

The founder
The Yakut Science Centre
of Complex Medical Problems
The Siberian Branch
The Russian Academy of Medical Sciences

The editor-in-chief
Tomskiy M. I.

Editorial board:
Assistant to the editor-in-chief:
Petrova P.G.

The scientific editor
Platonov F.A.

The Edition manager and the responsible
secretary
Nikolaev V.P.

Editorial council:
Aftanas L.I., MD, Professor, Acad. RAMS
(Novosibirsk)
Voevoda M.I., MD, Professor, Corresponding
Member RAMS (Novosibirsk)
Ivanov P.M., MD, Professor (Yakutsk)
Kryubezi Eric, MD, Professor (France)
Maksimova N.R., MD (Yakutsk)
Mironova G.E., Doctor of Biology, Professor
(Yakutsk)
Mikhailova E.I., Doctor of Pedagogics,
Professor (Yakutsk)
Nelson Debora, MD, professor (USA)
Nikitin Yu.P., MD, Professor, Acad. RAMS
(Novosibirsk)
Odland John, MD, Professor (Norway)
Puzyrev V.P., MD, Professor, Acad. RAMS
(Tomsk)
Reutio Arya, MD, PhD, Professor (Finland)
Fedorova S.A., Doctor of Biology (Yakutsk)
Husebek Anne, MD, Professor (Norway)
Khusnutdinova E.K., Doctor of Biology,
Professor (Ufa)

The editor
Chuvashova I.I.

Translation
Semenova T.F.

Cover
Ignatyev V. N.

Computer imposition
Nikolashkina A.A.

The edition address:
677019, Yakutsk, Sergeljahsky highway, 4,
M&ChHCC NCM, unit S1-01,
tel.(4112) 32-15-26; 39-55-52
The telefax (4112) 32-19-81
E-mail: ysc_tech@sakha.ru
yscredactor@mail.ru
<http://www.ymj.ykt.ru>

The articles are presented in the
author's translation.

ISSN 1813 1905
3(47) `2014



YAKUT MEDICAL JOURNAL

SCIENTIFIC - PRACTICAL JOURNAL
OF THE YAKUT SCIENCE CENTRE OF
COMPLEX MEDICAL PROBLEMS
THE SIBERIAN BRANCH OF
THE RUSSIAN ACADEMY OF MEDICAL
SCIENCES

Quarterly

*It is registered by Sakha-Yakut
Territorial administration of the Ministry of the
Russian Federation on press affairs, telecasting
and means of mass communications from
October, 30th, 2003*

Registration number ПИ №19-0465

*Subscription index: 78781
Free price*

*«The Yakut medical journal» is included in
confirmed by the Higher certification commission
of the Russian Federation «List of leading
reviewed scientific magazines and editions in
which the publication of the basic scientific results
of dissertations on competition of scientific
degrees of the doctor and the candidate on
biological sciences and medicine, in edition from
25/02/2011 is recommended*

*The journal is included in the international
directory system under periodic and proceeding
editions "Ulrich's International Periodicals
Directory"*

CONTENTS

Original researches

Kirillina M.P., Loskutova K.S., Lushnikova E.L., Nepomnyashchikh L.M.

Immunohistochemical analysis of epithelial cells in mammary tumors in Republic Sakha (Yakutia)

Borisova E.P., Kylbanova E.S.

Clinico-functional features of concomitant chronic bronchitis and chronic obstructive pulmonary disease with metabolic syndrome in the Yakut ethnic group

Kornilova A.G., Kogoniya L.M.

Risk groups stratification of patients with gastrointestinal stromal tumors: defining the feasibility of adjuvant therapy and its duration

Borisov I.M., Shapovalova T.G.

Methods of evaluation of the pneumonia severity and their comparative analysis in the servicemen

Ivanov S.V., Sukhov G.M., Ivanov I.S., Cukanov A.V., Goryainova G.N., Obyedkov E.G., Gafarov G.N.

Features of the skin and fascia structure in patients with ventral hernias

Chizhov Yu.V., Ushnitsky I.D., Plonina V.S., Baginski A.L., Kazantseva T.V., Varlamov P.G.

Features of orthopedic treatment of dentition defects of HIV-infected patients with fixed dentures

Duglas N.I., Gur'eva A.B., Rad' Y.G., Pavlova T.Y., Baisheva N.S.

Features of ultrasonic, anthropometric parameters of teenage girls and women of Yakutia

Konstantinova L.I., Mironova G.E., Okhlopko E.D., Efremova A.V.

Effect of "Valetok-SP Aktiv" vitamin and mineral food supplement on the state of pro- and antioxidant balance of Yakutia athletes

Methods of diagnosis and treatment

Egorova T.V., Savvina N.V., Savvina D.V., Lazareva A.A., Govorova M.D., Pavlova O.N.

Identification of risk factors in schoolchildren of the Sakha (Yakutia) Republic: the results of a comprehensive survey in the Health Centre for Children

Mikhailova A.E., Zakharova R.N., Timofeeva A.V.

Difficulties in diagnosis of reactive arthritis in an outpatient clinics

Skachkov D.P., Shtilerman A.L.

Initial results of treatment of patients with bullous keratopathy by corneal collagen cross-linking method

Bashirov E.V., Polina M.L., Duglas N. I.

Perspectives of the study of adaptive-immune reactions spectrum after different treatment technologies of uterine fibroids



Organization of healthcare, medical science and education

Tarabukina S.M., Akimova A.M.

Organization of drug supply in rural areas on the example of Megino-Kangalassky region of the Republic Sakha (Yakutia)

Evseeva S.A., Chasnyk V.G., Dranaeva G.G., Burceva T.E.

Opinion study of medical staff of Northern and Arctic regions of the Republic Sakha (Yakutia) about the system of medical care

Nelunova T.I., Chasnyk V.G., Burceva T.E., Son E.D., Afanasyeva N.A., Yakovleva A.I., Neustroeva T.S.

Analysis of the structure of neonatal CHD in RS (Y) according to the Republic Hospital № 1 - NCM data for 2011-2013

Dorofeev A.L., Pestushko N.A., Pjatnickaja S.V.

Distance education technologies in the training of highly skilled medical personnel

Hygiene, sanitation, epidemiology and medical ecology

Gerasimova V.V., Maksimova N.R., Levakova I.A., Mukomolov S.L.

Molecular epidemiology of hepatitis B virus in Yakutia

Mordovskaja L.I., Gur'eva O.I.

Clinical and immunological features of drug-resistant tuberculosis in children and adolescents

Semenchenko I.Yu., Sharafetdinov H.H., Plotnikova O.A., Lapik I.A., Alekseeva R.I., Sentsova T.B.

The role of specialized food for enteral nutrition in the treatment of type 2 diabetes

Muradov S.V., Sel'minskaja O.V., Rogatyh S.V.

Paratunskoye resort (Kamchatka Krai) therapeutic muds and drugs on their basis as a means of etiotropic and pathogenetic therapy of periodontal disease

Tyaptirgyanova V.M., Tyaptirgyanov M.M.

Influence of water quality in Yakutia reservoirs on the fish organism (at the example of Vilyuy, Khroma, Indigirka and Kolyma Rivers)

Tyaptirgyanov M.M., Tyaptirgyanova V.M.

Ecological and hygienic evaluation of the accumulation and distribution of cadmium compounds in organs and tissues of Yakutia freshwater fish

Grigorieva A.A., Mironova G.E.

Assessment of the distribution of heavy metals in meat foods of Central Yakutia inhabitants

Reviews and lectures

Potupchik T.V., Evert L.S., Zajceva O.I., Panicheva E.S., Miroshnichenko E.V.

Adaptation of the first-graders in the school



Experience exchange

Lyadova M.V.

The study of medical records of defects in the formulation and confirmation of the diagnosis in patients with injuries of ligaments

Protodjakonova G.P Donchenko VN

Effectiveness of different types of corks at mycobacteria cultivation

Starostin V.P., Nezgovorova A.M., Pestereva M.I.

Features of rehabilitation in pediatric tuberculosis sanatorium in the North

Lebedeva U.M., Rumyantseva A.N., Stepanov K.M., Ignatieva M.E., Egorov I.Y., Kornilova M.V., Borisova N.B.

Items of optimizing the structure of the population nutrition and improving the quality and safety of food production in the Republic Sakha (Yakutia)

Shepeleva L.P.

Differential diagnostic criteria of normal and altered tuberculous process of intrathoracic lymph nodes

Events Chronicle

Our jubilees

Starostin V.P., Grigoriev N.N.

75th anniversary of the Republic Sakha (Yakutia) pediatric sanatorium named after T.P. Dmitrieva

75th anniversary of I.Ja. Egorov



Immunohistochemical Analysis of Mammary Epithelial Cells at Tumoral Growth in Republic of Sakha (Yakutia)

M.P. Kirillina, K.S. Loskutova, E.L. Lushnikova, L.M. Nepomnyaschih

ABSTRACT

The analysis of histological examination results of surgical material of breast cancer from 294 women with subsequent immunohistochemical determination of estrogen (ER) - and progesterone (PgR) - receptors, proliferative activity (Ki-67), expression of the mutant suppressor gene (p53) and gene-inhibitor apoptosis (bcl-2) was carried out. The obtained data testify that IHC-research of the tumor progression markers is a defining part in the forecast of course, optimization of therapeutic approaches with an individualization of chemo-, hormonal and beam therapy of mammary cancer, the decision of a question of medicamentous and/or surgical shutdown of the ovaries, based on the research results of the biological activity markers of the tumor.

Keywords: breast, cancer, immunohistochemistry.

Relevance. Currently one of the most urgent problems not only in oncology but also health care in general is the prevention of breast cancer (BC), due to the rapid, steady growth and widespread incidence of this form of cancer, which became on top of the structure of morbidity for women with malignant neoplasms [1].

Immunohistochemistry (IHC) is the method of pinpointing the precise localization of particular cell or tissue antigen, allowing carrying out the immunoassay of tissue sections while maintaining the cell morphology. Thus, the most important biological characteristics of tumors having a value in the forecast of disease include proliferative activity (PA) (antigen Ki-67) of tumor cells, their differentiation level, hormone receptor status, intensity of apoptosis (as markers of bcl-2 and p53), which are determined by immunohistochemical methods [2].

Despite the widespread adoption of immunohistochemical techniques in the diagnosis of cancer, it should be noted that in this area the knowledge about the changes in expression of certain markers of proliferation, differentiation and cell death is still being accumulated. Most of the studies evaluated the expression of a limited number of markers, which does not allow us to identify the most informative predictors of malignancy amplification. It is also important to note the need for diagnostic examinations considering ethnicity, since

It is also important to point out, that there is a need of diagnostic examinations considering ethnicity, since ethnic and genetic factors play significant role for many types of cancers, including breast cancer [3].

The **objective of research** is to examine expression patterns of molecular biological markers for breast cancer, depending on age and ethnicity on the example of Republic of Sakha (Yakutia).

MATERIALS AND METHODS

In our research work the material from 294 women who were held surgical treatment and / or puncturing biopsy in Yakutsk Republican Oncology Center and 2nd surgical department of the Clinical Center SBD Sakha (Yakutia) "Republican Hospital № 1 - National Medical Center" was investigated. In our research, as indigenous were considered Yakuts, Evens and Evenki people, as non-indigenous - all persons of other nationalities, who arrived at different times from regions of Russia and CIS countries. There were 118 (40.1%) of indigenous women and 176 (59.9%) women of non-indigenous nationalities. All studies were performed with the approval of the Local Committee on Biomedical Ethics "Yakut Scientific Center of complex medical problems" SB RAMS.

Histological processing of the material was carried out according to conventional techniques. Immunohistochemical study was performed on serial paraffin sections. Staining was performed by indirect immunoperoxidase method after unmasking the antigenic determinants. Sections were incubated for 40 - 60 min with primary monoclonal antibodies to the antigens of estrogen (ER), progesterone (PgR), Ki-67, p53, bcl-2 (used RTU-ER-6F11, RTU-PGR-312, RTU-Ki-67-MM1, RTU-p53-DO7, RTU-bcl-2/100/D5, «Novocastra», UK). Staining was performed according to the manufacturer's instructions.

When evaluating the results of the research for the ER and PgR were performed determination of the fraction of stained cells in points [4,5]: 0 - total absence of nuclear staining, 1 - 10% of the cells in the investigated material have nuclear staining, 2 - 1/3 of the cells with nuclear staining, 3 - from 1/3 to 1/2 of the cells with nuclear staining, 4 - from 1/2 to 2/3 of the cells with nuclear staining, 5 - from 2/3 to 100% of the cells with nuclear staining. Determination of antibody expression intensity was also performed in points: 0 - complete absence of expression in the nuclei of tumor cells, 1 - weak nuclear staining, 2 - mild nuclear staining, 3 - strong nuclear staining. Upon receiving the total result which is less than or equal to 2, the reaction was considered negative (-), 3 or more - a positive (+).

Index of Ki-67 positive cells (proliferative activity - PA) was determined by analysis of at least 100 nuclei by the following formula:

$$PA = \frac{\text{"the number of Ki - 67 positive cells x 100"}}{\text{"the total cell number"}}$$

Low PA corresponded to Ki-67 index of less than or equal to 15%; high PA - with Ki-67 index of more than 15%.

Low expression of p53 was detected in the presence of expression of less than 25% of the cells; high expression of p53 – in the presence of expression of more than 25% of tumor cell nuclei (nuclear stain).

Low expression of bcl-2 was detected in the presence of expression of less than 25%; High expression of bcl-2 - in the presence of expression of more than 25% of tumor cells (cytoplasmic staining).

Statistical analysis was performed using the statistical package SPSS STATISTICS 17.0 (SPSS Inc.).

RESULTS AND DISCUSSION

The average age of the operated women was $54,2 \pm 12,1$ years, most were women over 50 years old - 96 women (32.6%), 60 - 69 years old - 64 women (21.8%), in ages of 40 - 49 years - 60 women (20.4%), and under 39 years old - 37 women (12.6%), and over 70 years old - 37 women (12.6%) (Table 1).

Table 1						
Distribution of material by age and ethnicity						
Age group	Indigenous		Non-indigenous		In total	
	abs. / rel.	the average age	number abs. / rel.	the average age	number abs. / rel.	the average age
under 39 years old	15/12,7	33,7 \pm 5,3	22/12,5	33,8 \pm 3,6	37/12,6	33,7 \pm 4,3
40 – 49 years old	28/23,7	45,3 \pm 2,9	32/18,2	45,0 \pm 2,8	60/20,4	45,1 \pm 2,9
50 – 59 years old	31/26,3	54,8 \pm 2,7	65/37,0	54,1 \pm 2,9	96/32,6	54,3 \pm 2,9
60 – 69 years old	25/21,2	63,4 \pm 2,6	39/22,1	62,9 \pm 3,1	64/21,8	63,1 \pm 2,9
over 70 years old	19/16,1	74,2 \pm 2,9	18/10,2	73,3 \pm 3,3	37/12,6	73,8 \pm 3,2
Total number:	118/100	54,8 \pm 12,9	176/100	53,8 \pm 11,5	294/100	54,2 \pm 12,1

It should be noted that the breast cancer, which is traditionally considered as a disease of women older than 50 years, today became much "younger" - there are cases of disease of women of forty and thirty years old, and even women in their twenties. [6] This tendency was observed in our research. For example, there are twice more women aged over 50 years than those under 50 years (197 versus 97), the largest number recorded is significantly more frequent in the age group of 50 - 59 years old (96 cases or 32.6% of total surveyed) . In second place in frequency of our research is the age group of 40 - 49 years old (60/20, 4%). Also, studies were conducted in women aged under 39 years (37/12, 6%) and women aged over 70 years (37/126%). These results are comparable to those of developed countries, where about 75% of cases of breast cancer occur among women in postmenopause[7].

To determine ER and PgR immunohistochemical examine was carried out (Fig. 1, 2) and 4 groups with various combinations of steroid receptors in tumor cells were allocated: ER + / PGR-(7,8%), ER-/PGR + (5,4%), ER -/PGR- (35%), ER + / PGR + (51,7%).

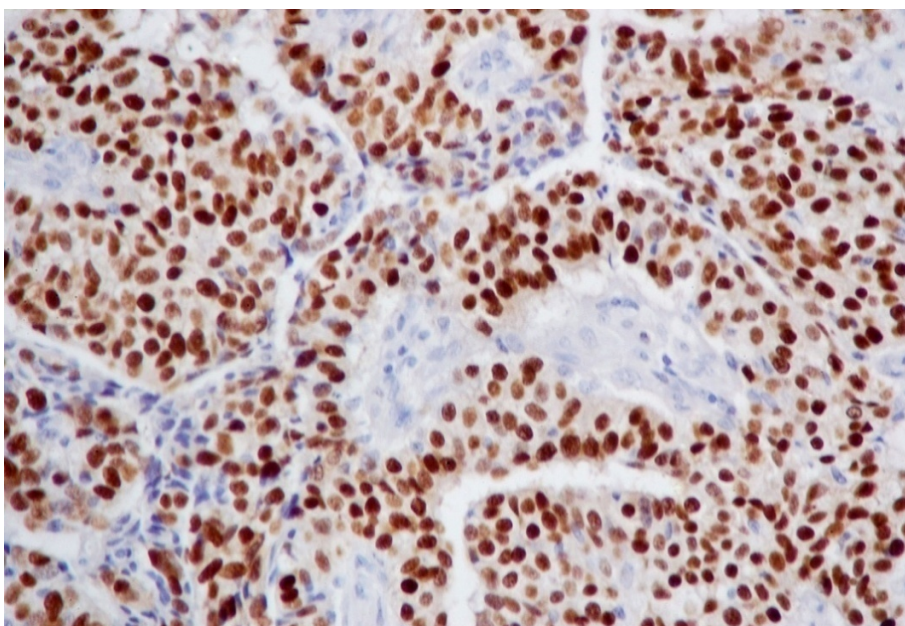


Fig. 1. Infiltrative ductal breast cancer.x200.

The immunohistochemical reaction with the monoclonal antibody to ER.

Proportion of stained cells in scores = 5 (from 2/3 to 100% of the cells with nuclear staining), the intensity of expression in scores = 3 (strong nuclear staining), the sum score = 8. Result: ER-positive breast cancer.

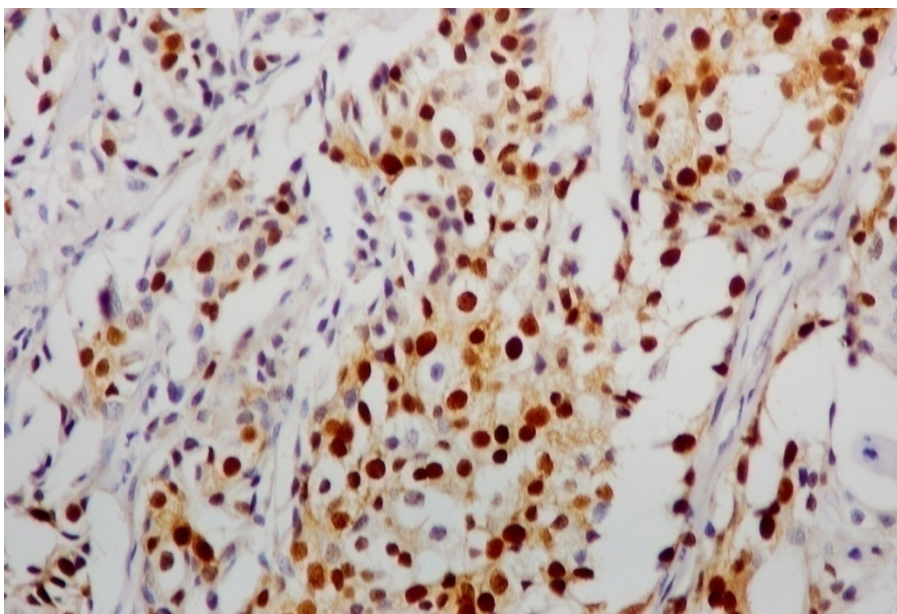


Fig. 2. Infiltrative ductal breast cancer x200.

Immunohistochemical reaction with monoclonal antibodies to PgR.

Proportion of stained cells in scores 4 = ($\frac{1}{2}$ to $\frac{2}{3}$ of the cells with nuclear staining), the intensity of expression in scores = 3 (strong nuclear staining), the sum score = 7. Result: PgR-positive breast cancer.

Collectively receptor-positive tumor cells in breast cancer were significantly higher than the receptor-negative ($p < 0.05$) - 191 cases (64.9%) of the total number of studies: aged under 50 years - 60 cases (31, 4%), over 50 years - 131 cases (68.6%). Analysis of the dynamics of change of the receptor status of breast cancer according to age revealed no statistically significant differences ($p = 0.14$), but set a trend toward increased frequency (percentage) receptor-positive breast cancer with increasing the age (Fig. 3). Thus, in a group under 39 years old, they made 56.7% and in the group over 70 years old - 75.6%. At the same time, in both groups receptor-positive breast cancer profile prevailed (correspondingly 48.3 and 54% of cases in indigenous and non-residents); receptor-negative breast cancer profile was less frequent (correspondingly 38.1 and 32.9% of cases).

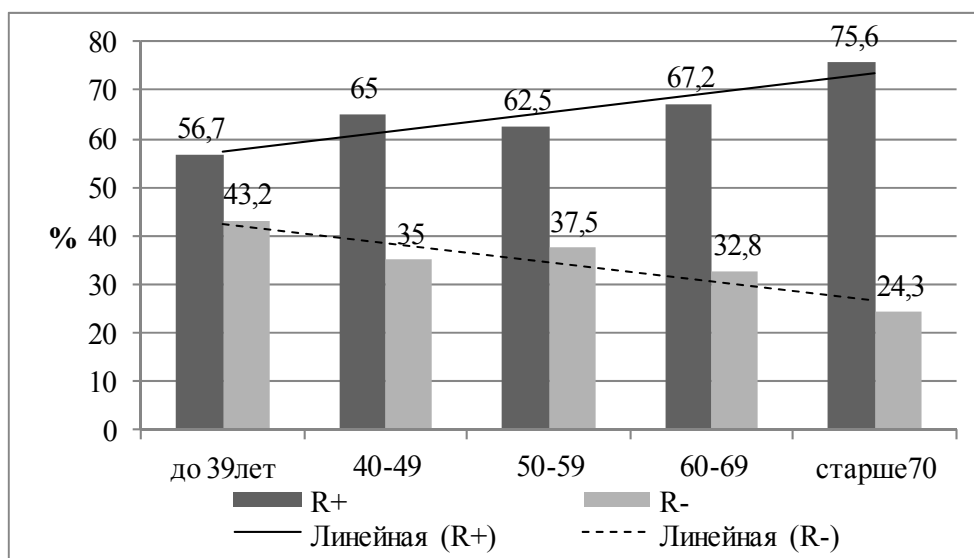


Figure 3. Dynamics of changes in receptor status of breast cancer according to age.

The connection between the age of patients and the expression of ER ($p = 0.03$). If under the age of 39 years, the average total score estimates of the proportion of positive cells and the intensity level of ER expression was equal to 3.2, the following age groups indicated a steady rise in these indicators up to 3.7 points at patients with breast cancer who were older than 70 years. In assessing the changes in the level of expression of PgR similar linear relationship is not detected ($p = 0.54$).

By the statistical analysis of the data according to ethnicity we have revealed differences among the indigenous women and women of non-indigenous nationalities. There was a tendency to a slight increase in the expression level of ER of indigenous women with the age, while increase of the expression level of ER of women of non-indigenous nationalities was statistically significant ($r = 0,20$, $p = 0,01$). Other authors have also noted differences in the content of hormones in the blood of women of different ethnic groups in Siberia, in particular, higher levels

of estradiol of indigenous (Tyva, Hakass, Buryat) at a lower the incidence of breast cancer [8]. A comparison of the degree of malignancy of tumors with the presence of ER and PgR (Fig. 4).

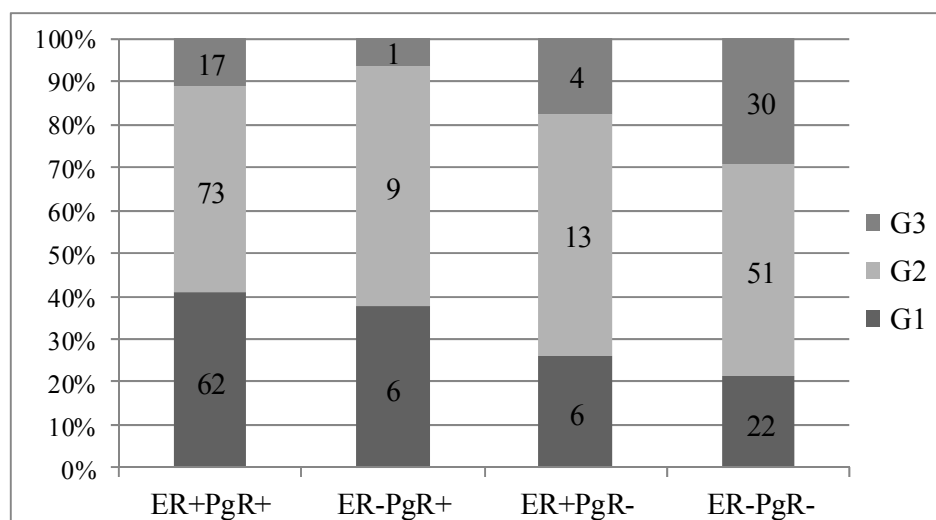


Fig. 4. Distribution of degrees of malignancy (by Elston& Ellis) at various hormone profile of breast cancer

The obtained data demonstrate certain dependence of histological grade of breast cancer on receptor profile of tumor cells ($\chi^2 = 20.40$, $df = 6$, $p = 0.002$). Thus, G1 at the receptor-positive tumors was detected 2 times more frequently (40.8% of the tumors in this group) than in the receptor-negative (21.3%) and only the ER-positive tumors (26.1%) and PgR positive (37.5%). G2 was detected equally often in receptor-positive and receptor-negative breast cancer (48 and 49.5%, respectively), while it was the vast majority of tumors with only ER-positive (56.5%) and only PgR-positive (56.2%) profile. Though G3 in the general totality was diagnosed more than 2 times less than remaining degrees, it constituted 29.1% of tumors with a receptor-negative profile and 11.2% - with a positive profile and was found in only 17.4% with ER-positive, and 6.2% of the PgR-positive profile.

Thus, by increasing the degree of malignancy receptor-negative tumors are significantly more observed ($p < 0.05$), while receptor-positive rate decreases.

Proliferative activity of breast tumor cells was determined using a universal proliferation marker Ki-67, which is expressed in almost all phases of the mitotic cycle and reflects the value of the proliferative tumors pool [9]. In our research Ki-67 expression was detected in 272 cases (92.5%) – less than 15% of tumor cells (low PA). We observed Ki-67 expression in 22 women (7.5%) – more than 15% of tumor cells (high PA) (Fig. 5-6).

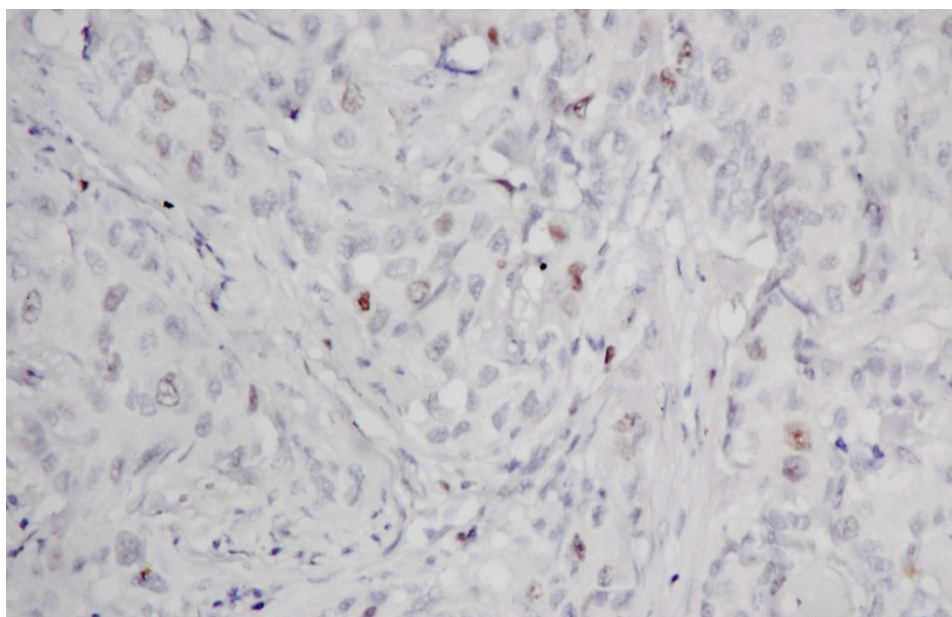


Fig. 5. Infiltrative ductal breast cancer X200.

The immunohistochemical reaction with the monoclonal antibody Ki-67. Expression of 20%.

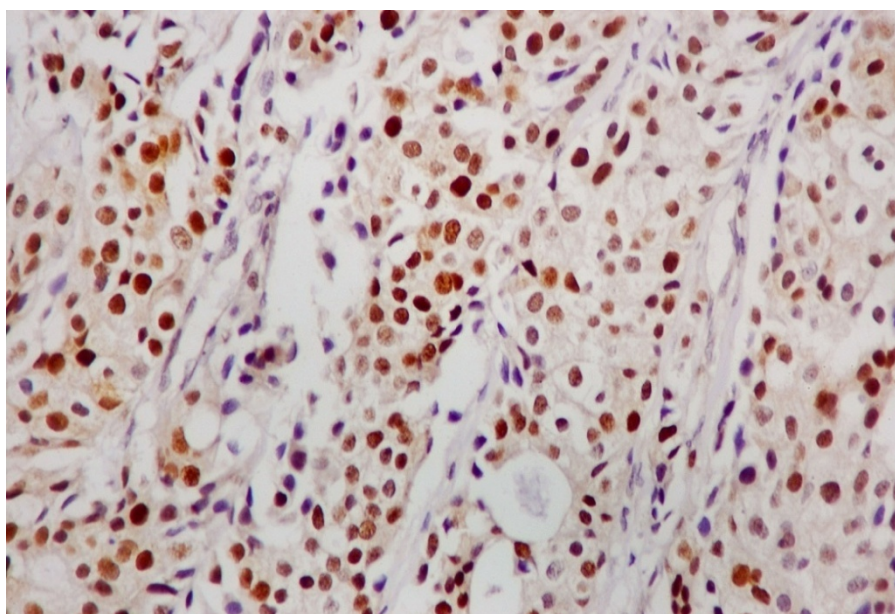


Fig. 6. Infiltrative ductal breast cancer x200.

The immunohistochemical reaction with the monoclonal antibody Ki-67. Expression of 90%.

Analysis of the expression pattern of Ki-67, depending on the age revealed that the expression level of Ki-67 antigen was independent of age ($\chi^2=4.1$, $df=4$, $p=0.39$). High PA of tumor cells occurs in both elderly patients and younger aged ones. In aggregate indicators in groups of indigenous and non-indigenous population in breast cancer statistically significant correlations with PA ethnicity has not been found ($\chi^2=1.6$, $df=1$, $p=0.20$). Numerous studies have shown that PA of tumor cells in breast cancer is directly correlated with the histological degree of malignancy [10,11]. The results obtained in our study indicate that the expression of Ki-67 antigen significantly differ between the different histological variants of breast cancer ($\chi^2=3.58$, $df=1$, $p=0.05$): there was a tendency of increasing the histological degree of malignancy while increasing the expression of Ki-67 (Fig. 7).

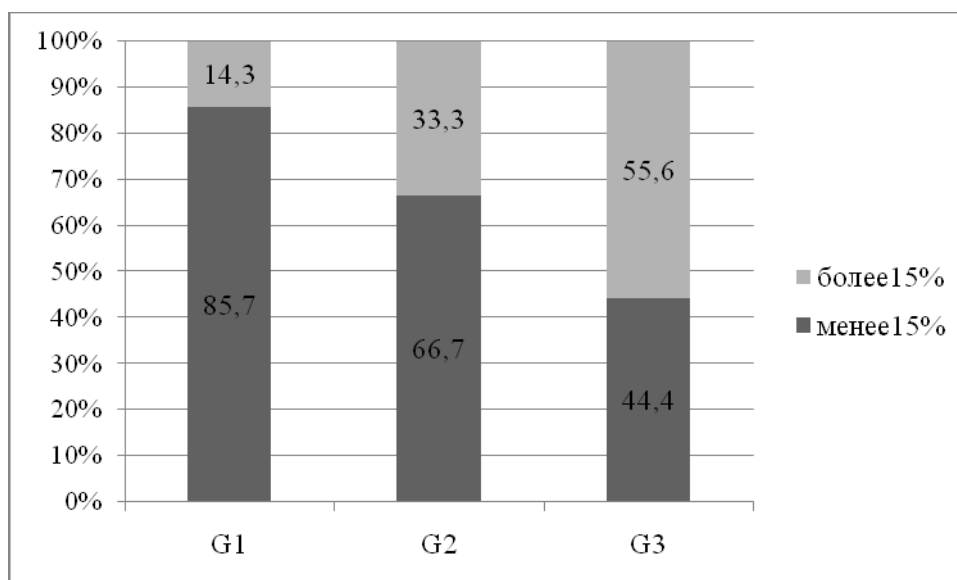


Fig. 7. Dependence of histological degree of malignancy on the level of Ki-67 expression.

These results do not contradict to the literature data on the Ki-67 antigen as a marker of adverse outcome of the disease [12,13,14]. Importantly, PA of tumor cells serves as an independent prognostic indicator of relapse, overall and disease-free survival [16], as well as a predictive factor in determining the sensitivity to radiotherapy and chemotherapy [17,18]. Our analysis confirmed the dependence between the degree of histological malignancy and proliferative activity of tumors, which proves the necessity of accounting PA of tumor cells in the evaluation of malignant potential and prognosis of breast cancer.

In immunohistochemical study of mutant tumor suppressor gene p53 low expression (less than 25% of tumor cells) was observed in 197 (67.0%) cases, whereas high expression (more than 25% of tumor cells) - 97 (33.0%) cases (Fig. 8, 9).

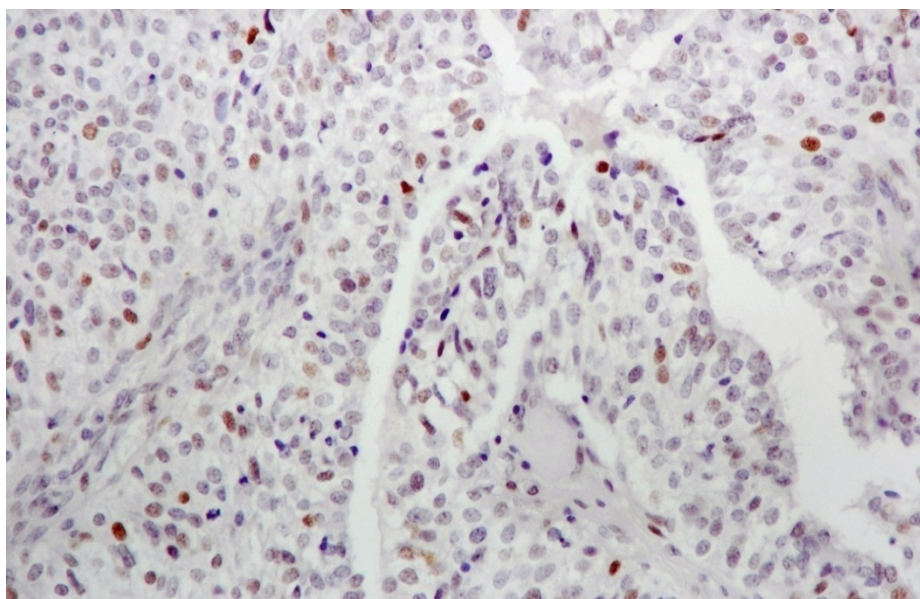


Fig. 8. Invasive breast cancer x200.

The immunohistochemical reaction with monoclonal antibodies to p53. Expression of 15%.

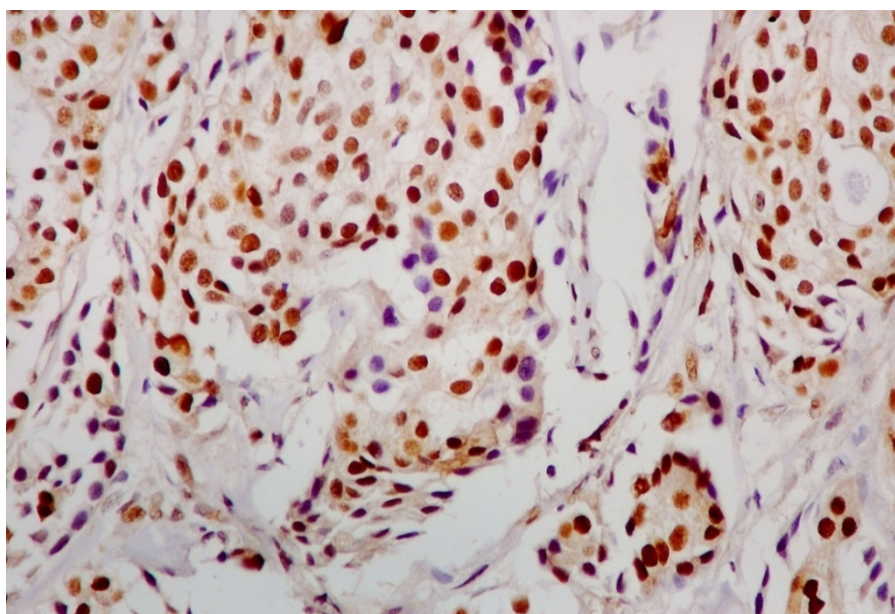


Fig. 9. Infiltrative ductal breast cancer X200.

The immunohistochemical reaction with monoclonal antibodies to p53. Expression of 100%.

In the analysis of this indicator based on ethnicity, we have established that indigenous women have statistically significant weak positive correlation ($r = 0,21$, $p = 0,02$) between age and the expression of p53. Low expression of p53 was observed in indigenous women aged 40 - 49 years (27.2%), while non-indigenous - aged 50 - 59 years (36.7%). In aggregate indicators in

both groups statistically significant age differences were not found ($\chi^2 = 1,8$, $df = 4$, $p = 0.76$). The positive relationship between the level of p53 expression and increased histological tumor grade was found ($\chi^2=7.9$, $df=2$, $p=0.01$), which proves the need to consider the severity of the process of cell apoptosis in evaluating the malignant potential of the tumor and prognosis of breast cancer (Fig. 10).

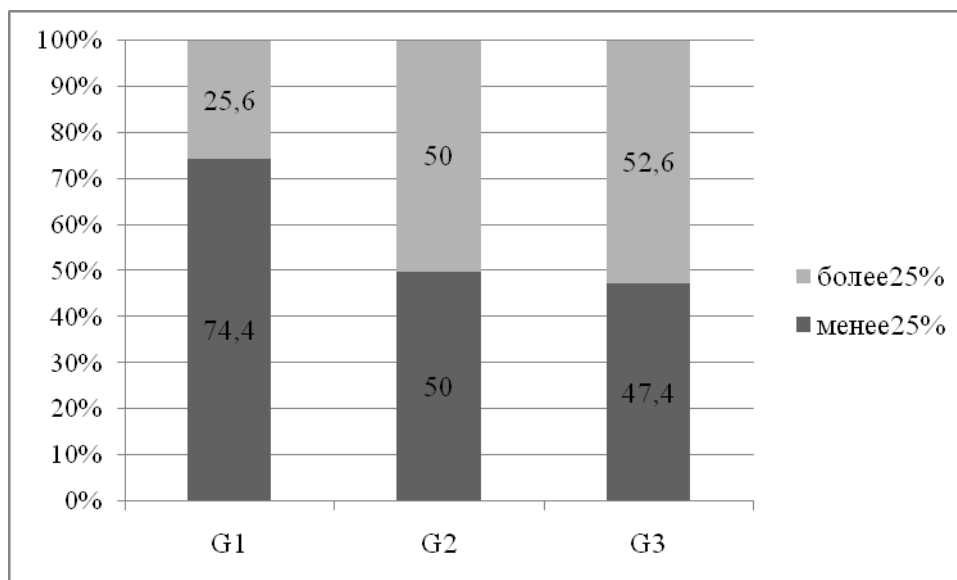


Fig. 10. Dependence of histological grade on the level of p53 expression.

By immunohistochemical study of the expression of anti-apoptotic tumor-suppressor gene bcl-2 we found low expression of bcl-2 in 142 cases (48.3%), high expression - in 152 cases (51.7%) (Figure 11).

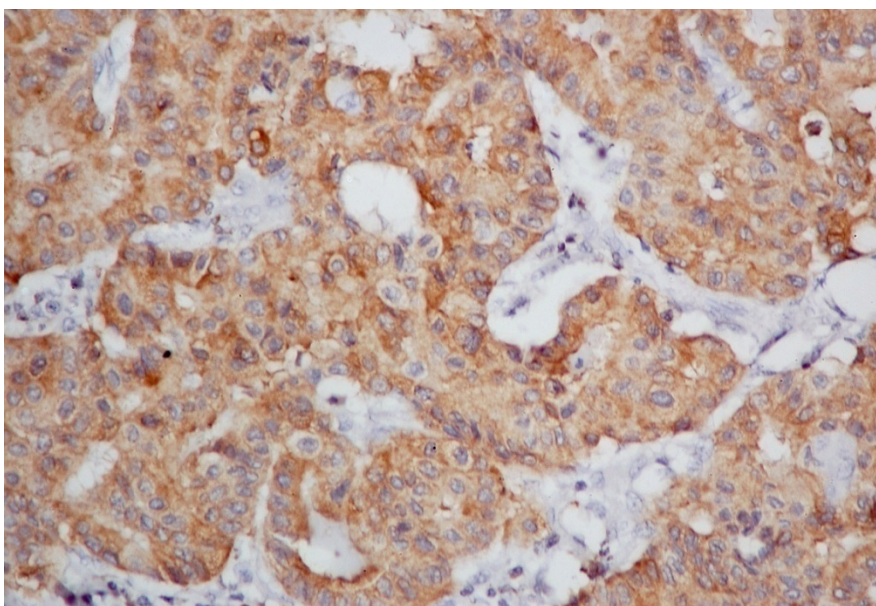


Fig. 11. Invasive papillary breast cancer x200.

The immunohistochemical reaction with the monoclonal antibody bcl-2. Expression of 98%.

Data analysis based on ethnicity did not reveal differences in the frequency of cases with low and high expression of bcl-2 ($\chi^2=0.23$, $df=1$, $p=0.64$). Low expression of bcl-2 in indigenous and non-indigenous women most frequently was recorded at the age of 50 - 59 years (respectively 33.9 and 36.1%). High expression of bcl-2 was more common among indigenous women aged 60 - 69 years (27.1%), in non-indigenous women - aged 50 - 59 years (37.6%).

According to the literature, bcl-2 is a tumor-suppressor gene affecting cell death mechanisms and suppressing apoptosis [15]. According to many authors, the increased expression of bcl-2 is associated with increased survival of patients after adjuvant therapy. Perhaps this is due to the close relationship between the expression of bcl-2 and the expression of ER and PgR, and low PA. However, bcl-2 is not an independent prognostic factor [15]. We have established a negative correlation between the expression of bcl-2 antigen, and the degree of histological malignancy of tumor ($r = -12.9$, $p=0.03$), i.e. tumors with a high degree of malignancy were characterized by low expression of bcl-2, which describes by preserving the regulation of apoptosis in normal levels (Fig. 12).

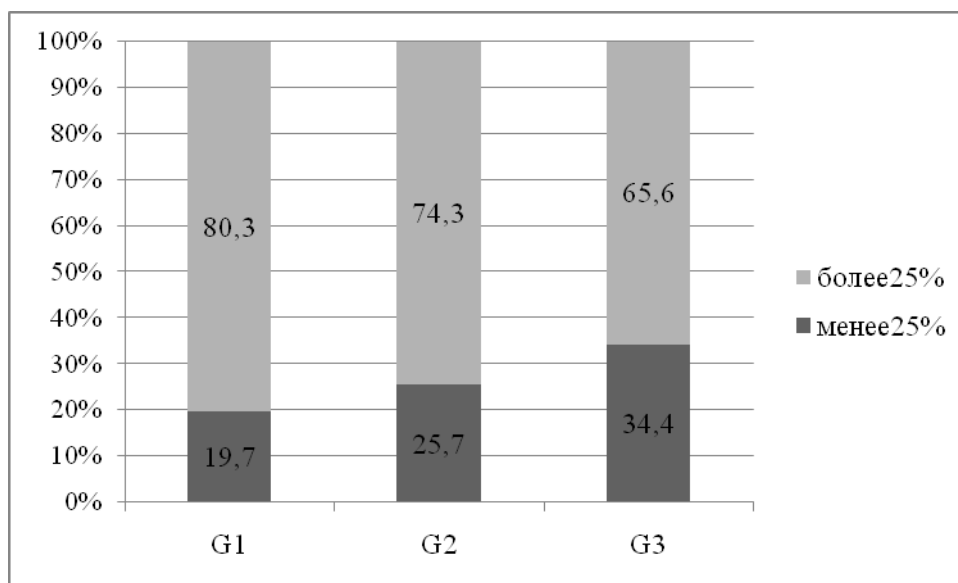


Fig. 12. Dependence of bcl-2 expression on the degree of malignancy.

Thus, the data of comparative immunohistochemical study of some molecular biological markers for breast cancer analysis of their expression levels showed:

- According to clinical and morphological analysis, breast cancer develops most often in representatives of non-indigenous nationalities of the Republic of Sakha (Yakutia) (60%) than those belonging to indigenous nationalities (40%). With the highest rate recorded in women of indigenous and non-indigenous nationalities in the age group 50 - 59 years (32.6%) and 60 - 69 years (21.8%).

- In breast cancer tumors with the presence of steroid hormone receptors are predominant (65%).

- With increasing age tumor cells of breast cancer the level of ER expression increases ($p = 0.03$).

- Tumors with a high degree of malignancy are characterized by low expression of estrogen receptors and progesterone receptors ($p < 0.05$).

- The tendency of tumor grade increasing by increasing the expression of p53 and Ki-67 is found.

- The level of expression of bcl-2 antigen and its prevalence is positively correlated with the presence of ER and PgR receptors on tumor cells and low-grade tumors.

- The most informative criteria of increasing breast cancers are the decrease in expression of estrogen and progesterone receptors, increased expression of Ki-67 and p53 and decreased expression of bcl-2.

- The most informative criterias of increasing of breast tumors malignancy are the decrease in expression of estrogen and progesterone receptors, increased expression of Ki-67 and p53 and decreased expression of bcl-2.

