport:

- training athletes to psychology training;
- managing the dynamics of the athletes mental stress;
- the establishment of athletes motivational attitudes in training;
- regulation of mental athletes readiness for competitions; prevention of psychogenic and neurotic athletes reactions;

- prevention of alcoholism, smoking, drug abuse and so on.

The contents of the specific psychoprophylactic work is determined by the athletes individual characteristics and nature of the violations.

Thus, prevention is an integral element in the sport, which requires timely measures to prevent and taking into account the individual characteristics of athletes.

Analyzing the psychological literature on sport and sporting achievements, we conclude that the main directions of psychological preparation in sport include: the formation of sport motivation; education volitional qualities; ideomotor training; improving responsiveness; improve specialized skills; the regulation of mental distress; to develop a tolerance to emotional stress; manage starting conditions of the athletes.

The hygiene is the branch of medical psychology that studies the influence factors and environmental conditions, education and self-education on the mental development and mental state of a person, is developing recommendations for the preservation and promotion of mental health of society and individuals.

The main task of mental health in sport is also providing the right psychological athletes mood, adequacy and balance of their reactions to stimuli (external stimuli) of the environment in which it operates.

Psychogun measures may be intended to protect the athletes psyche from the influence of irritants, which can cause negative emotions, to do this ensures that players are not subjected to criticism from sports leadership, to long before the competition was set and communicated to the athletes the team that will help calm the athletes who have doubts in their abilities, but also eliminate the spirit of unhealthy rivalry in the team.

Account of all possible factors of negative psychological impact on athletes: a stimulating effect fans, the acclaim sports press thought about the possibility of obtaining victory team.

So, the main areas of psycho-hygienic work in sports are:

- psychological assistance in formation of harmonious personality of the athlete;
- study of the effect on the athlete psyche in the conditions of sport environment with the aim of improving sporting achievements;
- warning overloading the athletes nervous system, mental disorders and neurotic reactions;
- development and implementation of sports practice measures aimed at ensuring the mental

health of athletes;

- elimination of the athletes neurotic reactions;
- implementation of measures of psycho-hygienic training conditions and competitive cycle;

•teaching athletes the autogenic training skills for the solution of psycho-hygienic problems in sport.

Psychotherapy is the use of psychological interventions for the patient's treatment, to improve feelings of psychological well-being.

In the work of sports psychologist similar method of psychological help is called personality-oriented (reconstructive) psychotherapy.

It is aimed at:

1) the study of the patient's personality, his emotional reactions, attitudes, identifying the reasons for the occurrence and persistence of neurotic condition;

2) aid to the patient in the awareness of the psychological disease causes in the change of attitude towards stressful situations;

3) correction of inadequate reactions and behaviours.

In the process of psychotherapeutic conversation with the patient he is asked direct or indirect questions, about his behavior in different situations of life, peculiarities of relations system.

**Conclusion.** Thus, the analysis of scientific and methodological literature and best practice sports showed that the psychological aspects of physical culture provide for the implementation of such areas as diagnostics, sports selection, diagnosis as well as athletic abilities; prevention; hygiene; psychological education of athletes and coaches; psychological correction of negative conditions, reactions, and maladaptive behaviors of athletes; ensuring the sport psychological process; psychological assistance in the team's chemistry; psychological counseling of athletes and coaches and methodological work in the sport.

The methods of psycho-diagnostics in the system of physical culture and sport and the contents of psychoprophylaxis and mental health in sport were showed. We can summarize that the goal is the formation of psychological stability of athletes to defeat willingness to participate in the competition and the optimal effective functioning in sport.

The success of psychological support and psychological support of work on the athletes preparation is directly associated with the

diagnostic work in the field of sports.

**Prospects for further research.** Sports psychology is among very young applied branches of psychological science. The concept of "sports psychology" first appeared in articles of Pierre de Coubertin, the founder of the modern Olympic games. They were published in the beginning of the XX century and had descriptive character. In 1913, at a special Congress of sport psychology organized on his initiative the International Olympic Committee in Lausanne and received their "baptism."

In the history of Russian psychology by the time of the psychology birth of physical education and sport can be considered as the publication date of the first scientific papers. The first researches were in 1925-1926 performed by Professor P. A. Rudik at the Department of psychology ("the Influence of muscular work on the process of reaction", "reaction in the application the main issues of physical culture") and T. G. Nikitin ("the Value of suggestion and imitation in the case of physical education").

Socio-cultural and economic changes that occur in the state, can not touch the sports system, which in modern conditions is also in need of transformation and must change to meet the new social requirements. These transformations relate, in particular, professional activity of the psychologists in the field of sport, and provide qualitative changes in the system of sport psychologists training, the psychological readiness formation to professional activities with regard to its features [4].