REFERENCES

1. Berstein L.M. Sovremennaya ehndokrinologiya gormonzavisimyykh opukholej [Modern endocrinology of hormone-depended tumors], Moscow, 2002, V.48, № 4, PP. 496 - 503.
2. Loskutova K.S., Argunov V.A. Immunomorfologicheskaya kharakteristika gormonal'nogo statusa pervichnogo raka molochnoj zhelezy v Respublike Sakha (Yakutiya) [Immunomorphological characteristics of the hormonal status of primary breast cancer in the Republic of Sakha (Yakutia)] .Yakutsk, 2009, № 1, PP. 46 - 49.
3. Pozharissky K.M., Leenman E.E. Znachenie immunogistokhimicheskikh metodik dlya opredeleniya kharaktera lecheniya i prognoza opukholevykh zabolevanij [Value of immunohistochemical techniques to determine the nature of the treatment and prognosis of tumor diseases]. Moscow, 2000, № 5, PP. 3 - 11.
4. Petrov S.V., Reichlin N.T. Rukovodstvo po immunogistokhimicheskoy diagnostike opukholej cheloveka [Guidelines for immunohistochemical diagnosis of human tumors]. Kazan, 2004, P. 452
5. Pisareva L.F., Odintsov I.N., Shivit-ool A.A., Sirazitdinova A.K. Ehpideologicheskie osobennosti zlokachestvennykh novoobrazovaniy molochnoj zhelezy v regione Sibiri i Dal'nego Vostoka [Epidemiological features of breast cancers in the region of Siberia and the Far East.]. Tomsk, 2006, P. 10.
6. Pisareva L.F., Odintsov I.N., Ananina O.A. Gormonal'nyj status zhenshhin razlichnykh natsional'nostej regiona Sibiri i Dal'nego Vostoka [Hormonal status of women of different ethnicities in the region of Siberia and the Far East.]. Tomsk, 2011, № 2 (44), PP. 5 - 10.
7. Uporov A.V., Semiglazov V.F., Pozharissky K.M. Immunogistokhimicheskoe izuchenie kletok raka molochnoj zhelezy s ispol'zovaniem raznykh markerov proliferatsii [Immunohistochemical study of breast cancer cells using a variety of proliferation markers]. Moscow, 2000, № 2, pp.26-30.
8. Anderson W.F. Chatterjee N., Ershler W.B. Estrogen receptor breast cancer phenotypes in the Surveillance, Epidemiology, and the Results database. Brawley Breast cancer Res.Treat. – 2002. – Vol. 76. – P.27-36.
9. Buchholtz T.A. David D.W., McConcey D.J.et al. Chemotherapy-induced apoptosis and bcl-2 levels correlate with breast cancer response to chemotherapy. Cancer. – 2003. – Vol.9/



- P.33-41.

10. Costarelli L., Piro F.R., Fortunato L. Hormone-dependence and C-ERBB2: relationship between estrogen receptor expression, estrogen-regulated proteins, and C-ERBB2 in breast carcinoma. *SupplTumori*. - 2005.- Vol.4.- P.171.

11. Choi D.H. Kim S., Rimm D.L. et al Immunohistochemical biomarkers in patients with early-onset breast carcinoma by tissue microarray. *Cancer J*. - 2005.-Vol.II (5). - PP.404-411.

12. Ferrara N. The role vascular endothelial growth factor in pathological angiogenesis. *Breast Cancer Res. Treast*. -1995. – Vol.36, №36, №2. – P.127-137.

13. Hoonkop A.H., van-Diest P.J. Prognostic role of clinical, pathological and biological characteristics in patients with locally advanced breast cancer. *Br. J. Cancer*. – 1998. – Vol.77. – P. 621 – 626.

14. Imamura, H. Haga S., Shimizu T. et al. MIB 1 determined proliferative activity in intraductal components and prognosis of invasive ductal breast carcinoma *Jpn. J. Cancer Res*. – 1997. – Vol. 88. – P. 1017 – 1023.

15. Jacobson M.D, Burne J.F., King M.P. et al. Bcl-2 blocks apoptosis in cells lacking mitochondrial DNA. *Nature*. – 1993. – Vol.361. – P.365 – 368.

16. Keshgegian A. Cnaan A. Proliferation markers in breast carcinoma: mitotic figure count, S-phase fraction, proliferating cell nuclear antigen, Ki-67 and MIB-1. *Am. J. Clin. Pathol*. – 1995. – Vol. 104. – P. 42 – 49.

17. Kronqvist P., Kuopio T., Nykanen M., Helenius H. Predicting aggressive outcome in TINOMO breast cancer. *Br. J. Cancer*. – 2004. – Vol. 91 (2). – P. 277 – 281.

18. Rozan, S. Vincent-Salomon A., Zafrani B. et al. No significant predictive value of c-erbB-2 or p53 expression regarding. *Int. J. Cancer*. – 1998. – Vol.79. – P.27-33.



The authors

Kirillina Maria Petrovna – PhD (Biology), Head. lab. of MI NEFU named after M.K. Ammosov, junior researcher YSC CMP SB RAMS, e-mail: kirillinamp@mail.ru; Yakutsk, Russia;

Loskutova Kyunnyay Savvichna - PhD, Head of Laboratory YSC CMP SB RAMS, doctor pathologist of the highest qualification category, Head of Dpt Pathology RH № 1 - NCM, chief out-of-staff pathologist MH Sakha (Yakutia), Yakutsk, Russia;

Lushnikova Elena Leonidovna – Doctor of Biology, prof., Acad. RANS, Head of lab. Institute of Regional Pathology and Pathomorphology SB RAMS, Novosibirsk, Russia;

Nepomnyashchikh Lev Moiseevich - MD, RAMS corresponding member, prof., Director of the Institute of Regional Pathology and Pathomorphology SB RAMS, Novosibirsk, Russia.

E.P. Borisova, E.S. Kylbanova

Clinico-Functional Features of Concomitant Chronic Bronchitis and Chronic Obstructive Pulmonary Disease and Metabolic Syndrome in the Yakut Ethnic Group

ABSTRACT

Objective. Studing of clinical and functional characteristics of the combined course of chronic bronchitis (CB) and chronic obstructive pulmonary disease (COPD) and metabolic syndrome (MS) in Yakut ethnic group.

Materials and methods. We have examined 88 patients Yakut with chronic bronchitis and COPD in combination with MS. The median age was $50,9 \pm 0,91$ years. The comparison group consisted of 60 patients Yakut with chronic bronchitis and COPD without metabolic syndrome, where the average age was equal to 48.9 ± 1.35 years. Peculiarities of clinical manifestations and indicators of bronchial patency were also studied.

Results. In the combined course of CB/COPD and MS in Yakut ethnic group, we found more severe clinical manifestations in comparison with the group without metabolic syndrome, in the form of a more severe cough syndrome, more severe dyspnea, sputum gain and changes its character, increasing the frequency of exacerbations. In the combined course of chronic bronchitis and chronic obstructive pulmonary disease and metabolic syndrome in Yakut ethnic group, we found that lung function compared with isolated over these diseases were not significantly different. However, in the combined courses more pronounced disorders of respiratory function in the form of reduced forced vital capacity (FVC), decline in forced expiratory volume in one second FEV_1 , FEV_1/FVC ratio increase $> 70\%$ were observed in our research.

Conclusion. Combined course of CB/COPD and MS is characterized by more severe changes in the clinical manifestations. Our findings indicate the presence of more pronounced changes in respiratory function in patients with associated course of CB/COPD and MS.

Keywords: metabolic syndrome, chronic bronchitis, COPD, respiratory function.

INTRODUCTION

Respiratory diseases in the Republic of Sakha (Yakutia) occupy one of the leading places in the structure of morbidity and determine largely the level of temporary disability, disability and mortality.

According to WHO, chronic obstructive pulmonary disease (COPD) is one of the most common diseases, it is expected to become the third leading cause of death in 2020. During the

last decade, the concept of COPD has been recognized as a disease with systemic manifestations, which include cardiovascular disease, cachexia, muscle dysfunction, osteoporosis, anemia, clinical depression, metabolic and endothelial dysfunction [7].

Currently, WHO experts consider metabolic syndrome (MS) as "pandemic of the XXI century". Its prevalence in the adult population of Russia according to All-Russian Scientific Society of Cardiologist in 2009 is 20-40 % and more frequently, it occurs in middle-aged and older. The prevalence of MS according to the International Diabetes Federation among the aboriginal population of Yakutia is 8.8 % [1].

Today, however, the combined features of chronic bronchitis and COPD with MS in domestic science devoted to the study unit and the available literature, we found no data on the combination of chronic bronchitis and COPD with MS Yakut ethnic group.

The aim of this study was to investigate the clinical and functional characteristics of the combined course of chronic bronchitis and chronic obstructive pulmonary disease and metabolic syndrome in Yakut ethnic group.

MATERIALS AND METHODS

We conducted a comprehensive clinical and functional, instrumental examination of 148 patients based on the Department of Emergency Medicine of the Republican Hospital № 2 - emergency medical center of Yakutsk from 2009 to 2013. All patients signed the informed consent to participate in the survey. The study was conducted within the framework of the research project «Metabolic syndrome and chronic non-communicable diseases among residents of Yakutia» (Registration number YSU 11 - 01M.2009.).

Study group comprised 88 patients with metabolic syndrome in combination with chronic bronchitis (CB) and chronic obstructive pulmonary disease (COPD) Yakut. The median age was equal to $50,9 \pm 0,91$ years, gender: women 69.3%, men 30.7%. The study included patients with a diagnosis of «COPD» 44.3%, with a diagnosis of «chronic bronchitis» 55.7%.

The comparison group consisted of 60 patients Yakut with chronic bronchitis and COPD without metabolic syndrome. The average age of $48,9 \pm 1,35$ years as the age of the main group , by gender, women were 80% , men 20% of patients with a diagnosis of "COPD" 41.7% , with a diagnosis of "chronic bronchitis" 58.3%. For statistical analysis found that the study groups did not significantly differ by age, gender, and the ratio of CB and COPD diagnoses. Regular smokers in the respective groups were 28.4% and 28.3% of those surveyed patients ($p = 0.644$). Analysis of smoking index showed that the value of this indicator in patients with comorbidity is higher at $8,89 \pm 1,51$ pack - years , compared with $4,5 \pm 1,01$ pack - years in patients with isolated over CB / COPD ($p = 0.003$).

Diagnoses of "chronic bronchitis" and "COPD" is established based on complaints, medical history, physical examination, spirometry, in accordance with international consensus documents: identification of experts of the World Health Organization, "Global Initiative for Chronic Obstructive Lung Disease" revision 2011, international classification of Disease X revision. Metabolic syndrome is established based on recommendations from the All-Russian Scientific Society of Cardiologist 2009.

The survey was carried out taking into account the patients developed questionnaire approved by the ethics committee, which included questions on blocks: socio-demographic characteristics, medical history, the study of heredity, behavior and health, a validated questionnaire to assess respiratory symptoms in patients with COPD symptoms scale (PL Paggiaro), scale severity of dyspnea Medical Research Council Dyspnea Scale (MRCDS). Spirometry was performed on a hardware-software complex for functional studies "Valenta" (St. Petersburg). Calculated following volume and speed post-bronchodilator lung function: forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), and the ratio of these two parameters (FEV_1/FVC). Statistical data processing and analysis was performed using SPSS statistical software package for Windows. Quantitative measures described in the study groups using the mean values (M) and standard error (m). Check the laws of distribution of quantitative indicators was performed using the Kolmogorov-Smirnov test. Test results showed that the distribution of many quantitative indicators are not subject to the normal law. Therefore, a comparative analysis of quantitative indicators used nonparametric Mann-Whitney test. Study the interaction between qualitative attributes were analyzed using the classical chi-square test of Pearson. Threshold of significance for all statistical tests used accepted meaning of $p < 0,05$.

RESULTS AND DISCUSSION

With the purpose of studying the clinical manifestations of the combined course of chronic bronchitis/chronic obstructive pulmonary disease (CB/COPD) and metabolic syndrome (MS), we analyzed the clinical data in the main group of the combined course of CB/COPD and MS ($n = 88$) and a group of isolated CB/COPD ($n = 60$). We have found statistically significant differences in many clinical manifestations.

Thus, in the group of the combined course of CB/COPD and MS compared to the group of isolated CB/COPD were significantly more patients complained of cough in winter: 86,4% vs 68,3%, $p = 0.008$ (Table 1). The intensity of cough in combination of CB/COPD and MS was pronounced than in isolated CB/COPD. 46.6 % of patients of the main group were characterized as mild cough, while the comparison group - 48.3 % of patients. Intensification cough up average recorded in 37.5 % of individuals in the group combined flow versus 18.3 % in patients

with isolated chronic bronchitis/COPD ($p = 0.003$). Expressed cough was noted 8.0% in the main group and only 5% in the comparison group without MS. At the same time increased cough and sputum for the last 3 years was determined in 60.2 % in the case of nosology syntropy CB/COPD and MS and only in 28.3 % of patients with isolated CB / COPD ($p = 0.000$).

Thus, we identified heavier cough syndrome in the case of combination of CB/COPD and MS. Our data are consistent with the literature, according to which abdominal obesity causes increased productive cough [9].

By the intensity of sputum we also found statistically significant differences. Thus, the absence of sputum noted only 20.5 % of patients combined course of CB/COPD and MS patients versus 65 % of the comparison group, $p = 0.000$ (Table 2). For a small amount of sputum complained 60.2 % of patients of the main group against 30.0% of patients at an isolated CB/COPD. Moderate sputum noted 18.2 % of patients with chronic bronchitis/COPD and MS, and only 5 % of patients in the comparison group ($p = 0.000$). The color of sputum, reflecting the intensity of inflammatory changes in the bronchopulmonary system, we also recorded a statistically significant difference. The high intensity of inflammation was observed with a combination of chronic bronchitis/COPD and MS - light yellow expectoration in 18.2 % of those in the primary group vs 8,3% in the comparison group; green sputum 18,2% vs 6,7%, respectively, $p = 0.001$. Thus, the associated flow CB/COPD and MS is characterized by increased sputum and change its nature, due to more severe inflammatory changes in the intensity of the bronchopulmonary system.

Abdominal obesity, a major component of MS, causes increased shortness of breath on exertion, reduces the functionality of the body [9]. Shortness of breath syndrome analysis showed (Table 3) that the association CB/COPD and MS significantly more likely to have wheezing and whistling in the chest (38,6% vs 23,3%, $p = 0.05$), shortness of breath with wheezing (28,4% vs 15,0%, $p = 0.05$). In combined course of CB/COPD and MS we found an absence of dyspnea observed only 7.8% of patients, whereas in the case of CB/COPD without MS similar figure was higher at 32.8%, dyspnea during light load was observed in 13.6 % of cases in the study group, and only 1.7 % of cases in the comparison group ($p = 0.000$). Thus, the syndrome of lack of air more pronounced in the case of combined course of CB/COPD and MS.

Significant differences in the frequency of exacerbations were found in the two groups. Patients with isolated chronic bronchitis/COPD more than half the cases (66.7%) had only one exacerbation per year, whereas the conjugate disease exacerbations were recorded 2 times a year 51.1% , 3 or more in 15.9 %, $p = 0.000$ (Table 3).

Thus, when we observed associated course of CB/COPD and MS we found more severe clinical manifestations comparison with the isolated CB/COPD due to a more pronounced change in intensity inflammatory bronchopulmonary system due to MS connection that corresponds to the literature data, whereby COPD is characterized by chronic airway obstruction and related endocrine and metabolic disorders, worsen the clinical course and prognosis of patients [8]. Abdominal obesity is associated with the appearance of respiratory symptoms and is another source of systemic inflammation in COPD [2].

Obesity also affects lung function and lung volumes, and is associated with a decrease in expiratory reserve volume and functional residual capacity due to its restrictive extrapulmonary components [3,5]. In the study of respiratory function we found that FEV₁ in the study group was lower than in the comparison group and amounted to $80,3 \pm 2,09\%$ vs $84,71 \pm 2,62\%$, respectively (Table 4). Similar association between obesity and central airways obstruction as described in several studies. So, K-B.H. Lam and al., 2010, showed that abdominal obesity was associated with airway obstruction, regardless of smoking status: OR = 1.43 , 95% CI 1,09-1,88 [4]. The study N. Leone, 2009, showed that MS and abdominal obesity is closely associated with lower FEV₁ and FVC, regardless of potential confounding factors [5]. Obesity is associated with restriction of respiratory excursions with reduced lung vital capacity and increased FEV₁/FVC ratio > 70% [6]. In our study, FVC in the study group was $77,53 \pm 1,88\%$, which is slightly smaller in comparison with isolated course of CB/COPD , where this option - $78,50 \pm 2,38\%$. FEV₁/FVC ratio in patients with the association of CB/COPD and MS - $106,8 \pm 1,51\%$, which is also somewhat lower than in patients CB/COPD without the presence of MS - $110,05 \pm 1,24\%$. However, the observed differences in the parameters of respiratory function were not statistically significant.

Thus, in case of comorbidity of chronic bronchitis/COPD and MS we revealed more severe changes in the clinical manifestations. Also, our findings indicate the presence of more pronounced changes in respiratory function in patients with associated course of CB/COPD and MS.

CONCLUSIONS

1. In the combined course of CB/COPD and MS in Yakut ethnic group, we found more severe clinical manifestations in comparison with the group without metabolic syndrome, in the form of a more severe cough syndrome, more severe dyspnea, sputum gain and changes its character, increasing the frequency of exacerbations.

2. In the combined course of chronic bronchitis and chronic obstructive pulmonary disease and metabolic syndrome in Yakut ethnic group, we found that lung function compared



with isolated over these diseases were not significantly different. However, in the combined courses more pronounced disorders of respiratory function in the form of reduced forced vital capacity, decline in FEV_1 , FEV_1/FVC ratio increase $> 70\%$ were observed in our research.

Table 1

Characteristic of the cough syndrome in the study groups, %

Sign		CB/COPD + MS, Yakut n = 88	CB/COPD, Yakut n = 60	P ¹
Cough in the winter		86,4	68,3	0,008
Increased cough and sputum for 3 years		60,2	28,3	0,000
Cough intensity	no	8,0	23,8	0,003
	easy	46,6	48,3	NS
	moderate	37,5	18,3	0,003
	expressed	8,0	5,0	NS

Note: ¹p - significance of differences chi-squared Pearson

Table 2

Character of sputum in the study groups, %

Sign		CB/COPD + MS, Yakut n = 88	CB/COPD, Yakut n = 60	P ¹
Sputum production	no	20,5	65,0	0,000
	small	60,2	30,0	0,000
	moderate	18,2	5,0	0,000
	large	1,1	0,0	NS
Color	colorless	3,4	21,7	0,001
	white-gray	60,2	63,3	NS
	light yellow	18,2	8,3	NS
	green	18,2	6,7	0,001

Note: ¹p - significance of differences chi-squared Pearson

Table 3

Dyspnea syndrome and the number of exacerbations in the study groups, %

Sign		CB/COPD + MS, Yakut n = 88	CB/COPD, Yakut n = 60	P
Wheezing and whistling in the chest		38,6	23,3	0,050
Shortness of breath with wheezing		28,4	15,0	0,050
The intensity of dyspnea	no	7,8	32,8	0,000
	at moderate load	77,3	65,0	NS
	under light load	13,6	1,7	0,000
	at minimum load	2,3	0,0	NS
The number of exacerbations per year	to 1 times	33,0	66,7	0,000
	to 2 times	51,1	28,3	0,000
	3 or more per year	15,9	5,0	0,000

Note: ¹p - significance of differences chi-squared Pearson

Table 4

Indicators of spirometry

Indicator	CB/COPD + MS, Yakut n = 88	CB/COPD, Yakut n = 60	p ¹
	M±m	M±m	
FVC	77,53±1,88	78,50±2,38	0,857
FEV ₁	80,3±2,09	84,71±2,62	0,196
FEV ₁ /FVC	106,8±1,51	110,0±1,24	0,250

Note: ¹p - significance of differences chi-squared Pearson

References

1. Osakovskiy V.L., Gol'dfarb L.G., Klimova T.M., Sambuugin N., Odgerel Z., Yakovleva M.N., Ignat'ev P.M., Alekseeva L.L., Baltakhinova M.E., Timofeev G.A., Krivoschapkin V.G., Platonov F.A. Metabolicheskiy sindrom u aborigennogo naseleniya Yakutii [Metabolic syndrome in aboriginal population of Yakutia]. Yakutskiy meditsinskiy zhurnal [Yakut Medical Journal]. 2010; 2:98-102.
2. Furutate R., Ishii T., Wakabayashi R., Motegi T., Yamada K., Gemma A., Kida K. Excessive visceral fat accumulation in advanced chronic obstructive pulmonary disease. Int. J. Chron. Obstruct. Pulmon. Dis. 2011; 6:423-430.
3. Gifford A.H., Leiter J.C., Manning H.L. Respiratory function in an obese patient with sleep-disordered breathing. Chest. 2010 Sep; 138(3):704-715.
Int. J. Chron. Obstruct. Pulmon. Dis. 2011; 6:423-430.
4. Lam K.B., Jordan R.E., Jiang C.Q., Thomas G.N., Miller M.R., Zhang W.S., Lam T.H., Cheng K.K., Adab P. Airflow obstruction and metabolic syndrome: the Guangzhou Biobank Cohort Study. Eur Respir J. 2010 Feb;35(2):317-323
5. Leone N., Courbon D., Thomas F., Bean K., Jégo B., Leynaert B., Guize L., Zureik M. Lung function impairment and metabolic syndrome the critical role of abdominal obesity. Am. J. Respir. Crit. Care Med. 2009 Mar 15; 179(6):509-516.
6. Nakajima K., Kubouchi Y., Muneyuki T., Ebata M., Eguchi S., Munakata H. A possible association between suspected restrictive pattern as assessed by ordinary pulmonary function test and the metabolic syndrome. Chest. 2008 Oct; 134(4):712-718.



7. Tkacova R. Systemic Inflammation in Chronic Obstructive Pulmonary Disease: May Adipose Tissue Play a Role? Review of the Literature and Future Perspectives. Tkacova R. Mediators Inflamm. 2010; 5:859-889.
8. Torres-Sánchez I., Valenza M.C., Carrasco F., Cabrera-Martos I., Valenza-Demet G., Cano-Capellaci M. Endocrinometabolic disorders in chronic obstructive pulmonary disease. Nutr. Hosp. 2013 Jul-Aug; 28(4):1022- 1030.
9. Zutler M., Singer J.P., Omachi T.A., Eisner M., Iribarren C., Katz P., Blanc P.D. Obesity, but not undiagnosed airflow obstruction, is linked to respiratory symptoms and decreased functional capacity in adults without established COPD. Prim. Care Respir. J. 2012 Jun; 21(2):194-201.

The authors:

Borisova Ekaterina Petrovna (Borisova E.P.) - postgraduate student of the Department of internal medicine and General practice (family medicine) faculty of postgraduate education of physicians Medical Institute Federal state Autonomous educational institution of higher professional education «North-Eastern Federal University named after M.K.Ammosov», the physician of the Department of emergency medicine of Republican Hospital № 2 - Emergency medical center of Yakutsk

Address: 27 Oyunskiy street, Yakutsk, Russia, 677013

E-mail: borisovaep75@mail.ru

Kylbanova Elena Semenovna (Kylbanova E.S.) - doctor of medical sciences, professor, Head of the Department of internal medicine and General practice (family medicine) faculty of postgraduate education of physicians Medical Institute Federal state Autonomous educational institution of higher professional education «North-Eastern Federal University named after M.K.Ammosov»

Address: 27 Oyunskiy street, Yakutsk, Russia, 677013

E-mail: kyles@list.ru

Risk Group Stratification of Patients with Gastrointestinal Stromal Tumors to Determine Expediency and Duration of Adjuvant Therapy

A.G. Kornilova¹, L.M. Kogonia², V.G. Mos'kin², S.V. Mordanov³, O.S. Oksenyuk³

¹ MHCI 'The Podolsk City Clinical Hospital' <doc.kornilova@mail.ru>

² CBHCI of the MOH "The Moscow Regional Research Clinical Institute named after M.F. Vladimirsky" <lali51@yandex.ru>

³ The Rostov State Medical University

ABSTRACT

Experience of adjuvant therapy of patients with gastrointestinal stromal tumors (GISTs) has demonstrated high efficacy allowing almost two-fold increase of patients' recurrence-free survival. Currently, low risk patients after radical surgical treatment are closely followed up; moderate risk GIST patients are recommended adjuvant therapy with Imatinib for 1 year whereas those of high risk – for 3 years. This article presents the review of significant predictors, analysis of which shall let a clinical oncologist stratify patients into risk groups most precisely thus improving the efficacy of target therapy.

Keywords: gastrointestinal stromal tumors, adjuvant therapy, risk group, Imatinib

New discoveries in the area of molecular biology, immunohistochemical assay (IHA), studying prognostically significant morphological features of the malignancies' structure as well as advances of target therapy allowed developing and introducing new approaches to differential diagnosis and treatment of patients with mesenchymal tumors of the gastrointestinal tract to clinical practice.

For the first time, gastrointestinal stromal tumors (GISTs) were segregated as a separate disease only in 1983 [24]. Until that time, given neoplasms fall into the category of 'other' types of sarcomas.

GISTs belong to rare tumors accounting for 0.1- 3% of all GI malignancies; however, their proportion among all sarcomas of the GI tract is as high as 80% [29,40]. Besides, many GISTs remain unidentified: 20% of tumors present themselves the endoscopic findings or are accidentally encountered on radiological examination of the abdominal cavity; microscopic GISTs are found in 35 out of 100 patients operated on for stomach cancer; 10 unrecognized GISTs are found per 1,000 autopsies [32,20].

In a number of clinical trials, correlation between the efficacy of surgical treatment of GIST patients and degree of local spread of the disease/radicalism of a surgical intervention has been shown. Thus, the recurrence rate is equal to 35% for the localized lesion and amounting to 90% for the locally disseminated process. On an average, the 5 year-survival of patients after surgical treatment varies from 35% to 65%. Recurrences occur within two years in 80% of observations [9,34]. In case of recurrence or diagnosis of the primary non-operable/disseminated process, median survival is 10-20 months [10,36]. As a rule, surgical removal of the recurrent lesions does not lead to improved prognosis [33].

Experience of using systemic chemotherapy for treating this group of tumors has demonstrated lack of satisfactory outcomes. Most often, Doxorubicin and Dacarbazine were used. However, neither mono-chemotherapy nor most commonly used combination MAID has not been efficacious: by different authors, the response rate varied from 0% to 27% whereas overall median survival was 14-18 months [3, 35, 45]

Discovery of the major pathogenetic mechanism responsible for GIST – hyperactivation of the c-KIT receptor [17,21] – as well as results of preclinical trials of the STI-571 drug laid the foundation for assessing the effectiveness of the targeted drug Imatinib and its incorporation into broad clinical practice for treating GIST patients, which permitted twofold extension of life expectancy of this patient population [43,44].

Within the framework of a large randomized double-blinded clinical trial ACOSOG Z9001 carried out in the US that enrolled 713 patients with localized types of GISTs from 230 hospitals in the US and Canada, the efficacy of 1-year adjuvant therapy after radical surgical treatment of this patient cohort has been proven [5]. Exclusion criteria were as follows: patient age older than 18 years, tumor over 3 cm in diameter, CD117-positive tumors. Patients were divided to two groups: the first group (n=359) has been prescribed Imatinib 400 mg/day during one year; the second group (n=354) has been given placebo. It was found that adjuvant therapy with Imatinib has contributed to the improvement of recurrence-free survival indicators from 83% in the control group to 97% in the group of postoperative treatment [5]. Two-year recurrence-free survival of high-risk patients with localized GISTs turned out to be almost two times higher with Imatinib versus placebo: 77% and 41%, respectively (Table 1) [5].

Table 1

The 2-year recurrence-free survival of GIST patients by degree of risk (phase III of clinical trial Z9001)

Degree of risk	Group of Imatinib adjuvant therapy	Control group (placebo)	<i>p</i>
Low	98%	98%	0.92
Moderate	98%	76%	0.05
High	77%	41%	<0.0001

Such a significant difference in recurrence-free survival prompted a decision made by protocol's developers on unblinding study's results, and patients from the placebo group were offered treatment with Imatinib.

Results of the clinical trial ACOSOG Z9001 served as a basis for approving Imatinib as a drug for 1-year adjuvant therapy of c-kit+ GISTs in the US in 2008 and in Europe and Russia in 2009.

Similar results were obtained in a number of other clinical trials. In particular, Zhan W.H. et al. studied the efficacy of Imatinib adjuvant therapy in GIST patients at high risk of recurrence (tumor size over 5 cm and presence of 5 or more mitoses in 50 fields of vision at 400x magnification) [46]. Fifty seven patients with high risk GISTs were enrolled in this study. From 2004 to 2005, all patients underwent radical surgical treatment for the primary tumor followed by adjuvant therapy with Imatinib 400 mg/day. With median follow-up of 12 months, metastases occurred only in 2 (3.5%) patients. The median recurrence-free period was 12.8 months [46].

Within the framework of the clinical trial EORTC 62024, results of which were presented at the 2013 ASCO meeting, the efficacy of Imatinib adjuvant therapy versus surgical treatment with subsequent dynamic follow-up was studied in patients with high and moderate GIST risk. 908 GIST patients enrolled in the study were divided to two groups of 454 individuals each: in the first group, adjuvant therapy has been given for two years; in the second group, targeted therapy after surgery has not been given. By results of this trial, the 3-year recurrence-free survival in the adjuvant treatment group amounted to 84%; in the dynamic follow-up group – 66%. Upon completion of the program, investigators came to conclusion that Imatinib adjuvant therapy in populations of patients with moderate and high risk GISTs should have been given for more than 1 year [13].

In the Scandinavian multicenter prospective randomized clinical trial SSG XVIII/AIO, 2 options of duration of Imatinib adjuvant therapy of 400 high risk GIST patients were compared. Follow-up lasted for a median of 54 months. In this trial, a significant advantage of 3-year Imatinib adjuvant therapy has been found. 5-year recurrence-free survival in the group receiving treatment for three years was 66% as opposed to 48% in the group of 1-year targeted therapy. The 3-year recurrence-free survival in the group of 3-year therapy was 92% compared to 82% in the group of 1-year therapy. Tolerability of Imatinib therapy, in general, was good. A proportion of patients who quit taking Imatinib during the period of their participation in the study for any reasons excluding GIST recurrence was 26% in the 36 month adjuvant therapy group and 13% – in the group receiving Imatinib for 12 months [18].

Based on this trial, in 2012 changes have been made to the European Society for Medical Oncology (ESMO) guidelines: for patients with high risk GISTs after a radical surgical operation, Imatinib adjuvant therapy is recommended for 3 years [12].

In accordance with the International Classification of Diseases for Oncology, there are benign, dubious prognosis and malignant GISTs. There is an opinion concerning both potentially malignant nature of all GISTs and benign nature of tumors smaller than 2 cm and those with minimal mitotic activity. At the same time, cases of recurrences and metastases of any size GISTs are described [20].

At present, making diagnosis of GIST is based on morphological and immunohistochemical data. Main histological types of GIST are spindle cell (70%), epithelioid cell (20%) and mixed (10%). In the study carried out by Singler S. et al., it was found that the 5-year recurrence-free survival in the setting of spindle cell GIST amounted to 61%, epithelioid – 33%, and mixed – 23% ($p=0.002$) [41].

The Joint Working Group of the National Institutes of Health (NIH) established for studying GIST recommends using the system of determining ‘risk of aggressiveness’ that takes into consideration just tumor size and a number of mitoses in 50 representative fields of vision at x400 magnification (Table 2) [27].

Table 2.

Assessment of the GIST malignant potential

Risk level	Tumor size	Mitotic index
High	does not matter	$\geq 10/50$
	≥ 10 cm	does not matter
	≥ 5 cm	$\geq 5/50$
Medium	5-10 cm	$\leq 5/50$
	≤ 5 cm	6-10/50
Low	2-5 cm	$\leq 5/50$
Extremely low	≤ 2 cm	$\leq 5/50$

While differentiating GISTs by degree of malignancy, some authors rely upon the system of criteria suggested by the French National Federation of Cancer Centers that was developed for histological grading of sarcomas along with assessment of the severity of cell polymorphism, indicators of tumor cellularity, presence of mucosal invasion and sites of necrosis [15].

At the same time, guidelines of the European Society for Medical Oncology (ESMO) and the US National Comprehensive Cancer Network (NCCN) reflect the fact that localization of the primary tumor possesses even more significant prognostic value (Table 3) [8,11].

Table 3.

Risk of GIST progression by mitotic index, tumor size and localization

Mitotic Index (number of mitoses in 50 fields of vision)	Tumor size (cm)	Risk of disease recurrence (%)			
		Stomach	Duodenum	Small intestine	Rectum
≤ 5	≤2	0	0	0	0
	>2, ≤5	1.9	8.3	4.3	8.5
	>5, ≤ 10	3.6	*	24	*
	>10	10	34	52	57
>5	≤2	*	*	*	54
	>2, ≤ 5	16	50	73	52
	>5, ≤ 10	55	*	85	*
	>10	86	86	90	71

Note: *No accurate data is available

Significance of the primary tumor as a prognostic factor has been also demonstrated in papers by M. Miettinen. This author came to conclusion that patients with the primary tumor in their gut would have worse prognosis [27].

In 2008 in order to clarify indications for adjuvant therapy, H. Joensuu has made a suggestion to modify the classification of risk groups with consideration of primary tumor's localization (Table 4) [19].

Table 4.

Risk of GIST progression

Risk	Tumor size, cm	Mitotic index	Tumor localization
Very low	<2	≤ 5	Any
Low	2.1-5.0	≤ 5	Any
Intermediate	2.1-5.0	>5	Stomach
	<5	6-10	Any
	5.1-10.0	≤ 5	Stomach
High	Any	Any	Tumor rupture
	>10	Any	Any
	Any	>10	Any
	>5.0	>5	Any
	2.1-5.0	>5	Outside the stomach
	5.1-10.0	≤ 5	Outside the stomach

Likelihood of recurrence in 2 and 6 years after radical surgical treatment may be calculated with the use of nomograms presented in the paper by J. S. Gold: risk assessment is done by tumor size, its localization and mitotic index [14].

Besides, the ESMO guidelines recognize the importance of tumor capsule's rupture (both spontaneous and due to surgical resection) as an unfavorable prognostic factor given accompanying contamination of the peritoneum [11].

High Ki-67 proliferation index (over 10% of nuclei expressing Ki-67) and loss of expression of neurogenic and smooth muscle cell differentiation's markers by the tumor cells are also currently perceived as objective signs of unfavorable prognosis [38].

The need for accurate stratification of recurrence risk became especially pressing after the introduction of Imatinib into common clinical practice as a drug for adjuvant therapy. According to modern data, genotype of the primary GIST determining its response to Imatinib therapy is the most important predictor (Table 5) [25,26,30,39].

Table 5.

Clinical significance of various mutations of the c-kit and PDGFRa genes

Mutation site	% of all mutations	Clinical significance
c-kit, exon 11	5-15	All localizations, good response to Imatinib
c-kit, exon 9	60-70	Many tumors of the small intestine. Less sensitivity compared to exon 11 mutations; escalating the daily dose of Imatinib up to 800 mg is effective
c-kit, exon 13	1	Imatinib is efficacious
c-kit, exon 17	1	Imatinib is efficacious
PDGFRa, exon 12	1	Tumors are localized in the stomach; Imatinib is efficacious
PDGFRa, exon 14	Less than 1	Extremely rare cases
PDGFRa, exon 18	5	Stomach tumors are more common, variant D842 is sensitive to Imatinib
Wild type	10-15	Only 40% of tumors respond to Imatinib; pronounced primary resistance
GIST in children	3	Mutations in the c-kit and PDGFRa genes are absent
Carney triad	Less than 1	Mutations in the c-kit and PDGFRa genes are absent
GIST in a combination with neurofibromatosis	Less than 1	Mutations are rather absent; possible mutation in the NF1 gene

It's noteworthy that in contemporary literature controversial opinions on prognostic value of KIT exon 11 mutations are reflected. Some authors link this type of mutation to high degree of tumor's malignancy [22,42]. Others believe that KIT exon 11 mutations are frequently seen in benign GISTs [1]. However, stromal tumors of the GI tract with the KIT exon 11 mutation are the most sensitive to Imatinib: complete regression of the tumor is noted in 6% of cases; partial regression – in 61%; process stabilization – in 25% and progression – in 3% of cases [4, 37].

The therapeutic effect of Imatinib in patients with KIT exon 9 mutations is not that good: complete regression of the tumor is noted in 5% of cases; partial regression – in 29%; process

stabilization – in 47%; disease progression – in 17% of cases [4, 37]. Efficacy of this therapy is achieved through escalating daily doses of the drug up to 800 mg. It should be noted that, by literature data, there are no significant differences in survival between patients with stromal tumors with deletions in exons 9 and 11 of the KIT [28, 29, 3].

GISTs with the mutation in exon 13 of the KIT are associated with more aggressive course of the disease as opposed to GISTs with the mutation in exon 17 in patients with stromal tumors of the stomach. At the same time, clinical course of stromal tumors of the small intestine with mutations in exons 13 and 17 of the KIT gene is not different from that of other stromal tumors of the same localization [2].

GISTs with PDGFRa mutations, in general, are associated with low mitotic activity and more favorable clinical course. Most frequently, these tumors are localized in the stomach [6, 7].

Primary resistance to Imatinib is observed in patients with mutations in exon 17 of the KIT and exon 18 of the PDGFRa [4, 37].

In small groups of GIST patients, other clinical and pathological prognostically important factors have also been demonstrated. Thus, in the paper by Martin J. et al., high cellularity has been described as an independent factor of low 5-year recurrence-free survival compared to moderate or low cellularity tumors [23]. Hassan I. et al. have demonstrated in their works that prognosis in patients with clinical symptoms of the disease upon diagnosis was worse than that in asymptomatic patients [16].

By now, prognostic value of many other biological and histopathological GIST factors such as DNA ploidy, tumor necrosis, expression of CD44, insulin-like growth factor-1 & 2, retinoblastoma protein, degree of cellular atypia, expression of S-100, telomerase activity, microvascular density and lack of KIT gene expression is considered. However, due to the small size of samples and retrospective nature of these studies it's difficult to identify the impact of single clinical and pathological factors on disease course's prognosis. Besides, these indicators in the majority of observations were associated with other high risk factors (large tumor size or big number of mitoses), which further decreased independence of their prognostic value.

For intermediate risk of GIST progression, approaches to adjuvant therapy are not yet defined. Research in this area continues.

To date, importance of identifying risk factors of GIST progression for a prognostic purpose does not cause any doubts. A hefty number of clinical trials devoted to studying these signs have been conducted. Summarizing the results yielded, the largest oncology societies worldwide came to conclusion that in order to increase the duration of efficacious therapy and,

as a consequence, improve GIST patients' survival, one would need to consider a broad range of factors permitting the assessment of tumor aggressiveness.

Risk stratification is a matter of paramount importance for selecting GIST patients who are indicated adjuvant therapy with Imatinib. Assessing risk of disease progression based on the analysis of such prognostic factors as neoplasm's size, its localization, mitotic rate, rupture of the tumor capsule and mutation site shall allow more thorough dividing patients into risk groups entailing the improved recurrence-free and overall survival of GIST patients.

REFERENCES

1. Nikulin M.P. Gastrointestinal stromal tumors (GISTs). Epidemiology, diagnosis, modern approaches to treatment / M.P. Nikulin, I.S. Stilidi // *Journal of Modern Oncology. Extra issue.* – 2007.- P. 3-50
2. Snigur P.V. Stromal tumors of the duodenum / P.V. Snigur, O.A. Anurova // *Surgery.* – 2003.- № 11.- P. 46-48.
3. An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas / K. Antman [et al.] // *J Clin Oncol.* – 1993.- № 11(7). - P. 1276-1285.
4. Benjamin R.S. For the Sarcoma Intergroup. Phase III dose-randomized study of imatinib mesylate (ST1571) for GIST: Intergroup S0033 early results / R.S. Benjamin, C. Rankin, C. Fletcher // *Proc Am Soc Clin Oncol.* - 2003. - № 22. - P. 814.
5. Blackstein M.E. Risk assessment for tumor recurrence after surgical resection of localized primary gastrointestinal stromal tumor: North American Intergroup phase III trial ACOSOG Z9001/ M. E. Blackstein // *GI ASCO.* – 2010.- №6.
6. Corless C.L. PDGFRA mutations in gastrointestinal stromal tumors: frequency, spectrum and in vitro sensitivity to imatinib / C.L. Corless, A. Schroeder, D.J. Griffith // *Clin. Oncol.* – 2005. - № 23. - P. 5357–5364.
7. Daum O. Diagnostic morphological features of PDGFRA-mutated gastrointestinal stromal tumors: molecular genetic and histologic analysis of 60 cases of gastric gastrointestinal stromal tumors / O. Daum, P. Grossmann, T. Vanecek // *Ann. Diagn. Pathol.* – 2007. - № 11. – P. 27–33.
8. De Matteo R.P. Tumor mitotic rate, size, and location independently predict recurrence after resection of primary gastrointestinal stromal tumor (GIST)/ R.P. De Matteo [et al.] // *Cancer.* - 2008. - №112. - P. 608–615.

9. De Matteo R.P. Two hundred gastrointestinal stromal tumors: recurrence patterns and prognostic factors for survival / R.P. De Matteo [et al.] // Ann Surgery. – 2000. - №231. - P. 51-58.
10. Dougherty M.J. Sarcomas of the gastrointestinal tract. Separation into favorable and unfavorable prognostic groups by mitotic count / M.J. Dougherty [et al.] // Ann Surgery. – 1991. - №214(5). - P. 569-74.
11. ESMO Clinical Recommendations for diagnosis, treatment and follow-up. – 2010.- P. 147- 153.
12. ESMO Update Clinical Practice Guidelines. Ann of Oncol. - 2012.- №23.- Supplement 7.
13. European Organisation for Research and Treatment of Cancer. EORTC 62024 study protocol. Phase III randomized study of adjuvant imatinib mesylate versus observation only in patients with completely resected localized gastrointestinal stromal tumor at intermediate- or high-risk of relapse.
14. Gold J.S. Development and validation of a prognostic nomogram for recurrence-free survival after complete surgical resection of localised primary gastrointestinal stromal tumour: a retrospective analysis / J.S.Gold [et al.] // Lancet Oncol. - 2009. - №10(11). - P. 1045-52.
15. Guillou L. Prognostic factors in soft tissue sarcoma in the adult/ L. Guillou, J.M.Coindre // Ann Pathol. - 1997. - №17(6). - P. 375-377.
16. Hassan I. Surgically managed gastrointestinal stromal tumors: a comparative and prognostic analysis / I. Hassan, Y.N.You., R.Shyyan // Ann Surg Oncol. - 2008. - №15(1).- P. 52-59.
17. Hirota S. Gain-function mutations of c-kit in human gastrointestinal stromal tumors/ S. Hirota [et al.] // Science. – 1998.- №279.- P. 577-580.
18. Joensuu H. One vs three years of adjuvant imatinib for operable GIST: a randomized trial/ H. Joensuu [et al.] // JAMA. – 2012.- №307(12).-P.1265-72.
19. Joensuu H. Risk stratification of patients diagnosed with gastrointestinal stromal tumor/ H. Joensuu H// Hum Pathol. – 2008.- № 39(10).- P.1411-1419.
20. Kawanowa K. High incidence of microscopic gastrointestinal stromal tumors in the stomach/ K. Kawanowa [et al.]// Human Pathol. - 2006.- №37(12).-P. 1527-1535.
21. Kindblom L.G.Gastrointestinal pacemaker cell tumor (GIPACT): gastrointestinal stromal tumors show phenotypic characteristics of the interstitial cells of Cajal / L. G.Kindblom [et al.]// Am J Pathol. – 1998.- №152(5).- P.1259-69.

22. Lasota J. Clinical significance of oncogenic KIT and PDGFRA mutations in gastrointestinal stromal tumours /J.Lasota, M.Miettinen// Histopathology. – 2008. -№ 4.- P.4–16.
23. Martin J. Deletions affecting codons 557-558 of the c-KIT gene indicate a poor prognosis in patients with completely resected gastrointestinal stromal tumors: a study by the Spanish Group for Sarcoma Research (GEIS)/ J.Martin, J. Poveda, A.J. Llombart-Bosch //Clin. Oncol. – 2005.- №23.- P. 6190– 6198.
24. Mazur M.T. Gastric stromal tumors: Reappraisal of histogenesis/ M.T. Mazur, H.B.Clark // Am J Surg. Pathol. – 1983.-№7.- P.507-519.
25. Miettinen M. Evaluation of malignancy and prognosis of gastrointestinal stromal tumors: a review / M.Miettinen, W.El-Rifai // Hum Pathol. – 2002.- №33.- P. 478–483.
26. Miettinen M. Gastrointestinal stromal tumors in patients with neurofibromatosis: a clinicopathologic and molecular genetic study of 45 cases / M.Miettinen , J.F.Fetsch, L.H. Sobin // Am. J. Surg. Pathol. - 2006.- №30.- P. 90–96.
27. Miettinen M. Gastrointestinal stromal tumors - definition, clinical, histological, immunohistochemical, and molecular genetic features and differential diagnosis / M. Miettinen , J. Lasota // Virchows Arch.-2001.-№438(1).-P.1-12.
28. Miettinen M. Gastrointestinal stromal tumors: definition, occurrence, pathology, differential diagnosis and molecular genetics / M. Miettinen , J.Lasota // Pol. J. Pathol. – 2003.- №54.- P.3–24.
29. Miettinen M. Gastrointestinal stromal tumours: review on morphology, molecular pathology, prognosis, and differential diagnosis / M. Miettinen // Arch Pathol Lab Med. - 2006.- №130.- P.1466–1478.
30. Miettinen M. Gastrointestinal stromal tumors (GISTs) of the jejunum and ileum: a clinicopathologic, immunohistochemical and molecular genetic study of 906 cases prior to imatinib with longterm follow-up / M. Miettinen [et al.]// Am. J Surg. Pathol. - 2006.- №30.- P. 477–489.
31. Miettinen M. Gastrointestinal stromal tumors of the stomach—a clinicopathologic, immunohistochemical and molecular genetic study of 1756 cases with long-term follow-up / M. Miettinen , L.H. Sobin, J. Lasota // Am. J. Surg. Pathol. - 2005.- №29.- P. 52–68.
32. Minute gastric sclerosing stromal tumors (GIST tumorlets) are common in adults and frequently show c-KIT mutations /A. Agaimy [et al.] //Am J Surg Pathol. – 2007.- №31(1).- P.113-120.