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## ANALYSIS OF FOLIC ACID LEVEL IN THE BLOOD OF WOMEN WITH FETAL LOSS SYNDROME

**Abstract.** *The article presents the level of folic acid in plasma of pregnant women with fetal loss syndrome. An inverse correlation between the level of folic acid in the blood and the number of miscarriages and abortions in the anamnesis of patients has been found. The correction of folic acid deficiency at the dose of 400 mcg per day with the subsequent determination of the control level has been suggested. Against the ground of treatment the level of folic acid was normalized, the value was statistically significant.*

**Ключові слова:** *фолієва кислота, синдром втрати плода, перинатальні втрати.*

**Introduction.** Folic acid – N-{4'-[(2-amino-4-oxy-6-pteridyle)-methyl]-aminobenzoil}-L-(+)-glutamic acid – obtained from spinach leaves in 1941 and synthesized under the supervision of Yellapragada Subbarow, an Indian-American biochemist, in 1945. It is not accumulated in the body, and supplied with the intake of fresh vegetables, liver, mushrooms, egg yolks, legumes, brans and cereals. In addition to exogenous way of intake there is also endogenous bacterial synthesis of folates in the large intestine. Absorption of this substance is accomplished in the upper part of the small intestine. With thermal treatment of food approximately 90% of folic acid is lost (up to 50 % with boiling eggs, up to 95 % after meat is fried). Regular consumption of alcoholic drinks results in reduced amount of folic acid in the body.

Folacin takes an active part in oxidation-reduction processes, supports the immune system, prevents fatty infiltration of the liver, possesses anti-anemic action, promotes normal maturation and functioning of the placenta, has estrogen-like effect, reduces the signs of postpartum depression. Folic co-enzymes promote biosynthesis of purine and pyrimidine bases, nucleic acids, amino acids, increase the body intake of glutamic acid and tyrosine, influence upon rapidly growing tissues. In case folic cycle is disturbed, the risk of development of the following pathological processes increases:

- complications of pregnancy (placental dysfunction, gestosis, exfoliation of the normally

located placenta) due to microscopic clots formation with disorders of microcirculation and formation of spiral arteries pathology;

- developmental defects of the fetus;
- prenatal death of the fetus;
- cardio-vascular disorders;
- osteoporosis;
- lens ectopia;
- cancerogenesis;
- intensification of side-effects after chemotherapy.

**Objective:** to examine the level of folic acid in plasma of women with fetal wastage syndrome.

**Materials and methods.** To perform our investigation the group of 20 pregnant women was formed aged from 19 to 35 with fetal wastage syndrome without comorbid extragenital pathology and bad habits. The patients were informed about necessity to undergo additional examinations, and their informed written consent was obtained. The criterion to be included into the study was absence of biochemical and USD-markers of fetal pathology with reproductive loss available in anamnesis. The study was performed in the licensed certified laboratory in Kherson region. The data obtained were statistically processed in the program package Statistica. Critical index of Student t-criterion was detected with significance level  $p=0,05$ . Reference values of folic acid content were from 3,1 to 20,5 ng/ml. The pregnant women gave their blood for analysis on empty stomach since 12 to 20 weeks and 30 weeks of gestation.

### Results and discussion

The retrospective analysis has found that outcome of pregnancy of 8 patients (40%) was miscarriage in the term of 10-12 weeks, 2 patients (10%) – still birth in the term of 24 weeks, in 1 patient (5%) experienced early neonatal death (during 4 hours after birth), 9 women (45%) experienced miscarriage of more than three pregnancies in the term of 6-8 weeks, in 5 examined women three pregnancies were interrupted by medical abortions. In all the women the content of folic acid was not higher than that of the lower normal level. It was within the range of 1,7-2,3 ng/mg in 5 patients, from 2,4 to 3,0 ng/ml in 7 patients, and in the rest 8 women – 3,0-3,1 ng/ml. The analysis of the information obtained has found a reverse correlation between the level of folic acid in the blood of women and clinical signs of fetal loss syndrome. In order to correct folate insufficiency folic acid in the dose of 400 mcg per day was indicated to the patients for the period of 1 month with the control of indices after the treatment. Folic acid content in the blood plasma of patients normalized against the ground of the therapy initiated. The value ranged from 5,5 to 10,5 ng/ml ( $p < 0,05$ ), which is statistically reliable.

**Conclusion.** The investigation performed has found that in women with fetal loss syndrome folic acid level is considerably lower of that the normal one in spite of comorbid somatic pathology unavailable. Additional intake of folic acid in the dose of 400 mcg per day during a

month enables to normalize the values of folate content in the blood of patients.

**Prospects of further studies.** The data obtained are rather perspective to elaborate the plan of pre-conceptual preparing and management of both pregnant women with fetal loss syndrome and those pregnant for the first time.

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## **DIAGNOSTICS OF THE FRONTAL SINUS DEVELOPMENT WITH ADJACENT STRUCTURES IN THE PRENATAL PERIOD OF HUMAN ONTOGENESIS**

**Abstract.** *The article deals with the development of the frontal sinuses and adjacent structures in the prenatal period and childhood of human ontogenesis. By means of a comprehensive morphometry vertical, transverse, anterior-posterior sizes of the frontal sinuses and adjacent structures are detected; in the prenatal period the shape of the frontal sinuses is mostly slit-like (56%) and oval (44%), in childhood – pear-shaped (33%), oval (30%) and triangle (27%), that will promote better efficacy of diagnostics of congenital developmental defects.*

**Key words:** *frontal sinuses, fetus, childhood, ontogenesis, anatomy.*

**Introduction.** Diagnostics and treatment of the frontal sinuses are known to be one of the most complicated tasks as compared to diseases of other paranasal sinuses. It is stipulated by insufficient awareness of specialists with modern anatomical-physiological and instrumental methods of their examination and treatment [1]. Advanced methods of endoscopic intranasal surgery require a comprehensive spatial image concerning 3-D structure of the nasal cavity and paranasal sinuses [2, 3]. Numerous studies deal with anatomy of the frontal sinuses. However, the problem of topographic anatomy of the frontal-nasal junction and its surrounding structures remains one of the confusing and disputable issues concerning the structure of the paranasal sinuses [4]. A distinctive feature of the frontal sinuses is their absence at the moment of birth. They develop during the following eight years, and are completely formed only after puberty period. Considering the fact that the frontal sinuses are hollow structures covered with the mucous membrane, they can be afflicted with viral or bacterial infections. Harmful microbes penetrate together with the inhaled air [5]. In case of a low body resistance an inflammatory process may occur, therefore, it is important to follow the process of the frontal sinus development in the prenatal period and childhood.

**Objective:** to investigate development of the frontal sinuses with the adjacent structures in the

prenatal period and childhood of human ontogenesis.

**Materials and methods.** Dead fetuses, newborns and specimens of heads or separate complex of organs of different age human groups were fixed in formalin solution, and after external examination washed properly during 1-2 days under running water. Afterwards sagittal sections of the head and the complex of organs were performed so that the cut was passing close to the wall of the nasal septum. The place of the paranasal sinus opening was described on the anatomical specimens obtained. After that the frontal sinuses were opened, and their anterior-posterior, transverse and vertical sizes were measured, peculiarities of their walls were described.

For further microscopic examination of the frontal sinuses the specimens were fixed in 5-7 % formalin solution during 2-3 weeks. Afterwards the specimens were washed under the running water for 1-2 days depending on their sizes. Then the specimens were decalcified by means of their putting into 7% nitric acid solution for 1-3 days. To prevent swelling of the connective tissue the specimens were put into 5% sodium sulfate solution for 24 hours. The specimens were dehydrated by means of their processing through the battery of alcohols with an increasing concentration (from 30° up to absolute ethyl alcohol). The specimens were saturated with

paraffin. Chloroform was used as an intermediate medium between the absolute ethyl alcohol and paraffin. The series of histological sections 10-15 mcm thick were prepared from the paraffin blocks. Before processing in the battery of ethyl alcohol certain specimens were totally stained with boric carmine, and after histological sections were made they were additionally stained with hematoxylin-eosin, Lion blue or by Van Gieson method on the microscope slide which enables to obtain more differentiated staining of different tissues. After fixation in Canada balsam they were examined under the light microscope. The structures were measured with an ocular-micrometer and micrometric ruler.

**Results and discussion.** The rudiments of sinuses border on the cartilaginous capsule of the nasal cavity lateral walls. The shape of sinuses becomes close to oval. Their anterior-posterior size is  $(0,3 \pm 0,02)$  mm, transverse size –  $(0,05 \pm 0,02)$  mm and vertical –  $(0,06 \pm 0,02)$  mm. At the end of the 5<sup>th</sup> month of development the anterior-posterior size of the sinuses increases to 1,1-1,3 mm, transverse – to 0,15-0,18 mm, vertical – 0,13-0,22 mm. Their shape is oval. The ossification islets of a semi-oval shape are seen near superior lateral borders of a pear-shaped opening on X-ray images. Therefore, the rudiment of the frontal sinuses is found on the 5<sup>th</sup> month of development. It is presented by a small oval-shaped cavity. Although radiographic clear anatomical signs of the sinus borders are absent.

The rudiments of the frontal sinuses occur at the 5<sup>th</sup> month of the intrauterine development (fetuses 188,0-228,0 mm of PCL (parietal-coccygeal length) by means of the mucous membrane evagination of the middle nasal passage into the adjacent tissue. The rudiments of the frontal sinuses of 5<sup>th</sup>-month fetuses on the frontal sections are of an elongated oval shape. The inferior wall of the sinus is 1,0 mm higher from that of the supraorbital border. At this stage the gland of the mucous membrane of the sinuses begin to form by means of epithelium ingrowth into the adjacent mesenchyme. The mucous membrane becomes  $0,2 \pm 0,01$  mm thick. The anterior X-ray projection presents additional ossification islets in the area of the lower portions of the medial wall of the eye sockets. They are located laterally and higher from the borders of the pear-shaped opening. On the border between the superior-lateral portion of the pear-shaped

opening and medial wall of the eye socket there is a lucid interval found that should be considered the place of origin for the frontal sinus formation.