33. Mudan S. Salvage surgery for patients with recurrent gastrointestinal sarcoma: prognostic factors to guide patient selection / S. Mudan, K. Conlon, J. Woodruff // *Cancer*. – 2000.- № 88.- P. 66-74.
34. Ng E.H. Prognostic factors influencing survival in gastrointestinal leiomyosarcomas. Implications for surgical management and staging / E.H. Ng [et al.] // *Ann Surg*. – 1992.- №215(1). - P. 68-77.
35. Pidhorecky I. Gastrointestinal stromal tumors: current diagnosis, biologic behavior, and management / I. Pidhorecky [et al.] // *Ann Surg Oncol*. – 2000.-№ 7(9).- P.705-712.
36. Plaat B.E. Soft tissue leiomyosarcomas and malignant gastrointestinal stromal tumors: differences in clinical outcome and expression of multidrug resistance proteins/ B.E. Plaat [et al.] // *J Clin Oncol*. – 2000.- № 18(18).- P. 3211-3220.
37. Raut C.P. Surgical management of advanced gastrointestinal stroma tumors after treatment with targeted systemic therapy using kinase inhibitors / C.P. Raut [et al.] // *J. Clin. Oncol*. - 2006.- № 15.- P. 2325-2331.
38. Role of Ki-67 as a prognostic factor in gastrointestinal stromal tumors / B. Belev [et al.] // *World J Gastroenterol*. – 2013. - № 19(4). - P. 523-527.
39. Rutkowski P., Nowecki Z., Nyckowski P. Surgical treatment of patients with initially inoperable and/or metastatic gastrointestinal stromal tumors (GIST) during therapy with imatinib mesylate / P. Rutkowski, Z. Nowecki, P. Nyckowski // *J Surg Oncol*. – 2006.- №93.- P. 304–311.
40. Sarlomo-Rikala M. CD117: a sensitive marker for gastrointestinal stromal tumors that is more specific than CD34 / M. Sarlomo-Rikala [et al.] // *Mod Pathol*. - 1998.- № 11(8).- P. 728-734.
41. Singer S. Prognostic value of KIT mutation type, mitotic activity, and histologic subtype in gastrointestinal stromal tumors / S. Singer [et al.] // *J Clin Oncol*. – 2002.- № 20(18).- P. 3898-3905.
42. Tarn C. Analysis of KIT mutations in sporadic and familial gastrointestinal stromal tumors: therapeutic implications through protein modeling/ C. Tarn, E. Merkel, A. A. Canutescu // *Clin. Cancer Res*. - 2005.- № 11.- P. 3668–3677.
43. Van den Abbelle A. D. 18-FDG-PET provides early evidence of biological response to STI-571 in patients with malignant gastrointestinal stromal tumors / A.D. Van den Abbelle [et al.] // *Proc Am Soc Clin Oncol*. – 2001.- № 20.- P. 362.



44. Van Oosterom A.T. Update of phase I study of imatinib (STI 571) in advanced soft tissue sarcomas and gastrointestinal stromal tumours: a report of the EORTC Soft Tissue and Bone Sarcoma Group / A.T. Van Oosterom [et al.] // Eur. J. Cancer. – 2002.- № 38.- P. 83-87.

45. Zalupski M. Phase III comparison of doxorubicin and dacarbazine given by bolus versus infusion in patients with soft-tissue sarcomas: a Southwest Oncology Group study / M. Zalupski [et al.] // J Nat Cancer Inst. – 1991. - № 83(13). - P. 926-932.

46. Znah W.H. Efficacy and safety of adjuvant post-surgical therapy with imatinib in patients with high risk of relapsing GIST. ASCO 2007, Abstr. 10045. Available at: <http://www.cancer.gov/clinicaltrials/EORTC-62024>.

The authors:

Kornilova Anush G. – doctor oncologist MUZ PGKB, graduate student of Oncology and Thoracic Surgery HFC GBUZ MO MONICA named after M.F. Vladimirsky, e-mail: doc.kornilova@mail.ru;

Kogoniya Lali M. - MD, Professor of Oncology and Thoracic Surgery HFC GBUZ MO MONICA named after M.F. Vladimirsky, e-mail: lali51@yandex.ru;

Mos'kin Valery G. – doctor Radiologist GBUZ MO MONICA named after M.F. Vladimirsky, a senior laboratory assistant Oncology and Thoracic Surgery HFC GBUZ MO MONICA named after M.F. Vladimirsky, e-mail: makmos97@yahoo.com;

Mordanov Sergey V., MD, Head of the Laboratory of Medical Genetics of the Rostov State Medical University (SEI HPE RostGMU Russian Ministry of Health), e-mail: Labmed@mail.ru;

Oksenyuk Oksana S., MD, director of the biochemical department of the Central Research Laboratory of SEI HPE RostGMU Russian Ministry of Health, e-mail: Oksenuk_o@bk.ru.

Methods of Evaluation of the Pneumonia Severity and their Comparative Analysis in the Servicemen

I.M. Borisov, T.G. Shapovalova

ABSTRACT

Objective. Comparative analysis of two-step (non-severe, severe) and three-step (mild, moderate, severe) assessment of the severity of community-acquired pneumonia in the military men.

Materials and Methods. The study included 1177 patients with pneumonia, men, and soldiers performing military service at the age of 18 to 22 years (19.2 ± 0.19).

Results. It is shown that a three-stage evaluation of the severity of pneumonia allows more adequately assess the degree of severity of the disease and thus provide not only more accurate triage on site selection of treatment, but convincingly decide on the hospitalization need and determine the most rational treatment of the disease.

Keywords: community-acquired pneumonia, assessment of severity of pneumonia.

INTRODUCTION

The problem of diagnosis and treatment of community-acquired pneumonia (CAP) continues to be one of the most relevant in the modern health care. The paradox in this case is that, on the one hand, achieved impressive results in understanding the pathogenesis of infection, to improve diagnostic methods, to improve the effectiveness of chemotherapy, the availability of modern highly effective antibacterial drugs, and on the other - is stored a large number of patients with severe disease and relatively high mortality due to pneumonia than, as before, is a leader in the structure of morbidity and mortality from infectious diseases in developed countries [15].

In Russia, the incidence of community-acquired pneumonia in 2006 was 4, 1 ‰ [3]. However, the incidence of community-acquired pneumonia in the Armed Forces of Russian soldiers performing military service, is substantially higher for the past 15 years, 30 - 45 ‰ [3, 4, 7]. Mortality in community-acquired pneumonia in adults up to 50 years without concomitant diseases in Russia is 1 - 3% of patients requiring hospitalization in the intensive care unit (ICU), it comes to 30% [3]. In the European Union, North America and Japan, the death rate from pneumonia in 2003 - 2006 years. was 50 - 60 to 100 thousand people per year [15], in Russia - 30 cases per 100 thousand population [3, 4].

M.J. Fine et al. examined risk factors for a possible death of pneumonia, with a total point

value of these parameters, such as age, sex, laboratory findings, clinical examination of the patient on admission, presence of comorbidities [11, 14]. In accordance with the greater or lesser likelihood of death were identified five risk categories (I - V). The authors concluded that patients with I and II risk category, that is, the minimum probability of a fatal outcome, can be treated as outpatients. Patients with category III need a short hospital stay. When the amount of points corresponding to the IV and V categories of risk, requires unconditional admission [11, 14]. Were formulated new approaches to the management of patients with pneumonia, in which a significant number (80%) were invited and treated without hospitalization [3, 13].

The cost of outpatient treatment, of course, much lower than fixed. For example, if the treatment of hospitalized patients in the United States in 2007 was worth an average of 5700 dollars, the patient - only \$ 300. [8]. The economic benefits are more than obvious. Especially since the cost of treating patients with pneumonia in the United States in 2006 totaled \$ 10 billion, with more than 92% of them came from hospitals [12].

Thus choice of treatment of CAP (outpatient or inpatient) is very important, including economic value. As a result, there was a replacement concept actually assess the severity of the EP on the definition of criteria (or reading) to the formulation of criteria for hospitalization and severe course of the EP with the criteria of flow, requiring hospitalization in the ICU.

CAP moderate course with low risk of adverse outcome on the merits of the question. Meanwhile, it is not heavy for the CAP, which included the mild and moderate course of the disease is about 96% of all cases of CAP. Patients who make up this major part of all cases have different clinical manifestations, the evaluation of which is of great importance when choosing the type and amount of antibiotic, detoxifying and symptomatic therapy. Adequate assessment of the severity of pneumonia is of practical importance and is not limited to sorting on site selection criteria and treatment of heavy flow.

The purpose of the study. Comparative analysis of two-stage (non-severe, severe) and three-stage (mild, moderate, severe) assessment of the severity of community-acquired pneumonia in the military men.

Materials and methods. To fulfill this goal, a comparative analysis of the results of examination and treatment of patients with pneumonia in a pulmonary department of the military hospital in the period from 2004 to 2010. In the study included 1,177 patients with pneumonia, men, soldiers performing military service at the age of 18 to 22 years ($19, 2 \pm 0,19$).

The severity of pneumonia in all patients who participated in the study, determined sequentially: first, by a two-stage criteria (non-severe and severe), and then - according to the criteria of the three-stage (mild, moderate, severe) scales. The results were called, respectively,

two-and three-stage assessment of the severity assessment of the severity of pneumonia.

For two-step evaluation of the severity were used the criteria set out in the relevant methodological guidelines of the Main Military Medical Directorate of the Russian Defense Ministry on the diagnosis, treatment and prevention of community-acquired pneumonia in the military (2003 and 2009), and practical recommendations for the diagnosis, treatment and prevention of community-acquired pneumonia in adults (2003 and 2006) [2, 3, 4, 7]. The criteria for severe pneumonia, according to the methodological guidelines for the diagnosis, treatment and prevention of pneumonia in troops in 2003 [7] were: the plight of the patient (cyanosis, confusion, delirium, fever above 39,0 C); respiratory failure (respiratory rate >30 per minute, $PaO_2 < 60$ mm Hg, $PaCO_2 > 50$ mm Hg), arterial hypotension - systolic blood pressure < of 90 mm Hg. and (or) diastolic blood pressure of 60 mm Hg; marked tachycardia (heart rate per minute > 125); leukocytosis ($> 25 \cdot 10^9 / L$) or leukopenia ($< 4 \cdot 10^9 / L$) hemoglobin < 100 g / l; hematocrit < 30 %; common extensive pneumonia or bilateral pneumonic infiltration; progressive course of pneumonia, massive pleural effusion; cavity (s) of the collapse of the lung tissue; diuresis < 80 ml for 4 h, and (or) blood urea nitrogen > 7, 0 mmol / l (or) creatinine > 176, 7 mmol / l; secondary bacteremia, meningitis, pericarditis, hematogenous infection screenings. Extras were isolated and signs dire, life-threatening pneumonia flow presented in Table. 1.

According to the guidelines of the Main Military Medical Directorate of the Russian Defense Ministry on the diagnosis, treatment and prevention of community-acquired pneumonia in the Russian Defense Ministry troops in 2009 [4], the above criteria for severe pneumonia extremely became known as the criteria for severe (Table 2).

The criteria for severe in the methodological guidance of the Main Military Medical Directorate of the Russian Defense Ministry on the diagnostics, treatment and prevention of community-acquired pneumonia among military personnel of the Ministry of Defense of Russia in 2009 [4], were similar to the criteria for severe pneumonia recommendations for diagnosis, treatment and prevention of community-acquired pneumonia in adults in 2003 and 2006) [2, 3], with the exception of hemoglobin, and hematocrit values of azotemia.

The guidelines for the treatment and diagnosis of pneumonia as the Main Military Medical Directorate of the Ministry of Defence of Russia (2003, 2009) and in adult civilian patients (2003 and 2006) emphasized that the estimates for pneumonia heavy enough as one of the following criteria [2, 3, 4, 7].

In order to determine the severity of pneumonia for three-criterion evaluation of the severity we used the criteria developed by us [5]. They are presented in Table. 3.

In contrast to the recommendations of the methodological guidelines of the Main Military

Medical Directorate of the Ministry of Defense of Russia in 2003, 2009 and in civilian medicine in adults in 2003, 2006 [2, 3, 4, 7], according to the three-stage evaluation criteria it was proposed to determine the severity of CAP on the aggregation of all the available evidence and developed criteria for mild, moderate and severe disease.

Confirmed case of pneumonia was considered the presence of specific clinical and radiographic evidence of disease. Besides of physical signs there were analyzed electrocardiogram data, parameters of common peripheral blood, urine, biochemical studies, electrolyte (potassium, sodium, serum), protein composition, the coagulation system, renal excretory function and blood gas. All patients received antibiotic and symptomatic treatment in accordance with accepted standards and clinical guidelines [2, 3, 4, 6, 7].

Statistical processing of the results of the study were performed using software package Microsoft Office Excel 2007 and Statistica 6.0 (StatSoft, Inc. 2001). For comparison of quantitative indicators used Student's t test.

Results and discussion. According to the criteria for the diagnosis of acute respiratory failure (ARF) (respiratory rate > 30 min; $\text{SaO}_2 < 90\%$, $\text{PO}_2 < 60$ mm Hg), the number of patients with severe pneumonia for two-and three-stage assessment was essentially the same: two-stage assessment of severity - 4, 8% (56 people) and a three-stage assessment of severity - 4, 6% (54 people). By hypotension when using a two-stage assessment (systolic blood pressure < 90 mm Hg., Diastolic blood pressure < 60 mm Hg) The number of patients with severe pneumonia was 4, 2% (50 persons), on a scale three-stage assessment (systolic blood pressure ≤ 90 mm Hg diastolic pressure ≤ 50 mm Hg) - 4, 6% (54 patients). Thus, the criteria for acute respiratory failure and hypotension both systems rated severity of pneumonia showed similar results .

According to X-ray examination of the chest cavity, most of the patients (999 men; 84, 9%) in the inflammatory process involved only one segment, two and three segments - respectively in 164 people (13, 9%) and 14 (1, 2%) .

Pneumonic infiltrates were found in the lower lobe of the lower lobes of both lungs - 45 patients (3, 8%) in the upper lobe of the left and light in the middle right lung lobe - in 22 persons (1, 9%), the upper lobe of the left lung and the lower lobe of the right lung - in 27 persons (2, 3%), in the lower lobe of the left lung and the right middle lobe lung – in 14 patients (1, 2%).

Share a lot of lung damage among patients studied were found. The two share loss was observed in 108 people (9, 2%). If the criterion of "Two and a lot of equity of interstitial lung disease" on a scale of two-stage evaluation of the severity of patients with severe pneumonia was 108 people (9, 2%), then the scale of the three-stage assessment of the severity of these patients

were distributed as follows: mild course was in 69 people (63, 9%), moderate - in 36 people (33, 3%) and severe - in 3 people (2, 8%). Thus, by destruction of lung tissue of patients with severe when using the three-step evaluation of the severity scale was significantly less (54 pers.; 4, 6%) and corresponded to the number of patients with severe pneumonia criteria for acute respiratory failure and hypotension.

The correlation between the volume of infiltrative changes in the lungs according to radiography and the severity of the patient's condition is often absent. Thus, the practical experience so far shows that even minor radiological manifestations at the onset of pneumonia in the future may develop severe illness. Therefore, if properly assess the severity of pneumonia at the onset of the disease, focusing only on a small area of destruction of lung tissue in the future may develop life-threatening complications of the disease - infectious-toxic shock and acute respiratory failure due to incorrectly chosen tactic of the patient. At the same time, extensive inflammatory infiltration of the patient's condition may not significantly suffer, not objectively detect signs of severe pneumonia and not cause risk of developing complications, which confirmed the results of the use of a three-stage evaluation of the severity scale.

Leukopenia ($<4 \times 10^9 / L$) in the primary results of the study of peripheral blood was diagnosed only three people (0, 3%). These patients were admitted to hospital in a satisfactory condition, complaining of a rare unproductive cough without fever and other symptoms of infectious intoxication, with no signs of acute respiratory and circulatory failure and criteria of the scale three-stage evaluation of the severity of pneumonia among them was defined as mild, but on the scale of a two-stage assessment of severity as severe. However, no other criteria for severe pneumonia in these patients were found and white blood cell count returned to normal within the first 2 days after admission. Therefore, in view of the clinical picture, data, physical examination, and results of instrumental studies of the disease in the final version were considered easy. Leukocytosis as pneumonia severity criterion is not considered two-stage assessment of the severity [2, 3, 4], while the scale three-rated severity of [5], this figure, in most cases correlated well with disease severity. So, on a scale three-stage assessment of the severity of leukocytosis to $10 \times 10^9 / L$ was detected in 792 people (67, 3%), 10 to $20 \times 10^9 / L$ with a shift to the left leukocyte counts - in 337 people (28, 6%) and over $20 \times 10^9 / L$ toxic grit – 48 (4, 1%). Thus, to evaluate how severe pneumonia only one of the criteria, as required by a two-stage range [2, 3, 4] apparently impractical. There was an obvious need for a set of criteria to determine the severity of community-acquired pneumonia.

For an objective assessment of the patient's consciousness on a scale of severity we used a two-stage evaluation process recommended in the methodological guidelines of the Main

Military Medical Directorate of the Russian Defense Ministry on the diagnosis, treatment and prevention of pneumonia in military personnel (2003) [7]. To this end, we use the special scale H. Quereshi, H. Hodgkinson (1974), as amended by Stratchounski L.S. (2002), which includes 10 questions, the correct answer to each of which was estimated at 1 point. Amount of ≤ 8 points indicates a violation of consciousness. Questions asked by the patient, according to this scale: 1) age, 2) date of birth, and 3) the time (within hours), and 4) a year, and 5) the name of the hospital, and 6) the ability to recognize two people (eg, doctor, nurse) 7) address; 8) the date of the beginning of the Great Patriotic war, 9) the name of the President of the Russian Federation, 10) countdown from 20 to 1.

In our study, almost one-third of the patients (345 people, 29, 3%) scored less than 8 points, and, therefore, should be attributed to the group of patients with severe disease, as found signs of "disturbance of consciousness" [2, 3, 4]. Most often, patients, due to their low educational level, and made mistakes in questions 3, 5, 8, 9 and 10. However, during the observation and treatment, with a comprehensive evaluation of data and objective examination of the results of instrumental studies treat for pneumonia in 291 (24, 7%) patients had a severe extremely difficult. Severity of intoxication was defined as a minimum, acute respiratory and cardiovascular failure were absent, complications of the disease was not. When using a three-step scale assessing the severity of mild euphoria in patients was observed only in 10.7% of cases (126 pers.), and the confusion of all diagnosed in 14 people (1, 2%). Thus, the criterion of "disturbance of consciousness" is used as the sole criterion for assessing the severity of PE and defined in points on a special scale, may also contribute to an erroneous evaluation of the severity of CAP.

Patients with extrapulmonary foci of infection (meningitis, brain abscess, etc.), acute renal failure (anuria, blood creatinine > 0.176 mmol / L, urea nitrogen > 7.0 mmol / L) and anemia (hemoglobin < 100 d/l, hematocrit < 30 %) of the patients included in the study, was not.

When using a three-stage evaluation of the severity scale, based on a comprehensive analysis of all the criteria of severity of pneumonia at the time of admission to hospital for lung diseases were reported in significantly more patients (712 people, 60, 5%) than moderate and severe (respectively at 411 people., 34, 9 % and 54 people, 4, 6 %, $p < 0.01$ (χ^2). Using a two-stage evaluation of the severity scale, with a recommendation to regard the disease as severe if at least one criterion, showed different results: the so-, severe pneumonia was found in 427 people. (36, 3%). Due to the fact that the criteria for non-severe pneumonia flow on a scale two-stage assessment of severity are not differentiated, then it must be assumed that they are all left outside the heavy currents, the is – 750 people) (63, 7 %).

Feature of our study was the participation of patients with pneumonia, soldiers performing

military service. For this category of people is a mandatory hospitalization in case of pneumonia, and this gave us the opportunity to analyze the course of the disease including those patients who are on the scale of a two-stage evaluation of the severity of medicine in the civilian sector may be treated as outpatients. As a result of 712 people (60, 5%), who at the time of admission were recorded for lung pneumonia on a scale assessing the severity of a three-stage, 17 patients (1.4%) diagnostic views on the severity of the disease during the follow-up of the first two days have changed and the disease has been disease interpreted as moderately. On the contrary, for pneumonia in 13 patients (1, 1%), with the primary inspection deterministic as moderately, in the future, during the first day of observation, was seen as a slight. Of the 411 people (34, 9%), whose admission to hospital for pneumonia was diagnosed moderate scale three-stage assessment of severity, the next day the state has been revised as severe in 11 people (0, 9%), which required the translation of these patients in the intensive care unit. Therefore, if you do not differentiate between mild and moderate of pneumonia, assess disease only as "non-severe" and advise patients to outpatient treatment without proper medical supervision, not taking into account the possibility of adequate care and treatment in an outpatient setting, there are cases with exacerbation of pneumonia, which is equivalent in importance late admission. According to our data [1], during the first two days of the onset of the disease in the hospital received up to 3, 6% of patients with severe pneumonia, then on the third day the percentage of such patients increased to 8, 6 % and 4-th it has already reached 11, 8%. It is established that the hospital on the third and on the fourth day of onset of pneumonia during the weigh down 5% and 8, 2%, respectively, $p < 0, 05 (\chi^2)$ [1].

Conclusion. One of the reasons that the mortality from pneumonia still is one of the first places a leading cause of death from infectious diseases has traditionally holds the 1st place [15], and this is despite the availability of highly effective antibiotics, may be in the among other things, an inadequate system of assessing the severity of pneumonia. The desire to preferential treatment of pneumonia in an outpatient setting, with the aim of reducing insurance premiums, delaying hospitalization, lack of adequate medical supervision of the patient may also contribute to weighting of the patient, the development of life-threatening complications with the consequent fatal.

Patients, the severity of the pneumonia which qualifies under the three-stage system as a mid-weight, two-step on the scale is usually assessed as non-severe, and patients are encouraged to outpatient treatment. But after a while, after failure of outpatient, but significantly cheaper treatment, these patients swell group of patients with severe, complicated course of the disease and that they tend to require ICU admission and increase the percentage of deaths in pneumonia.

This circumstance is connected and the highest mortality from pneumonia among men of working age [3]: severe illness is diagnosed, the patient is not hospitalized, is assigned to outpatient treatment, and the patient often continue working as long as the disease does not acquire a severe course.

Most importantly, what convinces clinical experience in the diagnostic process need to be defined disease severity. Moreover, a more detailed examination of any pathology, including the CAP, and promotes a more accurate assessment of its clinical manifestations. Any simplification, including the separation of pneumonia only a mild and severe, leading to the erosion of the task of evaluating the severity of the disease and the inevitable, in view of this, errors.

If many authors [9, 11, 14] recommend distinguish three groups of patients with pneumonia (ambulatory patients requiring hospital treatment and indications for hospitalization in intensive care units), the stratification of the severity of the disease involves yet only two options - either heavy or non-severe. Obviously, using the three-stage assessment of the severity of pneumonia would eliminate this drawback. In this case, patients with mild pneumonia could be recommended outpatient treatment, patients with moderate course - admission to the therapeutic (pulmonology) department, and patients with severe disease were sent to the ICU.

Conclusions.

1. Sorting pneumonia severity considering only one criterion, a two-stage scale according to the recommendations are insufficient and could lead to an incorrect evaluation of the severity of the disease, indicating the need for comprehensive analysis of all clinical criteria.

2. Using a three-step scale provides a more accurate triage site selection treatment.

References

1. Borisov I.M. Shapovalova T.G. Pnevmonia u vakcinirovannich pnevmococcovoy vaccinoj [Pneumonia in vaccinated with pneumococcal vaccine]. Saratov, 2012. 190 p.
2. Chuchalin A.G., Sinopalnikov A.I., Jakovlev S.V. Vnebolnichnaja pnevmonia u vzroslich: prakticheskie rekomendacii po diagnostike, lecheniu I profilaktike [Community-acquired pneumonia in adults: guidelines for diagnosis, treatment and prevention] Clin. Mikrobiologija I antimicrobnaja chimioterapija [Clin. Microbiology and antimicrobial. Chemotherapy]. 2003, № 5, pp. 198 - 224.
3. Chuchalin A.G i dr. Vnebolnichnaja pnevmonia u vzroslich: prakticheskie rekomendacii po diagnostike, lecheniu I profilaktike [Community-acquired pneumonia in adults: Practical guidelines for the diagnosis, treatment and prevention]. Moscow: Izdatelskiy dom M-Vesti [Publishing house M-News], 2006, 76 p.
4. Diagnostika, lechenie I profilaktika Vnebolnichnoy pnevmonii u

voennosluzaschich MO RF: metodicheskie rekomendacii GVMU MO RF [Diagnosis, treatment and prevention of community-acquired pneumonia in servicemen of the Russian Federation Ministry of Defense: Defense guidelines Main Military Medical Management of the Russian Federation Ministry of Defense]. Moscow, 2009, 53 p.

5. Borisov I.M., Kraynyuk P.E., Shapovalov T.G., Borisova M.S. Patent 2458626 RU, (51) IPC A61V 5/0205 (2006.01) Sposob otsenki stepeni tajzesti pnevmonii [A method for assessing the severity of pneumonia]. № 2011109430/14; Zajavleno [Stated] 11.03.2011, Opubl. [Publ]. 20.08.2012, Bull. № 23.

6. Standarti (protokoli) diagnostiki i lechenija bolnich s nespecificheskimi zabolevaniami legkich: prikaz MZ RF 9.10/1998 № 300 [Standards (protocols) diagnosis and treatment of patients with nonspecific lung diseases: an order from the Russian Ministry of Health] 9.10.1998 № 300 Biblioteka jurnala kachestvo medicinskoy pomoshi [Library Journal, Quality of care] № 1. Moscow: Grant, 1999, 40 p.

7. Ukazania po diagnostike, lecheniu i profilaktike vnebolnichnoy pnevmonii u voennosluzaschich: metodicheskie ukazaniya GVMU MO RF [Guidelines for the diagnosis, treatment and prevention of community-acquired pneumonia in the military: Defense guidelines Main Military Medical Management of the Russian Federation Ministry of Defense]. Moscow, 2003, 79 p.

8. Ambrose P. G. Bhavnani S.M. Owens R.S. Antimicrobial Pharmacodynamics in Theory and Clinical Practice. New York, NY: Informa Healthcare, 2007. - pp.177-188.

9. American Thoracic Society. Guidelines for the management of adults with community-acquired pneumonia. Diagnosis, assessment of severity, antimicrobial therapy, and prevention. Am J Respir Crit Care Med, 2001, pp. 1730 – 1754.

10. Dambrava P.G. Torres A. Valles X. Adherence to guidelines empirical antibiotic recommendations and community-acquired pneumonia outcome. Eur. Respir. J., 2008; pp. 892 – 901.

11. Fine M. J. Auble T.E. Yealy D.M. A prediction rule to identify low- risk patients with community-acquired pneumonia. N. Engl. J. Med., 1997. Vol. 336. pp. 243 – 250.

12. Mandell L.A. Wunderink R.G. Anzueto A. Infectious Diseases Society of America/ American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis., 2007. Vol.44. pp. 27-72.

13. Metersky M. L. Community-acquired pneumonia: process of care studies. Curr Opin Infect Dis, 2002, № 15, pp. 169-174.

14. Metlay J P. Fine M. J. Testing strategies in the initial management of patient with



community-acquired pneumonia. An Intern Med, 2003; № 138, pp. 109-118

15. National Vital Statistics Report. Vol. 57, Number 14, April 2009. Deaths: Final Date for 2006. Centers for Disease Control and Prevention.

Available at www.cdc.gov/nchs/data/nver/nver57/nver57_14pdf

The authors

Borisov Igor Michaylovich, PhD (Candidate of Medicine)

Head of Pulmonology, Branch №12 1602 District Military Hospital, Znamensk, Russia

Address: 416540, Astrakhan Region, Znamensk, st. Lenin, 31

Phone: 8(85140)22762, mobile phone: 8902 1113 492.

E_mail: askbo@mail.ru.

Shapovalova Tatjana Germanovna, Doctor of Medicine

Razumovsky Saratov State Medical University, Professor of Department of Therapy of Pediatric and Stomatological Faculties, Saratov, Russia

Address: 410012, Saratov, st. Bolshaja Kazachja, 112

Phone: 8(8452)502396, mobile phone: 8927 1058 499

E_mail: t.g.shapovalova@gmail.com.

Features of the Skin and Fascia Structure in Patients with Ventral Hernias

S.V. Ivanov, G.M. Sukhov, I.S. Ivanov, A.V. Tcukanov, G.N. Goryainova, G.E. Obedkov,
I.A. Ivanova, G.N. Gafarov

ABSTRACT

Nowadays ventral hernias still remain the actual problem of abdominal surgery. The disorders of collagen formation and collagen types ratio in the connective tissue play the major role in the pathogenesis of ventral hernias. The peculiarities of collagen structure in the skin and aponeurosis were investigated in 95 patients with and without ventral hernias. All patients were divided in two groups.

The first group included 46 patients, suffering from the anterior abdominal wall hernias, the patients of the second group presented no signs of hernia disease or signs of connective tissue dysplasia.

The specimens of the skin and aponeurosis were taken during planned surgical operations. They were used for the investigation of the quality contents of the connective tissue collagen fibers. The specimens were stained with Sirius Red dye, and investigated with the usage of polarization microscope Altami Polar 2, magnification $\times 250$ и $\times 400$, in ordinary and polarization regimes. Photos of microspecimens were made with digital ocular camera Altami 3 Mpx., there were taken 10 fields of view in each magnification. Analysis of the results was fulfilled with MS Excel program.

The investigation of collagen fibers presented the heterogeneity of their structure. In each bunch of fibers there were found longitudinal fibrillation. The comparison of the results of aponeurosis architecture investigation in patients with anterior abdominal wall pathology revealed that in the control group (patients with ventral hernias) collagen fibers are localized in different directions and plans in 42% of all cases, in 53% the collagen fibers were branching in separate thin fibers, in 63% of the main group patients interfiber spaces are significantly more in sizes in comparison with the aponeurosis architecture in patients of the control group (without ventral hernias). The patients with the hernias of the anterior abdominal wall possess lower index of collagen fibers density and interfiber spaces in the skin in comparison with patients without this pathology.

The collagen fibers of aponeurosis in patients with ventral hernias possess more porous structure. This causes weakness of the anterior abdominal wall and leads to hernia defects formation.

Keywords: ventral hernia, polarization microscopy, collagen.

INTRODUCTION

Surgical treatment of ventral hernias (VH) still remains the actual problem of the modern abdominal surgery. During the last years one can observe the tendency towards the increase in the rate of hernias in general structure of surgical pathology. Technical mistakes can lead to relapse of the disease in 14 – 54% of all cases. Up to 25% of the operations, performed in surgical departments are hernioplastics. Among them 22% are the operations in case of VH, about 35% of them are fulfilled in emergency due to infringement. VH of the anterior abdominal wall is a comparatively frequent pathology, complicating laparotomy in 10-13% [3,4,8,11].

In aging the rate of the middle VH increases, and contributes from 57 to 83% of all post operation anterior abdominal wall hernias. Nowadays the results of VH treatment are not satisfactory, despite using of the new surgical technologies.

It was pointed the considerable role of collagen metabolism in the mature connective tissue formation and in the possible further VH development. The disorders can influence upon the characteristics of the connective tissue, contributing to reparative processes in the focus of hernioplastics, in the postoperation scar formation, and thus to the development and relapse of hernias [5,6,10].

Nowadays there are no exact, approved with scientific research indications for different types of plastics, accounting the grade of the connective tissue dysplasia. Thus it is still actual a choice of the method of different localization hernias treatment.

In surgical treatment of the patients with VH the methods including using of synthetic materials are the most effective. However, despite the results of VH treatment have been improved in case of plastics without intention and with using of synthetic materials, there are certain problems of the synthetic endoprosthesis and the method of surgical treatment choice [1,2,7,9].

The purpose of investigation: to reveal the differences of collagen fibers structure in skin and aponeurosis of patients with VH and without VH.

MATERIALS AND METHODS

The research is based on the investigation of the skin and aponeurosis structure in 95 patients, examined and treated from 2010 till 2012 years in clinics of surgical diseases № 1 of Kursk State Medical University based in Kursk Regional hospital.

There were examined 30 males (31,6%) and 65 females (68,4%). The control group (group № 1) presented 46 patients with VH, (group № 2) group of investigation or main group consisted

of 49 patients without VH. The patients of the second group were operated on due to complications of cholelithiasis.

For microscopic examination the pieces of the skin and aponeurosis were taken in planned operations. In the specimens there was examined quality content of the connective tissue collagen fibers. The specimens were stained with Sirius Red and examined by the ordinary light and by the light of polarization with the help of polarization microscope Altami Polar 2, of $\times 250$ and $\times 400$ magnifications.

The comparison of the histological structures was performed with microscope $\times 400$ magnifications, as it helps to visualize all structures the best way. The photos of microspecimens were taken with ocular camera Altami 3 Mpx., there were taken 10 fields of view with microscope different magnification. The statistics of the results was performed with the help of Microsoft Excel-2003 supplements and Statistica 6.0 program.

There were determined quantity index (M), the standard error of mean (m), and standard deviation (σ). The significance of mean differences was estimated with Student index. Correlation analysis was performed with using of ranging correlation Spirman's index. Critical level of significance (p) was 0,05.

RESULTS AND DISCUSSION

The examination of histological specimens of control group patients (without VH), stained with Sirius Red in polarization light (pic. 1, a,b), revealed that bunches of collagen fibers are arranged in several layers, and wavy bunches are parallel to each other. The collagen fibers of bunches go from one layer to another, connecting them.

Architecture of the skin and aponeurosis in patients with VH possesses certain peculiarities (pic. 2, a, b). There is a lot of not properly arranged collagen fibers of different directions and are localized in different planes.

In examination of the collagen fibers and interfiber spaces density in the skin specimens with the help of ImageJ2x program, there were got the following results: in patients of the 1 group the collagen fibers density is $259,4 \pm 48,3$ pixel/inch; and interfiber spaces density is $178,2 \pm 30,4$ pixel/inch; In patients of the 2 group (without VH) the collagen fibers density is $362,8 \pm 39,7$ pixel/inch; and interfiber spaces density is $266,8 \pm 51,3$ pixel/inch; (table) in equal optic magnification.

In patients with VH the interfiber spaces density is $178,2 \pm 30,4$, and in patients without VH it is significantly higher - $266,8 \pm 51,3$ ($p \leq 0,05$) (pic. 3,a).

At the same time in comparison of the collagen fibers density it is revealed that in patients with VH their density is $259,4 \pm 48,3$, and in patients without VH it is $362,8 \pm 39,7$. Thus, in patients without VH the collagen fibers density is significantly higher ($p \leq 0,05$) (pic. 3,b).

In investigation of aponeurosis specimens stained with Sirius Red by the light of polarization collagen fibers are of 1 to 2 micrometers in patients of main group (without VH) (pic. 4, a). In patients of the group with VH microscopic examination presents thinning of collagen fibers and widening of interfiber spaces (pic. 4, b).

CONCLUSION

Analysis of the results of the aponeurosis architecture examination in patients with the anterior abdominal wall pathology revealed that in the group of patients with VH in 42% of specimens collagen fibers are of different directions and are localized in different planes. In 53% of specimens collagen fibers are branching into thin fibers of 1-2 micrometers. In 67% of the control group cases the specimens demonstrate wider interfiber spaces in comparison with the architecture of the aponeurosis in the main group (patients without VH). Patients with VH possess less index of collagen fibers density in the skin than the patients without this pathology.

The results of investigation present the significant differences in the architecture of the connective tissue structural elements of the anterior abdominal wall in patients with VH in comparison with patients without VH. These differences are important for understanding of the disorders of the aponeurosis, which provides structural and functional characteristics of the anterior abdominal wall. Thus, it is causative to use preoperation diagnostics with the help of polarization microscopy.

REFERENCES

1. Bagirova A.R. Aspekty abdominoplastiki [Aspects of Abdominoplasty] Hirurgija [Surgery]. 2001, № 1, P. 64-66.
2. Bogdanov D.Ju., Rutenburg G.M., Naurbaev M.S. Sravnitel'nye harakteristiki gernioplastik pri posleoperacionnyh gryzhah zhivota [Comparative characteristics of gernioplastics in postoperative abdominal hernias] Jendoskop.hirurgija [Endoscop. Surgery]. 2008, № 6, P. 3-13.
3. Vol'nyj S.V. Kliniko-morfologicheskie osobennosti pahovyh gryzh v svete narushenij kollagenovogo obmena: avtoref. dis. ... kand. med.nauk [Clinical-morphological characteristics of inguinal hernias in the disorders of collagen metabolism: PhD thesis]. Moscow, 2010.

4. Gorskij V.A., Agapov M.A., Ovanesjan Je.R. Metody predotvrashhenija obrazovaniya gryzh posle laparoskopicheskoyholecistjektomii [Methods of hernias prevention after laparoscopic cholecystectomy] Vestn. Gerniologii [Herniology Herald]. Moscow, 2008, p. 57-61.
5. Kuchkin Ju.V., Kutukov V.E., Pecherov A.A., D.Ju. Shpeht. Sposoby alloplastiki bol'shikh i gigantskikh posleoperacionnykh gryzh [Methods of large and giant postoperative hernias alloplastics] Gerniologija [Herniology]. 2005, № 1, p. 30-32.
6. Nikitin V.N., Perskij E.S., Utevskaia L.A. Vozrastnaja i jevoljucionnaja biohimija kollagenovykh struktur [The Age and evolutionary biochemistry of collagen structures]. Kiev: Naukova dumka, 1977, 297 p.
7. Pushkin S.Ju., Belokonev V.I. Rezul'taty lechenija bol'nykh sredinnoj ventral'noj gryzhej s primeneniem sinteticheskikh jendoprotezov [Results of treatment of patients with the median ventral hernia with synthetic implants] Hirurgija. Zhurn. im. N.I. Pirogova [Surgery. N. I. Pirogov]. 2010, № 6, p. 43-45.
8. Rastegaev A.V. Vybor sposoba ustraneniya posleoperacionnoj ventral'noj gryzhi: avtoref. dis. ... kand. med. nauk [Selection of ways to avoid postoperative ventral hernia: PhD thesis]. SPb., 2009, 24 p.
9. Serov V.V., Shehter A.B. Soedinitel'naja tkan' (funkcional'naja morfologija i obshhaja patologija) [Connective tissue (functional morphology and pathology)]. Moscow: Medicina, 1981, 312 p.
10. Timoshin A.D., Jurasov A.V., Shestakov A.L. Konceptija hirurgicheskogo lechenija posleoperacionnykh gryzh perednej brjushnoj stenki [Concept of surgical treatment of postoperative abdominal hernias]. Gerniologija [Herniology]. 2004, № 1, p.5-4.
11. Toskin K.D., Zhebrovskij V.V. Lechenie posleoperacionnykh gryzh perednej brjushnoj stenki s primeneniem transplantatov tverdoj mozgovoju obolochki [Treatment of postoperative abdominal hernias with the use of grafts of dura mater]. Klinich. Hirurgija [Clinical surgery]. 1979, № 5, p. 67.

The authors:

Department of Surgical Diseases №1, "Kursk State Medical University", Kursk, Russian Federation:

1. Ivanov S.V., Professor, MD, E-mail: sv.ivanov@rambler.ru;
2. Suhov G.M., Assistant, E-mail: hernia2009@mail.ru;
3. Ivanov I.S., Associate Professor, MD, E-mail: ivanov.is@mail.ru;
4. Cukanov A.V., Ph.D., Assistant, E-mail: tsandrej@yandex.ru;

5. Goryainova G.N., Ph.D., Associate Professor, Gorjainovagn @ kursksmu.net;
6. Obyedkov E.G., clinical intern, E-mail: evgenij-obodkov @ yandex.ru;
7. Ivanova I.A., Ph.D., Associate Professor, E-mail: ia.ivanova@mail.ru;
8. Gafarov G.N., PhD, postgraduate student, E-mail: doktor_h@mail.ru.

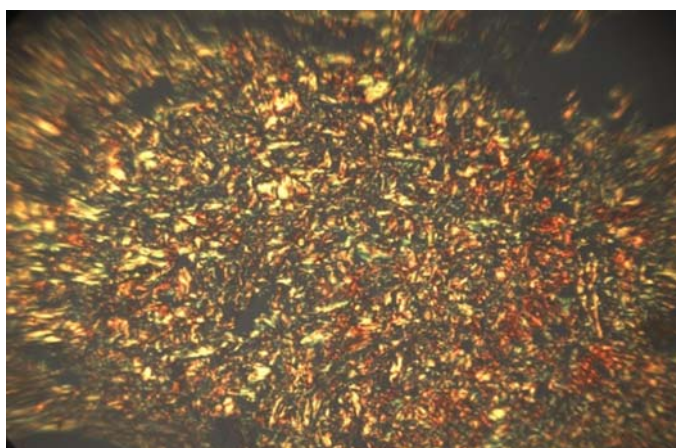


Fig. 1a. Microscopic picture of skin specimen (patient without VH). Sirius Red staining. X 400.

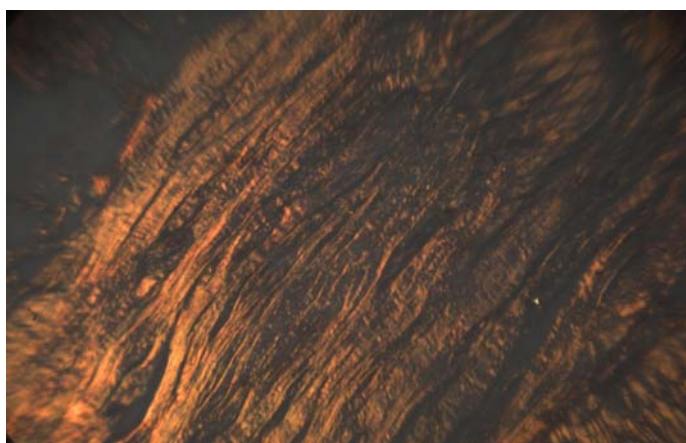


Fig. 1b. Microscopic picture of aponeurosis specimen (patient without VH). Sirius Red staining. X 400.

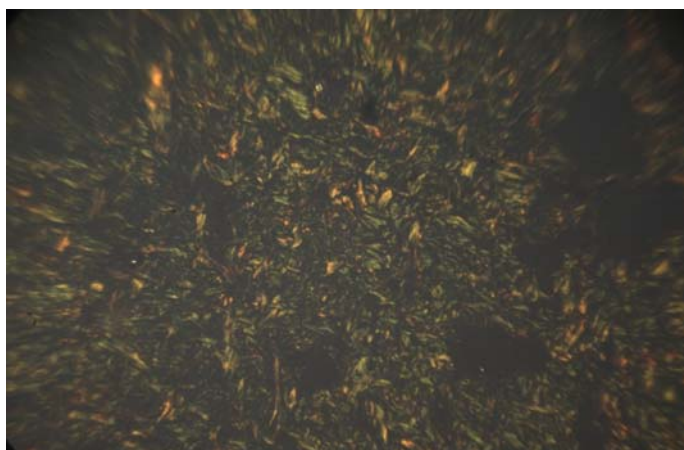


Fig. 2a. Microscopic picture of skin specimen (patient with VH). Sirius Red staining. X 400.

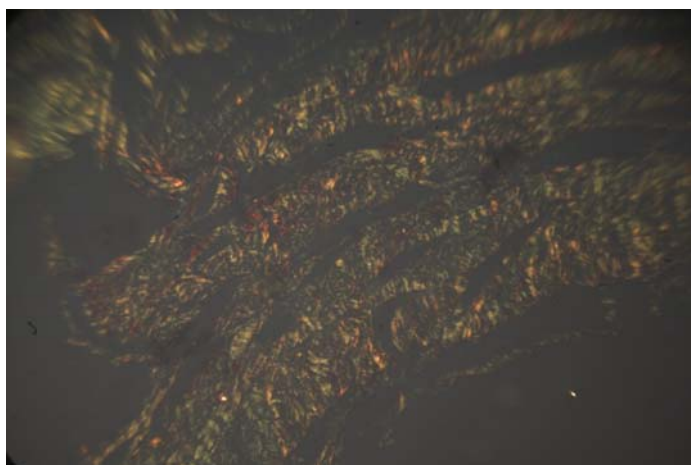


Fig. 2b. Microscopic picture of aponeurosis specimen (patient with VH). Sirius Red staining. X 400.

Table 1.

The density of the collagen fibers and interfiber spaces in the skin of patients

Note: «*» - the differences are significant, $p < 0,05$.

Group of patients	density of the collagen fibers (pixel/inch)	density of interfiber spaces (pixel/inch)
1 - Patients with VH N = 46	259,4±48,3*	178,2±30,4*
2 – patients without VH N = 49	362,8±39,7*	266,8±51,3*

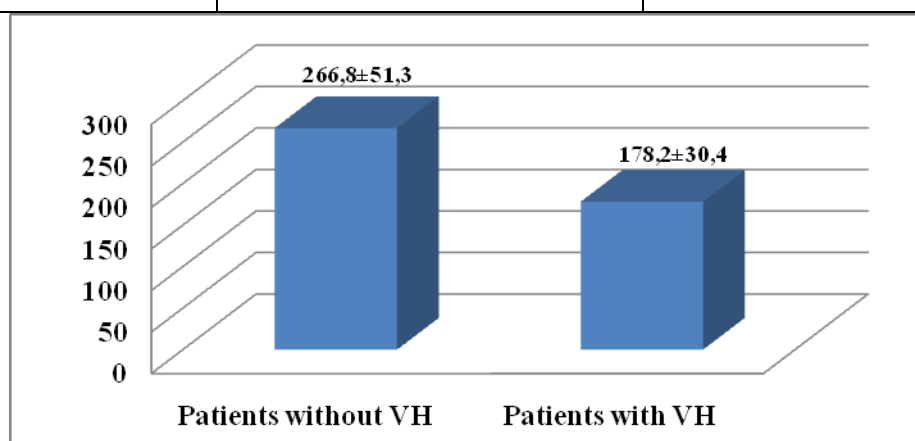


Fig. 3. Density of interfiber spaces in the skin of patients with VH and without VH (pixel / inch).

Features of Orthopedic Treatment of Dentition Defects of HIV -Infected Patients with Fixed Structures

Chizhov Yu.V., Ushnitsky I.D., Plonina V.S., Baginski A.L., Kazantseva T.V., Varlamov P.G.

ABSTRACT

In 100 HIV-infected men aged 20-25, who need prosthetics, with generalized forms of periodontitis and candidal glossitis / stomatitis special antifungal therapy of oral mucosa was conducted. Application of this technique has allowed increasing the effectiveness of orthopedic treatment of patients, as well as at orthopedic treatment stages, and at the control examinations after 4-6 months. With this technique inflammations, bleeding, soreness of the oral mucosa were eliminated or significantly reduced, a fungal infection was eliminated.

Keywords: HIV-infected patients, orthopedic treatment of dentition defects, special preparation of the oral mucosa to prosthetics.

INTRODUCTION

The current epidemiological situation of HIV infection in the Russian Federation is characterized by the increasing number of newly diagnosed patients infected with HIV, at varying ways of transmission. In this regard, HIV infection has become a major health and social problem, since in addition to the direct social values - the illness and death of millions of people, AIDS is also an economic and political damage, which allowed the infection to be one of the most important modern sociopathies. Infection of young people with above mentioned infections viruses leads not only to a quantitative increase in the incidence of HIV infection, but also has important medical and social importance, since the HIV-infected remain long-term asymptomatic sources of infection and die from AIDS in the fertile and working age. [5,6].

Pathogenesis of HIV infection. When HIV infects the body, it affects a number of very important cells, including CD4 (T-lymphocytes), in which it multiplies. When a cell is infected, it ceases to function normally, and after HIV reproduces itself, it can destroy the cell. This virus infects not only CD4, but it is important for the control of cell infection. Number of CD4 - the main indicator of immune health with HIV. When most CD4 cells are infected or destroyed, the body loses its ability to resist severe and life-threatening diseases [1,3,6]. It is known that HIV-infected, against secondary immunodeficiency activated conditionally pathogenic flora,

contributing to the development of infectious diseases. Lesions in the oral cavity are the earliest and most important indicators of HIV infection (table).