In 5-month fetuses the anterior-posterior size of the right frontal sinus is 2,0-2,2 mm, transverse – 0,18-0,21 mm, vertical – 0,25-0,3 mm; and the left one: 1,8-2,0; 0,16-0,19; 0,23-0,25 mm respectively.

In 7-8-month fetuses the anterior-posterior size of the right frontal sinus is 5,4-5,9 mm, transverse – 0,8-1,0 mm, vertical – 2,0-2,5 mm, and the left one: 5,2-5,7; 0,7-0,9; 1,9-2,4 mm respectively. On the frontal sections the frontal sinuses are of the following shapes: in the right in 52 % cases an oval shape is found, in 32 % – spherical and in 16 % – spherical-oval. In the left a spherical shape of the sinus was found in 56 % cases, oval – in 34 %, spherical-oval – in 10 %. Radiological images in 7-8-month fetuses detect the areas of the frontal sinus localization in the anterior projection more distinctly than in fetuses of the previous age group.

On the basis of examination of 9-10-month fetuses from 311,0 to 375,0 mm of PCL it was found that the frontal sinuses are located higher from that of the supraorbital border. The sinuses are located at the distance of 2,0 mm from the upper and middle nasal passages. The anterior-posterior size of the right frontal sinus is 6,5-7,0 mm, transverse – 1,4-1,6 mm, vertical – 2,8-3,0 mm, and the left sinus: 6,4-6,9; 1,3-1,5; 2,6-2,8 mm respectively. On the frontal sections the sinus is of the following shapes: in the right in 54 % cases it is oval, in 35 % – spherical and in 11 % – spherical-oval. In the left a spherical shape of the frontal sinus is found in 57 % cases, oval – in 36 %, spherical-oval – in 7 %. Radiograms of heads of 9-10-month fetuses in the frontal projection present enlargement of ossification islets of the sinus walls as compared to 7-8-month fetuses. The sinus is connected with the nasal cavity in the place of the semilunar opening between the hamulus and ethmoidal bulla.

Variability of shapes of the frontal sinuses in newborns is found. The right sinus: oval (52 %), spherical (32 %), spherical-oval (16 %); the left sinus: oval (34 %), spherical (56 %), spherical-oval (10 %). It is of a slit-like shape on X-ray images.

In the period of early childhood (1-3 years) the frontal sinuses on all the specimens are detected higher from that of the supraorbital border. Its vertical size is 7,5-8,0 mm, transverse – 5,7-6,0



mm, anterior-posterior – 13,9-14,5 mm. The walls of sinuses are covered with the mucous membrane.

Frontal sinuses are characterized by age variability of radiological forms: in the prenatal period the shape of sinuses is more frequently slit-like (56%) and oval (44%), in childhood – pear-shaped (33%), oval (30%) and triangle (27%). Development of the frontal sinuses in childhood is accompanied by enlargement of the cavity volume. Formation and topographic-anatomical correlation of the nasal walls together with the adjacent structures during infancy (10 days – one year) demonstrated that the hamulus length was ( $8,0 \pm 0,13$ ) mm, width – ( $2,0 \pm 0,1$ ) mm. They are located obliquely in the anterior-posterior direction. Evagination of the frontal bundle on the examined specimens increased and was ( $2,6 \pm 0,05$ ) mm.

An intensive development of the frontal sinuses occurs in the period of the second childhood (8-12 years) and teen age (13-16 years).

**Conclusion.** The vertical, transverse, anterior-posterior sizes of the frontal sinuses and adjacent structures are detected by means of a comprehensive morphometry; in the prenatal period the shape of the frontal sinuses is more often slit-like (56%) and oval (44%), in childhood – pear-shaped (33%), oval (30%) and triangle (27%), promoting better efficacy of diagnostics of congenital developmental defects.

**Prospects of further studies.** Further investigation of blood supply and innervation of the mucous membrane of the frontal sinuses in other age periods is being planned.

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## BLOOD SUPPLY OF THE CERVICAL REGION OF THE VERTEBRAL COLUMN DURING THE FETAL PERIOD AND IN NEWBORNS

**Abstract.** *The peculiarities of the blood supply of the cervical region of the vertebral column of 35 human fetuses, 30 newborns have been studied by means of morphological methods of investigation. The development of the blood vessels of the cervical region of vertebral column in health and also individual divergences during different age periods, the peculiarities of the blood supply of the parts of the vertebra as well as intervascular anastomoses along the vertebral column have been studied.*

**Key words:** *vertebral column, blood supply, ontogeneis, human.*

**Introduction.** The treatment of patients with compression syndromes is an urgent task of modern medicine. According to the WHO, 2/3 of the population suffers from radicular and joint pain of varying degrees of severity, leading to temporary and partial disability. Back pain is one of the main causes of economic losses in manufacturing [2, 3, 5, 6, 8, 9]. The results of the study conducted in the USA showed an increase in the total cost of diagnosis, treatment, and disability compensation to workers due to this pathology has increased from 15.6 billion dollars in 1997 to 28 billion dollars in 2000, that can makes this disease one of the most cost-effective [7, 10].