It is known that the most early and compulsory sign of the manifestation of HIV - infection is a manifestation of it in the mouth [4]. So among the earliest widespread HIV indicator diseases include HIV - associated periodontal diseases, which are characterized by a rather persistent and prolonged course resistant to conventional treatment [5,6]. Clinical sign of HIV periodontitis is bystroprogressirovannaya destruction of alveolar bone and periodontal tissue. With severe inflammation, pain, spontaneous gingival bleeding in Figure 1 (left), joining a fungal infection in Figure 1 (right), contributes to the development of resistance to conventional therapies.



Figure 1. Lesions in the oral cavity at HIV- infection: left - gingival bleeding, right - a fungal infection.

The orthopedic treatment of inflammation of the gums could complicate the process of preparation for a crown, especially the establishment of the ledge, removing double impression silicone masses, and then fixing bridges. These complications ultimately lead to a decline in the quality of prosthetics. In addition, significant bleeding gums can lead to viral contamination print and prosthesis in the intermediate stages , creating a risk of infection and the doctor equipment .

The purpose of research - to improve orthopedic treatment of dentition defects in HIV-infected , by special preparation of the oral mucosa to prosthetics.

MATERIALS AND METHODS.

100 HIV-positive at the age of 20-25 years male were surveyed. Of the surveyed revealed that 88 people (88.0 %) need prosthetics fixed prosthesis, 12 (12.0%) men do not need prosthetics. Dental status was assessed by conventional research and classifications instrumental inspection of the oral cavity and periodontal status. To estimate the prevalence and intensity of caries, periodontal disease oral hygiene status was used : the index of the intensity of dental caries (CPU) and hygiene index, the index needs in the treatment of periodontal disease - CPITN. Dentition examination determined by classification AI Gavrilova. All the examinees performed microscopic smears for the presence of oral fungi of the genus *Candida*. Number of needy people in the prosthesis 88 (100.0 %) identified two groups: basic 45 patients (51.1 %) and a control group of 43 people (48.9 %). After a dental examination and selection of prosthetic performed oral hygiene, occupational health. Further, patients of the main group received the following training : application to the oral mucosa p- m -1ml./4raza clotrimazole 1% per day, per / os tab. Fluconazole 50mg / 2 times a day after meal number 10. The second group of patients in need of prosthetics further training was conducted by the standard technique - administered iodine rinse mouth with water (5-10 drops of tincture of iodine , a glass of water), 2 times a day for 10 days. Statistical processing of the results was performed using the programs «Microsoft Excel» «Statistica 6 », «SPSS 17.0 for Windows» [2].

RESULTS AND DISCUSSION

By examination we revealed the following: gums color of 10.0% of surveyed - pale pink, at 78.0% - gums hyperemic, swollen, bleeding gums - at 60.0 %. The presence and depth of periodontal pockets 3-4 mm. - 58.0 % 4-5 mm. - 30.0 % 6 mm. - 12.0 %. By tooth mobility: 1stepen - 48.0 % 2 degree - 35%, grade 3 - 17.0% . On microscopic examination of smears of the oral cavity revealed the presence of fungi of the genus *Candida* - in 70.0 % of cases. Observed correlation relationship in patients with the presence of periodontal pockets to a depth of 5 mm. and the presence in them of fungi *Candida* $r = 0,501$ ($p = 0.001$) . The index definition caries intensity (KPU) showed that 85.0 % of the patients the mean value of the Communist Party was $11,1 \pm 0,74$ (high intensity level of dental caries). Oral hygiene index was $2,2 \pm 0,05$, which is unsatisfactory. In the analysis of the dentition and exhibiting clinical diagnosis was determined that 62.0 % had grade 3 dentition defects (defects included unilateral lateral parts of the dentition) 24.0% - Grade 4 (bilateral defects included lateral parts of the dentition), 11 0 % - 5 class (included defects of the anterior dentition) , 3.0 % - Grade 6 (combined defects).

1 month later we revealed that the proposed method allows the preparation of the oral cavity in 25 people (55.6%) to increase the effectiveness of orthopedic treatment of secondary

partial edentulous and shorten training in oral prosthetics by reducing generalized periodontitis and Candida glossitis / stomatitis in HIV-infected patients. In the control group of HIV -infected patients with secondary partially edentulous and chronic generalized periodontitis, candidiasis glossitis / stomatitis, which for local drug treatment used the standard scheme, the timing of local treatment were stretched to 14-19 days, while after 4 months at 34 people (80.0 %) HIV-positive relapsed generalized periodontitis and candidiasis.

Analysis of the results after 6 months confirmed the resistance effect of a medical complex in 25 patients (55.6 %) patients. Thus, the proposed method for the preparation of oral prosthetics HIV-positive, purposeful action provides an infection that most often occurs in these patients. Proposed treatment improves local immunity of the oral mucosa with preserved persistent clinical effect, a reduction in terms of preparation of the oral cavity, as well as prolong the life of fixed prostheses .

CONCLUSIONS

1. Providing treatment for HIV-infected patients in need of dental prosthetics, with generalized forms of periodontitis and candidal glossitis / stomatitis, antifungal therapy: application to the oral mucosa of klotrimazol 1% -1ml. 4 times per day , per / os tab. Fluconazole 50mg / 2 times a day after meal №10, can significantly reduce the time of preparation for prosthetics of patients with HIV and more durable clinical results.

2 . Correlation relationship in patients with generalized periodontitis (periodontal pockets to a depth of 5 mm.) and the presence in them of fungi Candida $r = 0,501$ ($p = 0.001$) is observed.

3. Medical staff working in a dental office should observe the utmost caution in all kinds of manipulations, avoid contact with skin and mucous membranes with blood and saliva of the patient. Personnel must strictly comply with the requirements for the prevention of occupational infections, strictly observe the rules of personal hygiene: when working with patients not to touch the hands of his eyes, nose, mouth, hair: do not touch and do not comb wounds, cuts, and other damage. Each case of damage associated with possible contamination of blood or other body fluids while performing their duties is to notify the department head (or chief physician) to register them in the register of accidents.

References

1. Bezrukov V.N., Alimskij A.V., Azrel'jan B.A. Osnovnye napravlenija razvitiia nauchnyh issledovanij po jepidemiologii stomatologicheskikh zabolevanij: Nekotorye itogi i perspektivy [Main directions of researches on the epidemiology of dental diseases: Some results and prospects] *Novoe v stomatologii* [New in dentistry]. 1995, №4, p. 18-21.

2. Glanc S. Mediko-biologicheskaja statistika [Biomedical Statistics]. Moscow: Praktika, 1999, 459 p.
3. Klinicheskie rekomendacii. VICH-infekcija i SPID [Clinical guidelines. HIV and AIDS] pod red. V.V. Pokrovskogo [ed. V.V. Pokrovsky]. Moscow: GJeOTAR-Media, 2009, 128 p.
4. Mirgorodskaja L.V. Kulik I.V. VICH-infekcija. Projavlenija v polosti rta [HIV infection. Manifestations in the oral cavity] Institut stomatologii, 2011, №11, p. 36-40.
5. Onishhenko G.G. Profilaktika infekcionnyh zabolevanij – vazhnaja povestka dnja (Bol'shoj Vos'merki) Prevention of infectious diseases - important agenda (Big Eight) Zh. Immunologija [J. Immunology], №5, Vol. 27, 2006.
6. Saakjan M.Ju. Special'naja podgotovka polosti rta k protezirovaniju pri ortopedicheskom lechenii zabolevanij parodonta [Special training in oral prosthetics at orthopedic treatment of periodontal disease]: Uchebno-metodicheskoe posobie [manual]. N.Novgorod: Izd-vo NGMA, 2001, 30 p.
6. Saakyan M. J.: / M. J. Saakyan. N-Novgorod: NGMA Publ. H., 2001, 30 p.

The authors:

Chizhov Yuri V., MD, professor of dentistry clinics, Krasnoyarsk State Medical University named after V.F. Voyno- Yassenetsky, Krasnoyarsk, Russia;

Ushnitsky Innokentii D., MD, professor, head of medical, surgical , prosthetic dentistry and pediatric dentistry Medical Institute North- Eastern Federal University named after M.K. Ammosov, Yakutsk, Russia, e-mail: incadim@mail.ru;

Plonina V.S., dentist FC LPU KTB №1, Krasnoyarsk, Russia;

Baginski Alexei L., PhD, chair of dentistry clinics, Krasnoyarsk State Medical University named after V.F. Voyno- Yassenetsky, Krasnoyarsk, Russia;

Kazantseva Tamara V., PhD, assistant professor of dentistry clinics, Krasnoyarsk State Medical University named after V.F. Voyno- Yassenetsky, Krasnoyarsk, Russia;

Varlamov Peter G., Ph.D, Associate Professor, Head of Department of medical, surgical , prosthetic dentistry and pediatric dentistry Medical Institute North- Eastern Federal University named after M.K. Ammosov, Yakutsk, Russia.

Features of Ultrasonic and Anthropometric Parameters among Teenage girls and Women of Yakutia

N.I. Douglas, A.B.Gur'eva, Ya.G.Rad' , T.Yu.Pavlova, N.S. Baisheva

ABSTRACT

In the study comparative characteristic of ultrasonic and anthropometric parameters in adolescent girls and women of indigenous and non - indigenous population of Yakutia was conducted. Adolescent girls and women of Russian nationality are significantly higher at comparison with the indigenous women of the RS (Y). From 10-11 years in all the girls of the Yakut and Evenki origin rapid expansion of the pelvic bones begins. Uterine size in adolescent girls of the RS (Y) indigenous population was significantly smaller at comparison with the girls of the Russian nationality.

Keywords: adolescent girls, height, weight, size of the uterus, ovaries, ultrasound investigation.

Individual human development proceeds and is changing under the influence of two major interacting factors - genetic and environmental programs. Any growing organism, owing to the incompleteness of its morphofunctional development immaturity of some of its regulatory mechanisms, high liability of a certain age group, is the most sensitive to the effects of environmental factors that can destabilize homeostasis (D.A.Farber, 2001 [6]; E.Casino, 2003 [4]; A.A.Baranov, 2006 [3]).

The influence of environmental factors on the condition of the body is not limited to the moment of their impact, but the impact itself affects further development and formation. This defines the search for optimal ways of approaching physiology of children and adolescents and those mechanisms that provide adaptive character development at each stage of ontogeny in the specific conditions of the North.

Specificity of natural, cultural and ecological conditions of the North is reflected in the physiological state voltage of functional systems and complex restructuring homeostasis (V.P. Treasurers, 1980 [5]; Avtsyn A.P., 1985 [1], with N.A. Aghajanian, 2006 [2]).

One of the most important characteristics of the health of adolescent girls is the indicators of their physical development, which are closely interrelated and interdependent with the processes of formation of the reproductive system.



Materials and methods: In order to try to find a solution for the matter mentioned above 578 women were examined, including 102 women of Russian nationality, who were in the control group, born and living in the Republic of Sakha (Yakutia). The study group included 476 indigenous women of Yakutia, including 296 and 180 of Yakut and Evenk nationalities respectively.

The control group included 50 adolescent girls and 52 women of reproductive age. 186 teenage girls and 110 women of reproductive age were Yakut. 82 teenage girls 98 women of reproductive age were Evenk.

We conducted anthropometric survey, external dimensions of the pelvis.

Ultrasonographic method of smaller hip diagnosis was done by means of an ultrasound machine called “LOKA-1700” with the use of abdominal transducer frequency of 3.5. MHz and vaginal transducer frequency of 6.5 MHz, as well as using another device – “Voluson - 730 ProV” with the following sensors: IC5-9H/GIN, RAB2-5/OB.

RESULTS AND DISCUSSION

Evaluation of the growth index showed that adolescent girls and women of Russian nationality were significantly higher comparing to the indigenous women of the Republic of Sakha (Yakutia).

Pelviometre tests revealed the increasing of external dimensions of the four bony pelvises in 10-11 year old girls; this is the age when all girls regardless of nationality begin developing rapidly in the area of the pelvic bones. The next increase of all external transverse dimensions of the pelvis was observed in the beginning of the late prepubertal period. The vast majority of 17 year old girls both Yakut and Evenk (81.2%) had lag on all the outer dimensions of the pelvis as opposed to 17 year old girls of Russian nationality. Average external dimensions of the pelvis were less than those of the Russian girls by 0.5-1.2cm, especially in relation to distantiaspinarum and conjugateexterna.

Ultrasound examination of the pelvic organs, performed in phase I and II of the menstrual cycle, (Table 1.2) showed that uterine size (length, width, anteroposterior dimension) in adolescent girls of indigenous inhabitants of the Sakha Republic (Yakutia) were significantly lower comparing to the same parameters in girls of Russian nationality. These differences were discovered on the 5-7 day of the menstrual cycle, and on 22-24 day of the menstrual cycle. Thus, the length of the uterus on 5-7 day of the menstrual cycle in the control group was 4.4 ± 0.2 cm and that of the indigenous women was significantly lower: Yakut girls - 4.0 cm and Evenk girls - 0.2, 3.8, 0.2.

There were no statistically significant differences in endometrial thickness. In all cases the endometrium was defined as M-echo regular oval, of uniform intensity. The minimum thickness of the endometrium was registered in the first days of menstruation (I phase). Maximum endometrial thickness occurred on 21-23 day of the menstrual cycle (II phase).

Evaluation of ultrasonic parameters of ovaries also revealed the fact of a statistically significant reduction of the sizes of the ovaries of girls and adolescents among indigenous women of the Republic when compared with girls of Russian nationality (Table 3). Separate study of right and left ovaries showed no significant difference in their development, which is an indication of equal participation of both ovaries in a normal menstrual cycle of girls during puberty.

There were no statistically significant differences in the size of the uterus and ovaries of women of reproductive age.

Table 1

Sonographic parameters of uterus on the 5-7 days of the menstrual cycle, cm

Groups		n	Length	Width	Anteroposterior dimension	Endometrium
Control	teenage girls	50	4,4 \pm 0,2	3,9 \pm 0,2	3,1 \pm 0,2	1,9 \pm 0,2
	women of reproductive age	52	4,9 \pm 0,7	4,4 \pm 0,3	4,3 \pm 0,9	3,4 \pm 1,2
Yakut	teenage girls	186	4,0 \pm 0,2*	3,4 \pm 0,2*	2,6 \pm 0,2*	1,8 \pm 0,2
	women of reproductive age	110	4,7 \pm 0,7	4,3 \pm 0,3	4,5 \pm 0,7	4,1 \pm 1,1
Evenk	teenage girls	82	3,8 \pm 0,2*	3,33 \pm 0,2*	2,6 \pm 0,2*	1,8 \pm 0,2
	women of reproductive age	98	4,9 \pm 0,5	4,4 \pm 0,3	4,6 \pm 0,8	3,9 \pm 1,9

Note: * $p < 0.05$ - reliability of differences established by comparison with the control group.

Table 2

Sonographic parameters of uterus on the 22-24 day of the menstrual cycle, cm

Groups		n	Length	Width	Anteroposterior dimension	Endometrium
Control	teenage girls	50	4,5±0,2	4,5±0,2	3,5±0,2	4,4±1,8
	women of reproductive age	52	4,9±0,7	4,8±0,5	4,4±0,9	7,4±2,2
Yakut	teenage girls	186	4,1±0,2*	3,8±0,18*	2,9±0,2*	4,1±1,2
	women of reproductive age	110	4,7±0,7	4,3±0,3	4,5±0,7	4,1±1,1
Evenk	teenage girls	82	4,1±0,2*	3,8±0,18*	2,9±0,2*	4,1±1,2
	women of reproductive age	98	4,9±0,5	4,4±0,3	4,6±0,8	3,9±1,9

Note: * $p < 0.05$ - reliability of differences established by comparison with the control group.



Table 3 Sonographic parameters of ovarian on the 5-7 day of menstrual cycle, cm.

Groups		n	Right ovary			Left ovary		
			Length	Width	Thickness	Length	Width	Thickness
Control	teenage girls	50	3,3 \pm 0,3	2,5 \pm 0,3	2,0 \pm 0,2	3,3 \pm 0,3	2,7 \pm 0,3	2,0 \pm 0,2
	women of reproductive age	52	3,4 \pm 0,3	2,8 \pm 0,3	2,8 \pm 0,2	3,6 \pm 0,3	2,8 \pm 0,3	2,6 \pm 0,2
Yakut	teenage girls	186	3,0 \pm 0,1	2,0 \pm 0,1*	1,8 \pm 0,2	2,9 \pm 0,2*	2,1 \pm 0,1*	1,7 \pm 0,2
	women of reproductive age	110	3,3 \pm 0,3	2,8 \pm 0,3	2,8 \pm 0,2	3,6 \pm 0,3	2,8 \pm 0,3	2,6 \pm 0,2
Evenk	teenage girls	82	2,7 \pm 0,2	2,0 \pm 0,1*	1,8 \pm 0,2	2,8 \pm 0,2*	2,0 \pm 0,1*	1,8 \pm 0,2
	women of reproductive age	98	3,1 \pm 0,3	3,0 \pm 0,2	2,6 \pm 0,2	3,6 \pm 0,3	2,6 \pm 0,2	2,8 \pm 0,1

Note: * $p < 0.05$ - reliability of differences established by comparison with the control group.

A more detailed assessment of ultrasonic parameters of the uterus and ovaries of girls and female adolescents (Table 4, 5) showed that the growth of the uterus and ovaries occurs gradually and moderately. The girls of Russian nationality showed increase in length, width and anterior-posterior of uterine size. This was observed among girls aged 12 to 13 years of age (the length of the growth of the uterus - 1 cm, width - 1.4 cm, and anterior-posterior size - 1.1 cm). Then increase in the size dropped dramatically and ranged from 0.1 to 0.3 cm per year.

In the group of Yakut and Evenk girls the uterine length was significantly smaller when compared to that of the Russian girls. Statistically significant differences were evident among the girls of the age groups of 10-11 years old and 12-16 years of age inclusively. A similar situation is observed with respect to parameters such as the "width" and "anteroposterior dimension." 17 year old girls were noted to have a statistically significant difference and the discernible trend towards a decrease in uterine size of adolescent girls of indigenous inhabitants of the Sakha Republic (Yakutia) was registered.

Examination of the size of the ovaries of girls and adolescents showed that the significant increase in the ovarian length of Russian girls occurred between 11 and 12 years of age (the length increased by 0.6 cm), and the increase of the thickness of ovarian tissue was observed at 13 years (an increase of 0.8 cm). Indigenous residents were observed to have an increase as well (maximum increase did not exceed 0.4 cm.)

In the group of girls Yakut and Evenk girls' ovaries were significantly smaller comparing to those of the girls of Russian nationality in the age group of under 17 year olds. For 17 year old girls a tendency of reducing sizes of the ovary was registered, but there was no statistically significant difference.

Comparison of the size of the uterus and ovaries with age at menarche showed high correlation ($r = 0,65$).

Table 4

Size of the uterus of girls and adolescents of the Republic of Sakha (Yakutia).

Group, years		Uterus, I phase			Uterus, II phase		
		Length	Width	Anteroposterior dimension	Length	Width	Anteroposterior dimension
Control	10-11	2,5±0,1	2,2±0,1	1,2±0,1	-	-	-
	12	2,8±0,1	2,7±0,1	1,9±0,1	-	-	-
	13	3,8±1,2	4,1±0,2	3,0±0,1	4,1±0,2	4,1±0,2	3,1±0,2
	14	4,1±0,1	4,2±0,2	3,2±0,1	4,1±0,2	4,1±0,3	3,3±0,2
	15	4,4±0,2	4,1±0,2	3,2±0,1	4,1±0,2	4,9±0,2	3,8±0,2
	16	4,5±0,3	3,9±0,2	3,0±0,1	4,4±0,2	4,5±0,2	3,5±0,2
	17	4,3±0,1	4,2±0,1	3,3±0,1	4,4±0,1	4,5±0,1	3,8±0,3
	18	4,4±0,1	4,3±0,1	3,5±0,1	4,6±0,1	4,5±0,1	4,0±0,1
Yakut	10-11	2,0±0,1*	2,0±0,1	1,2±0,1	-	-	-
	12	2,4±0,1*	2,2±0,1*	1,5±0,1	-	-	-
	13	2,8±1,2*	3,0±0,2*	1,7±0,1*	3,1±0,2	3,1±0,2	1,7±0,2
	14	3,3±0,1*	3,2±0,2*	1,9±0,1*	3,4±0,2	3,1±0,3	1,9±0,2
	15	3,7±0,2*	3,3±0,2*	2,2±0,1*	4,0±0,2	3,4±0,2	2,3±0,2
	16	4,0±0,3*	3,6±0,2	2,9±0,1*	4,0±0,2	3,7±0,2	2,5±0,2
	17	4,2±0,1	3,8±0,1	3,1±0,1*	4,4±0,1	3,8±0,1	3,3±0,3
	18	4,2±0,1	3,9±0,1	3,0±0,1*	4,1±0,1	3,9±0,1	3,1±0,1
Evenk	10-11	1,9±0,1*	2,0±0,1	1,2±0,1	-	-	-
	12	2,4±0,1*	2,2±0,1	1,5±0,1	-	-	-
	13	2,8±1,2*	3,0±0,2	1,7±0,1	3,1±0,2	3,1±0,2	1,7±0,2
	14	3,3±0,1*	3,2±0,2	1,7±0,1	3,4±0,2	3,1±0,3	1,8±0,2
	15	3,6±0,2	3,3±0,2	2,2±0,1	4,0±0,2	3,4±0,2	2,3±0,2
	16	4,0±0,3	3,6±0,2	2,8±0,1	4,0±0,2	3,7±0,2	2,5±0,2
	17	4,1±0,1	3,8±0,1	3,1±0,1	4,2±0,1	3,8±0,1	3,0±0,3
	18	4,2±0,1	3,8±0,1	3,0±0,1	4,1±0,1	3,9±0,1	3,1±0,1

Note: * $p < 0.05$ - reliability of differences established by comparison with the control group.

Table 5

Dimensions of the ovaries in girls and female adolescents of the Republic of Sakha (Yakutia)

Group, years		Uterus, I phase			Uterus, II phase		
		Length	Width	Anteroposterior dimension	Length	Width	Anteroposterior dimension
Control	10-11	2,0 \pm 0,1	1,6 \pm 0,1	1,2 \pm 0,1	-	-	-
	12	2,6 \pm 0,1	1,5 \pm 0,1	1,6 \pm 0,1	-	-	-
	13	2,7 \pm 0,2	2,4 \pm 0,2	2,4 \pm 0,1	2,7 \pm 1,2	2,4 \pm 0,2	2,4 \pm 0,1
	14	3,3 \pm 0,1	2,5 \pm 0,2	2,1 \pm 0,1	3,3 \pm 0,1	2,5 \pm 0,2	2,1 \pm 0,1
	15	3,3 \pm 0,2	2,5 \pm 0,2	2,0 \pm 0,1	3,3 \pm 0,2	2,5 \pm 0,2	2,0 \pm 0,1
	16	3,8 \pm 0,3	2,5 \pm 0,1	2,1 \pm 0,1	3,8 \pm 0,3	2,5 \pm 0,1	2,1 \pm 0,1
	17	3,4 \pm 0,1	2,8 \pm 0,1	2,3 \pm 0,1	3,4 \pm 0,1	2,8 \pm 0,1	2,3 \pm 0,1
	18	3,4 \pm 0,1	2,9 \pm 0,1	2,5 \pm 0,1	3,4 \pm 0,1	2,9 \pm 0,1	2,5 \pm 0,1
Yakut	10-11	1,7 \pm 0,1	1,5 \pm 0,1	1,2 \pm 0,1	-	-	-
	12	1,6 \pm 0,1	1,7 \pm 0,1	1,3 \pm 0,1	-	-	-
	13	2,0 \pm 0,2	1,6 \pm 0,2	1,4 \pm 0,1	2,1 \pm 0,2	1,6 \pm 0,2	1,3 \pm 0,1
	14	2,3 \pm 0,1	1,8 \pm 0,2	1,6 \pm 0,1	2,3 \pm 0,1	1,8 \pm 0,2	1,6 \pm 0,1
	15	2,7 \pm 0,2	2,0 \pm 0,2	1,8 \pm 0,1	2,7 \pm 0,2	2,0 \pm 0,2	1,7 \pm 0,1
	16	2,8 \pm 0,3	2,1 \pm 0,1	2,0 \pm 0,1	2,9 \pm 0,3	2,1 \pm 0,1	2,0 \pm 0,1
	17	3,0 \pm 0,1	2,5 \pm 0,1	2,0 \pm 0,1	3,0 \pm 0,1	2,3 \pm 0,1	2,0 \pm 0,1
	18	3,2 \pm 0,1	2,7 \pm 0,1	2,3 \pm 0,1	3,2 \pm 0,1	2,6 \pm 0,1	2,2 \pm 0,1
Evenk	10-11	1,6 \pm 0,1	1,3 \pm 0,1	1,1 \pm 0,1	-	-	-
	12	1,6 \pm 0,1	1,4 \pm 0,1	1,1 \pm 0,1	-	-	-
	13	1,9 \pm 0,2	1,6 \pm 0,2	1,4 \pm 0,1	2,0 \pm 0,2	1,6 \pm 0,2	1,3 \pm 0,1
	14	2,3 \pm 0,1	1,8 \pm 0,2	1,6 \pm 0,1	2,3 \pm 0,1	1,7 \pm 0,2	1,6 \pm 0,1
	15	2,6 \pm 0,2	2,0 \pm 0,2	1,7 \pm 0,1	2,7 \pm 0,2	2,0 \pm 0,2	1,7 \pm 0,1
	16	2,8 \pm 0,3	2,1 \pm 0,1	2,0 \pm 0,1	2,7 \pm 0,3	2,0 \pm 0,1	2,0 \pm 0,1
	17	3,1 \pm 0,1	2,4 \pm 0,1	2,0 \pm 0,1	2,9 \pm 0,1	2,3 \pm 0,1	2,0 \pm 0,1
	18	3,2 \pm 0,1	2,6 \pm 0,1	2,3 \pm 0,1	3,2 \pm 0,1	2,6 \pm 0,1	2,1 \pm 0,1



Note: * $p < 0.05$ - reliability of differences established by comparison with the control group.

CONCLUSION:

The results obtained showed that Russian adolescent girls and women of Russian nationality are significantly more developed in comparison with the indigenous women of the Republic of Sakha (Yakutia). The features of the age dynamics of the pelvic organs of adolescent girls and indigenous women of Yakutia are as follows: uterine size (length, width, anteroposterior dimension) was significantly lower comparing to the same parameters of Russian girls; increase in size of the uterus occurs gradually and moderately with leveling statistically significant difference at the age of 17; girls of Russian nationality show significant increase in the length of the ovary between 11 and 12 years of age, and increase in the thickness of the ovarian tissue was observed at the age of 13.

The native inhabitants showed a more gradual and moderate development and increase in the size of their ovarian tissue. In the course of the study it was also revealed that the regional characteristics of the physical development of the indigenous inhabitants of the Sakha Republic (Yakutia) comparing to the migrant population showed a reduction in the size of the pelvic bone from 0.5 to 1.2 cm.

REFERENCES

1. Avtsyn A.P., Zhavoronkov A.A., Marachev A.G., Milovanov A.P. Patologiya cheloveka na severe [Human pathology in the North] - M.: Medical, 1985 - 415.
2. Aghajanian N.A., Baevsky R.M., Berseneva A.P. Problemi adaptatsii i ucheniye o zdorovie [Problems of adaptation and teaching about health] – RUDN [Moscow People's Friendship University], 2006 - 284
3. Baranov A.A., Kuchma V.R., Tutelian V.A., Velichkovski B.T. Noviyе vozmozhnosti profilakticheskoy medicine v reshenii problem zdorovia detei i podrostkov [New possibilities of preventive medicine in addressing health problems of children and adolescents] Kompleksnaya programma nauchnykh issledovaniy "Profilaktika naibolee rasprostranennykh boleznei detei i podrostkov na 2005-2009g." [Comprehensive program of research "Prevention of the most common diseases of children and adolescents in 2005-2009."] - M.: GEOTAR Media, 2006 - 120



4. Kazin E.M., Blinov N.G., Dushenina T.V., Galeev A.R. Kompleksnoe longnitudialnoe issledovaniye osobennostey fizicheskogo I psihofiziologicheskogo razvitiya uchashchihsya na etapah detskogo, podrostkovogo I yuneshoskogo periodov ontogeneza [Comprehensive longitudinal study of physical and psycho-physiological features of student development at the stages of child, adolescent and youth periods of ontogenesis] Fiziologiya cheloveka [Human Physiology] - 2003 - T. 29 - № 1 - P.70 -71

5. Treasurers V.P. Sovremenniy aspekt adaptatsii [Modern aspects of adaptation] - Novosibirsk : Nauka, 1980 . - 191 p.

6. Farber D.A., Bezrukih M.M. Metodologicheskiye aspekti izucheniya fiziologii razvitiya rebenka [Methodological aspects of the study of the physiology of child development] Fiziologiya cheloveka [Human Physiology] - 2001 - T. 27 - № 5 - 8- 16

The authors

Douglas Natalia Ivanovna, MD, Head of the Department of the Faculty of the doctors' advanced training MI NEFU, e-mail: nduglas@yandex.ru;

Gur'eva Alla Borisovna, PhD, guryevaab@mail.ru;

Rad' Yana Gennadevna, PhD, Associate Professor, e-mail: rig787@yandex.ru;

Pavlova Tatiana Yurevna, PhD, e-mail: tatyanaupavl@mail.ru;

Baisheva Nurgouyana Semenovna - assistant of the Department of the Faculty of the doctors' advanced training MI NEFU, e-mail: kosmos80-80@mail.ru.

Effect of "Valetek-SP Aktiv" Vitamin and Mineral Food Supplement on the State of Pro- and Antioxidant Balance of Yakutia Athletes

Konstantinova L.I., Mironova G.E., Okhlopkova E.D., Efremova A.V.

ABSTRACT

The state of lipid peroxidation (LPO) and antioxidant system (AOS) in athletes – freestyle wrestlers of Yakutia before and after taking vitamin drink "Valetek-SP Active". We examined 39 wrestlers, aged 21 to 29 years. Athletes were divided into two groups: who drank and not drank a drink. Analysis of survey findings showed that after 20 days of taking a drink in the first group of athletes, TBA-RP concentration decreased by 24%. The total content low molecular antioxidants in both groups of athletes increased, but the increase in the first group was more pronounced than in the second group, 50% ($p < 0,0001$) and 22% respectively. CAT activity in the first group of athletes decreased by 15% ($p < 0,001$), while the second group decreased three-fold compared with the first group accounting for 51% ($p < 0,001$). The intensity of the enzyme superoxide dismutase for the whole period of ingestion of drink remained at the same level.

Thus, it was found that vitamin and mineral complex "Valetek-SP Active" reduces the intensity of lipid peroxidation and has a supportive effect of antioxidant protection of athletes.

Keywords: lipid peroxidation, antioxidant system, pro-and antioxidant balance, wrestlers.

INTRODUCTION

At the moment, the possibility of correction of free-radical processes in the athletes organism antioxidant preparations attracts an increasing number of researchers.

The organism of sportsmen, training in the North, is subject to long-term influence of the severe climatic and ecological factors: cold temperatures, hypoxia, causing the accumulation of reactive oxygen species (ROS) and lipid peroxidation (LPO) [2,4,6,9]. In the few publications shows that LPO play a big role in the development of fatigue and reduced physical performance [3].

However, as the analysis of published data, the state of the pro-and antioxidant balance in freestyle wrestlers' organism training in the Republic of Sakha (Yakutia), has been little studied [5].

The purpose of research was to evaluate the state of the pro- and antioxidant balance in athletes – freestyle wrestlers of Yakutia before and after drank vitamin and mineral complex "Valetek-SP Active".

MATERIAL AND METHODS

We examined 39 freestyle wrestlers of Institute of Physical Culture and Sports M.K. Ammosov North-Eastern Federal University and "High school sports" (Yakutsk), aged 21-24 years. Athletes were divided into two groups: 21 people daily drank vitamin-mineral complex "Valetek-SP Active", and the second – 18 people. Do not take this vitamin-mineral complex and not receiving additional sources of vitamins and minerals.

For one portion of the vitamin-mineral 10 g of the dry drink mix was dissolved in 250 ml of bottled water at room temperature. Ready to drink "Valetek-SP Active" sportsmen took 1 times a day, after the evening workout for 20 days in the presence of researchers.

Material for the study served as serum and heparinized blood taken from the cubital vein in the morning on an empty stomach in a state of relative muscular rest.

Lipid peroxidation was evaluated in erythrocyte suspended matter by education trimetin complex of thiobarbituric acid TBA-RP [10].

Parameters of antioxidant defense system was determined by the total content of low molecular weight antioxidants (LMAO) [7], the activity of enzymes superoxide dismutase (SOD) [8], catalase (CAT) [1].

Research LPO and antioxidant protection (AOP) were performed spectrophotometric methods on a spectrophotometer «Specord 40».

Statistical processing was performed using the software package SPSS 19.0. For quantitative indicators were calculated the mean and standard error, denoted as $M \pm m$. Estimation of the importance differences of average in the comparison groups performed using the Mann-Whitney. For all the criteria used for the threshold level of significance accepted value of $p < 0,05$.

The study was approved by the decision of the local ethics committee at "Yakutian Scientific Center of complex medical problems" SB RAMS.

RESULTS AND DISCUSSION

Table 1 shows the status of lipid peroxidation (LPO) and antioxidant system (AOS) in athletes organism before and after taking vitamin drink "Valetek-SP Active".

Comparative analysis of the data showed that in the first day of the study the concentration of TBA-RP, reflecting the intensity of lipid peroxidation (Fig. 1), and the content of low molecular weight antioxidants and super super oxide mutase activity, characterizing the state of non-enzymatic and enzymatic level of antioxidant defense, in both groups of athletes did not differ statistically significantly. Differences were detected in the antioxidant enzyme activity – catalase activity, which, in the first group of athletes was increased by 27% ($p < 0,001$) compared with athletes second group (Table 1).

On the tenth day of the study was noted no statistically significant increase of TBA-RP concentration in the first group of athletes at 8%, in the second group of athletes changes in the concentration of TBA-RP was observed, compared with the first day of the study (Fig. 1). The total content LMAO at this stage of the study in both groups of athletes increased, but in the first group, this increase was manifested most brightly (44%) ($p < 0,001$) than in the second group (6%).

Changes in the activity of antioxidant defense enzymes have the same dynamics. CAT activity on the 10th day of the study in both groups decreased in the first group of athletes by 11% ($p < 0,05$), the second – by 8%, while SOD activity did not change compared with the initial day of the study (Table 1).

On the twentieth day of the study in the first group of athletes who took vitamin drink "Valetok-SP Active" TBA-RP concentration decreased by 24%, indicating a decrease in lipid peroxidation is an indicator of adaptation of organism to the intensive psycho-physiological loads during training gathering in this group. In the second group of athletes who did not take vitamin drink "Valetok-SP Active", for 20 days, the concentration of TBA-RP increased by 20% compared to the first day of the study, indicating that the voltage adaptation processes during training gathering.

The total content of LMAO in both groups of athletes continued to increase, but an increase in the first group was more pronounced than in the second group, 50% ($p < 0,0001$) and 22% respectively. Increased LMAO in both groups of athletes, probably due to the fact that in the organism is synthesized daily LMAO (glutathione, uric acid, urea, succinic acid, etc.), which the organism uses for its own needs. For stress and increasing psychophysiological loadings the need for these substances increases, there is tension in the chain of metabolic flow rate increases antioxidants, there is a deficiency that accompanies fatigue, and reduces working capacity. A significant increase in the total content LMAO in the organism of first group of athletes, is a good indication of an improvement the state of non-enzymatic antioxidant defense and shows the effectiveness of receiving vitamin drink "Valetok-SP Active" for twenty days.

At the end of the study there was a reduction of CAT activity in both groups. However, compared with the first day of the study, the athletes in the first group showed a decrease of activity by 15% ($p < 0,001$), while the second group – CAT activity three times lower compared with the first group accounting for 51% ($p < 0,001$). Consequently, taking vitamin and mineral complex "Valetok-SP Active" has supporting action of antioxidant protection.

The intensity of the enzyme superoxide dismutase for the whole period of ingestion of drink remained at the same level.

To determine the status of pro- and antioxidative balance calculated the coefficient C_{AOD} / LPO by the formula:

$$KAOD / POL = LMAO + CAT / TAC-RP$$

At baseline the coefficient of pro- and antioxidant balance in the first group of athletes was 15% higher than in the second group (Fig. 2), this can be explained statistically significant difference in the activity of CAT, which in the first group was higher (Table 1).

On the tenth day of the study there was a decrease $KAOD / LPO$ in the first group of athletes at 10%, and the second – by 6%. On the twentieth day of taking a drink was marked activation of antioxidant protection. Which was reflected in the first group was up 20% $KAOD / LPO$ compared with the first day and 36%, compared to the tenth day of the study. In the second group there was the reverse reaction of $KAOD / LPO$ values, reflected in a sharp decline on 50 and 53%, respectively, due to reduced antioxidant protection of non-enzymatic and enzymatic chain.

Thus, vitamin and mineral complex "Valetok-SP Active" has an antioxidant effect. 20-day intake of vitamin and mineral complex "Valetok-SP Active" inhibits the activation of lipid peroxidation products and increases antioxidant protection of athletes, which gives grounds to recommend the use of this complex dietary supplement as a means of effective antioxidant support of athletes' organism.

REFERENCES

1. Koroljuk M.A. Metod opredeleniya aktivnosti katalazy [Method for determination of catalase activity]. Lab. delo [Lab. Business], 1988, № 1, pp.16-19.
2. Krivoshapkin V.G. Regional'nye standarty osnovnykh fiziologicheskikh pokazatelej cheloveka na Severe (v tablicah i risunkah) [Regional standards of basic human physiological indicators in the North (in tables and figures)]. Yakutsk: Izd-vo Departamenta NiSPO [Publishing House of the Department of INEC], 2001, 146 p.
3. Lankin V.Z. Svobodno-radikal'nye processy v norme i pri patologicheskikh sostojaniyah [Free-radical processes in normal and pathological states]. RKNPK MZ RF [RKNPK Health Ministry]. Moscow, 2001, 78 p.
4. Mironova G.E. Hronicheskij obstruktivnyj bronhit v usloviyah Krajnego severa (znachenie antioksidantnogo statusa i antioksidantnoj terapii) [Chronic obstructive bronchitis in the far north (the antioxidant status and antioxidant therapy)]. Krasnoyarsk, 2003, 169 p.
5. Ohlopkova E.D. Adaptivnye reakcii organizma k intensivnym fizicheskim nagruzkam sportsmenov Jakutii: avtoref. dis. kand. biol. nauk [Adaptive reactions of the



organism to intense physical stress athletes of Yakutia: Author. dis. Candidate. biol. Science]. Yakutsk, 2011.

6. Petrova P.G. Jekologija, adaptacija i zdorov'e [Ecology, adaptation and health]. Moscow, 1996, 132 p.

7. Rogozhin V.V. Metody biohimicheskikh issledovanij [Biochemical research methods]. Yakutsk, 1999, pp.91-93.

8. Spravochnik po laboratornym metodam issledovanija / Pod red. L.A. Danilovoj [Handbook of Laboratory Methods / Eds. L.A. Danilova]. – St. Petersburg.: Piter [Peter], 2003, 541 p.

9. Stepanova G.K. Morfologicheskie i funkcional'nye priznaki adaptivnosti molodyh muzhchin raznyh jetnosov Respubliki Saha (Jakutija) / Aftoref. Dis... dokt. biol. nauk [Morphological and functional features of adaptability of young men of different ethnic groups of the Sakha Republic (Yakutia) / Aftoref. Dis ... Doctor. biol. Sciences]. Moscow, 2005, 38 p.

10. Uchiyama M. Determination of malonaldehyd precursor in tissues by thiobarbituric acid test / M. Uchiyama, M. Michara //Anal. Biochem. - 1978. - Vol.86. - №1. - P. 271-278.

Table 1

Indicators of antioxidant defense athletes

	Group 1 (drank a drink) (n = 21)			Group 2 (did not take a drink) (n = 18)		
	1st day	10th day	20th day	1st day	10th day	20th day
LMAO, mg eq / ml Eritrea.	0,065 ± 0,00	0,098 ± 0,00**	0,130 ± 0,01***	0,068 ± 0,00	0,072 ± 0,00	0,087 ± 0,00
SOD, umol / min. ml	0,061 ± 0,00	0,060 1± 0,05	0,061 ± 0,00	0,061 ± 0,01	0,062 ± 0,00	0,061 ± 0,00
CAT	0,700 ± 0,03 ⁺⁺	0,625 ± 0,05*	0,592 ± 0,05*** ⁺⁺	0,509 ± 0,05	0,467 ± 0,04	0,251 ± 0,03

*p<0,5; **p<0,001; ***p<0,0001 in the first group in comparison with the first day of study; +p<0,5; ++p<0,001; +++p<0,0001 in comparison with the second group.

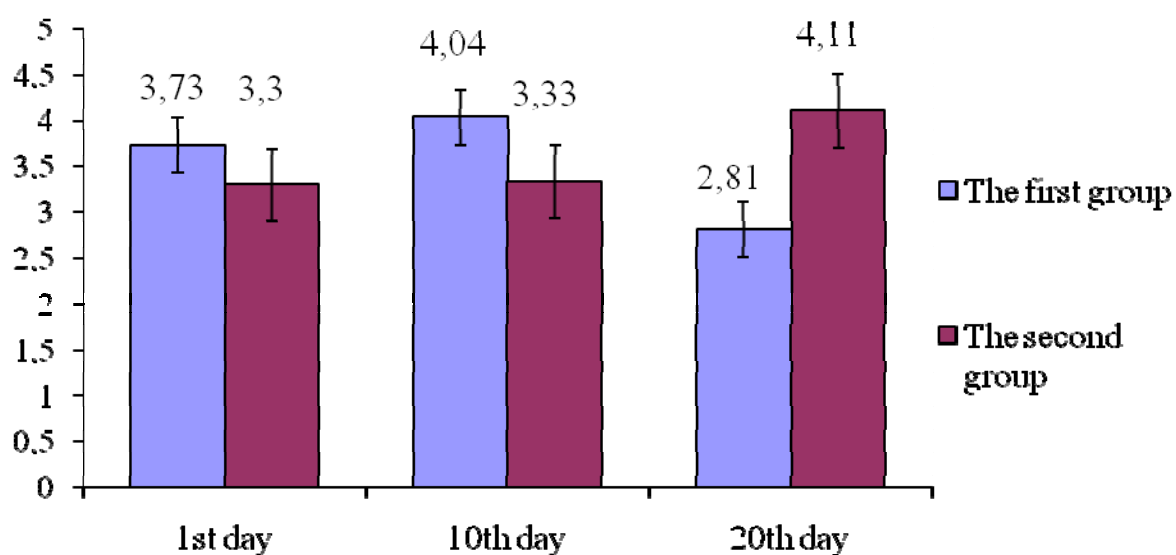


Fig. 1. TBA-RP concentration (nmol / L) in athletes who drank and not drank a vitamin drink "Valetek-SP Active", within 20 days.

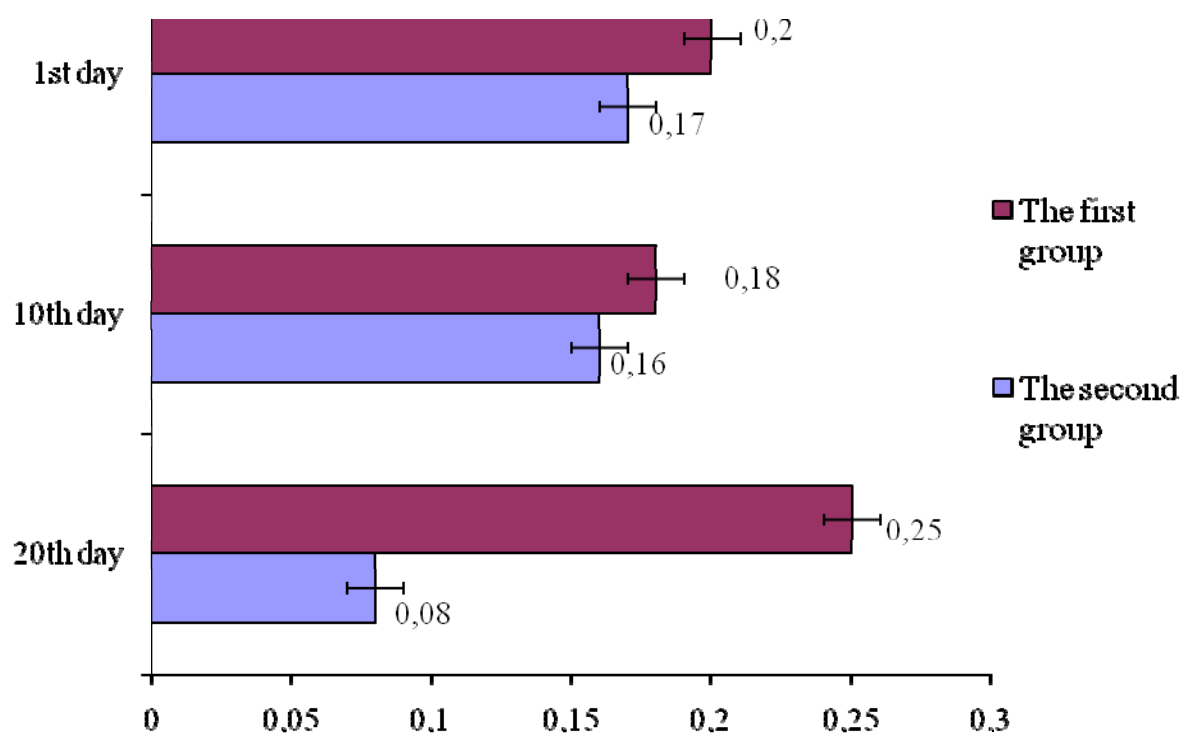


Fig. 2. Level indicator antioxidant balance before and after vitamin drink "Valetek-SP Active"



Information about authors

Konstantinova Lena I. – junior researcher, YSC CMP SB RAMS, Yakutsk, Republic Sakha (Yakutia), konstanta.l@mail.ru;

Mironova Galina E. – MD, PhD (Biology), prof., M.K. Ammosov North-Eastern Federal University, YSC CMP SB RAMS, Yakutsk, Republic Sakha (Yakutia), mirogalin@mail.ru;

Okhlopko Elena D. – PhD (Biology), junior researcher, YSC CMP SB RAMS, Yakutsk, Republic Sakha (Yakutia), elena_ohlopko@mail.ru;

Efremova Agrafena V. – PhD (Biology), junior researcher, YSC CMP SB RAMS, Yakutsk, Republic Sakha (Yakutia), a.efremova01@mail.ru.



Identification of Risk Factors in Schoolchildren of the Sakha (Yakutia) Republic: the Results of a Comprehensive Survey in the Health Centre for Children

Egorova T.V., Savvina N.V., Savvina A.D., Lazareva A.A., Govorova M.D., Pavlova O.N.