The normal development of the bone as an organ is in full compliance with the blood supply and the load. Variations in blood supply, load change will inevitably affect the structure and shape of the organ. [3] These relationships are defined by the following rules: the increase of the support load without an adequate increase of blood supply does not increase the bone mass; the increase of the support load accompanied by the increase of blood supply increases the bone mass; the decrease of the support load with sufficient blood supply promotes the bone resorption; preservation of the original support with reduced blood supply reduces osteogenesis; an equable reduce of the load and blood supply reduces the osteogenesis.

The dependence of bone structure and shape on an adequate blood supply and load made it possible to change the shape of the organ.

It is known that skeletal development is closely related to the circulatory system. The bone is not only a solid supporting substance but also a determined combination of special cellular elements of the blood-forming and blood-circulating system. The topicality of the task is determined by the need to find solutions to complex Orthopedic problem - a bloodless treatment of patients with spinal curvatures.

We believe that changing of the spinal shape can occur for various reasons, but surely one of the possible factors is the inadequacy between blood supply and the load. It also leads to changes in the shape of the spine, which results in scoliosis.

To investigate the problems of changing the shape of the spine, we examined its blood supply within norm.

Although the blood vessels of the spine were studied by many authors (KA Yudin, 1950; GA Ilizarov, 1981 et al.), but in the prenatal and neonatal ontogenesis such studies have not been fully conducted that makes the study urgent [1].

**Objective:** to examine the development and formation, as well as individual differences in the structure of blood vessels in normal spine and explore the symmetry and asymmetry of extra- and intraosseous vascular bed, the anatomical features of blood supply of the parts of the vertebra, and intervascular Materials and methods. The study was conducted on 35 human fetuses and 30 newborns. The research of vertebral arteries consisted of several stages: 1. The study of injected extraorganic arteries by anatomical dissection and radiography. 2. The study of

intraorganic arteries by making macroscopic samples, followed by X-ray in frontal, sagittal and horizontal planes. 3. The study of the spatial distribution of arteries in the vertebrae by enlightenment. A minium was chosen as a contrast substance which aids in getting a clear X-ray image. However, unlike other authors, we used a water suspension of minium, by the method of B.V.Ognev.

**Results and their discussion.** As the study of cervical arteries revealed the sources of blood supply of the cervical vertebrae in newborns include vertebral artery, ascending and deep cervical arteries, thyro-cervical trunk, inferior thyroid, superior intercostal, subclavian, external carotid and intercostal arteries, that arise from the thoracic aorta. In fetuses an ascending pharyngeal artery and transverse colli artery should be added to this list, excluding the external carotid artery. The number of sources of blood supply of cervical part of vertebral column in fetuses ranges from 3 to 6, usually 4, and in newborns - from 4 to 8, usually 4 (68% of cases). The differences in the number of sources of arterial blood supply according to sex were not found. Vertebral, ascending and deep cervical, intercostal and ascending pharyngeal arteries form branches to supply cervical vertebrae equally on the right and left, others (thyro-cervical trunk, inferior thyroid and subclavian arteries) supply the cervical vertebrae unequally from both sides. Transverse cervical artery and external carotid artery give branches only to one corresponding side.

Vertebral artery (8 newborns' specimens) originates from the right and left side of the subclavian artery. In two specimens it starts left rising from the ascending part of the aortic arch and right subclavian artery. The caliber of right and left vertebral arteries in 20 specimens was identical, in 7 - different. The trunk of vertebral artery was relatively straight in 21 out of 30 cases, in 9 it was tortuous: on both sides in 5 cases and 4 on one side. Different levels and penetration of the vertebral artery in the openings of the transverse processes of the vertebrae; in 28 preparations the artery entered the transverse opening of VI vertebra, and in two cases some peculiarities were found: in one specimen it entered the transverse opening of V vertebra on rightside and leftside of VI one, in other case it entered the transverse opening of IV vertebra rightside and leftside of IIIrd.

The study of 35 cervical vertebrae of fetuses

shows that vertebral artery arises from the subclavian. The right and left arteries in all cases were of the same caliber. In 10 cases a winding vertebral artery was seen, and in 25 - straight. In 30 cases the artery entered the opening of the transverse process of the VI vertebra, in 5 cases - VII.

The ascending cervical artery always arises from the thyro-cervical trunk. Its branches came towards vertebrae in 100%. The caliber of the right and left arteries was identical in 28 newborn's specimens and in 2 it was different. The diameter of arteries in fetuses was the same. In 3 out of 30 specimens of vertebrae in infants and in 4 fetuses the ascending cervical artery was tortuous.