ABSTRACT

In the article the possibilities, value and a role of screening researches in the Health Centre for formation of a healthy way of life for children and teenagers are considered. The state of health of children is studied on the basis of results of the testing on a hardware-software complex and inspections on the installed equipment. In structure of morpho-functional pathologies on the 1 place are functional infringements of cardiovascular system; on the 2 place is oral cavity pathology, further – disharmonious physical development.

Keywords: children, teenagers, Health Centre, complex inspection, formation of a healthy way of life.

Urgency. The problem of high level of death and depopulation in the Russian Federation requires the safety of children's and teenager's health. This problem has the special medical and social importance. The increasing number of diseases, death, social conditioned diseases of teenager's - a labor potential of society, bring up the problem of their health in rank of national safety.

The World organization of the public health has defined the health as condition of physical, emotional and social welfare, but not only absences of diseases or physical defects. The definition of "full health" includes physical, mental and spiritual health. Physical health is a normal work of all systems, absence of the diseases. Mental health is a general emotional comfort of the person, who lives in harmony with himself and surrounding world. Moral or spiritual health is a system of values and life's aims, motives, respect of human values, morals and laws [1].

Many forms of the pathological conditions develop in childhood under the influence of unfavorable surroundings factors. For instance, atherosclerosis, diabetes and particularly hypertension disease begin at childhood. Functional and morphological deviations of children quite often pass to chronic diseases. So prevention of the chronic diseases must include increasing of the resistant power of the organism and liquidation of the health state's pathologies [3].

Permanent residence in the Far North promotes at children and teenagers forming of the row resistant risk factors of diseases of cardiovascular system. Being long indoors creates the

condition for hypoxia and hypodynamia. The shortage of the motion with not well-balanced diet brings lipid metabolism disturbance and overweight at the expense lipopexia in hypodermic cellulose. Direct cardio – angiotrophic effect, rendered by complex polar circle factors, promotes increasing of the arterial pressure and the following development of arterial hypertension, being as the most important predictor and complication of diseases cardiovascularsystem, so and independent nosologic form. The spread of arterial hypertension among adult population of the Sakha Republic is 30,3% [4].

Functional and morphological deviations of children quite often pass to chronic diseases so prevention of the chronic diseases must include the growth of a resistant power of the organism and liquidation disturbances of the health state [3].

Objective: revealing of risk factors of non- infectious diseases development of schoolchildren by the comparative analysis of results examinations of children in countryside by the mobile Health Centre for children on organizing healthy lifestyle for 2012.

Research papers and methods. The Health Centre for children was opened on the functional base of children's hospital in December 2010. In December 2011 due to Program of the Modernization was purchased the Mobile Health Centre, which has allowed to widely practicing the exit inspections in regions of the republic.

The Object of the research is the healthstate of children and teenagers aged 6-17 (the school children) from Yakutsk and 8 regions of the republic (Amginsky, Ust-Aldansky, Momsky, Eveno-Bytantaysky, Olekminsky, Gorny, Hangalassky, Kobyaysky). By these inspections was organized the analysis of 4095 medical cards of patients of the Health Centre (the registration form 025). From them: the number of school children from Yakutsk was 3135 (76,5%), number of rural schoolchildren was 960 (23,5%). 76,4% of the examined children belong to age group from 6 to 14 years, a quarter - to age group from 15 to 17 years. All children of the general schools from Yakutsk were directed on complex inspection by medical workers of the educational institutions, rural children – by medical organizations on the permanent residence.

THE MATERIAL OF THE RESEARCH: report form number 68 "Information about activity of the Health Centre" for 2012 (adopted by order Russian Ministry of Health and Social development from 19.08.2009 number 597); report form number 50 "Information about activity medical organizations of the Sakha Republic, directed to organizing healthy lifestyle and implementation preventive medical activities" for 2012 (adopted by order Ministry of Health of the Sakha Republic) from 01.12.2011 number 01 - 8/4 - 1950); facts of the 4095 medical cards of the patients of the Health Centre(the report form 025).

The Physician defines on the grounds of results of the testing on hardware-software complex and inspections on installed equipment the most probable risk factors, functional and adaptive reserves of the organism with provision for age particularities, forecast the health state, makes clear about a healthy lifestyle, forms the individual program on healthy lifestyle and correcting program of the health deviation.

Educational activity of the Health Centre is obligatory. In the Health Centre are organized studies at health school, consultations, seminars and lectures for children, conferences for parents on forming healthy lifestyle. The physicians of the Health Centre, who pass special training, carry on studies. The Specialists of the Centre closely cooperate with educational institutions of the town.

Statistical processing of results was conducted with the using of the program SPSS.13 and computer program of the processing Microsoft Excel. Probability of the error $r < 0,05$ was estimated as signified.

RESULTS OF THE RESEARCH AND DISCUSSION

Distribution of children on groups of health has revealed the low factor health children among rural schoolboy 8,7 % against 17,3% town schoolboy ($r < 0,05$). Functional deviations are revealed at 82,6% of town schoolchildren and 92,3 % rural schoolchildren ($r < 0,05$) (table 1). For all schoolchildren with risk factors of the diseases development were recommended individual plans on correcting of the health deviation and on healthy lifestyle.

Table 1

Distribution of schoolchildren from Yakutsk and regions of the Sakha Republic on group of health (absolute number, %)

Group of health	Yakutsk n=3135		Regions n=960	
	Absolute number	%	Absolute number	%
1 group	544	17,3	84	8,7
2 group	2567	79,9	721	75,0
3 group	79	2,5	111	11,5
4 group	8	0,25	24	2,5
total	3135	76,5	960	23,5

The comparative analysis of results complex examination has shown that practically each second rural pupil (47,6%) needs in oral hygiene (tabl.2). 30% of rural children have only tooth decay. If procedures on oral hygiene were conducted regularly, they were ascribed to group of healthy children. In some regions (Eveno - Bytantaysky, Ust - Aldansky, Momsky) is extremely low organization of stomatology services; also exists low responsibility of the parents for health of their children and low medical activity of the parents. As to schoolchildren who lives in Yakutsk, conditions of oral hygiene are much better, but percent of children, who needs for oral hygiene is remain high 36,7% ($r < 0,05$).

Table 2

Comparative results of the complex examination schoolchildren of Yakutsk and regions of the Sakha Republic (abs. number, %)

Indicators(risk factors)	Yakutsk n=3135		Regions n=960	
	abs.number	%	abs.number	%
Short height	331	10,5	135	14,0
High height	526	16,7	166	17,0
Overweight	351	11,1	117	12,1
Lack of weight	111	3,5	82	8,2
Increasing of the arterial pressure	159	5,07	18	1,8
Low arterial pressure	32	1,02	8	0,8
Pathologies of the warm-vascular system	676	21,5	144	15,0
Increasing of glucose levels in blood	258	8,2	28	2,9
Increasing of cholesterol in blood	234	7,4	24	2,5
Increasing of carbon dioxide	561	17,8	60	6,2
Number of children who needs oral hygiene	1152	36,7	457	47,6
Anxiety	554	17,6	137	14,2
Pathologies of body composition	668	21,3	287	29,8
Declining of the lung capacity	756	24,1	117	12,1
Declining of oxygen saturation	10	0,31	7	0,7
The number of absolute healthy children	544	17,3	84	8,7

Each fourth pupil from Yakutsk and each third rural child have a declining in physical development ($r > 0,05$). Motor development and puberty are closely connected with physical development. The expressed deviation from standard of the physical development, as a rule,

means the pathologies of the processes of the growing and maturation of the organism. At the same time significant rapid physical development can be sometimes even more dangerous than essential retarding of the physical development, which nearly is indicative of presence hormone disturbance. The pathology of the body composition is high among rural schoolchildren, as effect of the deviation in physical development.

The truly difference is revealed in pathology of the functioning the cardiovascular system that reveals itself basically in the violation of the heart rhythm more among the town schoolchildren on 6,5%, also on 3,27% above children with arterial hypertension.

The express analysis glucose and cholesterol level on the blood periphery has shown that among the town children in 2,5 - 3 times above than among rural schoolchildren. This is explained with the features of nutrition, the low consumption of the natural products, as fish, meat, dairy products, and cereals. Yakut national dishes are used very seldom; moreover town children much often use sugar, sweets, carbonated water and pastries. Also in town conditions it is difficult to keep the regime of diet.

The daily routine of modern town schoolchildren is characterized by declining motor activity, that confirmed by results of the complex examination. The High level of the carbon dioxide 17,8% against 6,2% among rural schoolchildren, declining the lung capacity 24,1% against 12,1% ($r < 0,05$). In fundamental study of the professor A.G. Sucharev is revealed closely correlation dependency between level of the motor activity and development of the muscular, cardiovascular and respiratory systems by children, as well as the degree of their power to resist the disease (1999). The deficit of the motor activity is accompanied with the disturbance of the physical development, the reduction of the functional possibilities of the organism (general physical abilities to work) and adaptive status, development inadequate reaction a cardiovascular system on load and vegetative dysfunctions, weakness supporting-motor device [2].

In the each sixth town schoolboy and each seventh rural schoolboy high level of anxiety ($r > 0,05$) is revealed. The stress reasons of schoolchildren can be a big volume of the educational program at schools and lack of time to do it.

The Complex examination on hardware-software complex has allowed reveal multilateral notion about psycho-emotional and functional conditions town and rural schoolchildren.

CONCLUSION

Thus, complex examination at the Health center revealed a high level of risk, foreground were functional disorders of the cardiovascular system, chronic foci of infection (caries), abnormalities in physical development (overweight, underweight, short stature), functional disorders of breathing.



In the context of increased physical and psychological stress in modern schoolchildren screening allows early detection and correction of various deviations of health and disease states, it is extremely important from the standpoint of the prevention of chronic diseases and early compensation of somatic pathology.



References

1. Iljina I.P. Obrazzhizni i zdorovye: Uchebnoe posobie [Lifestyle and Health]: Textbook, Yakutsk: Publishing House of the Yakutsk State University, 2003.
2. Kozhin A.A. Kuchma V.R. Zdorovy chelovek i ego okruzhenie: uchebnik [Human health and the environment]: Textbook, Moscow: "Akademia", 2006, p.96.
3. Konnikova E.E., Popova I.E. Osnovy medicinskikh znany: Uchebnoe posobie [Bases of the medical knowledge]: Textbook/ Ministry of the Sakha Republic (Yakutia), Sakha State Teacher's Academia: Yakutsk, 2005, p.144.
4. Sochranenie i ukreplenie zdorovya detey i podrostkov v obrazovatelnykh uchrezhdeniyakh: nauchnye trudy i materialy konferensii [The Conservation and promotion of the children's and teenager's health in educational institutions]: research and conference paper. Yakutsk, 2008: Yakutsk Publishing House of the Yakutsk State University, 2008, p.94.

The authors

"CHILDREN'S HOSPITAL", Yakutsk, the Russian Federation:

Tatyana V. Egorova - pediatrician, Head of Health Centre for Children, postgraduate NEFU named after M.K Ammosov, Arkady1990@mail.ru. 677000, Yakutsk Republic Sakha (Yakutia) Mkr" Sterh", str. Ermolaeva, 1; Nadezda V. Savvina - Ph.D., Professor, Head of Department NEFU named after MK Ammosov; Anastasia D. Savvina - MD, associate professor NEFU named after MK Ammosov, Head of consultation-polyclinic Dep; Aytalina A. Lazareva - pediatrician; Maria D. Govorova – deputy head physician, Olga N.Pavlova – physician.

The Problems of Diagnosis of Reactive Arthritis in an Outpatient Clinic

A.E. Mikhailova, R.N. Zakharova, V.G. Krivoschapkin

ABSTRACT

Objective: to study the clinical characteristics of reactive arthritis in outpatients.

Material and methods. 40 pts visited out-patients were under questionnaire, including 60% female and 40% male, mean age 34.1 ± 9.6 years. They underwent a clinical examination, laboratory and X-ray diagnostics.

Results. Depending on the duration of the disease, patients were divided into three categories: patients with acute course was - 9 (22.5%) patients, subacute - 2 (5%) and chronic - 29 (72.5%). Clinical examination showed that the majority of patients had mono-oligoarthritis of the lower limbs, enthesiopathies and concomitant Chlamydia infection.

Conclusion. Thus, in order to reduce the incidence of chronic disease research it is needed to identify the cause of the infection in the early stages of the disease, to assess the condition of the joints through ultrasound. Due to the fact that the reactive arthritis refers to seronegative spondyloarthritis, determination of the presence of HLA-B27 would be of practical and scientific value.

Keywords: reactive arthritis, Chlamydia infection, mono-oligoarthritis.

INTRODUCTION

The term "reactive arthritis" (ReA) as a nosological form was first proposed in 1969 by Finnish researchers P. Ahvonen, K. Sievers and K. Aho, to describe arthritis in patients who had undergone *Yersinia enterocolitis* (Ahvonen P. et al., 1969). According to modern ideas, ReA is divided into 2 groups - urogenital (Chlamydia) and postenterocolitic (*Yersinia*, *Salmonella*, *Campylobacter* and *Shigella*).

Reactive arthritis is an immune inflammatory disease of the joints, initiated foci of infection in the intestine or urogenital tract, having the characteristic clinical picture with the involvement of the peripheral joints and spine, and often takes a chronic course [1, 2].

The incidence of ReA adult population of Russia in 2000-2010 (absolute number, thousand) according to statistical data MH Russia, shows that the total number of registered patients with ReA remained fairly stable throughout the period, with the lowest rate in 2006 - 44.4 thousand, to Unfortunately, in 2010 it increased to 51.1 million (6.7 million, or 13.2%). The

number of patients with a primary diagnosis of ReA was in 2006 16,252, and in 2010 - 19 385, ie 16.2% [3].

ReA usually get sick of working age, causing temporary, but sometimes persistent disability. Because of this, the disease has a social significance.

The purpose of this study was to investigate the clinical characteristics of reactive arthritis in the outpatient cohort of patients.

MATERIALS AND METHODS

For the diagnosis of reactive arthritis have been applied criteria of the American Rheumatism Association [2]:

- 1) asymmetrical seronegative arthritis;
- 2) urethritis or cervicitis, diarrhea;
- 3) inflammatory changes of the eye;
- 4) skin and mucous membranes.

All patients had clinical, laboratory and radiological diagnosis. To verify the causal infection patients underwent testing of biological material from the urethra and / or cervix by *Chlamydia trachomatis*, *Ureaplasma urealiticum* and *Mycoplasma hominis* using the polymerase chain reaction (PCR), and immunofluorescence method used and the formulation of the indirect hemagglutination with *Yersinia* and *Salmonella* antigen, seeding Fecal dysentery group.

RESULTS AND DISCUSSION

The study included 40 patients with a mean age of $34,1 \pm 9,6$ years. Among the patients were women - 24 (60%) and men - 16 (40%). An acute illness with a duration of 1 month and 6 months was observed in 9 (22.5%) patients, subacute - with a duration of 6 months. 12 months - y 2 (5%) and chronic over 12 months. - In 29 (72.5%) patients.

It should be noted that the acute course was observed in young people, where the average age was $22 \pm 3,5$. Joint disease characterized mono arthritis in 3, oligoarthritis in 6, it should be noted all observed enthesiopathies. Development of disease after chlamydial infections, genitourinary was found in all patients.

In subacute during a mean age of $27,5 \pm 0,7$, also had connections with *Chlamydia* infection was detected mono arthritis.

During the chronic mean age was $38,3 \pm 7,5$, disease duration $1,9 \pm 0,7$. These data show a trend of increasing age of chronic disease. The chronic course of the 29 patients, 3 (10.3%) occurred enterocolitic arthritis. Of these, one patient had chest X-ray revealed bilateral sacroiliitis I stage. Joint damage was characterized by oligoarthritis in 2 and one mono arthritis. Pain in the lumbosacral region were moderate and the movement of the spine remained.

If ReA chlamydial origin often met oligoarthritis - 19 (73.1%) than mono arthritis - 7 (26.9%). Unilateral sacroiliitis was observed in 8 (30.8%) patients.

In addition, 14 (53.8%) patients had clinical manifestations enthesitis - inflammatory changes in tendon insertions (ligaments, joint capsule) to the bone.

Regardless of the duration of the disease in 9 (22.5%) patients had a history of eye disease. At the time of the inspection 2 (5%) of the patients were examined and treated, and the rest were no inflammatory changes. An objective examination of skin lesions in patients at the time of the inspection were found. At the time of the survey the current chlamydial infection was detected in 15 (37.5%) of these patients and in 5 (33.3%) of the patients was associated with ureaplasma and 9 (60%) patients with mycoplasma infection. The patient was assigned to antibiotic therapy.

Of the 24 women, 11 (45.8%) showed an inflammatory disease of the genitourinary system, among men - in 7 (43.7%). It should be said that all patients with acute and subacute diseases of the genitourinary system had. Among patients with chronic disease of the genitourinary system were found in 7 (24.1%).

More frequent were clinical manifestations of inflammation in the knee and ankle joints. When X-rays of the affected joints in 7 (17.5%) patients had initial symptoms of osteoarthritis of the knee and heel spurs, 3 (7.5%), while the majority - no changes detected.

According Gaponova T.V. ultrasound of the joints is significantly more informative than X-rays. Unfortunately, due to the lack of ultrasound examination of the joints, the survey conducted [4]. As a result of changes in the joints is detected only for chronic conditions.

As is known [5] determining Chlamydia DNA using dot hybridization of nucleic acids using polymerase chain reaction, has a high specificity and sensitivity. Unfortunately, this study is not carried out in many encampments, as a result of patients fails to receive adequate therapy, which in turn leads to chronic arthritis. Also, the question remains diagnosis of genetic predisposition to seronegative spondyloarthritis patients, particularly in non-differentiated arthritis, which is to determine the presence of HLA-B27 antigen class 1 human major histocompatibility complex.

CONCLUSIONS: In inflammatory lesions of the joints, especially in young patients, it is necessary to investigate the presence of an infectious agent. And it would also be advisable to conduct ultrasound joints at the mono-oligoarthritis. Due to the fact that the reactive arthritis refers to seronegative spondyloarthritis, determination of the presence of HLA-B27 would be of practical and scientific value.



REFERENCES

1. Agababova E.R. Reactive arthritis and Reiter's disease / In.: Rheumatic Disease: A Guide for Physicians. Ed. V.A. Nasonova, N.V. Bunchuk. // Moscow: Medicina. - 1997. - P.324 - 335.
2. Asner T.V. Modern aspects of urinogenous reactive arthritis (diagnosis and treatment) / T.V. Asner, A.N. Kaliagin. // Siberian Journal of Medicine. - 2010. - № 2. - P. 142-144.
3. Balabanova R.M. Dynamics of the prevalence of rheumatic diseases included in the thirteenth class of ICD-10 in the adult population of the Russian Federation for 2000-2010 / R.M. Balabanova, Sh.F. Erdes. // Scientific-Practical Rheumatology. - 2012. - № 3. -P. 10-12.
4. Gaponova T.V. Clinical and immunological relationship with reactive arthritis of various etiologies // PhD thesis. - St. Petersburg, 2009.
5. The criteria for the diagnosis of reactive arthritis (draft) // Agababova E.R., Bunchuk N.V., Shubin S.V. [et al.] / Scientific-Practical Rheumatology. - 2003. - № 3. - 82 – 83 p.

Information about the authors

Mikhailova A. E. - PhD, NEFU Institute of Health. 677710, Yakutsk, Sergelyakhskoe Highway 4, building C-2, office. tel. 361536, e-mail: nsvnsr.66 @ mail.ru;

Zakharova R.N. - PhD, Head of the epidemiology and prevention of rheumatic diseases NEFU Institute of Health. 677710, Yakutsk, Sergelyakhskoe Highway 4, building C-2;

Timofeeva A.V.- PhD, senior researcher.

D. P. Skachkov, A. L. Shtilerman

First Results of Treatment of Patients with Bullous keratopathy by Corneal Collagen Cross - Linking Method

ABSTRACT

Cross - linking method is based on the combined use of ultraviolet radiation and photosensibilizer. The method relies on increasing the number of inter-and intra fibrillary covalent links between collagen fibers. In recent years, researches on the applicability of cross-linking in patients with endothelial- epithelial dystrophy of the cornea were held. 8 patients (8 eyes) with bullous keratopathy were observed who underwent the cross-linking of the cornea. Conducting cross-linking of corneal collagen in patients with bullous keratopathy in the early postoperative period can reduce swelling, increase the transparency of the cornea, and improve visual acuity and corneal arrest syndrome.

Keywords: cross-linking, collagen, keratopathy.

INTRODUCTION

Bullous keratopathy is a dystrophic disease of the cornea that develops as a result of the loss or dysfunction of endothelial cells. As a consequence there is penetration of intraocular fluid in the cornea, impregnating her layers and disruption of water and salt metabolism. As a result, there is swelling, corneal opacity, which is manifested decrease in visual acuity, as well as the formation of bubbles in the epithelium - "Bull", which, torn form erosive surface and thereby cause severe pain, tearing and photophobia [3].

Drug treatment of bullous keratopathy and ineffective is that a symptomatic drugs.

Currently, a new method of treatment of corneal pathologies - corneal collagen cross linking [4,5].

Cross linking is based on the combined use of ultraviolet radiation and photosensibilizer helps to strengthen collagen fibrils and increase biomechanical stability of the cornea. The method relies on increasing the number of inter-and intra fibrillary covalent links resulting from exposure to ultraviolet radiation on riboflavin, with the release of free radicals, which induce the formation of cross-links between collagen molecules [1,2].

Designed Seiler T., Wollensak G. 2003 collagen cross-linking method has been used successfully in the treatment of progressive corneal ectasia different etiology [6,7].

In recent years, research on the applicability of cross-linking in patients with endothelial-epithelial dystrophy (EED) of the cornea [1,5].

Purpose - to determine the efficacy of corneal collagen crosslinking treatment bullous keratopathy.

MATERIAL AND METHODS

The Department of Eye Microsurgery of the Amur Regional Hospital under observation were 8 patients (8 eyes) aged 65 - 83 years from the bullous form of induced corneal dystrophy (photo № - 1), which in the acute phase was conducted cross-linking of corneal collagen.

Indication for the procedure UV - irradiation with riboflavin was bullous stage endothelial - epithelial corneal dystrophy with severe corneal syndrome.

Contraindication for cross linking was the presence in patients with a history of herpetic keratitis, increased intraocular pressure, corneal thickness less than 400 microns, allergic reactions to riboflavin.

All patients underwent pre-and postoperative period received a standard eye examination. Besides it the patients underwent pachymetry.

During the night before the operation antiinflammatory (diclofenac 0.1 % solution) and antibiotics (ciprofloxacin 0.3 % solution), 4 times a day were prescribed. The operation was performed by standard procedure. Local anesthesia was carried instillation of 0.4 % solution oxibuprocaine. After blefarostat installing there was performed corneal deepitelization, short 1 - 2 mm to limb area. Thorough and complete removal of the epithelium is necessary in order to more easily riboflavin below lying in a penetrated layers of the cornea , which is necessary to protect the corneal endothelium , lens and retina from the damaging effect of UV light. Thereafter, the patient was instilled a solution containing 0.1% of riboflavin, for 30 minutes every 3-5 minutes. The unit UFalink (Russia) effects on the cornea was performed with ultraviolet irradiation (370 nm, $E = 3,0 \text{ mW/cm}^2$) for 30 minutes. During UV- irradiation continued instillation of riboflavin solution every 5 minutes. After an automatic shutoff device cornea was washed with saline was instilled into the conjunctival cavity antibacterial drops - ciprofloxacin 0.3%, imposed a soft contact lens. Postoperatively topically administered antibiotic (ciprofloxacin 0.3% solution), anti-inflammatory (diclofenac 0.1% solution) and reparative (korneregel) therapy (photo № - 3). Contact lens removed after complete epithelialization of the cornea.

Follow-up examinations were carried out on the 1st, 7th, 14th day and at 1, 2, 3 months postoperatively.

RESULTS AND DISCUSSION

As a result of surgery all patients had preserved the integrity of the cornea, docked and inflammatory pain. Corneal epithelialization process was completed in an average of $6,1 \pm 1,2$ day. Biomicroscopy after removing the lens epithelium full (photo № - 2). According pachymetry after 14 days there was a tendency to a decrease of the average cornea thickness of $65 \pm 3,1$ mm and hence the reduction of edema. After 3 months pachymetry indicators were below baseline by $134 \pm 2,6$ mm. By the end of the first week after crosslinking was an increase in visual acuity from 0.01 to 0.06. In one case, an increase in visual acuity from 0.05 to 0.4. Increased considerably and the transparency of the cornea was stable, even at day 7 became more clearly the detailed structure of the anterior chamber (photo № - 3). 6 patients showed a significant decrease corneal syndrome throughout the observation period in 2 patients operated relapse pain of varying severity that required additional medical correction destination.

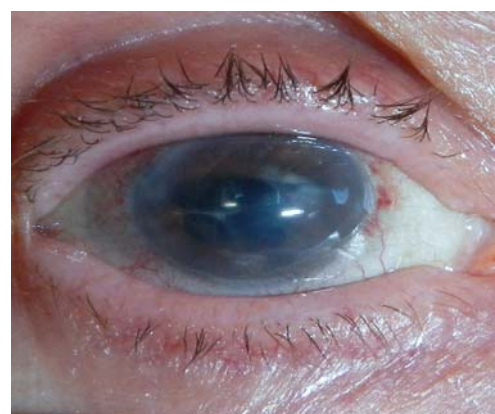
Positive clinical corneal collagen cross linking effect in patients with bullous keratopathy , presumably associated with the effect of " contraction " which occurs when reducing the area for the number of existing corneal endothelial cells , they can improve the barrier function of [1,2] . Also occurs after exposure to strengthen the links between collagen fibers prevent the penetration of intraocular fluid in the layers of the cornea .Using the method of cross-linking of collagen in the treatment of patients in the advanced stages of EED requires further research and analysis of long-term results.

CONCLUSIONS

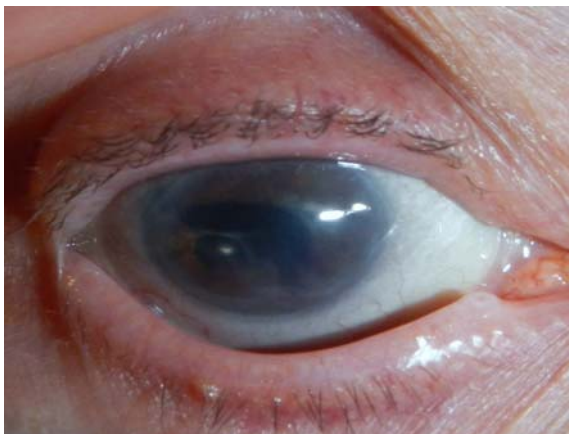
Conducting cross-linking of corneal collagen in patients with bullous keratopathy in the early postoperative period can reduce swelling, increase the transparency of the cornea, and improve visual acuity and corneal arrest syndrome.



a



b



c

The patient's eye before cross linking (a), after 1 day (b) and 7 days after cross linking.

References

1. Bikbova G.M., Bikbov M.M. Terapevticheskij potencial krosslinkinga i lechenie bulleznoj keratopatii [The therapeutic potential of cross-linking and treatment of bullous keratopathy] Oftal'mohirurgija [Ophthalmosurgery]. Moscow, 2009, № 2, p. 7-8.
2. Bikbov M.M. Bikbova G.M. Habibullin A.F. Primenenie krosslinkinga rogovichnogo kollagena v lechenii bulleznoj keratopatii [Corneal collagen cross-linking application in the treatment of bullous keratopathy] Oftal'mohirurgija [Ophthalmosurgery]. 2011, № 1, p. 12-13.
3. Kasparov A.A., Kasparova E.A., Trufanov S.V., Borodina N.V. Posleoperacionnaja bulleznaja keratopatija: transplantacionnye i netransplantacionnye metody lechenija [Postoperative bullous keratopathy: transplantation and non-transplantation therapies] Tezisy dokladov Devjatogo s#ezda oftal'mologov Rossii 2010 [Abstracts of the 9th Congress of the Russian Ophthalmologists 2010]. Moscow, 2010, p. -307.
4. Moroz Z.I., Kovshun E.V., Gorokhova M.V. Keratoplastika s ispol'zovaniem krosslinking-modificirovannogo donorskogo materiala pri fistule rogovicy [Keratoplasty using crosslinking -modified donor material for corneal fistula]. Oftal'mohirurgija [Ophthalmosurgery]. Moscow, 2012, № 4, p. 11-12.
5. Neroev V.V., Petukhova A.B., Gundorova R.A. Sfery klinicheskogo primeneniya krosslinkinga rogovichnogo kollagena [Fields of clinical application of corneal collagen cross-linking] Oftal'mologija [Ophthalmology]. Moscow, 2012, № 1, p. 24-26.
6. Wollensak G., Spoerl E., Seiler Th. Stress Strain Measurements of Human and Porcine Corneas after Riboflavin / Ultraviolet-A Induced Crosslinking // J. Cataract Refract. Surg.; Sep. 2003. -Vol. 29. -P. 1780-1785.



7. Wollensak G., Spoerl E., Seiler Th. Riboflavin / Ultraviolet-A Induced Collagen Crosslinking for the Treatment of Keratoconus // Am. J. Ophthalmol. 2003. -Vol. 135. - P. 620-627 .

The authors:

D. P. Skachkov, ophthalmologist, Amur Regional Hospital, 675000, st. Voronkov 26, tel.: 8 (4162) - 42-95-12, Blagoveshchensk, Russia, e-mail: doc8012@rambler.ru;

A.L. Shtilerman, professor, Head of Department Eye Diseases AGMA, Blagoveshchensk, Russia.

Perspectives of the Study of Adaptive-Immune Reactions Spectrum after Different Treatment Technologies of Uterine Fibroids

E.V. Bashirov, M.L. Polina, N.I. Douglas

ABSTRACT

The study included women with uterine myoma after various treatment technologies (laparotomy and laparoscopic myomectomies, uterine artery embolization). The features of adaptive variability and immunoreactivity in the early and late postoperative period were under study.

These adaptive- immune profile features allow predicting the likelihood of complications and disease recurrence after breast-conserving various interventions depending on the availability of therapeutic measures.

Keywords: uterine myoma, conservative myomectomy, uterine artery embolization, adaptive response, immunoreactivity.

INTRODUCTION

Urgency of the problem of optimization approaches in the management of women with uterine myoma determined decrease in their quality of life, coupled with the symptoms of the disease, a combination of hyperplastic endometrial diseases, infertility, and postoperative complications urogynecological which result becomes a statement of annual demographic and economic losses of society [4,5,9, 15].

Contrary to the appearance and the introduction of advanced endovideosurgical and endovascular treatment of uterine fibroids, the frequency of recurrence of the disease requires an analysis of the adequacy of the choice of intervention [7, 10, 11, 12].

Change radical approach - hysterectomy, often practiced in routine gynecological practice as well as due to late treatment of patients for medical help in symptomatic uterine myoma larger organ for treatment technology identified the need to revise the priority choice of access.

Modern contingent of women with uterine myoma much «younger», a quarter of them are infertile, others to be realized reproductive function [2, 3, 9]. That is why the problems of doing such a multifaceted group of patients are not only to eliminate the symptom of the disease and relapse prevention, but also in maintaining their child-bearing potential.

Obviously, improving the treatment of uterine fibroids technology requires not only to the effective conduct of conservative plastic operations with respect for reproductive functional

reserve, but also to minimize their negative effects on all body systems. However, these domestic and foreign literature about the immediate and long-term effects of interventions with uterine fibroids are ambiguous, the different priorities of choice - from the standpoint of the age of patients, localization of nodes, the presence of concomitant hyperplastic processes of the uterus, the technical skills of the surgeon [13,14].

Fears of complications of laparoscopic approach consequences - endoscopic scar ruptures during childbirth identified priority in favor laparotomic myomectomy competition which began to make uterine artery embolization (UAE) [8,14]. The data collected in the field of interventional radiology gynecological convince this method obviously alternative surgical interventions, especially - with the technical complexity of myomectomy or its accompanying unjustifiably high risk of trauma [7, 10, 15].

However, the conclusions about the competitiveness of UAE with other interventions due to the almost complete disappearance or significant reduction of clinical symptoms in contrast with the data on the feasibility of its implementation in women interested in childbirth. [20]

It seems that the debate on the preferred technology for the treatment of disease, the risk of complications and recurrence of fibroids after various interventions on the absence of rehabilitation algorithm that undoubtedly affects on formation of the integral characteristics of the quality of life [2, 10, 17, 18].

There were attempts to study predictive adaptive responses significance for aggregate analysis of gynecological patients after laparotomic interventions from the pathophysiological positions [6]. Essentially, the methodology based on the principles of H. Selye (1960) about status and reactions of the whole organism, elaborated by L.H. Harkavy (1999) [1] on the variability of the body's response to stress, reduces the possibility of prenosological diagnosis of adjustment disorders.

At individual data on the nature of AR after realized surgery stress in gynecological patients the range of immunological disorders, measured using the ELI-P test, remains poorly studied.

It seems that an extensive analysis of complex adaptive variability organism of patients, depending on the chosen method of treatment of uterine fibroids (myomectomy, laparoscopic and laparotomy, uterine artery embolization) subject to the availability and scope of rehabilitation measures will form the evidence base the validity of such tactics.

In connection with this we set a goal: to assess the effectiveness of rehabilitation after various treatment technologies patients with uterine myoma (UM) based on analyzing the nature of adaptive responses and immunoreactivity.

MATERIAL AND METHODS

To achieve the objective a prospective study of 265 women with uterine fibroids, applied to the clinic for conservative myomectomy and UAE was done. Preoperative examination provided for pelvic sonography with Doppler, hysteroscopy, histological examination of scrapings of the endometrial, the treatment of chronic persistent inflammatory diseases of the genitals, if necessary, antibiotic therapy was performed.

Comprehensive rehabilitation after the intervention included the prevention of adhesion, growth of relapse fibroids, immunocorrection treatment of hormone-dependent diseases dishormonal bodies' recovery eubioz of genitals and women's reproductive function.

Contingent of women, depending on the technology of treatment of uterine fibroids and the presence of postoperative rehabilitation was divided into groups : I - laparotomic after myomectomy (LTM) ((n = 68) - after a comprehensive rehabilitation (CR), II - after the LTM and without CR (n = 16), III - after laparoscopic myomectomy (LPC) and CR (n = 82), IV - after LPC and remediation without (n = 12), V group - after UAE and CR (n = 76), VI group - after UAE without rehabilitation (n = 11).

Embolization was performed by the standard technique, with advanced angiographic study sonography nodes Doppler velocimetry; emboli were used as particles of polyvinyl alcohol (PVA) in size from 350 to 900 or hydrogel (AAA Company, Russia). UAE is made if there are contraindications to other organ-preserving treatment options or inefficiencies (hormone), nodes larger than 10 cm in diameter.

On postoperative phase evaluated the nature of adaptation reactions (AR) on the 7th day, and a month after the intervention, depending on the availability of the CD and in her absence on the basis of leukocyte count in the peripheral blood smear procedure LH Harkavy et al. (1990). Isolated types of adaptive responses: response training (RT), calm reaction activity (CRA), reaction increased activation (RIA), reaction to chronic stress (RCS).

To study the serum immunoreactivity, reflecting the number and affinity of some natural autoantibodies embryotropic interacting with proteins - regulators of embryogenesis method was applied " ELI-P - 1 Test » (ELISA-detected probably of pathology), based on a standard ELISA. Studies were performed one day after the various treatment technologies, month and 3 months.

Statistical processing of the results was performed using the statistical software package Statistica v.6.0. program and Microsoft Office Excel 2003.

To identify the significance of differences between the parameters of the random variables we used Student's test. The level of statistical significance adopted $p < 0.05$.

RESULTS AND DISCUSSION

Spectrum of AR in a month after the intervention showed a predominance of RCS is rehabilitation compared with those in groups where practiced introduction of therapeutic measures, regardless of the method effects on uterine tissue: twice as often in the LTM (68.8%) ($p < 0.05$) and LPC (41.7%), four times at least - at the UAE (45.4%) ($p < 0.05$) (Fig. 1).

After CR RCS prevailed in LTM - a third - and a half times more frequently than in the LPC, three times - in UAE (10.5%).

Following rehabilitation measures identified in the dynamics of the increase in CRA in comparison with the results on the 7th day after the intervention: after LTM - from zero to 23.5%, LPC - from 19.5% to 34.1%, UAE - from 27.6% to 42.1%, whereas in the absence of CR - only 7.9% of the women on average. Dominant PCA defined in UAE - almost five times more compared to the rate in the group without treatment complex (9.1%) ($p < 0.05$). Month after various technologies treatment of uterine fibroids increased frequency RT just outside the Kyrgyz Republic, the highest rate was determined after LPC - a third of women (33.3%), 1.2 times higher than after UAE (27.3%), almost twice - after LTM (18.8%).

With the help of ELI-P test that evaluates the amount of embryotropic autoantibodies - integral marker systemic immunity, revealed the prevalence of abnormal immunoreactivity in all groups by day (average, 94.8%), regardless of the type of intervention, as a natural corollary to the operational stress vectoring in immunodeficient state (after the most significant LTM - 83.3%) (Fig. 2).

Predictions of improving the quality of life for a number of parameters analyzed scale was based on the statement of normoreactivity month after intervention with the implementation of the CR: LTM - at 22.0%, LPC - 59.7%, UAE - 53.9% of women.

Prognostically unfavorable in terms of UM relapse after intervention is believed to be abnormal immunoreactivity recorded in the absence of the CR. Hyporesponsiveness predominant in women after LTM (68.7%) - in contrast to half of the figure, after the LFM (41.7%), two times - after the UAE (36.4%) ($p < 0.05$).

Hyperactive answer is therapeutic measures rarely recorded: one-third (33.3%) after LPC, almost half (45.4%) who underwent UAE, and only 6.2% - after LTM (Fig. 3).

Adherence to treatment and health cures before and after treatment of MM determined predominance of normoreactivity in 56.8% of women on average, describing the mode of action on the tissue at the LPC and UAE as gentle; in LTM - twice less, only 22% ($p < 0.05$). Hyperreactivity after KR met twice more after UAE than after LPC (27.6% and 14.6%, respectively) ($p < 0.05$).

Validity of optimization approaches in the treatment of women with MM and implementation of restorative course after various interventions, as is the importance of doing an adequate preoperative evaluation confirms dynamic immunoreactivity after 3 months.

In the absence of therapeutic measures was diagnosed with abnormal production of autoantibodies embryotropic: hyporesponsiveness in 75.0 % of women after LTM - 1.7 times more than the LPC and after embolization ($p < 0.05$), hyperreactivity - a third (34.8 % on average) after UAE and LPC and only 6.2% - after LTM (Fig. 4).

Normoreactivity in the absence of health course after various treatment technologies MM revealed less: 2.6 times - after LTM (18.7%), 4.3 times - after LPC (16.7%) and the UAE (18.2%) ($p < 0.05$).

Reduced quality of life in patients with uterine myoma conditioned the negative symptoms, reflected on the parameters associated with physical activity, pain, psychological health, most are concerned with women metrorrhagia. Regression of symptoms after 6 and 12 months after various treatment technologies until the normalization condition, with the most dynamic quality of life after UAE LPC and testified about the effectiveness of therapeutic interventions and pathogenetic validity reductive repetition rate in the postoperative period.

CONCLUSIONS

These results suggest that post-operative evaluation of neurohumoral reactivity with testing for ELI-P-test and adaptation profile and subsequent correction of diagnosed disorders allows to predict the optimal recovery of functions of the reproductive system to the achievement of "comfortable" quality of life. It is found that the positive changes in the state of women after various treatment technologies for uterine myoma is accompanied by a shift of stress in Antistress reactions, negative - in adverse, most pronounced in the aggressive influence on uterine tissue. This confirms the priority of UAE and LSM by less traumatic influence compared with LTM. Type of immunoreactivity in conjunction with AR is not only a predictor of complications during the postoperative period, long-term recurrence of the disease, but also to measure the usefulness of ongoing rehabilitation course.

REFERENCES

1. Garkavi L.H., Kvakina E.B., Kuz'menko T.S. Antistressorniye reaktsii i aktivatsionnaya terapiya: Reaksiya kak put' k zdoroviu cherez prosessi samoorganizatsii [Antistress reaction and activation therapy Reaction activation as a way to health through self-organization processes] Moscow: Imedis, 1999, p.655.

2. Gurieva V.A. Mesto embolizatsii matochnich arteriy v terapii miomi matki [Place of uterine artery embolization in the treatment of uterine fibroids] Rossiyskiy vestnik akusherstva I ginekologii [Russian herald of Obstetrics and Gynecology] 2008, № 2, pp. 40 - 44.
3. Davydov A.I. Vosstanovitelnoe lecheniye posle organosberegayushich operatsiy u bolnich podslizistoy miomoi matki I adenomiozom [Rehabilitation treatment after surgery in patients with organ- submucosalmyoma and adenomyosis] Voprosi ginekologii, akusherstva I perinatologii [Questions gynecology, obstetrics and perinatology] 2011, № 10 (6), pp.13 -21.
4. A.N. Strizhakov, A.I. Davydov, S.A. Kondrashin and others. Diskussionniye aspekty embolizatsii matochnich artriya pri lechenii bolnich miomoi matki [Controversial aspects of uterine artery embolization in the treatment of patients with uterine myoma] Voprosi ginekologii, akusherstva I perinatologii [Questions gynecology, obstetrics and perinatology] 2004, T. 3, № 5, pp. 72-76.
5. A.N. Strizhakov, A.I. Davydov, V.M. Pashkov Dobrokachestvenniye zabolevaniya matki [Benign disease of the uterus] Moscow: GEOTAR - Media, 2011, p - 28.
6. Dolgov G.V. Gnoino-vospalitelniye oslojneniya v operativnoi ginekologii. Prognozirovaniye. Profilaktika: [Pyo- inflammatory complications in operative gynecology. Prediction. Prevention: Proc. allowance for higher honey. Textbook. Institutions] St. Petersburg: ELBI-SPb, 2001, pp.172
7. V.G. Breusenko, I.A. Krasnov, S.A.Kapranov, etc. Nekotoriye diskussionniye voprosi embolizatsii matochnich arterii pri lechenii miomi matki [Some controversial issues of uterine artery embolization in the treatment of uterine fibroids] Akusherstvo I ginekologiya [Obstetrics and Gynecology] , 2006, pp. 23-26.
8. A.N. Strizhakov, P.V. Budanov, A.I. Davydov and others. Spontanniyy razriv matki v rodah posle laparoskopicheskoi miomektomii [Spontaneous rupture of the uterus during childbirth after laparoscopic myomectomy] Voprosi ginekologii, akusherstva I perinatologii [Questions gynecology , obstetrics and perinatology, 2012, № 5, pp. 79-82.
9. A.L. Tikhomirov, A.A. Ledenkova, A.E. Bataeva. Patogeneticheskoe obosnovaniye profilaktiki miomi matki [Pathogenetic substantiation prevention of uterine fibroids] Voprosi ginekologii, akusherstva I perinatologii [Questions gynecology, obstetrics and perinatology], 2011, Vol.10, № 1, pp. 75-78.
10. G.M.Saveliev, V.G.Breusenko, S.A.Kapranov et al. Embolizatsiya matochnih arteriy v lechenii miomi matki: dostizheniya I perspektivy [Uterine artery embolization in the treatment of uterine fibroids: achievements and prospects] Akusherstvo I ginekologiya [Obstetrics and Gynecology], 2007, № 5, pp. 54 -59.

11. Agdi M., Tulandi T. Endoscopic management of uterine fibroids // Best Pract Res Clin Obstet Gynaecol. – 2008. – V.22. – N 4. – P.707-16.
12. Bhardwaj R. Uterine artery embolisation. Indian Heart J // 2012. – V.64. – N 3. – P.305-8.
13. Bradley L.D. Uterine fibroid embolization: a viable alternative to hysterectomy // Am J Obstet Gynecol. 2009. – V.201. – N 2. – P.127-35.
14. Bulman J.C., Ascher S.M, Spies J.B. Current concepts in uterine fibroid embolization // Radiographics. – 2012. – V.32. – N 6. – P.1735-50.
15. Gupta J.K., Sinha A., Lumsden M.A., Hickey M. Uterine artery embolization for symptomatic uterine fibroids // Cochrane Database Syst Rev. – 2012. – V.16. – N 5. - CD005073.
16. Kahn V., Fohlen A., Pelage J.P. Role of embolization in the management of uterine fibroids // J Gynecol Obstet Biol Reprod (Paris). – 2011. - V.40. – N 8. – P.918-27.
17. Kasum M. Fertility following myomectomy // Acta Clin Croat. – 2009. - V. 48. – N 2. – P.137-43.
18. Levy B.S. Modern management of uterine fibroids // Acta Obstet Gynecol Scand. – 2008. – V.87. – N 8. – P. 812-23.
19. Parker W.H. Laparoscopic myomectomy and abdominal myomectomy // Clin Obstet Gynecol. - 2006. – V. 49. – N 4. – P.789-97.
20. Van der Kooij S.M., Ankum W.M., Hehenkamp W.J. Review of nonsurgical/minimally invasive treatments for uterine fibroids // Curr Opin Obstet Gynecol. – 2012. – V.24. – N 6. – P. 368-75.

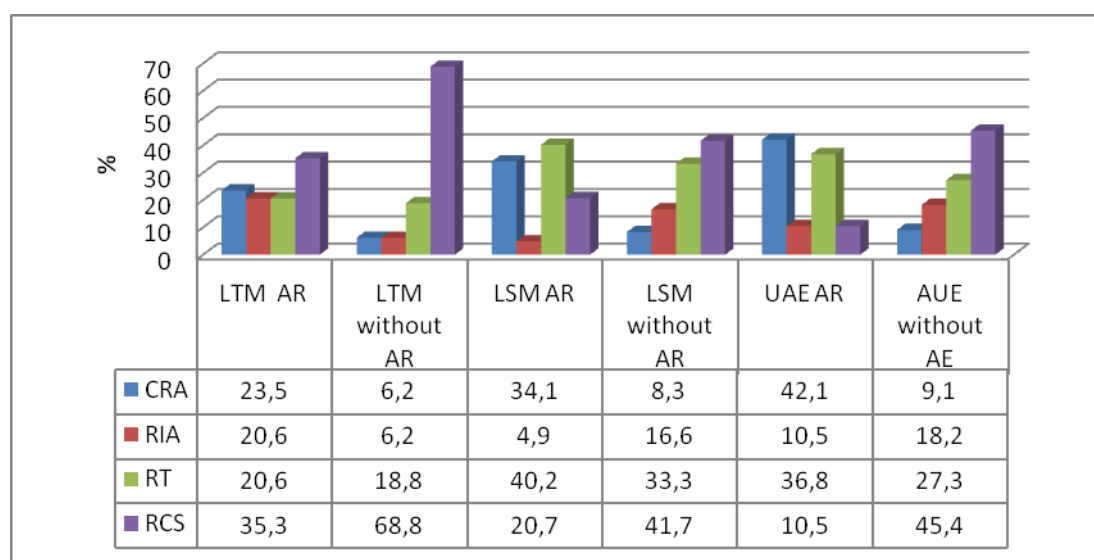


Fig. 1. Adaptation Character Profile month after various treatment technologies for uterine uterus depending on the presence/absence of rehabilitation therapy

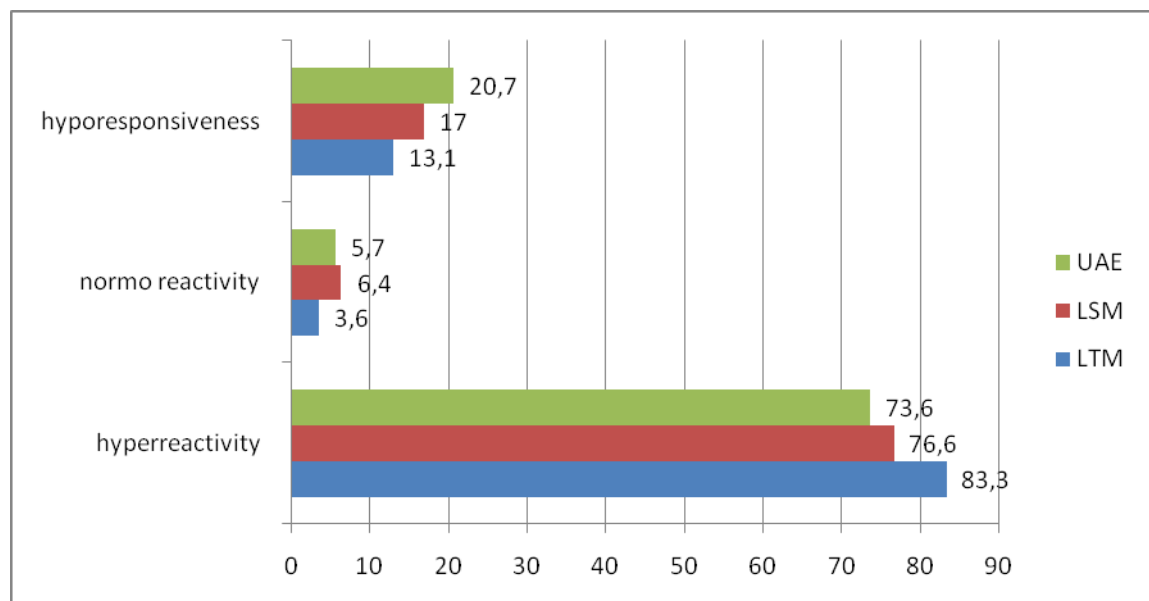


Fig. 2. Types of immunoreactivity day after surgery.

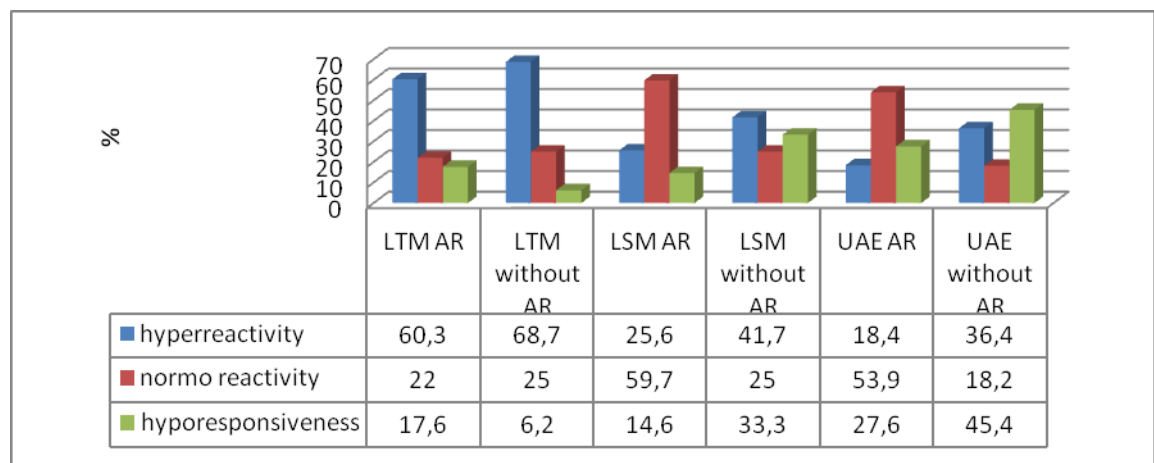


Fig. 3. Option of immunoreactivity month after various treatment technologies uterine myoma, depending on the presence/absence of rehabilitation therapy

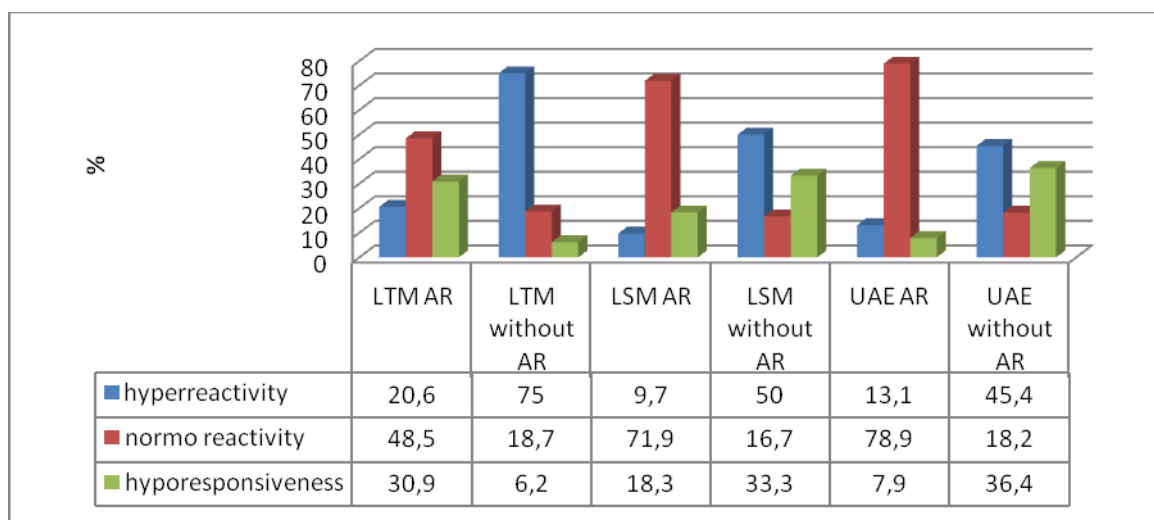


Fig. 4. Option of immunoreactivity after 3 months of treatment with different technologies uterine fibroids depending on the presence / absence of rehabilitation therapy

Authors:

Bashirov Eduard Vladimirovich - obstetrician-gynecologist, MD, Obstetric-Gynecologic Clinic Kuban State University of the Ministry of Health of the Russian Federation, Russia, 350072, Krasnodar, ul. Zhipovskaya 4/1; tel. 8 (988) 2425536, Fax: 8 (861) 2570509, E-mail: edikbashirov@rambler.ru;

Polina Miroslava Leonidovna - obstetrician-gynecologist, assistant professor of obstetrics, gynecology and reproductive medicine VPO Russian Peoples Friendship University, Russia, 117198, Moscow, Miklukho-Maklay St.,21, box. 3; tel. 8 (926) 6140549, E-mail: polina.ml@mail.ru;

Duglas Natalia Ivanovna - obstetrician-gynecologist, MD, Head. the Department of Ostetric and Gynecology Faculty of postgraduate training of doctors Medical Institute "North-Eastern Federal University named after M.K. Ammosov ", 8924662 67 22, E-mail: nduglas@yandex.ru.



Organization of Drug Supply in Rural Areas on the Example of Megino - Kangalassky Region of the Republic Sakha (Yakutia)

Tarabukina S.M., Akimova A.M.

ABSTRACT

Research organization of drug supply in rural areas, including changes with the introduction of the Federal Law of 12.04.2010 № 61-FZ "On Circulation of Medicines" were held. Availability medicinal aid in settlements of the region, the degree of public satisfaction, range and quality of pharmaceutical care in the area were evaluated.

Keywords: drugs and medical products, territorial subdivisions of district hospitals, drug supply, consumption of medicines per capita.

INTRODUCTION

Health care is a special sphere of social policy what provides citizens with medical and pharmaceutical care. Currently, the volume and quality of pharmaceutical care provided to the population largely differs depending on the place. For the rural population in remote areas it is influenced by a number of complex factors: low transport accessibility, low population density in rural areas, the reduction in the rate of social infrastructure, adverse socio-demographic situation; low income of rural residents; high rates of disease and injury. [1]

According to official statistics, almost one third of the population lives in rural areas, so the problem of organization of medicinal maintenance in rural areas, the problem of quality of providing pharmaceutical care and quantitative assessment of its level still remain relevant [7]. Due to Republic Sakha (Yakutia)'s geographical location and climate, extremes peculiarities of organization of medicinal maintenance in rural areas are even more complicated.

To solve the problem of drug supply in rural areas, where are no pharmacies, the notion of "rural settlements where there are no pharmacies" appeared in the Federal Law of the Russian Federation from 12.04.2010 # 61-FZ "On circulation of medicines".

According to the points of law, the organization of pharmaceutical activities, medical institutions and their separate subdivisions, located in rural areas, what do not have pharmaceutical organizations, are authorized to carry out retail trade in drugs. [9]

Objective: research of drug supply in rural areas on the example of the Megino-Kangalassky region.

MATERIALS AND METHODS

The objects of the study are the territorial subdivisions of the district hospital in 16 settlements of Megino - Kandalassky region, where there are no pharmacies, pharmacies three settlements of the district with the highest population density. During the study, the sociological questionnaires, group of the survey), statistical (sample analysis, content analysis), research methods were used. Information processing and results data were carried out using statistical economic-mathematical methods.

540 inhabitants of settlements with no pharmacies, 6 heads of pharmacies district, 16 employees of territorial subdivisions of the district hospital (paramedics) participated in the research.

RESULTS AND DISCUSSION

Megino-Kandalassky region is one of the agricultural areas inhabited by 3,2% from the total population of the RS (y), but it occupies a small area in comparison with other areas. It is referred to a group of river areas, where the typical seasonality of transport, which directly affects the system of drug supply. The research results can be applied to all areas lying beside the river taking into account correction factors related to each locality. Megino-Kandalassky region is located on central Asian lowland. The Western border of region passes through the branches of the river Lena. There are 3 plains situated on the territory of the district: Malinska, Nirukta, Tugulymsky. There are many lakes - Tanghulu, Balyktakh, Arylakh, also Abalak - lake with healing mud. Area - 11.7 thousand km². There are 31 municipal institution of education. Distance to Yakutsk: ground - 52 km, air - 70 km. The distance from the center of the district varies from 5 to 122 km. There are ground and air routes (the latter through sanitary aviation) between the settlement. The district main trade is agriculture, especially livestock (dairy cattle, beef herd horse breeding). Also, it includes grain-crops, potatoes, vegetables and fodder crops.

The number of resident population on January 1, 2014 was 30445 people. The population density is 2,65 people per 1 sq km (2013. - to 2.65). In the Republic of Sakha (Yakutia), the index is 0,31 people per 1 sq km.

Natural increase is 8.5 (2011), 9,4 (2012). Natural increase is growing. Death rate per 1,000 population is 9.4(2011), 9,6 (2012) [3,4].

There are 20 medical institutions in the district. In 2013, 123, 75 units of staff doctors are provided, 113,75 units of staff doctors are employed, individuals working 115 persons (2012. - 102), i.e. the proportion is 93%.

The system of drug supply of Megino-Kangalassky region presents only the retail level, and in localities with no pharmacies paramedic and midwife posts, district hospitals, medical clinics.

There are 17 organizations in retail trade, including any attached branches in total. 42, 85% of them belong to the state segment and 57, 15% belong to the private segment. It shows the equality of organization of drug supply in terms of ownership. The share of state-owned drugstores does not inferior to private due to opening branches Pharmacy # 25.

In the whole republic, the state and municipal forms of ownership of pharmacies began to decline since 2005, in view of insufficient profitability, especially in the Northern and Arctic regions. As a result of joint work of the line ministries with the heads of municipal formations, at least one state or municipal pharmacies was kept in each territorially isolated area.[8]

The number of inhabitants per one pharmacy organization is 2,5 thousand people. The availability of pharmacists per 10 thousand inhabitants is 1.9. The number of pharmacists provided per 10 thousand inhabitants is 6.6. Compared to other regions of the Republic it is average, although the Megino-Kangalassky region is the most densely populated.

Figure 1 shows the layout of pharmaceutical organizations, and FAP stations, medical clinics, district hospitals, which has the license for retail trade of drugs. The figure shows that there are only 7 pharmacies in the settlements of the region. Therefore, only 22.6 per cent of agricultural communities are covered. Pharmacies are concentrated mainly in the agricultural community, located at close distances between themselves and with good transport links, as well as with the highest population density. In settlements with no pharmacies pharmaceutical supplies shall be exercised by local district hospitals, medical clinics and FAP.

The district can be divided into 3 groups by the number of pharmacies: large settlements, medium towns and remote settlements. Pharmacies are concentrated, where the number of people is over 1000 people. FAP clinics, ambulances, district hospitals are located in all settlements, except those what are near to the Central district hospital (C. Petrovka, North Chuya). Comprising of district organizations what have license for pharmaceutical activity, is 81%.

Figure 2 shows that the bulk of medicinal maintenance of the population of the region accounts for pharmacy organizations. The share of the total turnover of separate subdivisions of district hospitals that have licenses for retail sale of medicines is only of 5.06%. Thus in these settlements account for 42 % of the district's residents.(figure 3)

In terms of turnover greater volume of service of the population belongs to the Pharmacy LTD. "Maya-Pharm" among private pharmacies. This pharmaceutical organization exists since

1994 and has branches in remote from each other settlements with largest populations. "OOO-Maya-Pharm" works in the system of supplementary provision of medicines, accepts applications from feldsher's stations of educational institutions of the Megino-Kangalassky region.

The survey population subjected 18 settlements of the three groups of 30 people. The total number of interviewed is 540. 310 respondents were female, 230 were male. Age categories: up to 20 years - 48 people, up to 40 years - 155, to 60 - 216, over 60 - 121.

Direct participation of the consumers let us consider the provision of pharmaceutical care not only as a set of objective characteristics, but also as a set of perceived subjective evaluations [2].

From figure 4 shows that the predominant number of people who apply for LAN 1 time per month. Moreover, the highest rate of 53% is occupied by the third group of settlements. Respondents to the third group of settlements comment on this situation as follows: departure to the district centre when necessary is difficult, and lack of time in connection with employment in the farm, financial condition does not allow to apply for a drug more than once a month. It turned out that from all three groups, the largest percentage of respondents need constant drug administration and has some chronic disease in history.

It should be noted that in the questionnaires stated the difference of prices for medicines in the Megino-Kangalassky region, and Yakutsk. This is because the approved limit retail markups on the list of essential drugs have different percentage. The city of Yakutsk refers to the first zone, where the percentage increase is 29%, Megino - Kangalassky region - a second zone where the percentage increase is respectively 47%. Due to the fact that the issue of pricing is a very sensitive topic, the difference in size of the markup population is marked as a significant disadvantage.

At this time, only 17 separate divisions by paramedics dispense drugs to the population, which is 74%. The remaining 26% of inhabitants of settlements receive medical help only by referring to the pharmacies the district center.

The method of random sampling was applied for the variability of the results of the questionnaire. Thus, the medical workers of 16 separate units of different settlements at a distance from 5 up to 122 km from the district center were subjected for the questionnaire.

In these structures employed specialists with higher education make 42,86%, middle make 57,14%, work experience varies from 3 to 38 years. One employee has a category of specialty what is the third. On average, separate units serve 450 - 520 inhabitants.

Values between 35 and 82 were given to the question "how many SKUs of drugs in your item is in stock?" List of medicines to be implemented by medical organizations having the license for pharmaceutical activity and their separate subdivisions, located in rural areas is regulated by the Ministry of healthcare of the Republic of Sakha (Yakutia)'s order from 24.09.2010, №01-8/4-994. According to the results of the survey, the average number of items is 67, as a percentage equal to 45,6%, which is less than half.

"Very poor" is the answer of 12,5% mainly medical personnel involved in separate divisions, located in the most remote from the Central regional hospital, which was to be expected. 31,25% answered "satisfactory", 18,75% responded "okay", and 37,5% answered "unsatisfactory" (Figure 6).

This 68,12% of interviewed medical workers answered "Yes" to the question "do you consider the available medical aid for the population in your community", considering that they sell drugs on applications of the population. 48,15% of these respondents work in the structural units located close to the district center.

Those who answered "no" 31,88% attributed to the fact that there is difficult transport links, the low solvency of the population and a number of other reasons.

It was noted by Federal service on surveillance in healthcare that residents of rural settlements that are located near cities and townswith no pharmacies, and with good transport links, are not interested in the purchase of medicines through the separate units of the medical organizations, including due to limited range and lack of discounts [5,6].

The question "Have actually improved medicinal assistance to localities with no pharmacies, after the introduction of a permit for retail sale for medical organizations?" was included to the questionnaire in order to evaluate the impact point in the area of retail trade geographically separate subdivisions of the district hospital of the Federal law of 12.04.2010 # 61-FZ "On circulation of medicines". According to 51,67% of respondents it has improved, and in the opinion of 48,33% of the interviewed health care workers it has not changed.

Six heads of pharmacies has taken part in questioning, irrespective of the organizational and structural forms of pharmaceutical organizations.

According to the survey the average age of the heads of pharmacies was from 45 to 55 years. Average of experience is 35 years. There were two pharmacists with higher category and two of the first category qualification.

Research has shown that opinions about the quality of pharmaceutical care of the heads of pharmacies are contrary to the opinion of the population living in settlements with no pharmacies.

All heads of pharmacies answered unanimously "Yes" to the question "How do you think: has drug use in communities with no pharmacies improved after the entry of Federal law №61. The answers were explained by the fact that it is unprofitable to open pharmacy organization with a staff unit in communities with small number of inhabitants, and the position of the Federal law legalized the retail sale of medicines if medical workers have a license.

It should be noted that in the course of the research showed that local hospitals are not included in the article of Federal law no. 61 in the implementation of pharmaceutical activity in separate divisions located in rural settlements lacking pharmacy organizations, the enumeration of the types of units (clinics, medical and first-aid stations, centers (departments) General medical (family) practice. Thus, 111 district hospitals out of 349 separate divisions have pharmaceutical license in the Republic, and in the Megino-Kangalassky region only 7 have it.

It is advisable to apply a standard that specifies the number of inhabitants served by only one pharmacy, or the density of the pharmacy network for optimal placement of the pharmacy network is. 3 models are developed for definition of this standard: separately for each subject of the Russian Federation, as well as for urban and rural areas.

Defining the number of inhabitants per pharmacy rural produced by the equation:

$Y_2 = 9,65 - (0,04773 \times X_3 + 1,475 \times X_4)$, where Y_2 - the number of inhabitants served by one rural pharmacy; X_3 - sale of medicines and medical products in calculation on one inhabitant for the analyzed year (thousand rubles). X_4 is the number of doctors per 1000,0 rural residents; 9,65 - constant coefficient equations; 0,04773 and 1,475 - the coefficients of the factors.

$Y_2 = 9,65 - (0,04773 \times 1,898 + 1,475 \times 4,8) = 2,5$ thousand people.

Based on these calculations in Megino - Kangalassky region should be of the order of 12 pharmacies.

CONCLUSION

Overall, the system of drug supply Megino-Kangalassky region operates repeating the characteristic tendencies of development of the system for the Republic and for the country. The share of pharmaceutical organizations is growing due to the opening of the private segment, production compounded pharmaceutical products, as well as throughout the country, is reduced. Pharmacies concentrated in towns with the largest populations. With the introduction of Federal law no. 61 "On circulation of medicines" drug coverage in separate divisions of the district hospital is expanded, including district hospitals, but today only 74 % of them operate. Turnover in separate divisions for the last year has increased significantly, but at the same time, studies have shown that it is insufficient. It takes only 5% of turnover in the area, although in these settlements 42% of the population inhabits. Less than half of the assortment of medicines

in respect of the approved by the Republic of necessary assortment is represented. In sociological research workers of separate units answered 12,5% - "very poor" and 31,5% - "unsatisfactory". There is a necessity of amendments in paragraphs of Federal law no. 61 "On circulation of medicines" in the part of regulation of pharmaceutical activity in settlements with no pharmacies, also inclusion in the list of separate units of the hospital yet, and district hospitals is required.

REFERENCES:

1. Balahanova E.G. Metodicheskie podhody k optimizatsii lekarstvennogo obespechenia jitelei sel'skikh naselennykh punktov [Methodological approaches of optimizing drug coverage to rural settlements] Dissertation author's abstract on scientific degree in pharmaceutical sciences, Perm, 2012, 23 p.
2. Buchnev B.P. Varsanidze S.L. Parfeynikov S.A. Kachestvennaya otsenka farmatsevticheskoi pomoschi [Qualitative assessment of pharmaceutical care] New Pharmacy, 2003, № 11, p. 25-27.
3. State Report on the Health of the Republic of Sakha (Yakutia) in 2011 / Ministry of Health of the Republic of Sakha (Yakutia), GBU Sakha (Yakutia) Yakut republican information-analytical center; (Redkoll.: Verbitskaya LI, et al), 2012, 148 p.
4. State Report on the Health of the Republic of Sakha (Yakutia) in 2012 / Ministry of Health of the Republic of Sakha (Yakutia), GBU Sakha (Yakutia) Yakut republican information-analytical center; (Redkoll.: Verbitskaya LI, et al), 2013, 139 p.
5. Dorofeyeva V.V. Sinaiskaia O.V. Razrapotka metodicheskogo podhoda k uluscheniyu kachestva okazaniya farmatsevticheskoi pomoschi aptechnymi organizatsiyami [Development of a methodological approach to improve the quality of pharmaceutical care pharmacy organizations] Vestn. People's Friendship University, 2004, № 4, p. 65-73.
6. Krupnova I.V. Lekarstvennoe obespechenie sel'skogo naseleniya – vajnyaya sotsial'no znachimaya zadacha [Drug provision of the rural population - an important socially significant problem] Herald Roszdravnadzor, "№ 1 (2011), 27 p.
7. Estimated population of the Russian Federation until 2030: Stat. Newsletter / Rosstat. Moscow, 2009, p. 7
8. Tarabukina S.M. Metodicheskie podhody k formirovaniyu regional'noi strategii lekarstvennogo obespecheniya naseleniya na primere Respubliki Sakha (Yakutia) [Methodological approaches to the formation of a regional strategy for drug coverage on the example of the Republic of Sakha (Yakutia)] Dissertation for the degree of candidate of pharmaceutical sciences, Tomsk, 2011, 223 p.
9. Federal Law 12 April 2010 N 61-FZ "On Circulation of Medicines".

The authors:

Tarabukina Sardana Makarovna - Candidate of Pharmaceutical Sciences, Associate Professor, Department of Pharmacology and Pharmacy MI NEFU, First Deputy General Director of JSC "Sahafarmatsiya", Yakutsk, Russia, e-mail: tcmx@mail.ru;

Akimova Agrafena M. - 5th year student of Pharmacy MI NEFU, Yakutsk, Russia.

Opinion Study of Medical Staff of Northern and Arctic Regions of the Republic Sakha (Yakutia) about the System of Medical Care

Evseeva S.A., Chasnyk V.G., Dranaeva G.G., Burtseva T.E.

ABSTRACT

The article is focused on the problem of medical care in the rural areas of the North, since this is the most socially significant task, and has a big load of negative experiences, gender stereotypes and scientific and methodological errors. The article presents the view of medical personnel of the northern and Arctic regions of the Republic to make management decisions in health care.

According to the respondents, the following factors: a shortage of specialized professionals, poor infrastructure, low levels of income affect the work in a health care institution. The proposals were introduced by the Ministry of health of the respondents in the framework of the modernization of the health care in 2012-2013, especially in salary, equipment facilities, equipping the new information technologies.

Keywords: problems of rural health care, satisfaction of medical staff, Yakutia.

INTRODUCTION

The problem, the volume and quality of medico-social assistance to the population in rural areas, first of all, depend on the distance from residence facilities, staffed with qualified personnel and equipment, to receive specialized medical treatment, the degree of implementation of the social security health regulations [1].

Negative effects of social and political change, economic problems of recent decades had an impact on the livelihood of the rural population, the destruction of the basic principles of organization of medical assistance for this social group. Reduction by one third in the number of community hospitals, uncompensated, usually an adequate development of outpatient care, worsening the shortage of doctors in rural clinics reduced the availability of primary medical care. Less accessible to the rural population has also become specialized medical assistance in hospitals and regional and national hospitals, in connection with material difficulties of travel [2-4]. Compared with rural doctors less security at 3.4 times and nurses-in 1.6 times. In this regard, the burden and responsibility on rural medical workers well above.

Study of the opinions of the medical personnel of the northern and Arctic regions is an important part of the system of administrative decision-making in health care, through feedback



mechanisms to adjustment programmes for the modernization of industry and increase their efficiency.

MATERIALS AND METHODS

We conducted an anonymous survey of health care workers of the Republic of Sakha (Yakutia) on the State of rural health in 17 areas in the period of 2011-2012: Mirnui, Hangalasskij, Zhigansky, Abyjskij, Amginskij, Neryungri, Aldansky, Namskij, Suntarskij, Kobâjskij, Verhnevilûjskij, Olenekskij, Olekminsky, Verhnekolymskij, Ust-Maya, Verkhoyansk. In total 274 people filled questionnaires (see table 1).

Table 1

Distribution of respondents by region of Sakha (Yakutia)

Areas	Number of respondents	Doctors diff.	Nurses	Physician Assistant	Midwives	Nurses
Mirniy	31	15	14	2		
Khangalasskiy	33	7	12	9	4	1
Zhiganskiy	10	4	5	1		
Abiyskiy	5	1	3	1		
Aldanskiy	31	6	20	3		2
Suntarskiy	10	2	7	1		
Kobyayskiy	9	3	3	3		
Olekminskiy	12	5	6	1		
Verkhnevilyuiskiy	40	7	15	4	4	5
Olenekskiy	22	5	7	5	5	
Verkhnekolimskiy	7	3	4			
Ust-Maya	4	3	1			
Verkhoyanskiy	11	2	7	2		
Amginskiy	44	12	18	13	1	
Neryungry	3	1	2			
Namskiy	7	1	6			
Total	274					

RESULTS AND DISCUSSION

An anonymous survey of health professionals working in the pediatric service of the Sakha (Yakutia), had revealed a number of negative health and social factors: health workers are not fully satisfied with the quality of medical care in a health care setting (80.6%). to work in a health care setting, according to respondents, the following factors:

1. Shortage of specialists of narrow profile -71.5%.
2. Poor material and technical base of -59%.
3. Lack of necessary medicines-41.6%.
4. The constraints States doctors - 40,1%.
5. The constraints States nurses -19,7%.

According to respondents the level of income of health workers is only enough for food and essentials - 79,1%.

When conducting medical examinations of children are having difficulty: not enough specialists-54.3%, parents do not have time to drive to the examination-43.7%, children do not want to miss school-21%. Most health professionals believe that the more time goes on the record of an outpatient card than the examination of the child. Over the years, has sharply increased paper work that impairs the preventive work. Do not fill the daily clinical journal and f. 30, reloaded the other paper work. There is no continuity between the specialists and employees school-preschool Department, as well as among specialists.

Almost all health professionals believe that over the years, the work is deteriorating and the figure was 97%.

Recycling is due to the following factors: a lot of paper work (84.3%), very many different inspections (39.7%), land (20.8%) and rebooted. Also consider that the work of specialists organized by the irrational, that unnecessarily visiting children and medical patients of congestion (according to respondents in 41.2% of cases).

In the hospital, the periodic travel in connection with numerous multiple exits in Yakutsk.

Many of them believe that if there was a continuity of work between doctors, school district preschool doctors, specialists would be reduced congestion and improved the clinical examination of children (67.8%).

63.5% of respondents indicated a huge technical and medical assistance provided by pediatric NCM. However, respondents believed that there are some factors hampering the assessment and treatment of children in an institution of higher level, such as: insufficient number of quota-34% and the complex system of referral to ACS NCM (for destinations in the PC with the child's parents to NCM, first go to the CSF, then in Yakutsk (NCM), i.e., if the locality of hard-to-reach, the parents have the extra spending to get directions) (76%).

There is a high percentage of interchangeability among doctors through: mostly doctors and nursing staff are women-many of them go on a decree that is the same and interchangeable during the holidays.

According to respondents in the last 5 years of health in the region was worse-12.5%; has not changed-48.5%; got better-30%. 21.5% of health care workers are satisfied with their work, 60.2%-somewhat satisfied. Most medical professionals do not completely satisfied with my work due to lack of time for self-education due to low wages, especially among nurses, bad equipment of hospitals, the paramedic obstetric stations, district hospitals do not have district pediatricians, because of the load feeding and sleep mode is often disrupted.

CONCLUSION

Questionnaire of health workers had identified numerous judgments and proposals that will be put into practice. Certain elements of the proposals have already been implemented by the Ministry of Health of the Republic within the framework of the Modernization of health care, especially in terms of remuneration, provision of equipment, equipping the new information technologies.

REFERENCES:

1. Lindenbraten A.L. Aktual'nye problemy sovershenstvovaniya zdavoohranenija v sub#ektah Rossijskoj Federacii [Actual problems of improving health in the constituent entities of the Russian Federation] Probl.social'noj gigieny, zdavoohranenija i istorii mediciny [Probl. social hygiene, health and the history of medicine]. Moscow, 2004, №4, p. 23-26.
2. Lisicyn Ju.P. Social'naja gigiena i organizacija zdavoohranenija (lekicii) [School of public health (lectures)]. Moscow: Medicina, 1973, 456 p.
3. Modestov A.A., Kosova S.A., Bondar' V.I., Nevolin Ju.S., Fedotkina S.A. Sostojanie zdorov'ja detskogo naselenija kak osnova razrabotki regional'nyh programm medicinskoj profilaktiki [The health of the child population as a basis for the development of regional programmes of preventive medicine]. Rossijskij pediatricheskij zhurnal [Russian Pediatric journal], 2013, №4, p. 56-57.
4. Jakovleva T.V., Ivanova A.A., Modestov A.A. Osnovnye napravlenija modernizacii sistemy ozdorovlenija detej i podrostkov [Main directions of modernization of the system of rehabilitation of children and adolescents]. Rossijskij pediatricheskij zhurnal [Russian Pediatric journal], Moscow, 2011, №3, p 37-9.

**Information about the authors:**

Evseeva Sardana A.- post-graduate State Pediatric Medical Academy of Saint-Petersburg pediatric university,

Dranaeva Galina Gavrilovna -PhD, researcher of Yakut science center,

Chasnyk Vyacheslav Grigorevich- MD, Professor of Saint Petersburg State Pediatric Medical University,

Bourtseva Tatyana Egorovna - MD, Deputy Director of Yakut science center

Address for correspondence: bourtsevat@yandex.ru.

**Analysis of the Structure of Neonatal CHD in RS (Y) according to the Republic
Hospital № 1 - NCM Data for 2011-2013**

T.I. Nelunova, V. G. Chasnyk. T.E. Burtseva, E.D.Son, N. A. Afanasyeva,
A.I. Yakovleva, T.S. Neustroyeva

ABSTRACT

The structure of congenital heart diseases (CHD) and large vessels in the newborn in the Republic of Sakha (Yakutia) was under study. All the share of septal defects group combined with functioning arterial duct and pulmonary artery valve stenosis was 82,20% of the all CHD (899). The CM of large vessels was 8, 90% (80) of all diagnosed cases of CHD. Complex, combined CHD were 4, 67% (46) of the total number of detected CHD.

Mortality rate was 1.22% (11 cases) of the total number of children with CHD (899) and was formed by obstructive lesions of the aorta and complex defects. The CHD structure has a preponderance of boys: 476/52, 94%. The absolute predominance of children Yakuts with CHD was revealed: 72, 08% (648) of all diagnosed cases of CHD.

Keywords: congenital heart disease, septal defects, developmental abnormalities of large vessels, complex congenital heart disease, structure of congenital heart disease in the Republic Sakha (Yakutia).

INTRODUCTION

Today in structure of children's incidence, disability and infantile mortality congenital developmental anomalies, (CHD) which meet at 4,0-6,0% of newborns are of all great importance, and their contribution to structure of death of children on the first year of life makes more than 20,0% [1,4]. In structure of congenital developmental anomalies the congenital heart diseases (CHD) and large vessels are high on the list (22% of all CD) and their frequency of birth rate worldwide makes 8-14 cases on 1000 newborns [2]. Frequency of occurrence of CHD among the live-born makes 0,7 on 1000 newborns. In 40% of cases CHD are the reason of perinatal losses and in 60% of death on the first year of life [5,8]. The researchers conducted in the USA and Great Britain, showed that at a natural current of CHD by the end of the 1st year more than 70% of children, in North America this pathology is a cause of death of 37% of babies, and in Western Europe – 45%. [3,9]]. Birth rate of children with heart diseases makes in the Russian Federation from 3,2 to 8,0 on 1000 newborns and tends to growth [6]. Republic of Sakha (Yakutia) -RS(Y) steadily is a part of the few regions of Russia in which the natural increase of the population remains. In dynamics, in three years, in RS (Y) the indicator of birth

rate increased by 4,8%. / to data of Territorial body of Federal State Statistics Service (TB FSSS) / In structure of infantile mortality for a number of years CD takes the second place (2012 - 23,1; 2011 - 16,5; 2010 - 11,8 on 10.000 been born live) after "diseases, specific for the neonatality period" (2012 - 45,5 on 10 thousand been born live; 2011 - 25,7; 2010 - 28,6). In 2012, in the republic, in connection with transition to nursing of newborns with extremely low body weight by criteria of WHO growth of coefficient of infantile mortality in comparison with 2010 by 1,4 times – 9,9 on 1000 been born (2011 – 6,3 is noted; 2010 - 7,2). In 2012, in connection with transition to criteria of registration of childbirth under the WHO recommendation from 22 weeks of pregnancy, the indicator of perinatal mortality according to MPI in comparison with 2010 grew by 1,6 times and made 13,7 on 1000 been born live and dead (2011 - 8,6; 2010 – 8,4). In structure of the reasons of **perinatal mortality** the specific weight of congenital anomalies of development – by 1,5 times significantly increased: 2012 - 23,9% (56 cases), 2011 - 15,7% (22 cases), 2010 - 16,3% (22 cases). Leaders in structure of congenital developmental anomalies are multiple developmental anomalies (33,9%), heart diseases and the central nervous system (on 21,4%). On disability the congenital developmental anomalies (CDA) of which 48,3% make anomalies of system of blood circulation are the main reasons of an exit of children. / the report of the minister of Health about states of health of the population of RS (Y); 2012/. According to the existing order MH Russian Federation No. 268 of September 10, 1998 "About monitoring of congenital developmental anomalies among children" and to No. 392 order MH Russian Federation of 02.11.1999 among all heart diseases and large vessels of obligatory registration and to the account only congenital anomalies of large arteries and "a syndrome of a left-side hypoplasia of heart" are considered. At present there is no uniform full monitoring of CH in RS (Y) in nosological forms since information on other nosological forms and anatomic options of CH drops out. Primary incidence of CHD of bodies of blood circulation of children's age, is generally formed by incidence of CHD among newborns. Thus, incidence growth among newborn children of CD, in which structure of CHD occupy one of leading places, in RS (Y); essential contribution of in formation of perinatal and infantile mortality, and an invalidization among children; insufficient data on a prevalence, frequency and CHD structure among newborns in RS (Y) formed the basis for carrying out studying of frequency and structure of CHD and large vessels among newborn children in RS (Y). Relevance of this problem is caused not only their big prevalence, but a tendency to increase in specific weight of more serious, combined CHD with a frequent fatal case on the first year of life [7] and need rendering the high-tech cardiac help. Data on a prevalence and structure of CHD are necessary for planning

and the organization of volumes of the specialized high-tech cardiac and cardiological help for children.

Purpose of research: to study structure of the congenital heart diseases (CHD) and large vessels among newborns in RS (Y) according to the Perinatal Center State Budgetary Institution RS (Y) RB No. 1NCM for 2011-2013.

MATERIALS AND RESEARCH METHODS

Research was conducted on the basis of the Perinatal Center of State Budgetary Institution RS (Y) RH1 NCM among live-born newborns: department of pathology of newborns (DPN), department of nursing of the prematurely born (DNPB), infectious department of newborns (IDN)

CHD were registered according to the nomenclature headings Q20-Q28 "Congenital anomalies of system of blood circulation" the XVII class "Congenital Anomalies [Developmental Anomalies], Deformations and Chromosomal Violations" of the International statistical classification of diseases and the problems connected with health (the 10th revision) (MKB10) as primary documentation are used: stationary magazines (form No. 010 order of MH USSR 04.10.1980 No. 1030); statistical cards of the inpatient (form No. 066/u-02 order MH RF 30.12.2002 No. 413) Nosological diagnoses of CHD are confirmed with data of an echocardiography of heart with a Doppler sonography of vessels (EHO-KG with DS), electrocardiograms (electrocardiogram), roentgenograms, computer tomograms in angiographic researches. The indicator of frequency was considered on 1.000, been born the live.

RESULTS AND DISCUSSION

The analysis of structure of CHD according to the Perinatal center State Budgetary Institution RS (Y) RH№1 NCM) showed the following results. According to our data, during 2011-2013 of all 899 cases of CHD, among the newborns who were born live and being on inspection, treatment, and as at the 2nd stage of nursing concerning prematurity in profile departments are registered. In total it is processed: in OPN 433, in DNPB, in IDN of 200 statistical cards. Received results are presented in табл.№1. According to these tab. No. 1 in CHD structure the general share of group of the septal defects made 59,29% (533), occupying a half of all revealed cases of CHD. On the first place among all revealed CHD defect of a interatrial baffle (DRIB)-303/33,7% was registered; further combination of defect of an interventricular septum(DIVS) and DRIB-of 109/12,12%; isolated P-of 84/9,34%. The septal defects won first place in group % DRIB 303 / 56,85; on the second place on frequency a combination of DRIB and DIVS-109/20,45 of %; on the third place of DIVS – 84(15,76%); on the fourth place DIVS, DRIB combination, valvate stenosis of a pulmonary artery (VSPA) of- 37/6,94%. The share of group of a combination the septal defects with the functioning arterial channel (FAC), VSPA made 22,91% (206). In this group first place won a combination of DRIB with FAC – 75/36,41% and DIVS with FAC-of 74/35,92%; second place combination of DIVS, DRIB to FAC-of 53/25,23%; on the last place on frequency the combination of DRIB to FAC and VSPA - 4/1,94% met. Thus all share of group of the septal defects (533) and groups the

septal defects in combination with FAC and VSPA (206) made 82,20% of all CHD (899). Defects of large vessels (isolated FAC, an aorta coarctation (Co Ao), abnormal drainage of pulmonary veins (ADPV), a stenosis of a pulmonary artery (LA stenosis)) made only 80 cases (8,9%) of the all revealed cases of CD, from them congenital malformations of large arteries unambiguously prevail – 72 cases. In structure of CD of large vessels isolated FAC – 51/63,75% most often met; on the second place Ko Ao – 21 cases / 26,25%; ADRV (total / 3 and partial / 1) - 4/5%; stenosis of LA of 4/5%. The share of a tetrad of Fallo (T. Fallo) made 1,11% (10) of all revealed CHD (899). The share of anomaly of Ebstein (4) and congenital anomalies of the tricuspid valve (1) made 0,56% (5). Share of valvate CHD: atresias of the tricuspid valve (atresia of TV) as a part of a syndrome of a hypoplasia of the right compartments of heart (1), atresias of the valve of a pulmonary artery it (APA) - (7), made 0,89% (8) of all revealed CHD. To the share of the atrioventricular channel (AVK) (10) fell 1,11% from all cases of CHD. The share of the transposition of the main vessels (TMV) made 0,45% (4) Share of a double - outlet right ventricle (DO from RV) 0,22% (2). Other CHD: single ventricle (SV) (OV) - 0,11% (1). Difficult, combined CHD made 4,67% (46) of all quantity of revealed CHD. In structure of difficult CHD, T. Fallo-of 21,74% (10) and AVK-21,74% (10) were the most often met. On the second place: It is AVC-15,22% (7), on the third place - TMS of 8,70% (4), anomaly of Ebshteyn-of 8,70% (4), total ADRV (TADLV) - 6,52% (3), on the fourth DO from RV - 4,35% (2), other defects: TC atresia as a part of a syndrome of a hypoplasia of the right compartments, single ventricle (SV), on 1 (on 2,17%).

The lethality made 11 cases that made 1,22% of total of children with CHD. (899). Among them: AVC – 2, obstructive damages of an aorta in combination with septal defects – 4, partially open AVC with a hypoplasia of an aorta-1, DO from RV-2, Edwards's syndrome with case DIVS, DRIB-2. Department of pathology of newborns: the general lethality during 2011-2013 made 5/0,92%. Department of nursing of the prematurely born: the general lethality, during 2011-2013 in CHD structure made 6/2,57%. Higher share of a lethality in DNPB probably is caused by specifics of department: nursing of deeply prematurely born children, including with extremely low body weight with gestation term of 25-26 weeks, with severe defeats of CNS, bronchopulmonary displasia (BPD), the syndrome of respiratory frustration (SRF) and accompanying MCHD and the genetic pathology, being on mechanical ventilation.

Studying of structure of CD according the sex revealed the following: distribution of boys and girls approximately identical, but boys were revealed 476/52,94%, slightly more, than girls 423/47,06. On national structure Yakuts made 72,08% (648 newborns), the Russian 16,70% (150), Evenks of 4.89% (44), Evens of 1,33% (12), Yukaghirs, Dolgans, Chukchi 0,11% (on 1)-

each, other 4,67% (42). In total indigenous Arctic ethnic groups (IAEGs) made 6,56% (59 newborns) of all revealed cases of CHD. In IAEGs structure: on the first place: Evenks of 74.58% (44), second Evens for 20.34% (12), further Yukaghirs, Dolgans, Chukchi 1,69% (1) - each. Absolute prevalence of children of Yakuts with CHD is revealed: 72,08% (648)

CONCLUSIONS

During 2011-2013, according to our data, among all revealed cases of CHD (899) the group the septal defects often met made 59,29% (533) and also group of a combination the septal defects with FAC and VSPA which made 22,51% (206). All share of group the septal defects (533) and groups of the septal defects in combination with FAC and VSPA (206) made 82,20% of all CHD (899), occupying the main part of all revealed CHD. The share of CD of large vessels (isolated FAC, Co Ao, ADPV, PA stenosis) made 8,90% of all revealed cases of CHD (80), from them unambiguously prevail CD of large arteries of-90%/72 case.

T. Fallo's share made 1,11% (10) of all revealed CHD (899). The share of anomaly of Ebstein (4) and congenital anomalies of the tricuspid valve (1) made 0,56% (5). Share of valvate CHD: tricuspid atresias as a part of a syndrome of a hypoplasia of the right compartments of heart (1), atresias of the PA (7) valve made 0,89% (8) of all revealed CHD. To the share of AVK 1,11%(10) fell from all cases of CHD. The share of TMS made 0,45% (4) the share of DO from RV is 0,22% (2). Other CHD: single ventricle (SV) - 0,11% (1). Difficult, combined CHD made 4,67% (46) of all quantity of revealed CHD. In structure of difficult CHD most often met a tetrad of Fallo-of 21,74% (10) and AVC-21,74% (10).

On the second place: atresia of the PA valve of-15,22% (7), on the third place - TMS of 8,70% (4), anomaly of Ebstein-of 8,70% (4), TADPV-6,52% (3), on the fourth DO from RV-4,35% (2), other defects: 1 (on 2,17%)- each. During 2011 for 2013 the lethality made 1,22% (11 cases) of total of children with CHD (899) and was formed due to obstructive damages of an aorta and difficult defects. In structure of CHD there is some prevalence of boys: 476/52,94%. On national structure: Yakuts made 72,08% (648 newborns), the Russian 16,70% (150), Evenks of 4.89% (44), Evens of 1,33% (12), Yukaghirs, Dolgans, Chukchi - 0,11% (on 1) - each, other 4,67% (42). In total indigenous Arctic ethnic groups made 6,56% (59 newborns) of all revealed cases of CHD. Absolute prevalence of children of Yakuts with CHD is revealed: 72,08% (648)

Table 1

Structure of CHD according to nosological entity conducted on the basis of the Perinatal
Center State Budgetary Institution RS (Y) RHN№1 NCM in 2011 -2013

Nosological entity CHD ICD 10	Total CHD 899	
	amount	%
Q21.8 000	40	4,45
Q21.0 DIVS	84	9,34
Q21.1 DRIB	303	33,7
Q21.0+Q21.1 DIVS+DRIB	109	12,12
Q21.0+Q21.1+ VSPA DIVS+DRIB+VSPA	37	4,12
Q25.0 FAC	51	5,67
Q25.0+ Q21.0 FAC+DIVS	74	8,23
Q25.0+ Q21.1 FAC+DRIB	75	8,34
Q25.0+ Q21.1+VSPA FAC+DRIB+VSPA	4	0,45
Q25.0+Q21.0+ Q21.1 FAC+DIVS+DRIB	53	5,9
Q25.1 Ko Ao	21	2,34
Q21.3 T. Fallo	10	1,11
Q26.2 T.ADPV	3	0,33
Q26.3 Ч. ADPV	1	0,11
Q22.8 Congenital anomaly TC	1	0,11
Q22.5 Ebstein's disease	4	0,45
Q22.8 Atresia TV	1	0,11
Q21.2 General AVC	10	1,11
Q20.3 TMS	4	0,45
Q22.0 APA	7	0,78
Q25.6 Stenosis JIA	4	0,45
Q20.8 SV	1	0,11
Q20.1 DO from RV	2	0,22



List of references

1. Bogantsev S.V. Analiz struktury vrozhdyonnykh porokov serdtsa u detei [The analysis of structure of congenital heart diseases among children]. Omskiy nauchnyi vestnik [Omsk Science Messenger], 2006, No. 3, PP.196-200.
2. Zeminskaya D.I. Detskaya invalidnost [Children disability]. Moscow: Med., 2001, PP.34-47.
3. Lyapin V.A. Sotsialno znachimaya patologiya detskogo naseleniya promyshlennogo tsentra Zapadnoi Sibiri [Social significant pathology of the children's population of the industrial center Western Siberia]. Sibir-Vostok [Siberia-East], 2005, No. 3, PP. 9-11.
4. Magomedova Sh.M. Epidemiologiya VPS u detei v razlichnykh klimatogeograficheskikh zonakh Respubliki Dagestan [Epidemiology CHD among children in various the climatic geographical zones of the Republic of Dagestan]. Avtoref. dis. na soiskanie uchenoi stepeni kand. med. nauk: spets. 14.02.02 Epidemiologiya [Abstract on scientific degree medical sciences: special 14.02.02 Epidemiology]. Mahachkala, 2006, P.48.
5. Moiseenko R.A. Volosovets A.P. Sovremennye problemy i zadachi detskoj kardiorevmaticheskoi sluzhby Ukrainy [Modern problems and tasks of children's cardiorheumatic service of Ukraine]. Materialy konferentsii Aktualnye voprosy detskoj kardiorevmatologii [Materials of the Topical Issues of Children's Cardiorheumatology conference]. Evpatoriya, 2006, PP.27-28.
6. Mutafyan O.A. Poroki i malye anomalii serdtsa u detei i podrostkov [Defects and small anomalies of heart among children and teenagers]. SPb.: SPbMAPO, 2005, P.479
7. Seidbekova F.O. Chastota vstrechaemosti vrozhdennykh porokov serdtsa sredi novorozhdennykh g. Baku [Frequency of occurrence of congenital heart diseases among newborn of Baku city]. Visnik problem biologii i meditsiny [Messenger of Problems in Medicine], 2013, Iss.1, Vol.2 (99), P.158
8. Boon R. Artifical chordac for pediatric mitral and tricuspid valve repair/R. Boon, M. Hazekamp, G. Hoohenkerk [et al.] // Enr. J. Cardiothorac. surg. -2007 . – Vol. 32, No. 1. - River 143-148.
9. Rosano A. Potto T I). Potting P. Mastroiaeoovo T. Infant mortality and congenital anomalies from 1950! o 1994: An international perspective//J. Epidemiol. Community Health. - 2000 . - Vol. 54 . - P. 660-666 .