In newborns the beginning of ascending cervical artery was observed at the level of VI and VII vertebrae (25 and 5 specimens respectively), and in fetuses on the same level (28 and 7 specimens). Branches of the 1st and 2nd orders enter the intervertebral foramina of III-IV, IV-V and V-VI vertebrae and openings between II-III and V-VI vertebrae in newborns. In fetuses they often arise between the openings of III-IV and Vth vertebrae, seldom - between II-III and V-VI vertebrae; in newborns they supply Vth vertebrae with blood and sometimes - IV, VI vertebrae. The blood supply of II, III and VII vertebrae is rare. In fetuses above named arteries often direct towards III-IV vertebrae and in some cases towards I-IInd.

Deep cervical artery arose from costo-cervical trunk. Its branches came to the cervical vertebrae in 100%. The beginning of artery was not always at the same vertebrae level. Thus, in 64% of cases it arose from costo-cervical trunk on the level of VII vertebra, and in 10% on the level of thoracic vertebra. In 26% of cases it begins on the level of VII cervical on the right, and I thoracic vertebra on the left. Deep cervical artery gives off branches on the level of different cervical vertebrae, in one specimen it reached atlas, in 9% - II vertebra in 41% - III in 37% - IV and in 10% - VII vertebra. In two cadavers of fetuses the right deep cervical artery reached the level of VI vertebra, and the left one - II vertebra. The branches of 1st and 2nd order from this artery enter the intervertebral openings: between V and VI vertebrae (in 14 cases), between VI and VII (61) and VII and cervical and thoracic vertebrae (6 cases). The most common was the approach to the outer surface of the vertebral arches and spinous processes of III-VII and rarely - I-II vertebrae.

The thyro-cervical trunk blood supplied the vertebrae in 34 cases (9 newborns and 25 fetuses specimens). At the level of VII vertebra a branch arose from it and reaches V or VI vertebrae, then goes down to I-II thoracic vertebrae. It gives rise to branches of the 2-3rd order. In 17 specimens they were facing each other, in 14 cases towards two and in 3 towards three vertebrae. Its branches reach the outer surface of the antero-external surface of V-VII cervical vertebrae.

The inferior thyroid artery supplies II to IV lower cervical vertebrae in 35 specimens, including 5 newborn's and 30 fetuses' cadavers. Its branches directed the vertebrae from on right side in 15 cases, on the left side in 8 and on both sides in 12 specimens. The artery gives branches to the front surface of bodies of III-VII vertebrae.

The superior intercostal artery supplies VII vertebra in 16 specimens (5 newborns and 11 fetuses). Its branches (2 to 6) approach the VII cervical vertebra on both sides.

The subclavian artery supplies the cervical vertebrae in 9 cases (3 newborns and 6 fetuses' specimens).

Its branches come to the body of VII cervical vertebra from one side (right) in 6 cases from two sides in 6 cases.

The branches of the first intercostal artery are involved in blood supply of VII cervical vertebra (2 cases).

The transverse cervical artery gives branches to V-VII vertebrae (4 fetus' specimens). From the right transverse cervical artery one or two branches penetrate the intervertebral foramen of VI-VII vertebrae.

The ascending pharyngeal artery supplies vertebrae of fetuses (5 specimens). From both arteries the branches go to the front surface of atlas and to odontoid process of axis.

The external carotid artery gives branches to two vertebrae: the posterior arch of the atlas and to transverse processes of V vertebra.

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The external carotid artery gives branches to two vertebrae: the posterior arch of the atlas and to transverse processes of V vertebra.

Thus the above described arteries are differently involved in the blood supply of the cervical spine. Obviously the various sources of blood supply of the cervical spine are possible in newborns and fetuses.

In newborns the vertebral, ascending and deep cervical arteries are permanent, others (thyro-cervical trunk, inferior thyroid artery, superior intercostal arteries) supply vertebrae mainly in fetuses, and only a few of them were seen in newborns. The subclavian and the first intercostal arteries and external carotid arteries supply cervical vertebrae in newborns only in rare cases. The ascending pharyngeal artery and transverse cervical artery were seen mainly in fetuses.

**Conclusions.** 1. Such sources of blood supply as thyro-cervical trunk, inferior thyroid, superior intercostal and first intercostal arteries tend to change with the body growth which leads to sharp limitation of their participation in the blood supply of cervical vertebrae. These arteries can be attributed to non-permanent additional sources of blood supply.

2. The number of permanent and non-permanent sources of the blood supply of vertebrae is different: for cervical vertebrae 3 to 6 in infants, and from 4 to 8 in fetuses.

3. The constant sources of blood supply (vertebral, ascending and deep cervical arteries) supply 1 to 7 cervical vertebrae, additionally - thyro-cervical trunk, inferior thyroid artery and superior intercostal, subclavian, first intercostal, ascending pharyngeal and transverse cervical

arteries supply with blood 1 to 4 cervical vertebrae.

4. There are more branches of 1st-2nd order, which rise towards the cervical vertebrae from permanent sources than those from additional; the latter, in turn, are more numerous in fetuses than in infants.

**Prospects for further research.** In future research the development and formation of blood supply of the thoracic spine during the prenatal and early neonatal periods of human ontogenesis and its features are planned to be studied.

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## THE INDICATORS OF STIMULATION ELECTRONEUROMYOGRAPHY IN PATIENTS WITH DIABETIC POLYNEUROPATHY

**Abstract** *The work is dedicated to researching of the effect of cocarnit on the functional state of the peripheral nerves based on the findings of stimulation electroneuromyography in multimodality treatment of diabetic polyneuropathy. The most positive influence on the amplitude of M-response of the nerves of the upper and lower extremities has been detected in case of use of cocarnit in comparison with the basic treatment.*

**Key words:** *peripheral nerves, diabetic polyneuropathy, cocarnit.*

**Introduction.** The clinical manifestations of diabetic neuropathy (DPN) are very diverse and occur in practice of specialists in various profiles. It is known that diabetic polyneuropathy increases the danger of amputation by 1.7 times, the danger of feet deformation by 12 times, and the danger of feet ulcers by 39 times. A significant prevalence of this pathology determines the importance of practical and theoretical perspectives. The most informative method of diagnosing lesions of the peripheral nervous system in patients with DPN is electroneuromyography. It is registration of oscillations of electric potentials in skeletal muscles that allows to examine the state of peripheral lesions of neuromotor apparatus effectively. Thus, when using this method, lesions detection frequency of functions of peripheral nerves increases up to 70-90%.

**Objective:** prove the expediency of application of cocarnit (CDF) in treatment of patients with DPN, depending on the duration of diabetes by studying the functional state of peripheral nerves according to finding of stimulation electroneuromyography. Examine the indicators of stimulation electroneuromyography in patients with DPN, depending on the duration of diabetes mellitus before and after treatment.

**Materials and methods.** We explored 86 patients with type II diabetes mellitus who were hospitalized in Chernivtsi Regional Clinical Endocrinological Dispensary. Among the patients there were 36 women and 50 men; the age of the patients ranged from 36 to 65 years. Diabetes

mellitus (DM) of moderate severity was observed in 82 patients, 4 patients were in a critical state; 12 patients were in position to compensate for the disease, 74 patients had subcompensation. Patients were divided into 3 groups: Gr.1 - patients who had diabetes up to 1 year (29 patients);

Gr.2- patients with diabetes up to 10 years (30 patients); Gr.3 - patients with diabetes for over 10 years (27 patients). Additionally patients were divided into two subgroups. Subgroup I - patients who have received basic therapy that included Diet number 9, maninil to 5 mg twice daily or insulin (2/3 of daily dose in the morning and 1/3 of dose in the evening, the rate of 0.7 - 1.0 U / kg body weight), pentoxifylline intravenously 5 ml per 250 ml isotonic sodium chloride, vitamin B (42 patients). Subgroup II - patients that along with basic treatment received CDF (1 ampoule intramuscularly 1 time per day for two weeks) (44 patients). The control group consisted of 20 healthy individuals. The study of the functional state of peripheral nerves was performed by stimulation electroneuromyography (ENMG) on the apparatus Neuro-refraction-4 (Neurosoft, Russia).

**Results and their discussion.** Determine the amplitude of M-response of peripheral nerves of upper extremities through stimulation ENMG.

While assessing the dynamics of the M-response amplitude n. medianus it was found out that group 1 patients with diabetes duration up to 1 year M-response amplitude n. medianus tended

to decrease by 24.3% compared with the control. Amplitude decreases with increasing of disease duration. Thus, in the second group of patients, M- response amplitude decreased by 28.1%, and the patients who had diabetes for over 10 years showed decrease of M- response amplitude n. medianus by 32% compared to the control ( $p < 0.05$ ), indicating the axonal lesions of peripheral nerves. Patients of group 1 manifested increase of M- response amplitude after basic treatment by 7%; after additional prescription of CDF along with the basic therapy M-response amplitude n. medianus significantly increased by 20.5%. In the second group, M-response amplitude n. medianus almost did not change after basic treatment (by 0.82%); after additional prescription of CDF there was a tendency to increase by 17.1% ( $p > 0.05$ ). In the third group of patients, a slight increase in the amplitude of M-response by 3.4% ( $p > 0.05$ ) was noted after basic treatment; after the additional appointments of CDF M-response amplitude increased by 20.2% ( $p > 0.05$ ).

We investigated the indicators of M-response amplitude n. ulnaris (m. abductor digiti minimi) before and after the conducted treatment in diabetic patients with DPN. In group 1 patients with diabetes up to 1 year, decrease in M-response amplitude n. ulnaris by 18.1% was noted compared to the control ( $p > 0.05$ ). Amplitude decreases with increasing of disease duration. Thus, in the second group of patients M-response amplitude decreased by 26.3% ( $p > 0.05$ ), and patients with diabetes over 10 years showed likely decrease in the M-response amplitude n. medianus by 29.2% compared with the control. Thus, even in patients with diabetes up to 1 year decrease in the amplitude of M-response was noted, indicating a predominantly axonal lesion of peripheral nerves. M-response amplitude decreases depending on the duration of diabetes.