**Data about authors:**

Nelunova Tuyara Ivanovna - postgraduate SPSMA, doctor cardiologist of cardiac department RH№1 NCM, nelunova-ti@mail.ru

Chasnyk Vyacheslav Grigoryevich – MD, prof., chair of depart. SPSMA, senior researcher YSC CMP SB RAMS

Bourtseva Tatyana Egorovna – MD, deputy Director YSC CMP SB RAMS

Son Eudokia Danilovna – PhD, associate professor of children's diseases of FPGS NEFU,

Afanasyeva Natalya Aleksandrovna – Head of department of newborns RH№1-NMC,

Yakovleva Anisiya Ilinichna - Head of department of nursing prematurely born RH№1-NCM,

Neustroyeva Tatyana Semenovna - Head of infectious department RH№1-NCM.

Distance Education Technologies in the Training of Highly Skilled Medical Personnel

A. L. Dorofeyev, N.A.Pestushko, S.V.Pyatnitskaya

ABSTRACT

Modern information and communication technologies in higher educational institutions allow more effective organization of medical workers professional improvement. The presented work is devoted to consideration of opportunities how to use distant learning in the course of training of healthcare workers. Distant learning in medicine has obvious pluses. Medical workers not only increase qualification according to significant issues of medical practice, but also have an opportunity to bring level of the vocational training to demanded accreditation indicators. There is interdependence between distant educational technologies in medicine and increase of productivity of rendering medical services. Continuing medical education assumes module curriculum, according to an individual plan of training. Within the programs of distant learning provided by a an educational institution of higher learning, development of each educational module is confirmed by receiving a positive evaluation by testing, and paper writing on the offered subject. The level of training is also checked by attendants' ability to solve clinical cases and by questioning and oral discussions. Distant learning according to the programs provided by public organizations includes tests at the end of each educational module. Within full-time tuition for course attendants, conferences, round tables discussions and seminars are held. The developed and approved technology of professional development is presented in the article, the difficulties connected with distant learning of medical workers are specified, perspectives of the organization of distant learning are analyzed and necessary conditions for training of highly skilled medical workers are considered.

Keywords: distance educational technologies, medicine, health care, distance learning, professional improvement.

For the last two decades computer and information technologies have become an everyday reality of people and their professional activities. Computers are used in different spheres – science, industries and at home. Computers help to process, store, exchange information, model natural processes and mathematic objects. It cannot but demonstrate a growing importance of information technologies and broadening of their implementation in everyday life [1, 2, 4].

Current information and communication technologies used in educational institutions help to organize a continuing education for the specialists in natural sciences and humanities [12].

Implementation of IT in education allows making a learning process effective stimulating creativity and research potentials of the learners [11].

Continuing education is the system of gaining new knowledge, skills that improve professional activities. In other words, this system is an obligatory condition for professionalism improvement and broadening of specialists/ competence. Continuing education is very important for healthcare providers. Medicine is dynamically changing. New knowledge on diseases, their diagnostics and treatment appear new medications are being tested and approved in medical practice.

Continuing education can be performed full time, part time on an individual schedule and simultaneously with work [8]. In medicine, professional training combined with work is very important.

According to the Labor Law of the Russian Federation (article 196), and the decree of the Ministry of Public Health on August 03 августа 2012 г. № 66н «On the order and duration of continuing education for health and pharmacy care providers” an employer is to guarantee to organize continuing education for all medical personnel at least once in five years [7].

Healthcare workers without a specialist’s license or a certain qualification have no right to provide medical services. According to the Labor Law of the RF (iss. 3 p. 1 art. 81), insufficient qualification of a medical worker or occupation inconsistent with qualification revealed during attestation may be the reason for laying out [10].

Continuing education system in medicine has its pluses. It allows gaining new knowledge without going away to special educational institutions that are usually located in large university centers. It cuts down or significantly decreases financial losses. Distant learning helps medical workers to renew knowledge, to receive new information on diseases, their diagnostics and treatment. The education becomes continuing going simultaneously with work. Medical workers implement new knowledge in their clinical practice. At the same time, taking into consideration a severe shortage of doctors and nurses such system of continuing education does not impede the functioning of medical institutions.

There is interconnection between medical continuing education and medical service efficacy. The studies of I.S. Rodikova show that IT technologies in a combination with pharmacological support algorithm in emergencies increased 1.7-time efficiency of hypertension crisis treatment. In addition, the number of hospitalization decreased 2.5 times, repeated calls for acute coronary syndrome dropped down 1.4 times, a number of lethal cases decreased 1.8 times [9].

The system of distant learning has been functioning in the Far Eastern State Medical University since 2009. The first training courses were organized and conducted under a supervision of Professor Voronina N.V.

At present qualification improvement by distant learning is conducted on for-profit basis. The most active departments participating in continuing education programs are therapy and preventive medicine, public health and healthcare, psychiatry and narcology, pharmacy organization and economics.

Healthcare workers not only improve their qualification but also raise their professional knowledge and skills to the requirement of accreditation indexes. Distant learning helps to provide the course attendants with the information on all the requirements to healthcare providers.

At the same time many continuing education courses attendants prefer a full time education. There are several reasons for it. First, many doctors consider continuing education as an additional “vacation” being overloaded at work. Second, contact hours with faculty members help to receive explanations and comments. Third, distant learning is assumed by many doctors to be an additional pressure during working hours.

Since December 2013, the Far Eastern Medical University has started a Pilot project on continuing education [6]. Two departments: therapy and preventive medicine and pediatrics with the course of neonatology of the continuing education faculty are involved in the project. The latter is based on a module principle when training is scheduled individually for each attendant.

Figure 1 demonstrates the system of continuing education that has been worked out and is being tested in our university.

After placing a request for training, an attendant receives the following documents: “appointment blank” a contract on educational services provision, consent on personal data processing. Three sides sign a contract: an attendant, a medical institution and the university. It is valid for one calendar year.

The documents are filled in by an attendant and are submitted to the faculty of continuing education. Personal data are installed into a computer database of the FESMU and an attendant receives a personal code for an access to the portal. He/she has to register at the site of Coordination Counsel on the development of continuing medical and pharmaceutical education to get an individual code allowing working with educational modules of public organization. (www.sovetnmo.ru)

The supervisor of a training course compiles an individual curriculum. It comprises 114 credits out of which 36 credits cover the educational programs recommended by public

educational institutions. The program includes two parts: full-time and distant provided by the university and by public professional organizations. .

After filling in all the necessary forms and making up an individual curriculum, a faculty member e-mails educational modules to course attendants. Lectures are delivered off-line. However, they are intended to be presented on-line.

Each educational module is supposed to be learned when a good grade is received. Knowledge level is checked by tests and a written work on suggested subjects. During full time education, know ledges are also evaluated by clinical tasks and questioning. Distant training according to the curricula approved by public organizations includes tests after each educational module. In the framework of full time training conferences, round table discussions and seminars are conducted.

A test is passed if an attendant gives 70% of correct answers. If the result is lower, a test has to be made one more time. Clinical tasks or case studies and questioning are assessed as “passed/ not passed”. After a training course of 144 hours and passing all tests and other evaluations, an attendant takes an exam on all the studied material. If everything is successful, an attendant receives a certificate on qualification improvement. If necessary, a certification examination may take place and after it, a certificate of a specialist is given.

During computerized distant learning, each attendant can contact a mentor or a course supervisor as well as experts who provide services in continuing education. All the experts have scientific degrees and had fellowships in leading Russian medical centers.

According to the standards of continuing medical and pharmaceutical education for primary care physicians and pediatricians, public organizations work out components of educational programs: conferences, round table discussions, master-classes, trainings, seminars. All these events have individual codes, which attendants receive after registration. It allows doctors adding information to the educational portfolio on the site of the Coordination Counsel. This site also has informational and educational manuals included into individual curricula of attendants.

To monitor the quality of educational services the dean’s office of the continuing education faculty anonymously questions attendants and their employers.

Transition to a distant training within the framework of this pilot project has revealed several difficulties connected with medical personnel qualification improvement. Many attendants have very low computer skills; they do not know how to use –mail, Internet and so on. That is why many doctors of older age express no wish to participate in distant learning programs.

We should emphasize it one more time that low computer skills or their total absence is the most serious problem that hinders implementation of distant learning programs for healthcare providers. Although there are computers at work places and more people are learning how to use them, only from 59,1% to 72,7% (instead of necessary 90%) of medical workers know how to use a computer [3, 5].

One of the perspective of distant learning must become a creation of unified information system with Russian and foreign medical universities and schools. It will help to exchange information, make up a database of tests, and organize interactive conferences, lectures and training courses.

Only if all the training programs attendants have a good computer skills and proficiency, a medical continuing education will become effective and successful. This goal may be achieved with the help of short training courses. A more complicated objective is setting up of universities' computer network that will help to organize unified information and educational space where conferences and seminars can be conducted.

REFERENCES

1. Agranovich N.V. Hodjayan A.B. Vozmojnosti i effektivnost distantsionnogo obucheniya v meditsine [Capacity and effectiveness of distance learning in medicine] Fundamentalnyie issledovaniya [Fundamental research], 2012, № 3, PP. 545-547.
2. Apolihin O.I. Sivkov A.V., Kazachenko A.V. i dr. Distantsionnyie obrazovatelnyie tehnologii v urologii: perspektivy, tendentsii razvitiya. Opyit FGBU "NII urologii" Minzdrava Rossii [Distance education technologies in urology: perspectives and trends. Experience FGBI "Institute of Urology" Russian Ministry of Health] Eksperimentalnaya i klinicheskaya urologiya. [Experimental and clinical urology], 2013, № 4, PP. 4-8.
3. Dzeranova N.G. Otsenka effektivnosti obucheniya meditsinskih rabotnikov informatsionnyim tehnologiyam [Evaluating the effectiveness of training of health workers Information Technology]: avtoref. dis. kand. med. nauk [abstract Ph.D. in Medicine] Moskva, 2013, 25 p.
4. Klintsevich S.I., Bertel I.M., Lukashik E.YA. Distantsionnoe obuchenie v meditsinskom obrazovanii [Distance learning in medical education] Fundamentalnyie mediko-biologicheskie nauki i prakticheskoe zdravooohranenie: sb. nauch. trudov 1-y Mejdunarodnoy telekonferentsii [Fundamental life sciences and healthcare practice: Collected papers] (Tomsk 20 yanvarya-20 fevralya, 2010). Tomsk: SibGMU, 2010, P.172 .

5. Kovalev V.P. Ispolzovanie informatsionnyih tekhnologiy v sovershenstvovanii meditsinskogo obslujivaniya naseleniya [Use of information technology in improving medical services] avtoref. dis. kand. med. nauk. [abstract Ph.D. in Medicine] Moskva, 2011, 25 p.
6. Prikaz Minzdrava Rossii ot 11.11.2013 N 837 "Ob utverjdenii Polojeniya o modeli otrabotki osnovnyih printsipov nepreryivnogo meditsinskogo obrazovaniya dlya vrachey-terapevtov uchastkovyih, vrachey-pediatrov uchastkovyih, vrachey obschey praktiki (semeynyih vrachey) s uchastiem obschestvennyih professionalnyih organizatsiy" [Order of the Ministry of Health of Russia from 11.11.2013 N 837 "On Approval of the model working out the basic principles of continuing medical education for physicians vrachej precinct, district pediatricians, general practitioners (family doctors) with the participation of professional organizations"].
7. Prikaz Ministerstva zdavoohraneniya Rossiyskoy Federatsii ot 3 avgusta 2012 g. №66n «Ob utverjdenii poryadka i srokov sovershenstvovaniya meditsinskimi rabotnikami i farmatsevticheskimi rabotnikami professionalnyih znaniy i navyikov putem obucheniya po dopolnitelnyim professionalnyim obrazovatelnyim programmam v obrazovatelnyih i nauchnyih organizatsiyah» [Ministry of Health of the Russian Federation dated August 3, 2012 №66n "On approval of the procedure and terms of improving health workers and pharmaceutical workers professional knowledge and skills through training on additional professional educational programs in the educational and scientific organizations"].
8. Prikaz Ministerstva obrazovaniya i nauki Rossiyskoy Federatsii ot 1 iyulya 2013 goda № 499 «Ob utverjdenii Poryadka organizatsii i osuschestvleniya obrazovatelnoy deyatel'nosti po dopolnitelnyim professionalnyim programmam» [Ministry of Education and Science of the Russian Federation from July 1, 2013 № 499 "On approval of the organization and implementation of educational activities for additional professional programs"].
9. Rodyukova I.S. Sovershenstvovanie farmakoterapii neotlojnyih sostoyaniy na dogospital'nom etape s ispolzovaniem distantsionnyih form obucheniya vrachey [Improving pharmacotherapy emergency conditions prehospital using distance learning doctors]: dis. kand. med. nauk.[abstract Ph.D. in Medicine] Moskva, 2006, 117 p.
10. Trudovoy kodeks Rossiyskoy Federatsii (TK RF) ot 30.12.2001 N 197-FZ (deystvuyuschaya redaktsiya ot 02.04.2014) [The Labour Code of the Russian Federation].
11. Revinskaya O.G., Kravchenko N.S. Training of students for search of optimum conditions of carrying out study experiment on physics by means of theoretical models Journal of International Scientific Publication: Educational Alternatives. - 2013 – Vol.11. - Part 3. - P.93-103. – Электрон. Дан. - Режим доступа: http://ogrevinskaya.narod.ru/Bulgaria_2013.pdf
Дата обращения: 15.04.2014.



12. Buncher Evaluation of a Teleform-based data collection system: A multi-center obesity research case study /Jenkins T.M., Boyce T.W., Akers R. [et al.] //Computers in Biology and Medicine. - Volume 49.- 2014. – P. 15–18

Information about the authors:

Dorofeev Aleksandr Leonidovich - Dean of the Faculty of training and retraining of specialists, head of the Department of general practice (family medicine) and outpatient therapy Far Eastern State Medical University, MD, PhD, Tel. 8-914-183-24-30, 680028, Kalinin st., 10, Flat. 195, Khabarovsk, Russia, E-mail: fesmu-ovp@yandex.ru;

Pestushko Natalia A. - leading Record Manager Deanery of training and retraining of specialists Faculty, Far Eastern State Medical University, Khabarovsk, Russia;

Pyatnitska Svetlana - Deputy Dean of the training and retraining of specialists Faculty, assistant professor of pediatric therapy and dental faculty Far Eastern State Medical University, Khabarovsk Russia.

Contact for correspondence: A. L. Dorofeyev, e-mail: fesmu-ovp@yandex.ru

Molecular Epidemiology of Hepatitis B Virus in Yakutia

Gerasimova V.V., Maksimova N.R., Levakova I.A., Mukomolov S.L.

ABSTRACT

Heterogeneity of hepatitis B virus and its link with clinical course of infection and its outcomes remains one of priority directions of researches in Republic Sakha (Yakutia), as the region with high incidence of this disease. Blood serum samples with chronic hepatitis, registered in dispensary of various regions of the Republic Sakha (Yakutia), have been investigated. On the basis of results of the research by means of molecular - biological methods in the republic a genotype D was considered as the dominating genotype at patients with CHB, and sufficiently a large number of patients are infected simultaneously by two genotypes, most intensively circulating in the territory of Republic (A, D, C). For adequate therapy of such diseases it is necessary to consider characteristics of excreted isolates.

Keywords: hepatitis B, genotypes, viral load, mutations, drug resistance.

INTRODUCTION

The Republic Sakha (Yakutia) is considered to be the region of high prevalence of parenteral viral hepatitis B [1,4,7]. This unfavorable epidemiological condition is connected with many factors, including climatic and geographic features of the Far North. Severe course of parenteral viral hepatitis, its further chronicity are connected with presence of immunodeficiency, the incidence considerably increasing in unfavorable ecological conditions. It is particularly characteristic for the Republics Sakha (Yakutia) [2,3,5,6].

The viral hepatitis B (HBV) is hepatitis B pathogen virus, refers to a family *Hepadnaviridae* [8] and is one of the most changeable DNA-containing viruses that is caused by complex replication cycle, including a stage of RnK-pregenom reverse transcription [11]. Despite very limited possibilities of coding, the virus is capable to be protected from patient's immune system and to remain during all life in infected hepatocytes. When using the reverse transcriptase during the replication, it can be modified during the selection of viral mutants, for example, by means of immune system or antiviral therapy. Besides, viral genomes of wild and mutant types are stably stored in a core of infected hepatocytes as an episomal DNA that provides isolation from cell replication or integration in patient's genome [9]. Such factors as HBV genotype, viral load and specific viral mutations can cause the disease progression. Among them, HBV genotype not only predicts clinical outcomes, but also causes the effectiveness of

treatment with interferon. At present 8 HBV genotypes and some subtypes have been identified, they having distinctive geographic location. Individuals with genotypes A and C are characterized by higher frequency of infection chronicity in comparison with individuals with genotypes B and D. Patients with genotypes A and B have lower indicators of spontaneous seroconversion (HBeAg) – anti-HBe as compared with patients with genotypes C and D. Isolates HBV of genotype C have higher frequency in basic core promoter (BCP) A1762T/G1764A, and are characterized with higher viral load, than the isolates of genotype B. The same findings have been revealed in genotype D with its higher prevalence (BCP) A1762T/G1764A, as compared with genotype A. Such supervisions allow revealing important distinctions between HBV isolates, referring to different genotypes. Particularly, patients with HBV of genotypes C and D suffer from more severe liver diseases, including cirrhosis and hepatocellular carcinoma (HCC). Patients with HBV genotypes A and B are better treatable with interferon, as compared with genotypes C and D [10].

One of priority directions of the research is studying of HBV heterogeneity and its influence on the clinical course of the infection. In particular, the information concerning prevailing genetic HVB types, frequency of viral mutant forms in various territories of Russia is insufficient and inconsistent.

The purpose of this research was definition of HVB genotypes, detection of mutations in pre-core and (BCP) of HVB genome, as well as mutations in the field of polymerase gene, responding for drug resistance of the pathogen virus at patients with chronic hepatitis B (CHB), not receiving therapy in Republic Sakha (Yakutia).

MATERIALS AND RESEARCH METHODS

The sampling was carried out on the bases FBEH “Center of hygiene and epidemiology in RS (Y)” (the head physician Ushkareva O. A) in each region of the republic. The detection of viral load, genotyping and sequencing were carried out in the laboratory of viral hepatitis of the Federal budgetary establishment of science of the St.-Petersburg scientific research institute of epidemiology and microbiology named after Pasteur (the Head of laboratory Dr. of Medicine Mukomolov S.L.). In the laboratory aliquots of samples were prepared, the part was applied for molecular-biological researches, and the rest was stored as a bank of samples of blood serum at - 80 ° C.

The blood serum samples of 1304 patients with chronic hepatitis have been investigated, of them 819 (62,8 %) women and 485 (37,2 %) men, middle age of all patients has made 43,2 years. All patients were included in dispensary registration of different areas of the Republic Sakha (Yakutia): Aldansky-72, Amginsky-96, Bulunsky-37, Verkhoyansk-19, Vilujskiy-100,

Zhigansky-30, Lensky-90, Megino-Kangalassky-5, Mirniy-100, Nerjungrinsky-129, Njurbinsky-61, Suntarsky-103, Tattinsky-64, Tomponsky-34, Khangalassky-100, Churapchinsky-59, Yakutsk - 205 patients. The serum was investigated on HBsAg by a method of immune-ferment analysis (IFA) by means of test systems manufactured by Joint-Stock Company "Vector-best" (Novosibirsk), according to the firm-manufacturer instruction. 700 blood serum samples of patients with HBV were selected on storage at -80⁰S.

Of 700 samples 345 blood serum indices have shown positive viral activity. The viral activity and viral load were revealed by means of PCR-TEST SYSTEM taking into account results in on-line mode «AmpliSensHbV-Monitor-Fl» ("InterLabServis", Moscow). Of the samples containing DNA HBV, 31 indices from citizens of various regions of Yakutia (Churapchinsky, Mirninsky, Suntarsky, Verkhoyansk, Bulunsky, Hangalassky, Njurbinsky, Amginsky, Tomponsky, Tattinsky, Aldan, Viljujsky, Nerjungrinsky улусы, Yakutsk) with CHB diagnosis concerned genotype A virus in 87 - mutations in pre-core and P genome with the use of test systems INNO-LIPAHBV Genotyping, INNO-LIPAPreCore, INNO-LIPAHBVMulti-DR (Innogenetics, Belgium). Besides, quantitative content HBsAg in blood serum by means of Alcor-Bio Test System (Saint Petersburg) was revealed at 87 patients.

RESULTS AND DISCUSSION

In Yakutia 3 genotypes (A, D, C) have been revealed at patients with CHB. At 77,8 % surveyed HBV isolates concerned genotype D, genotype A at 3,7 % and C at 3,7 %. In samples of 14,8 % patients simultaneous presence of two genotypes of the virus has been revealed: A+D (11,1 %), D+C (3,7 %) (Fig. 1). The domiciliary distribution of virus genotypes has shown the genotype D in all regions, the genotype A in Verkhoyansk and Yakutsk, the genotype A+D in Bulunsky, the genotype C+D- in Tattinsky regions.

At all surveyed patients the isolates with mutations of basic core promoter and pre-core (BCP+PC-28 codon) were at 37 %, this parameter being more frequent as compared to PC-28 codon (25,4 %) and BCP (5,3 %). Only 28,6% isolates were of wild type without mutations in the field of C gene.

In Yakutia the mutation BCP+PC28 is the most spread, it makes 37.3±4,3 % and is extended in the category of people aged 50 years and more. While the virus of wild type noted in 28,6±4,0 is diagnosed among 15-29 years (43,5 %) and middle aged (37,3 %). The wild type is noted more often at men of 15-29 years, at women the widespread mutation is BCP+PC-28 and makes 50 % (Table 1). The mutation PC-28 codon has higher prevalence both at men and women of more senior than 50 years (Fig.2). By analyzing the prevalence of mutations CHB in the field C gene depending on age of patients the mean age of patients without mutations in this

field of genome (wild type virus) was estimated on 37 ± 5 years. While the corresponding age characteristics of HBV patients with mutations in BCP and PC-28 codon has amounted 67 ± 6 years. It is necessary to note that HBeAg was detected at patients with wild type HBV, i.e. without mutations in the field of genome C.

The mutations in HBV polymerase gene responding for drug resistance were revealed at two CHB patients. In one case the patient from Aldan region had the mutation in position L-173 with combination of gene C (BCP+PC codon 28). In the second case the patient from Suntarsky region had the same mutation in T-194 with combination of gene C (BCP+PC codon 28) as well. In both cases the patients with mutations of resistance had no specific antiviral treatment, so the mutations can be characterized as primary resistance, it being of lower frequency (2,2%).

No distinctions in the distribution of levels of viral load depending on age were revealed. At 55, 7 % of men and 53,7 % of women the viral load appeared less than 150 ME/ml. The relatively higher viral load 10^5 at 5,6% men and 4,5% women (Table 1). The viral load correlated with quantitative content HBsAg. The lowest content HBsAg in serum – 261 ME/ML was detected in the viral load lower than 150 ME/ml. When the viral load increased, the average concentration HBsAg (ME/ML) increased proportionally as well. Thus the concentration of surface antigen in samples with viral load 10^4 ME/ML and higher, it amounting 459 ME/ML (Table 2). The higher concentration HBsAg is found out at patients having mutations BCP and PC28 simultaneously.

CONCLUSION

Thus, according to this research in the republic the genotype D is the dominating type at CHB patients. For the first time it has been revealed that sufficiently large number of patients is infected simultaneously by two genotypes of the pathogen virus, most intensively circulating in the Republic territory (A, D, C). Among most of the investigated patients with the genotype D HBV mutation in pre-core (PC28) and BCP genome has been confirmed. The higher concentration HBsAg is found out at patients having simultaneous mutations BCP and PC28. It is important that the frequency of primary resistance to nucleoside analogues was extremely low and made up 2,2 %.

The results testify to necessity for surveying patients with chronic forms HB by means of molecular - biological methods in order to make decision for adequate therapy, considering features of excrete isolates.



REFERENCES

1. Alekseeva M. N. Virusnye gepatity v Respublike Sakha (Yakutiya) [Viral hepatitis in the Republic Sakha (Yakutia)]: dissertatsiya ... doktora meditsinskikh nauk [diss. ... Dr. of medical sciences]. Saint-Petersburg, 2002, P. 285.
2. Alekseeva M. N. Grinenko L.E. Timchenko A.V. [et.al.] Virusnye gepatity v Respublike Sakha (Yakutiya) Virusnye gepatity i drugie aktualnye infektsii: Sb. nauch. tr. [Viral hepatitis and other actual infections: Coll. scient. works]. Saint - Petersburg, 1997, V. 2., P. 164-166.
3. Alekseeva M. N. Meltser I.M. Rafailova M. A. [et.al.]. Osobennosti techeniya gemokontaktnykh gepatitov v Respublike Sakha (Yakutiya) [Features of the course of haemocontact hepatitis in the Republic Sakha (Yakutia)] Mat. russko-yaponskogo med.simpoziuma: sb. nauch. trudov [Mat. of Russ.-Jap. Med. Symp.], Khabarovsk, 1998, P. 408.
4. Ivanov P.M. Tomskiy M.I. Chabyeva L.G. [et.al.]. Gepatologiya Severa [Hepathology of the North]. The Yakut scientific centre of CMP SB RAMS, Medical Institute NEFU named after M.K.Ammosov, Yakutsk: LTD «Publishing House Sphera», 2012, P.304.
5. Petrova P. G. Volozhin A.I. Ekologiya cheloveka v usloviyakh Severa [Ecology of a person in the conditions of the North]. Yakutsk, 1996, P. 182.
6. Petrova P.G. Ekologiya, adaptatsiya i zdorove [Ecology, adaptation and health]. Yakutsk, 1996, P. 262.
7. Sleptsova S.S. Semenova V.K. Nikitina S.G. [et.al.]. Khronicheskie virusnyy gepatity [Chronic virus hepatitis]. The Yakut Medical Journal, 2013, № 1, P.52-55.
8. Shahildjan I.V. Mihailov M.I. Onishchenko G.G. Parenteralnye virusnye gepatity (epidemiologiya, diagnostika, profilaktika) Parenteral viral hepatitis (epidemiology, diagnostics, prophylaxis).Moscow: GOU VUNMC MZ RF, 2003, P.384.
9. Glebe. D. The molecular virology of hepatitis B virus / D. Glebe, C. Bremer // Semin.Liver.Dis.-2013. – Vol.33 (2).-P.103-12.
10. Lin C. The clinical implications of hepatitis B virus genotype: Recent advances / C. Lin, J.Kao//GastroenterolHepatology.- 2011.-Suppl 1.- P.123-130.
11. Naturally occurring escape mutations in the S gene in carriers seropositive for antibody to hepatitis B surface antigen / K.Yamamoto, M.Horikita, F.Tsuda et al.//J.Virol.-1994.-Vol.68.-P.2671-2676

The Authors:

Gerasimova Vilena Vasilevna- research assoc. FSAEE HPE NEFU named after M.K.Ammosov, res. assoc. FSBE YSC CMP SB RAMS virlab@mail.ru, Yakutsk, Russia;

Maksimova Nadezhda Romanovna – Dr. of Medicine, Prof., Chief of Scientific laboratory «Genome medicine» FSAEE HPE NEFU named after M.K.Ammosov, FSBE YSC CMP SB RAMS

Levakova Irina Aleksandrovna – research assoc. FBES St.-Petersburg scientific institute of epidemiology and microbiology named after Pasteur, St.-Petersburg;

Mukomolov Sergey Leonidovich - Dr.of Medicine, Prof., Chief of Laboratory of viral hepatitis FBES St.-Petersburg scientific institute epidemiology and microbiology named after Pasteur, St.-Petersburg.

Clinical and Immunological Characteristics of Drug-Resistant Tuberculosis in Children and Adolescents

Mordovskaia L.I., Gur'eva O.I.

ABSTRACT

We studied characteristics of clinical progression and immunological indicators in children and adolescents with drug-resistant tuberculosis. Control group consisted of patients with drug-sensitive tuberculosis. It was concluded that drug resistance of *M.tuberculosis* adversely influences the clinical progression and results in markedly suppressed immune system indicators in children and adolescents.

Keywords: child, adolescent, drug-resistant tuberculosis, immune system.

INTRODUCTION

Extremely difficult epidemiologic situation for tuberculosis (TB) in general and pediatric populations is still existent in Russia [1,4]. TB incidence rate in children and adolescents is one of the most sensitive indicators of the epidemiologic situation. Under existing epidemiologic situation, pulmonary TB is present in two variants, with different clinical symptoms, progression and outcomes, and thoroughly different approaches to multimodality treatment: drug-sensitive (DS) pulmonary TB, cause by *M.tuberculosis* (MTB) with sensitivity to all first and second line drugs; drug-resistant (DR) pulmonary TB, caused by MTB with resistance to one, two or more drugs/drug combinations. There is a separate entity of multidrug-resistance (MDR), which is characterized by simultaneous resistance to isoniazid and rifampicin regardless of resistance to other drugs. Due to age-related specifics, the problem of DR TB, as well as MDR TB, in children and adolescents, needs a relevant approach to disease detection and treatment. Dependence between the disease progression pattern and MTB drug-resistance pattern is not excluded, as far as studies by Russian researchers report [2,3].

Aim: To study clinical progression and immunological indicators specific for pediatric DR TB.

MATERIAL AND METHODS

Clinical radiological findings and immunological data of 24 pediatric patients with DR TB and 19 with DS TB were comparatively studied. At the time of study (2009-2013), all children and adolescents were undergoing in-patient therapy at the Pediatric Department no.2, Research & Practice Center for TB ('Ftiziatriia'), Sakha Republic (Yakutia).

Clinical, bacteriological, immunological, x-ray and CT examinations were performed in all patients. During physical examination, attention was paid to presence of the following signs and symptoms: general intoxication symptoms (body weight loss, loss of appetite, pallor, low grade fever, fatigue, sweating). Mantoux skin test with 2 TU PPD-L was performed in compliance with the instruction on the use of tuberculin skin tests given in the Russian Federation Health Ministry Order no. 109 (dated 2003). Skin tests using Diaskintest (recombinant TB allergen in standard dilution (0.2mcg), 0.1 ml solution for intradermal administration) were performed in accordance with labeling.

Bacteriologic tests included luminescence microscopy, culture on solid and liquid media (BACTEC MGIT 960). For immunological analysis, we studied relative lymphocyte count and lymphocyte subset composition in peripheral blood ($CD3^+$, $CD4^+$, $CD8^+$, $CD20^+$). Immunophenotyping was done using immunofluorescence method with appropriate monoclonal antibodies produced by Becton Dickinson (USA). Immunofluorescence response was assessed using flow FACSCalibur cytofluorometer (Becton Dickinson, USA). Serum cytokine profile was determined using ELISA test system produced by ZAO Vektor-Best (Russia). Whole blood IFN-gamma induction was studied in the presence of MTB antigens (tuberculin, ESAT-6 /CFP-10), using Tubinferon test-kits (Russia).

RESULTS

Age-sex distribution of patients is shown in Table 1.

As is shown in Table 1, adolescence age group predominated. There were more girls than boys among patients with DR TB (16 (66.7%) vs. 8 (33.3%), respectfully). There was no difference in numbers of girls and boys in the group of patients with DS TB (9 (47.4%) vs. 10 (52.6%), respectfully).

Positivity for MTB was detected by culture in all 43 patients (100.0%). Acid-fast bacteria (AFB) were detected by microscopy in 15 (62.5%) patients with DR TB and in 8 (42.1%) with DS TB. MDR MTB were detected in 16 cases with DR TB (66.7%).

Study of DR spectrum in patients with DR TB (Fig. 1) showed that resistance developed more often to isoniazid (100%), streptomycin (94.5%) or rifampicin (88.9%). DR to kanamycin (27.7%), etambutol (16.7%) and capreomycin (16.7%) was less common. In adolescents, DR spectrum was identical to the infection source DR spectrum in 17 (70.8%) of cases. Contact with active TB was established in 20 (83.3%) patients with DR TB, intrafamilial contact occurred in all patients. Among patients with DS TB, contact with active TB was detected in 10 (52.6%) patients, 8 (42.1%) of them were intrafamilial, and moreover, MTB of the infection sources were sensitive to all drugs.

Of the patients with DR TB, 19 (79.2%) had marked symptoms of TB intoxication. In patients with DS TB, the majority had moderate (9 (47.4%)) or mild (7 (36.8%)) TB intoxication symptoms.

Laboratory tests showed marked alterations in blood pictures of patients with DR TB: heightened ESR in 24 (100%), leucocytosis in 18 (75%), and lymphopenia in 15 (62.5%) (Table 2).

Results of tuberculin skin tests with 2 TU PPD-L did not differ much between the patients with DR or DS TB. Mean papule sizes for Mantoux skin test with 2 TU PPD-L and Diaskintest are shown in Table 3.

As is seen from Table 3, mean papule size after skin test with 2 TU PPD-L was 17.3 ± 0.6 mm. (DR TB) and 16.5 ± 1.0 mm. (DS TB) ($p > 0.05$). Mean papule sizes after Diaskintest were 12.5 ± 0.5 mm. (DR TB) and 12.4 ± 1.0 mm. (DS TB) ($p > 0.05$).

Analysis of clinical forms of TB showed the presence of infiltrative pulmonary TB in the majority of patients: 20 (83.2%) cases in DR TB and 14 (73.7%) cases in DS TB ($p < 0.001$). (Fig. 2).

Fig. 2 shows that patients with DR disease had besides infiltrative lung TB the following diagnoses: nodular (focal) lung TB (2; 8.4%); caseous pneumonia (1; 4.2%); TB of the bronchi (1; 4.2%). Patients with DS disease were diagnosed, apart from infiltrative lung TB, with primary complex (3 15.7%), caseous pneumonia (1; 5.3%) and nodular (focal) lung TB (1; 5.3%).

Analysis of the x-ray findings showed that extensive (bilateral) pulmonary TB was seen most often in patients with DR (13; 54.2%) versus DS (3; 15.8%) cases ($p < 0.01$). Lung cavities were observed more often in DR TB, than in DS TB: 15 (62.5%) cases versus 7 (36.8%) cases ($p < 0.01$).

The results of the study of the immune status in patients with DR TB are shown in Table 4.

As is seen in Table 4, patients who isolated DR MTB had marked alterations in the T-cell component of the immune system: decreased $CD3^+$ counts in DR ($51.3 \pm 0.9\%$) vs. DS ($56.8 \pm 2.1\%$) TB ($p < 0.05$); decreased $CD4^+$ counts in patients with DR TB ($36.3 \pm 1.1\%$; $p < 0.001$), decreased $CD4^+/CD8^+$ ratio (mean decrease rate was 1.2; $p < 0.05$). $CD20^+$ counts were elevated in all patients and no meaningful differences were noticed between patients isolating DS or DR TB. Levels of $CD16^+$ were $17.3 \pm 1.1\%$ in DR group and $20.7 \pm 1.2\%$ in DS group ($p < 0.05$).

Levels of PPD-induced IFN-gamma production were 189.4 ± 47.8 mg/mL in patients with DR TB and were higher (247.0 ± 64.9 pg/mL) in patients with DS TB. The same difference was

true for blood specimens incubated in the presence of ESAT-6/CFP-10 antigens: levels of IFN-gamma in DR and DS TB were 74.0 ± 17.6 pg/mL and 136.8 ± 31.8 pg/mL, respectively ($p < 0.05$). Levels of antigen-induced IFN-gamma in whole blood of patients with pulmonary TB were inversely related to the disease extent and severity. Serum IFN-gamma production in patients with DR TB showed a clear declining trend, compared to patients with DS TB. IL-8 counts in patients with DR TB were elevated up to 71.0 ± 36.8 pg/mL (as compared to 12.6 ± 4.5 pg/mL in patients with DS TB). IL-4 content tended to increase in patients with DR TB.

CONCLUSION

Drug resistance of MTB is a factor that negatively influences TB disease progression in pediatric patients. DR TB in children and adolescents is associated with marked symptoms of tubercular intoxication, hyperergic reaction to Mantoux skin test with 2 TU PPD-L, destruction of lung tissue, and stable decline of the immune status indicators.

References:

1. Aksenova V.A. Tuberkulez u detei i podrostkov v Rossii (Problemy i puti ikh resheniia) [Tuberculosis in children and adolescents in Russia (Problems and solutions)]. In: Sb. materialov nauch.-prakt. konf. "Tuberkulez u detei i podrostkov" [Abstract book of the research & practice conference 'Tuberculosis in children and adolescents']. Moscow; 2009. p. 22-25. Russian.
2. Poluektova F.G. Osobennosti techeniia i effektivnost' lecheniia lekarstvenno-ustoichivogo tuberkuleza legkikh u podrostkov [Disease progression and treatment effectiveness in adolescents with drug-resistant pulmonary tuberculosis]. Synopsis of Cand.Med.Sc.(PhD) Thesis. Moscow; 2004. Russian.
3. Firsova V.A. et al. Techenie tuberkuleza legkikh u podrostkov v zavisimosti ot raznoi stepeni lekarstvennoi rezistentnosti [Pulmonary tuberculosis in adolescents in relation to different degree of drug resistance]. Problemy Tuberkuleza, 2002, no. 12, pp. 23-25. Russian.
4. Shilova M.V. Tuberkulez v Rossii v 2008 godu [Tuberculosis in Russia in 2008]. Moscow; 2009. Russian.

Authors:

Mordovskaia Larisa Ivanovna, Dr.Med.Sc. (MD), senior researcher, Head of the Immunological Laboratory, Research & Practice Center for Tuberculosis, mobile: +7(914)272-42-69, email: limordovskaya@mail.ru

Gur'eva Olga Ivanovna, Cand.Med.Sc. (PhD), Head of the Pediatric Department no.2,
Research & Practice Center for Tuberculosis, mobile: +7(924)176-93-54, email:
gurievaolga@mail.ru

The Role of Specialized Food for Enteral Nutrition in the Treatment of Diabetes Type 2

I.Yu.Semenchenko, H.H.Sharafetdinov, O.A. Plotnikova, Lapik I.A., Alekseeva R.I.,
Sentsova T.B.

ABSTRACT

Objective: To investigate the effectiveness of personalized diet therapy with the inclusion of a specialized food for enteral nutrition (EN) on the anthropometric and body composition, carbohydrate and lipid metabolism in patients with type 2 diabetes.

Patients and methods. The study included 231 patients with confirmed diagnosis of type 2 diabetes under subcompensation carbohydrate metabolism. In all patients, conducted a comprehensive survey of the patients included in the study with the use of multi-level evaluation of disorders of the nutritional status and the risk of nutrition-related diseases "Nutritest SP-3." Randomized patients were divided into two groups: group A - patients receive personalized diet therapy with the inclusion of a specialized food for EA, and group B - patients received a low-calorie version of the standard diet.

Results. Studies have shown that personalization of diet inclusion of specialized food for EA not only to optimize the protein, carbohydrate and fatty acid composition of the diet, but also contributes to the effective correction of the broken indicators of nutritional status in patients with type 2 diabetes and obesity I-III degree (weight loss, BMI, WC, ON, the content of body fat and visceral fat area, improved glycemic control and lipid profile parameters).

Conclusion. Personalization dietary diet using specialized food for EA modified protein, fat and carbohydrate composition contributes to effective correction of metabolic abnormalities in patients with type 2 diabetes with obesity I-III degree.

Keywords: obesity, personalized diet therapy, type 2 diabetes, enteral feeding.

INTRODUCTION

Diabetes mellitus (DM) is currently a global psychological, social and economic problem that is defined by the soaring incidence, high frequency, severity and progression of vascular complications leading to early morbidity and high mortality.

According to the International Diabetes Federation [1], now in the world there are 366 million diabetic patients aged 20-79 years, of which 85-95% are patients with type 2 diabetes. It is predicted that by 2030 the total number of patients with diabetes will increase by 1.5 times and

reached 552 million, mainly due to patients with type 2 diabetes. According to the UN and WHO, from diabetes every 7 seconds in 1 patient dies every 10 seconds 12 sick person; die each year about 4.6 million patients with diabetes [2] The high rates of prevalence and incidence of vascular complications, such as myocardial infarction, stroke, gangrene of the lower extremities, nephropathy, etc., determine the need for the development and introduction into clinical practice of high-tech diagnostic methods, treatment and prevention of diabetes.

In the development and progression of vascular complications, leading to significant economic costs, a key role is played by chronic hyperglycemia [3, 4]. Chronic hyperglycemia participates in the pathogenesis of macro-and microvascular complications, both directly and indirectly by initiating several biochemical processes, which include oxidative stress, excessive formation of glycosylation end products, increased synthesis of diacylglycerol and others [5]. In order to achieve optimal glycemic control and reducing the risk of vascular complications, along with basal glycemia and glycated hemoglobin plays an important role postprandial glycemia [6, 7], associated with an increased risk of retinopathy, increasing intima-media thickness of the carotid artery, a decrease in myocardial blood volume and myocardial flow. In this connection, correction and monitoring indicators of glycemic control is necessary from the viewpoint of prevention of macro-microvascular complications in patients with diabetes.

As you know, one of the objectives of diet therapy in type 2 diabetes is to ensure adequate nutritional support of patients, aimed at correcting metabolic disorders such as basal and postprandial hyperglycemia, hyperinsulinemia, dyslipidemia, etc. To this end, traditionally used specialized food products for enteral nutrition (EN), characterized by a modified carbohydrate and fat composition of including a complex of vitamins, minerals and trace elements. In numerous clinical studies have shown the advantage of specialized products for EPO compared with standard mixtures to achieve optimal glycemic control and improving blood lipid profile in patients with diabetes [8-10].

Results of a meta-analysis of 23 studies [10] have shown that the use of specialized mixes for CE leads to a significant reduction of postprandial hyperglycemia, smaller peak levels of glucose in the blood, decrease in the area under the glycemic curve, significant reduction in insulin requirements. Optimization of glycemic control in diabetic patients is closely related to the modification of the carbohydrate composition of EPO of specialized products, including those with the exception of mono-and disaccharides and their replacement on the maltodextrins with a low degree of hydrolysis, the inclusion of sweeteners, high-fiber, etc.

Company Nutricia Medical Advanced Nutrition («NVNutricia», The Netherlands) has developed a specialized food for EP "Nutrizon EDVANST diazonium" (certificate of state

registration number 77.99.19.4.U.4238.5.09 from 05/05/2009), intended for patients with diabetes as an additional source of energy and micronutrients. This product contains in its structure soy protein, fructose, modified starch, soluble mixture (80%) and insoluble (20%) dietary fiber composition has a fat-modified (69% mononenasaschennyh fatty acids) with an optimal ratio of polyunsaturated fatty acids, n: 6 / n: 3. The purpose of this research was to study the effectiveness of personalized diet therapy with the inclusion of a specialized food for EA anthropometric indicators and indicators of body composition, carbohydrate and lipid metabolism in patients with type 2 diabetes.

PATIENTS AND METHODS

The study included 231 patients with confirmed diagnosis of type 2 diabetes, 55% of women and 45% men, aged $46,1 \pm 0,8$ years, under subcompensation carbohydrate metabolism without insulinopotrebnosti repositories on a standard diet therapy with concomitant diseases that do not require intensive treatment. Mean level of glycosylated hemoglobin (HbA1c,%) was $7,4 \pm 1,1\%$. To assess the degree of compensation of type 2 diabetes using the criteria proposed by the experts of the European Group on Policy Diabetes International Diabetes Federation (IDF, 1999) in accordance with the "algorithm specialized medical care to patients with diabetes" (2011).

Exclusion criteria were insulin, nephropathy on proteinuria, chronic renal failure, use of nonsteroidal anti-inflammatory drugs.

All patients were overweight and obesity degree I-III: BMI group average was $37,9 \pm 1,87$ kg / m².

Of comorbidities most frequently detected digestive diseases - chronic calculous cholecystitis (at 9.1%), chronic cholecystitis nekalkulezny (36%), postcholecystectomy syndrome (at 12.1%), as well as related kidney disease - urolithiasis (y 6%) and chronic pyelonephritis (24%), chronic pulmonary disease (COPD, asthma) were detected in 9.9% of patients with hypertension - 30.2%. Patients with type 2 diabetes included in the study were randomly divided into two groups of the same type: the main group (n = 128 pers.) And a comparison group (n = 103 pers.) And comparative analysis as presented in Table 1.

In the main group, the number of obese patients I, II and III century. was 58, 34 and 36 in control group - 38, 34 and 31 resp.

Patients of the main group (group A, n = 128) received a personalized version of the diet with the inclusion of a specialized diet food for EA based on the calculation of individual energy

needs using the indirect calorimetry using a respiratory calorimeter portable «Fitmate» (firm COSMED, Italy).

Patients comparison group (group B, n = 103) was obtained in a low calorie diet version ACI (according to the order of Ministry of Health of the Russian Federation of 05.08.2003 № 330 "On measures to improve nutritional care in health care institutions of the Russian Federation" and the order of the Ministry of Health of Russia 21.06 .2013, the number 395n "On approval of rules of Clinical Nutrition"). In all patients, conducted a comprehensive survey of the patients included in the study with the use of multi-level evaluation of disorders of the nutritional status and the risk of nutrition-related diseases "Nutritest SP-3." All patients were examined for fasting glycemia and 2 hours after a meal, as well as the level of glycated hemoglobin (HbA1c). Using standard methods of anthropometric studies measured height (cm), body weight (kg), waist circumference (cm), hip circumference (OB, cm), and calculated body mass index (BMI, kg/m²) and a ratio of / ON.

Assessment of body composition (fat, lean and active cell mass, extra-and intracellular fluid) was performed using the bioimpedance by standard technique using bioimpedance analyzer «Inbody 720" company Biospace Technology (Korea).

Study of biochemical parameters in serum (determination of total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglycerides (TG), urea, creatinine, uric acid, alanine-activity (ALT) and aspartate aminotransferase (AST) was performed on the analyzer firm «Konelab 30i» (Finland).