When conducting ENMG research in the dynamics it was found out that group 1 patients had an increase in the amplitude of M-response after basic treatment by 1.57% (i.e. amplitude almost did not change); after the additional prescription of CDF it increased by 13.4% ( $p > 0.05$ ). In patients with diabetes up to 10 years a slight increase by 6.8% in the amplitude of M-response after basic treatment was noted; after the additional prescription of CDF it rose 23.5% ( $p < 0.05$ ). In the third group of patients after basic treatment there was a tendency to increase the

amplitude of M- response by 6.1%; after additional appointments of CDF it increased by 17.0% ( $p > 0.05$ ). Thus, patients of all three groups manifested decrease in the amplitude of M- response, which depended on the duration of diabetes. After basic treatment, M-response amplitude n. ulnaris almost did not change in group 1 and tended to increase in the second and third groups of patients ( $p > 0.05$ ). Patients of the first and the second groups who along with the basic treatment received CDF had significant increase of the amplitude of M- response n. ulnaris compared with patients before treatment. In the third group of patients who received CDF, a tendency to increase the amplitude of the M- response was observed ( $p > 0.05$ ).

We determined indicators of M-response amplitude n. tibialis (m. abductor hallucis). In group 1 patients with diabetes up to 1 year decrease in M-response amplitude n. tibialis by 21.5% was noted compared to the control ( $p < 0.05$ ). Amplitude decreases with increasing of disease duration. Thus, in the second group of patients the amplitude of M -response decreased by 38.6% ( $p < 0.05$ ) and in patients with diabetes over 10 years a likely decrease in the amplitude M-response n. tibialis by 54.0% was noted compared with the control.

Thus, even the patients with duration of diabetes up to 1 year had decrease in the amplitude of M-response n. tibialis, which indicates axonal lesions of peripheral nerves. M-response amplitude decreases depending on the duration of diabetes.

Patients of group 1 had an increase in the amplitude of M- response n. tibialis after basic treatment by 2.6% ( $p > 0.05$ ); after the additional prescription of CDF it increased by 20.7% ( $p < 0.05$ ). In the second group a slight increase by 9.6% ( $p > 0.05$ ) in the amplitude of M -response was noted after basic treatment; after additional appointments of CDF it was by 34.0% ( $p < 0.05$ ). Patients with diabetes over 10 years only manifested a tendency to increase the amplitude of M- response after basic treatment by 6.8%; after additional appointments of CDF it increased by 36.1% ( $p > 0.05$ ). Thus, after basic treatment in all three groups, a significant increase of the amplitude of M-response n. tibialis was observed. Patients of the first and the second groups, who along with the basic treatment received CDF, had an increase of the amplitude of M-response n.

tibialis.

We estimated the dynamics of amplitude of M-response n. peroneus (m. extensor digitorum brevis). The results of the study show that patients from group 1 with diabetes up to 1 year had a decrease in the amplitude of M-response by 33.5% ( $p > 0.05$ ) compared with the control. Amplitude decreases with increasing of disease duration. Thus, in the second group of patients, the amplitude of M-response significantly decreased by 42.9%, and in patients with diabetes duration of more than 10 years a decrease in the amplitude M-response n. peroneus by 46.0% was noted compared to control ( $p < 0.05$ ). In group 1 patients after basic treatment had a slight increase in the amplitude of M-response n. peroneus by 3.1% ( $p > 0.05$ ); after the additional prescription of CDF – by 28.1% ( $p < 0.05$ ). In the second group a slight increase by 7.98% ( $p > 0.05$ ) in the amplitude of M-response after basic treatment was noted; after the additional prescription of CDF – by 30.7% ( $p < 0.05$ ). Patients with diabetes duration of more than 10 years manifested a marginal increase of the amplitude of M-response after basic treatment by 3.4% ( $p > 0.05$ ); after the addition of CDF- by 20.2% ( $p > 0.05$ ). Thus, patients of the first and the second groups, who in addition to background of the basic treatment received CDF, had a considerable increase in the amplitude of M-response n. peroneus.

**Conclusions.** 1. Reduction of the amplitude of the M-response of nerves of upper and lower extremities is observed in the majority of patients of I, II groups and all patients of III group.

2. Under the influence of basic treatment M-response amplitude increases insignificantly. After the addition of Cocarnit a considerable

increase in the amplitude of M-response in patients I and II groups was noted.

Thus, as a result of instrumental studies it has been found out that even patients with diabetes at an early stage manifest significant changes of neuromotor peripheral apparatus. They are shown by a decrease in the amplitude of M-response. The severity and nature of these changes characterize the severity of the pathological process. This demonstrates a high diagnostic value of ENMG and the need to include it in a complex examination of patients with DPN. Severity detected is largely determined by the initial state of the neuromotor system depending on the duration and severity of diabetes. All this suggests the need for medical activities at an earlier stage of disease, before the development of severe structural changes in the peripheral nerves.

Further research in this area will significantly improve the treatment of patients with diabetes complicated by polyneuropathy, taking into account the duration of the underlying disease.

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