Analysis was performed using the software package SPSS 17.0 for Windows. Results are presented as mean values and standard error of the mean value ($M \pm m$). Evaluation of significance of differences of averages performed using Student t-test. The significance level was considered significant at $p < 0.05$.

RESULTS AND DISCUSSION

To achieve the objectives evaluated the clinical efficacy and tolerability personalized diet to include specialized product for EPO in patients with type 2 diabetes. Randomized, parallel, controlled study was conducted at two similar in age, BMI, comorbidity groups of patients.

Portability personalized diet with the inclusion of a specialized product for EPO was good, with no signs of intolerance to the product were observed.

All patients in the diet therapy, regardless of the variant used diet, there was a positive dynamics of clinical symptoms: decreased complaints of shortness of breath, headaches, dizziness, flashing "flies" before the eyes, general weakness, increased exercise tolerance.

Dynamics of anthropometric parameters in patients with type 2 diabetes with obesity I-III degree in the treatment process is presented in Table 2.

Of Table 2 shows that both groups of patients observations decreased body weight, BMI, WC and OB, relationship FROM / ON, while a marked positive dynamics studied anthropometric indices in patients of the main group. Thus, in the process of incorporating a personalized diet therapy specialized product for EPO (group A) showed a significant decrease in OT, OB and index FROM / ABOUT above baseline values as compared to the comparison group (group B).

Dynamics of body composition in patients with type 2 diabetes with obesity I-III degree in the treatment process is presented in Table 3.

From the results presented in Table 3 shows that both groups of patients observations regardless of the degree of obesity there was a significant reduction of body fat mass, the degree of reduction in fat mass was more pronounced in the main group of patients (group A) received a personalized ration with the inclusion of a specialized food for EA. No significant differences in the dynamics of body fat content between treatment groups were observed. Win skeletal muscle mass and lean body mass in patients of group A with I-III degree of obesity in 2 weeks tended to a slight decrease in patients of group B with I-III degree of obesity, a significant decrease of these parameters from baseline. Visceral fat area decreased to a greater extent in patients of group A compared with that in patients of group B. The results show the positive impact of a personalized diet to include specialized food for EPO on indicators of body composition in patients with type 2 diabetes with obesity I-III degree.

Dynamics of basal glucose and lipid metabolism markers in patients with type 2 diabetes with obesity I-III degree in the treatment process is presented in Table 4, which implies that both groups of patients observations regardless of the degree of obesity a significant decrease in fasting glucose serum, but the degree of reduction of basal glycaemia was more pronounced in the basic group of patients (Group A) as compared with the comparison group (group B). The findings suggest that personalized nutritional therapy with the inclusion of a specialized food for EPO This improved glycemic control in patients with type 2 diabetes with obesity I-III degree. To a certain extent this may be due to characteristics of the product composition comprising slowly absorbed carbohydrate, dietary fiber and monounsaturated fatty acids (MUFA), and may also be due to the improved insulin sensitivity and functional activity of β -cells of the pancreas, while the more pronounced reduce body fat and visceral fat area in patients with type 2 diabetes with concomitant obesity on background personalized diet therapy.

Comparative evaluation of markers of lipid metabolism in patients enrolled in the study (Table 4) showed that obese patients I Art. against the background of a personalized diet therapy with the inclusion of a specialized product for EPO (group A) showed positive dynamics of the lipid profile: reduction of total cholesterol, LDL cholesterol and triglycerides in the blood serum averaged 8.2%, 9.4% and 12.9% relative baseline values ($p < 0.01$, $p < 0.001$ and $p < 0.001$, respectively).. Content of HDL cholesterol in patients of group A increased on average by 22.2% ($p < 0.001$). Dynamics of lipid profile parameters in patients of group B with obesity I Art. was less pronounced and not statistically significant.

The content of total cholesterol, LDL cholesterol and triglycerides in the blood serum of patients with type 2 diabetes with obesity II Art. Group A patients decreased on average by 7.2%, 13.5% and 16.3% relative to baseline values ($p < 0.001$, $p < 0.01$ and $p < 0.001$, respectively). while increased HDL-C on average 28.6% ($p < 0.001$). Dynamics of markers of lipid metabolism in obese patients with Article II. (Group B) was less pronounced and not statistically significant (Table 4).

In patients with type 2 diabetes with obesity III century. against the background of a personalized diet therapy with the inclusion of a specialized product for EPO (group A), a significant decrease in total cholesterol, LDL cholesterol and triglycerides in the blood serum of 6.1%, 7.8% and 8.7% relative to baseline values ($p < 0.001$, $p < 0.01$ and $p < 0.001$, respectively).. HDL cholesterol levels in patients of group A increased on average by 10% ($p < 0.001$). Dynamics of lipid metabolism in obese patients with Stage III. (Group B) was less pronounced and not statistically significant (Table 4).

Thus, the comparative analysis of lipid profile in patients with type 2 diabetes with obesity degree I-III evidence of the positive impact of diet inclusion personalized specialized product for EPO on markers of lipid metabolism and risk factors for cardiovascular complications. The data obtained allow us to conclude that the inclusion of a personalized diet specialized product for EPO MUFA-rich, with the modification of protein and carbohydrate composition, enhances the effectiveness of diet therapy in the correction of lipid metabolism and risk factors for cardiovascular complications in patients with type 2 diabetes with a concomitant obesity.

Significant changes in blood biochemical parameters (urea, creatinine, uric acid, ALT and AST) in both groups on background diet were observed.

Thus, the personalization of dietary diet with nutritional support as specialized food for EA modified protein, fat and carbohydrate composition contributes to effective correction of disturbed eating and indicators of metabolic status of patients with type 2 diabetes with obesity I-

III degree in order to reduce the risk of cardiovascular complications and improve quality of life for these patients.

REFERENCES

1. Ametov A.S., Melnik A.V. Upravlenie saharnym diabetom: rol' postprandial'noj giperglikemii i vozmozhnosti ee korrektsii g [Diabetes Managin: the role of postprandial hyperglycemia and its correction]. J Breast Cancer, 2007, №15, p. 2053-2058.
2. Balabolkin M.I., Klebanov E.M., Kreminskaya V.M. Lechenie saharnogo diabeta i ego oslozhnenij [Treatment of diabetes and its complications]: Uchebno-metodicheskoe posobie [Study guide]. Moscow: OAO «Izdatel'stvo «Medicina», 2005.
3. Dedov I.I. Saharnyj diabet – opasnejshij vyzov mirovomu soobshhestvu [Diabetes - the most dangerous challenge to the world community]. Vestnik Rossijskoj akademii medicinskih nauk [Bulletin of the Russian Academy of Medical Sciences], 2012, № 1, p. 7-13.
4. Sharafetdinov H.H., Meshcheriakova V.A., Plotnikov O.A. Metodologija primeneniya pishhevyyh smesey, ispol'zuemyh v jenteral'nom pitanii, v dietoterapii bol'nyh saharnym diabetom 2 tipa [Methodology of nutritional mixtures used in enteral nutrition, diet therapy of patients with type 2 diabetes]. Voprosy pitaniya [Nutrition], 2005, №74, p. 17-22.
5. Coulston A.M. Enteral nutrition in the patients with diabetes mellitus. Curr.Opin.Clin.Nutr.Metab.Care. 2000; 3: 11-15.
6. Elia M., Ceriello A., Laube H. et al. Enteral nutritional support and use of diabetes-specific formulas for patients with diabetes. Diabetes Care 2005; 28: 2267-2279.
7. IDF Diabetes Atlas, 5th ed., 2011.
8. Ohkubo Y., Kishikawa H., Araki E. et al. Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. Diabetes Res.Clin.Pract. 1995; 28: 103-117.
9. Shiraiwa T., Kaneto H., Miyatsuka T. et al. Postprandial hyperglycemia is an important predictor of the incidence of diabetic microangiopathy in Japanese type 2 diabetic patients Biochem.Biophys.Res.Communit. 2005; 336: 339-345.
10. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with traditional treatment and risk of complications in patients with type 2 diabetes. Lancet 1998; 352: 837-853.

Data for correspondence:

Sharafetdinov Haider Hamzyarovich, MD, head of metabolic diseases FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel. 8 (499) 794-35-16.

Semenchenko Irina Yrievna, endocrinologist offices metabolic diseases FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel.8 (499) 613-11-89

Plotnikova Oksana Alexandrovna, PhD, senior researcher of metabolic diseases FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel.8 (499) 613-11-95

Lapik Irina Alexandrovna, Junior Researcher FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel.8 (499) 613-11-89

Alekseeva Ravilya Ismailovna, PhD, researcher at the Department of metabolic diseases FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel. 8 (499) 613-11-89

Sentsova Tatiana Borisovna, MD, Professor, Head of the Laboratory of Clinical Biochemistry, Immunology and Allergy FGBU "NRI", 115446 Moscow, Kashirskoye, 21, Tel.8 (499) 613-11-89

Index	Group	
	Summary	Comparisons
Age, years	44,1±2,6	49,1±2,9
Duration of disease, years	7,5±2,1	7,0 ±1,9
Body weight, kg	104,9±3,5	103,7±4,1
BMI, kg / m ²	37,4±0,9	37,3±1,2
The average level of glycated hemoglobin HbA1c,%	7,4±1,0	7,4±1,3

Table 2

Dynamics of anthropometric parameters in patients with type 2 diabetes with obesity I-III degree during treatment ($M \pm m$).

Index	Group	I obesity degree		Obesity II degree		III degree obesity	
		1	2	1	2	1	2
Body weight, kg	A	98,2±3,4	92,6±3,2***	105,6±3,4	99,4±3,2***	110,9±3,4	105,8±3,2***
	B	96,8±3,9	94,2±3,1	104,6±5,0	102,2±2,9	109,7±3,6	107,1±4,0
BMI, kg/m ²	A	33,7±0,9	31,7±0,6***	36,7±0,86	34,7±0,65***	41,9±1,4	38,8±2,1***
	B	34,2±0,6	33,7±1,5	36,2±0,73	35,1±1,5	41,6±1,7	39,7±2,5
Hip circumference, cm	A	97,9±2,8	94,2±2,3***	116,8±2,8	113,2±2,3***	117,4±2,8	114,7±2,3***
	B	93,3±4,0	92,1±2,9	113,6±3,2	112,1±2,9	119,3±3,2	117,4±2,9
Waist circumference, cm	A	88,6±1,8	84,7±1,8	109,2±1,8	104,7±1,8*	112,7±1,8	109,2±1,8*
	B	84,8±1,8	83,6±2,3	107,5±1,8	105,4±1,9	114,9±1,8	111,2±2,1
OT/OB	A	0,9±0,02	0,88±0,03*	0,93±0,06	0,91±0,05*	0,96±0,07	0,94±0,06*
	B	0,91±0,02	0,90±0,01	0,95±0,08	0,94±0,06	0,96±0,06	0,95±0,04

Note: hereinafter: 1 - before treatment; 2 - through 2 weeks after treatment; p - reliability of differences from baseline * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 3

The body composition indicators in patients with type 2 diabetes with obesity I-III in the treatment power ($M \pm m$).

Index	Group	I obesity degree		Obesity II degree		III degree obesity	
		1	2	1	2	1	2
Fat mass, kg	A	41,1±0,9	38,7±0,7**	49,1±0,6	45,8±0,5*	74,1±1,4	67,6±1,3*
	B	44,2±0,9	42,9±0,6*	49,7±1,0	47,3±0,5*	78,3±1,8	75,8±1,2*
Skeletal muscle weight, kg	A	31,2±0,5	30,6 ±0,8	34,2±0,8	34,3±0,6	38,0±0,6	37,5±0,8
	B	34,8±0,9	32,2 ±0,6*	36,8±0,7	34,6±0,7*	38,1±0,6	36,8±0,8*
Lean mass, kg	A	56,4±1,4	56,3±1,3	58,3±1,5	58,8±1,6	58,1±0,6	57,0±0,8
	B	54,7±1,2	52,1±0,9*	58,6±1,5	56,3±1,3*	58,2±0,7	55,8±0,6*
Visceral fat area, cm ²	A	169,8±5,1	162,2±2,1*	210,4±3,6	197,9±2,3*	310,3±7,2	289,7±5,4*
	B	179,5±4,8	174,1 ±2,6	206,4±1,8	200,6±1,8	309,5±7,2	295,7±5,0*

Table 4

Dynamics of basal glucose and lipid metabolism markers in patients with type 2 diabetes with obesity I-III degree during treatment ($M \pm m$).

Index	Group	I obesity degree		Obesity II degree		III degree obesity	
		1	2	1	2	1	2
Glucose, mmol / l	A	7,4±3,2	6,2±1,8 *	8,3±2,4	6,8±2,7 *	9,7±2,9	7,9±2,1 *
	B	7,5±3,2	6,5±1,6 *	8,2±2,4	7,0±2,3 *	9,5±2,8	8,0±1,9 *
Total cholesterol, mmol / L	A	6,1 ±0,6	5,6±0,6***	6,9±0,2	6,4±0,6***	8,2±0,4	7,7±0,6***
	B	6,2±0,5	5,9±0,6	6,8±0,4	6,7±0,3	7,9±0,5	7,7±0,4
TG, mmol / L	A	3,1±0,4	2,7±0,4**	4,3±0,8	3,6±0,4**	4,6±0,2	4,2±0,4**
	B	2,5±0,1	2,4±0,1	4,3±0,2	3,9±0,1	4,6±0,3	4,4±0,1
HDL-C, mmol / L	A	0,9±0,04	1,1±0,04***	0,7±0,06	0,9±0,04***	1,0±0,07	1,1±0,04***
	B	0,9±0,05	1,0±0,05	0,8±0,07	0,9±0,05	0,9±0,05	0,9±0,05
LDL-C, mmol / L	A	3,2±0,2	2,9±0,2***	3,7±0,2	3,2±0,2***	5,1±0,08	4,7±0,2***
	B	3,1±0,2	3,0±0,2	4,3±0,3	3,5±0,2	4,9±0,3	4,7±0,2

Paratunskoye Resort (Kamchatka Krai) Therapeutic Muds and Drugs on their Basis as a Means of Etiotropic and Pathogenetic Therapy of Periodontal Disease

Muradov S.V., Sel'minskaya O.V., Rogatykh S.V.

ABSTRACT

Among the many natural remedies that common in our region, is a special group of thermo-mineral waters, medicine mud and natural seawater. We concentrated our attention on medicine mud from Utinoye Lake, which was used as a medication AEM (aqueous extract of mud). Therapeutic methods of treatment are aimed to inflammation removing and relapse prevention and effect, especially on etiotropic and pathogenetic sections in the occurrence of periodontal disease. The range of drugs used for this purpose is very broad, but it is necessary to call attention to the health natural remedies. It is necessary to study the possibilities of using these natural remedies, particularly in the treatment of periodontal disease. Unlike conventional drugs, natural remedies do not have a toxic effect on the organism, is well tolerated, do not cause allergic reactions. The effectiveness of electrophoretic application of AEM medication during paradontium conditions was studied. The efficiency of electrophoretic applying of AEM in periodontal diseases of 45 patients was studied by us in the sanatorium. During the study were formed three groups of observation: I group - 7 persons, patients periodontal disease; II group - 26 persons periodontitis patients I-III degree of severity; III group - 12 persons, periodontal disease patients (2 people) and periodontitis I-II degree of severity (10 people) - a control. After treatment the final dental examination was conducted for observing of periodontal condition. Dental hyperesthesia of hard teeth tissues reduced at the end of course of treatment among all patients with amphotosis. Gingival hemorrhage, exudate discharge from dental pockets disappeared after the treatment completely among the patients with periodontitis. Thus, mud drug AEM applying in combination with mouthwash by thermal water leads to positive results in the treatment of inflammatory and degenerative diseases of the periodontium and is an example of effective using of natural remedies and treatment.

Keywords: paradontium, peloids, Kamchatka, electrophoresis.

INTRODUCTION

It is difficult to overestimate the importance of environmental factors in medical and health practice, due to their diversity, accessibility, complex effect on the body and efficiency in maintain of the adaptive properties of the organism. Academician V.P. Kaznacheev [1] marks the local natural remedies as key factors which are support and restore the adaptive mechanisms

of organisms in extreme regions, which include Kamchatka.

Among the many natural remedies that common in our region, is a special group of thermo-mineral waters, medicine mud and natural seawater. We concentrated our attention on medicine mud from Utinoy Lake, which was used as a medication AEM (aqueous extract of mud).

It is necessary to study the possibilities of using these natural remedies, particularly in the treatment of periodontal disease. Diseases of the tooth surrounding tissues are known from old times very well. With the progress of civilization, the prevalence of periodontal diseases, has risen sharply. According to WHO (1978), periodontal diseases are found in 46-80% of children (gingivitis) and almost the entire adult population of most countries of the world (periodontitis and mixed forms). [3] The problem of periodontal diseases is very crucial for the Kamchatka region as for all northern territories. A lot of factors are influence to origin and development of periodontal diseases. The complex of peculiar conditions, which can be attributed to the common factors of occurrence of periodontal disease, affects to the human organism in our region. It is a state of hypoxia, significant fluctuations of atmospheric pressure, geomagnetic field, solar radiation, the quality of nutrition, including vitamin deficiency, especially vitamin C. Diseases of the internal organs and body systems are common predisposing factors of periodontal diseases: pathology of the endocrine system, gastro-intestinal tract, atherosclerosis, cardiovascular diseases, collagen, etc. [4]. One of the key factors is the disorder of the immune system. For local causes of periodontal diseases, manifested in the mouth in the first place should include microbial factor of plaque and tartar, which, in combine with an altered immune reactivity is the leading element in the development of periodontal diseases - an inflammatory destruction of periodontal tissues [6]. Periodontal diseases clinically manifested by denudation of the necks and the roots of the teeth, inflammation and edema of the gingival papilla and gingival margin, frequent observe of bleeding gums when brushing your teeth and taking solid food. Under long-term chronic inflammation occurs dissolve of bone tissue around the teeth forming the abnormal tooth-gum pockets, often with serous or purulent discharge. In the cases of a emphasized destructive changes appears tooth mobility, they advance, change their position in the dental arch.

In present time the treatment of periodontal diseases is one of the most difficult problem in dentistry. It can be explained firstly by large prevalence of this disease in the population, and secondly by great number of common and local predisposing factors and their various combinations in each patient, which requires individual and integrated approach to the treatment of the patient. The complexity intends a combination of therapeutic, surgical and orthopedic treatments.

Therapeutic methods of treatment are aimed to inflammation removing and relapse prevention and effect, especially on etiologic and pathogenetic sections in the occurrence of periodontal disease. The range of drugs used for this purpose is very broad, but it is necessary to call attention to the health natural remedies. Unlike conventional drugs, natural remedies do not have a toxic effect on the organism, is well tolerated, do not cause allergic reactions. [3]

Applying of therapeutic mud and mud preparations for the treatment of inflammatory periodontal diseases should be interesting and promising direction in the medicine. During many years the mud of Utinoe Lake applied in our region with great success.

The structure of mud includes specific microbial community from bottom silt deposits and biologically active substances that produced during its life and have varied physiological effect. With using mud from Utinoe Lake we made a drug – AEM. AEM is a liquid with acidic reaction, low mineralized; the composition is match for a mud solution. The most important biomedical properties of this drug are its antibacterial action against pus-producing cocci and bacteria of enteric typhoid group, as well as in wound healing effect of thermal and mechanical damage [5]. Biologically active substances contained in the preparation have an immunostimulating effect in the local inflammatory processes.

The efficiency of electrophoretic applying of AEM in periodontal diseases of 45 patients was studied by us in the sanatorium of Defense Ministry "Paratunka". During the study were formed three groups of observation: I group - 7 persons, patients periodontal disease; II group - 26 persons periodontitis patients I-III degree of severity; III group - 12 persons, periodontal disease patients (2 people) and periodontitis I-II degree of severity (10 people) - a control.

All patients (45 people) got professional oral hygiene including removal of hard and soft dental plaque before performing medical procedures. Oral sanitation if necessary was conducted. Patient learned for careful and correct oral hygiene as well as mouthwash by thermal water 6-8 times per day. In the event of gums abscess antibacterial drugs used as in II, and in the control groups of observation. Patients of I and II groups got electrophoresis with the AEM drug.

The methodology of the procedures used device "Potok-1". The drug and physiological solution alternately applied to the electrode cushions which put on the area of gums and the middle third of the medial surface of the right forearm. Total number of procedures was 15. The duration of each daily procedure was 15 minutes.

RESULTS AND DISCUSSION

After treatment the final dental examination was conducted for observing of periodontal condition. The results of treatment are shown in Table 1.

All patients were well tolerated the treatment. Exacerbations of gum disease, deteriorations

of general condition and intolerance of AEM was not observed. Hypersensitivity of hard tissues of the teeth disappeared or significantly reduced under the influence of treatment at the end of it. However, the objective symptom of a degenerative process (pallor of the mucous membrane of the gums) has not changed. Bleeding gums and emission of exudate from periodontal pockets of periodontitis patients I-III degree of severity disappeared completely after treatment. Teeth mobility was observed in 72% of patients, but in significantly reduced form.

Thus, mud drug AEM applying in combination with mouthwash by thermal water leads to positive results in the treatment of inflammatory and degenerative diseases of the periodontium and is an example of effective using of natural remedies and treatment.

Table 1 – Changing the periodontal status under the influence of drug treatment AEM

	Symptoms of periodontal tissue pathology	I group – 7 pers.		II group – 26 pers.		III group (control) – pers.	
		Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
.	Hypersensitivity of hard tissues of the teeth	6	1	7	3	2	2
.	Pallor of the mucous membrane of the gums	7	7	–	–	2	2
.	Pain in the gums	3	1	9	–	1	–
.	Bleeding gums	2	–	25	–	10	4
.	The presence of exudate in the PZDK	–	–	14	–	5	3
.	Abscess of gum	–	–	7	–	1	–
.	Tooth mobility	–	–	15	10	4	3

REFERENCES

1. Kaznacheev V.P. Sovremennye aspekty adaptacii [Modern aspects of adaptation]. Novosibirsk: Nauka, 1980, 192 p.
2. Kankanjan A.P., Leont'ev V.K. Bolezni parodonta [Periodontal disease]. Erevan: Tigran Mec, 1998, 360 p.
3. Malinina I.A. Vlijanie kurortnyh faktorov na sostojanie protivomikrobnnoj zashhity u bol'nyh hronicheskim generalizovannym parodontitom [Influence of the resort factors on antimicrobial protection in patients with chronic generalized periodontitis] // Stomatologija XXI veka: novejschie tehnologii i materialy [XXI century Dentistry: the latest technology and materials]. Perm': PGU, 2000, pp. 84-85.
4. Modina T.N. Rol' faktorov riska v diagnostike i prognozirovanii bystroprogressirujushhih parodontitov [The role of risk factors in the diagnosis and prognosis of rapidly progressing periodontitis] Majestro stomatologii. 2001. № 5, pp. 25-40.
5. Muradov S.V. Jekologicheskoe reshenie problem sovremennogo grjazelechenija [Environmental solving of modern mud treatment problem]. Petropavlovsk-Kamchatskij: Izd-vo KamGU im. V.Beringa, 2007. 266 p.

6. Jarova S.P. Rol' giporeaktivnosti organizma v techenii jeksperimental'nogo parodontita [Role of organism hyporeactivity during experimental periodontitis] J Vestnik stomatologii. 1999. № 3, pp. 51-70.

Authors

Muradov Sergey Vasilievich, Research Geotechnological Centre, Far Eastern Branch, Russian Academy of Sciences, Severo-vostochnoe s., 683002, Petropavlovsk-Kamchatsky, Russia, e-mail: biolab@kscnet.ru;

Selminskaya Olga Vladimirovna, Regional dental polyclinic of Kamchatka, Koryakskay st., 683010, Petropavlovsk-Kamchatsky, Russia;

Rogatykh Stanislav Valentinovich, Research Geotechnological Centre, Far Eastern Branch, Russian Academy of Sciences, Severo-vostochnoe s., 683002, Petropavlovsk-Kamchatsky, Russia.



V .M. Tyaptiryanova, M. M. Tyaptiryanov

Influence of Water Quality in Yakutia Reservoirs at Fish Organism

(at the example of rivers Vilyuy, Khroma, Indigirka and Kolyma)

ABSTRACT

Objective:

The purpose of this study was to determine the influence of water quality in Yakutia reservoirs at fish organism.

Background:

We have studied the common types of fish that live in rivers of Yakutia (at the example of Vilyuy, Khroma, Indigirka and Kolyma Rivers) and are representatives of the food chain "water - fish - man."

Methods:

In summer, July 2009, we investigated the blood of perch and roach, below the village Syuldyukar (r.Vilyuy) at Haryyalah and Kuranyi rivers (July 2009), after which laboratory analysis showed the following blood picture: leukocytes - from 210 to 499; erythrocytes - 168 - 326; ESR - 0-2; hemoglobin – 3.7-8.9, averaging 6.1 g%. Judging from the literature [1, 2], this type of blood indicates very advanced toxicity processes in fish.

Results:

On the basis of clinical, pathological and hematological parameters of fish we revealed specific reactions and vulnerable «function target» to existing factors. A comparison of the structure of the fish population in the waters of Yakutia, revealed deterioration in water quality and changes in the population structure of invertebrate organisms, which reflected in the state of final producers - fish.

Conclusion:

Changes of the environmental conditions under the influence of chemical contamination, as a result causes tension of adaptation mechanisms, which can lead to the development of pathological changes in the human body.

Keywords: environment, human body, human health, food chain, fish productivity, fat accumulation, reproduction, reproductive period, toxicant, anemia, hematopoiesis, intoxication.

INTRODUCTION

In recent years, the acute problem of environmental pollution with harmful chemicals remains. Among these pollutants, primarily, one can include certain heavy metals of technogenic origin. Environmental pollution with toxic metals above all affects human health. Pathways of

the chemical elements in the human body are varied. It should be noted that most of the chemical elements is ingested with food and water. We have studied the common types of fish that live in rivers of Yakutia, are representatives of the food chain "water - fish - man."

Deterioration of water quality and changes in community structure of invertebrates reflected the state of ecosystem end-producers - fish. The total fish production of the studied reservoirs decreased

The structure of the fish population has changed in the direction of reducing the proportion of whitefish, and also the sig basic biological indicators changed. Due to the toxic load on the fish organism premature death in older age groups occurs also there is inhibition of growth. Along with a reduction in the growth rate metabolism in fish changes aside to fat accumulation instead of plastic substances consumption for protein growth, which is a reaction to adverse living conditions.

Processes of fish reproduction are broken. One of the reactions of fish to changing conditions is the transition to a shorter life cycle and reproduction. However more typical are slowing of fish maturation and frequent, prolonged spawning season passes. In the context of the toxic load fish hardly accumulate energy resources to spawn and are unable to compensate for them: the reproductive period of population is declining.

Whitefish are the most abundant fish species in the rivers of the Far North. On the basis of studying of the changes of morphological and physiological indicators one can see the impact on living organisms of wastewater discharge to subarctic waters, and the most vulnerable organs (called function - target) with respect to those or other toxicants are pointed out. In natural waters - rivers Vilyuy, Khroma, Indigirka and Kolyma, we found lithonephria (nephrocalcinosis), which is associated with the contaminated water. Also pathology in the skeleton of fish - pug snout, bending of gill stamens and ribs, hump and merging of the 2-3 vertebrae in the thoracic department were marked. At the organism intoxication the following liver and kidney abnormalities: cell death and appearance on their site of the connective tissue were detected. The same phenomenon, but in a more vibrant power was described in whitefish of Kola Peninsula as nephrolithiasis [11] and abnormalities of the spleen in Buryatia whitefish [6, 8]. These studies were the basis for the development of theoretical justification of anthropogenic impact on the valuation of the subarctic waters [15].

Fish blood system responds to the deterioration of habitat with large variety of pathological changes forms and the general laws of its transformation have been described. The first response of fish to the toxic agent effect is blood solidification: replace destroying cells in the blood stream young erythrocytes, monocytes, segmented and immature leukocytes ejected. The

concentration of hemoglobin in the blood, erythrocyte sedimentation rate and leukocytes increase [7, 10]. Blood picture is characterized by, along with before hemolized red blood cells, and many young immature cells. Further on, there is a gradual decrease in hemoglobin concentration due to intensive destruction of red blood cells and anemia develops. Changes in the blood system are reversible, until protective functions of hematopoiesis have been exhausted. As a criterion minimum limit of the amount of hemoglobin - 8% g was set. Its further decline is a hallmark of fish toxicity [12, 23, 25]. Based on these data the possibility of using lipid metabolism to assess the state of the Kola Peninsula of whitefish at different degrees of toxic effects is shown [13, 20, 24].

In summer, July 2009, we investigated the blood of perch and roach, below the village Syuldyukar (r.Vilyuy) at Haryyalah and Kuranyi rivers (July 2009), after which laboratory analysis showed the following blood picture: leukocytes - from 210 to 499; erythrocytes - 168 - 326; ESR - 0-2; hemoglobin - 3.7-8.9, averaging 6.1 g%. Judging from the literature [1, 2], this type of blood indicates very advanced toxicity processes in fish.

The general pattern of development of fish toxicity disclosed on the basis of studying the hematopoietic system reaction is characterized by four stages: I - contact, II - mobilization, III - destabilization, IV - degradation. Methodically toxicity stages are differentiated by destroyed (or pathological) and "normal" erythrocytes ratio at different concentrations of hemoglobin in the blood. Transition to irreversible changes and death of the organism is characterized by "critical point" separating "the norm and pathology", i.e. III and IV stage of toxicity at reducing the hemoglobin concentration less than 80% when in the blood mass erythrocyte destruction are observed. Analysis of long-term dynamics of the state of hematological parameters of fish showed a reduction of the fish number in the modern period (compared to 1970-1980.) being at the degradative toxicity stage, that indicates the reduction of toxic exposure.

Excess of heavy metals in aqueous medium leads to their accumulation in fish organism. The greatest accumulating effect in relation to one or another element have that organs which are functionally inherent: nickel accumulates in the kidneys, liver, gills and skin; copper - in the liver, kidney and gill skeleton; strontium - mostly in the bone tissues. Strontium concentration because of its accumulation may be comparable with the content of zinc, which in norm in the soft tissues is much greater. It was revealed that a violation of the microelement composition became one of the causes of fish pathologies. There is a strong dependence in the system: nickel in water → nickel in kidney → fish nephrocalcinosis. Excess of strontium can cause bone pathology.

Fish gills take the first blow caused by chemical changes in the aquatic environment, which often reflects in the biochemical indices in this organ [9].

The spleen is the most interesting as hematopoietic and immunocomponent organ. Many of the occurring in the body physiological and biochemical processes in extreme conditions with a strong change in habitat affect the hematopoietic and immune systems. It is known that any stress usually suppresses immunity of animals, while stress factors activate the body's defenses. [3]

It is interesting to note, that the same, sometimes unexpected results are obtained at ecological and biochemical study, what may be relevant at using eco-systems of biochemical monitoring in the early diagnosis of chronic changes in fish in the pond. For example, in the study of changes in the content of various lipids in different organs of Volga sturgeon in norm and "bundle" of muscles [14].

Violation of the structure and functioning of fish populations, the occurrence of deep pathologies and dysfunctions in their bodies led to a decline of fishery potential reservoirs of Yakutia.

Thus, in a result of processing enterprises in the mineral waters of the republic following trends in water quality were traced: salinity was growing, ionic composition changed in the direction of increasing the sulfate content, due to elevated levels of suspended particles water clarity decreased, bottom sedimentation with solid industrial waste occurred and water accumulated toxic compounds. This resulted in a violation of the structural and functional characteristics of biocenosis, and due to the development of pathologies and dysfunctions in the body systems fish mortality was observed, that in general, has led to the depletion of water resources and fish [4, 18, 19, 21]. Currently, the ability of reservoirs to cleanse itself is insufficient to recycle huge masses of pollutants. The highest lead content in all fish species is observed in the liver, as well as in carnivorous and at peace (benthophages and planktophages). The concentration of lead was higher in large individuals, compared with small young fish. Perhaps this is due to the fact that with a constant admission with feed lead does not manage to eliminate from the body and therefore accumulates in increasing concentrations, depending on the age of the fish.

The obtained data allow us to assert that, at cooking, in large specimens of fish it is advisable to remove the liver as the main accumulator of this element.

Often studied fish samples had no apparent pathological abnormalities, characteristic of poisoning with salts of mercury, lead and cadmium. Therefore of particular importance in veterinary-sanitary inspection of fish and fish products is chemical-toxicological research.

However, it should be noted that many researchers observed pathology characteristic for reservoirs polluted with heavy metals, and evidence of toxicity to aquatic environment.

In such fish color changes of the body, muscle turgor reducing, appearance of the anemic ring on the gills and gill rakers bending, the appearance of connective tissue growths and stones in the kidney, skeletal developmental disorder, etc. were observed. These pathologies are also described in fish living in waters of the Kola Peninsula contaminated by heavy metals [5, 12, 16, 17, 22].

Salmon and whitefish fish are narrowly adapted to survive in extreme conditions. Stenobiontic character causes high demands on water quality and prompt responsiveness to changing environmental conditions in the reservoirs [15].

On the basis of clinical, pathological and hematological parameters of fish organism we revealed specific reactions and vulnerable "target function" to existing factors. The lake Imandra fish at the tissue level common pathologies were: edema, exudates, hemorrhages, changes in blood vessels that testified exudate-hemorrhagic inflammation in the gills and furnace, protein and fat (toxic) liver dystrophy, leading to atrophy of the organ, connective tissue proliferation, epithelial changes, etc. Along with common pathologies in fish specific diseases, typical for each of the districts, appear. In the zone of influence of the copper-nickel waste – nephrocalcinosis, and in mixed with apatite-nepheline production sinks flow - myopathy and nephrocalcinosis. In subsequent years, in a period of reduced water pollution by heavy metals the incidence of fish decreased.

For evolutionarily young and "plastic" species *Coregonus lavaretus*, in conditions of more than 6 years of water pollution, changes in population characteristics occurred in the following direction: reduced growth rates, increased variability in the timing of puberty (both a delay, and premature maturation were observed), reducing of the spawning multiplicity and life expectancy. At the basis of these changes is hormonal and biochemical regulation, aimed at improving the support metabolism (increased catabolism) to the detriment of assimilated energy used on the processes of growth and maturation of the gonads.

Thus, for the period of anthropogenic loads ecosystem (as shown in the example of Lake Imandra) has undergone significant changes that affected all of its structural components. In the past - oligotrophic ultrafresh waters with bicarbonate-calcium mineralization with low concentrations of suspended material and trace elements in the period of anthropogenic load its hydrochemical regime transformed: the waters began to comply with class sulfates of technogenic nature, content of suspended solids increased. There was a severe water and sediment pollution with heavy metals. Despite the reduction of pollution, especially with heavy metals and suspended solids in the last decades, the water quality is still unfavorable. New communities with impoverished species composition, formed in a period of strong pollution,

acquired a tendency to increase the number and biomass. There is reason to believe that in the near future, all these processes will be reflected in the waters of Yakutia.

These materials show the main directions of anthropogenic successions of Arctic aquatic ecosystems under the influence of a large complex of anthropogenic factors that may occur in other water systems during the developing of the Arctic regions.

It should be emphasized that the quality of food raw materials, regardless of their origin in the first place depends on the state of the environment. Changes of the environmental conditions under the influence of chemical contamination, as a result causes tension of adaptation mechanisms, which can lead to the development of pathological changes in the human body.

REFERENCES

1. Andreeva A.M. Principy organizacii belkov krovi i stabilizacija vnutrennej zhidkoj sredy organizma ryb [Principles of the organization and stabilization of blood proteins inside the body fluid of the fish] // Fiziologicheskie, biohimicheskie i molekuljarno-geneticheskie mehanizmy adaptacii gidrobiontov [Physiological, biochemical and molecular genetic mechanisms of adaptation of aquatic organisms]: Materialy Vseros. konf. s mezhdunar. uchastiem [Proceedings of the All-Russia. conf. with intern. participation]. Borok, 2012, P. 9-14.
2. Arshanica N.M. Stekol'nikov A.A. Diagnostika toksikozov ryb i ocenka sredy ih obitanija [Diagnosis of fish toxicosis and their habitat evaluation] Ibid, P. 269-274.
3. Bogdan V.V. Ruokolajnen T.R. Markova L.V. Izmenenie pokazatelej lipidnogo obmena u sigov pri raznom urovne zagrijaznenija ozer Kol'skogo Severa [Change of lipid metabolism in whitefish at different levels of pollution in the Kola North Lakes] Csovmennye problemy Severa k 100-letiju so dnja rozhdenija O.I. Semenova-Tjan-Shanskogo [Modern problems of the North to the 100th anniversary of O.I. Semenov-Tyan-Shan]: Materialy Mezhd. konferencii 10-12 oktjabrja 2006 g. [Materials of the Int. Conference 10-12 October 2006] Apatity, 2006, Part 1, P. 145-146.
4. Vedemejer G.A., Mejer F.P., Smit L. Stressy i bolezni ryb [Stress and fish disease] Legkaja i pishhevaja promyshlennost'[Light and Food Industry], Moscow, 1981, 128 p.
5. Grubinko V.V. Smol'skij A.S., Konovec I.N., Arsan O.M. Gemoglobin ryb pri dejstvii ammiaka i solej tjazhelyh metallov [Fish Hemoglobin at the action of ammonia and heavy metal salts] Gidrobiologicheskij zhurnal [Hydrobiological journal]. 1995, vol. 31, № 4, p. 82-87.
6. Dyrheeva N.S. Pronin N.M. Soderzhanie metallov (Mn, Fe, Zn, Cu, Cd, Pb) v organah ryb s razlichnym tipom pitaniya (Chivyrkul'skij zaliv oz. Bajkal) [Metal content (Mn, Fe, Zn, Cu, Cd, Pb) in the bodies of fish with different types of food (Chivyrkul'sky Bay Lake. Baikal)]



Sovremennye problemy gidrobiologii Sibiri: Tezisy dokl. Vseros. konf [Modern problems of Hydrobiology Siberia: Proc. All- Russia. conf.] Tomsk, 2001, P. 114-115.

7. Kashulin N.A. Lukin A.A., Admunsen P.A. Ryby presnyh vod Subarktiki kak bioindikatory tehnogenogo zagrjaznenija [Subarctic Freshwater Fish as bioindicators of anthropogenic pollution] Apatity, 1999, P. 142.

8. Luk'janenko V.I. Vasil'ev A.S., Luk'janenko V.V. Geterogenost' i polimorfizm gemoglobina ryb [Heterogeneity and polymorphism of hemoglobin fish] St. Petersburg, Nauka, 1991, 392 p.

9. Moiseenko T.I. Izmenenie fiziologicheskikh pokazatelej ryb kak indikator kachestva vodnoj sredy [Changing the physiological parameters of fish as an indicator of water quality] Monitoring prirodnoj sredy Kol'skogo Severa [Environmental monitoring of the Kola Peninsula]. Apatity, 1984, P. 51-57.

10. Moiseenko T.I. Jekotoksikologicheskij podhod k ocenke kachestva vod [Ecotoxicological approach to water quality assessment] Vodnye resursy [Water Resources]. 2005, vol. 32, № 2, P. 184-195.

11. Nemova N.N., Vysockaj R.U. Biohimicheskaja indikacija sostojanija ryb [Biochemical indication of the fish status] Moscow, Nauka, 2004, 215 p.

12. Sidorov V.S. Jekologicheskaja biohimija ryb. Lipidy [Environmental biochemistry of fish. Lipid]. Moscow: Nauka, 1983, 240 p.

13. Uilkinson Dzh. Izofermenty [Isoenzymes]. Moscow, 1968, 220 p.

14. Feklov Ju.A. Gunicheva E.A. Gistopatologija pecheni ryby kak biomarker zagrjaznenija sredy [Histopathology of fish liver as a biomarker of pollution] Sovremennye problemy bioindikacii i biomonitoringa [Modern problems bioindication and biomonitoring]: Tez. HI Mezhd. simp. po bioindikatoram [Proc. XI Int. Symp. on bioindicators]. Syktyvkar, 2001, 195 p.

15. Flerova (Nazarova) E.A. Zabotkina E.A. Ul'trastruktura lejkocitov okuneobraznyh ryb Evropejskoj chasti Rossii [Ultrastructure of leukocytes of Perciformes fish of European Russia] Problemy immunologii, patologii i ohrany zdorov'ja ryb: rasshirennyj material III Mezhdunar. konf., Borok, 18-22 ijulja 2011 g. / pod red. d.b.n., prof. V.R. Mkrjakova, d.b.n., prof. A.M. Naumovoj, d.b.n., prof. A.L. Nikiforova-Nikishina, k.b.n., L.V. Balabanovoj, k.b.n. D.V. Mkrjakova. Moscow: izd-vo RGAU-MSHA imeni K.A. Timirjazeva, 2001, P. 165-169.

16. Chernjavskih S.D. Fedorova M.Z. Fagocitarnaja aktivnost' jeritrocitov i lejkocitov v krovi ryb [Phagocytic activity of erythrocytes and leukocytes in the blood of fish] Problemy immunologii, patologii i ohrany zdorov'ja ryb: rasshirennyj material III Mezhdunar. konf.



[Problems of immunology, pathology, and fish health: advanced material of the III Intern.conf.] Borok, 18-22 ijulja 2011 g. / pod red.d.b.n., prof. V.R. Mikrjakova, d.b.n., prof.A.M. Naumovoj, d.b.n., prof. A.L. Nikiforova-Nikishina, k.b.n., L.V. Balabanovoj, k.b.n. D.V. Mikrjakova. Moscow: izd-vo RGAU-MSHA imeni K.A.Timirjazeva, 2011, P.170-174.

17. Adams S.M., Ryon M.G. A comparison of health assessment approaches for evaluating the effects of contaminant – related stress on fish populations. Aquatic Ecosist. Health, 1994, vol.3. P. 15-25.

18. Attrill M.J., Depledge M.H. Community and population indicators of Ecosystem health: targeting link between levels of biological organization. Aquat. Toxicol. 1997, vol. 38, P. 183-197.

19. Cash K.J. Assessing and monitoring aquatic ecosystem health – approaches using individual, population, and community ecosystem measurements .N.O. Northern River Basing Study Project Report, 1995, P. 68.

Authors:

Victoria Matveevna Tyaptirgyanova - PhD, deputy chief physician FBUZ "Center of Hygiene and Epidemiology in the Sakha Republic (Yakutia) », vtyap@mail.ru, Yakutsk, Russian Federation;

Matvei Matveevich Tyaptirgyanov - PhD, Doctor of Biology, associate professor of CIM NEFU named after M.K. Ammosov, Yakutsk, Russian Federation.

M.M. Tyaptiryanov, V.M. Tyaptiryanova

Ecological and hygienic evaluation of the accumulation and distribution of cadmium compounds in organs and tissues of Yakutia freshwater fish

ABSTRACT

The paper analyzes the results of the accumulation of heavy metals – particularly cadmium in the organs and tissues of freshwater fish in the waters of Yakutia, which is one link in the food chain "water-fish-man." According to the toxicology cadmium is considered to be one of the most dangerous to human health ecotoxicants. There are very little data on the cadmium content in the organism of Yakutia freshwater fish. Meanwhile, these data are not only of theoretical but also of practical importance, since the toxicity of cadmium is independent from the form of its compounds, as one can observe in the case of lead and mercury compounds, "soluble" metal chemical forms (i.e., those which pass through a filter with a pore size of 0.45 microns) are equally toxic. Our studies have shown that the highest level of cadmium was found in the liver of large perch in the summer period with age from 4 + to 6 + years, caught in the river Vilyuy and had 0.411 ± 0.290 mg / kg of cadmium in the body wet weight. This amount exceeds 2.1 times the Maximum Permissible Level. Apparently, because of the change of feeding in the winter period, in small immature species some trend towards reduction of cadmium in the liver was observed.

It should be noted that the main commercial product is a muscle tissue of the studied fish from different water reservoirs of Yakutia, which at present have no particular risk to human health because cadmium in muscle tissue is present in amounts not exceeding the maximum allowable levels.

Keywords: human health, heavy metals, cadmium, toxic element, age groups, trend.

It is known that cadmium is one of the most dangerous ecotoxicants and is close to mercury and arsenic by toxicity [6, 7].

In nature, cadmium is not found in the free form and does not form special ores. Cadmium is produced commercially as a by-product of zinc and copper refining (Marcus, 1991). In the middle-aged humans there is about 50 mg of cadmium, 1/3 concentrates in kidneys, the remaining amount in the liver, lungs and pancreas. With age, the content of cadmium in the body increases, in the newborn cadmium is absent and it occurs at 10 months of life.

Daily intake of cadmium by the adult is about 215 micrograms. Cadmium is not an essential element for mammals [19].

Nonetheless, epidemiological data suggest cadmium's extreme danger to humans. Due to the fact that this element is very slowly eliminated from the human body (0.1% per day), cadmium poisoning may turn into chronic form. Its symptoms are the damage to kidneys, nervous system, lungs, sexual dysfunction, and joint pain. There is credible evidence of carcinogenic risk of cadmium. Today it is estimated that in about 5% of the population of the United States and Japan, the concentration of cadmium in the body has reached a critical level.

According to the Austria Institute of Food data no mercury or lead, namely cadmium is the most dangerous heavy metal.

The global annual intake of cadmium from natural sources is about 8.43×10^{-5} kg (Table-1) [17]. This is the result of plants vital activity, soil, dispersed by wind, volcanic aerosols and forest fires. Annual emission into the atmosphere as a result of the activities of the industry is estimated to be 7.19×10^5 kg. Atmospheric depositions effectively remove cadmium from the atmosphere. Therefore, the concentration of cadmium in rainwater may exceed 50 mg / l [18].

In the river uncontaminated and slightly contaminated waters cadmium is contained in submicrogram concentrations, in contaminated and waste water cadmium concentration can reach tens of micrograms per 1 dm^3 [4]. Cadmium rapidly migrates into acidic and soft water, as free ions and soluble compounds. Therefore, preferential presence in forms available to aquatic organisms is typical for cadmium [3].

The intensity of cadmium anthropogenic emission on the water surface reaches 132 tons per year [11]. Natural background concentrations of cadmium are generally less than 1 mg / l [10].

It was established that embryos of aquatic organisms are most susceptible to toxic effects of cadmium. Studies on minnows, and then on other fish species have shown teratogenic effects of cadmium compounds, demonstrated in a variety of spinal deformities. Behavioral effects of cadmium were also observed [10].

Toxic effects of cadmium on fish are not fully understood. It is known that cadmium accumulates mainly in the gills, liver and kidneys. However, the impact of the detected amounts of cadmium on the functioning of these organs is unclear, although there is some evidence that it is involved in osmoregulatory processes in the gills and kidneys. Cadmium is slowly cleared from the tissues of fish after transfer from the contaminated water to clean one, at the same time the accumulation occurs rapidly and causes death of organisms within a few days [1, 5, 8, 9]. All heavy metals, including cadmium, contained in the soil through natural propagation can be used for monitoring, as well as be the basis of forward-looking information relating to the pollution in the water column organisms [2]. The high content of heavy metals (cadmium, mercury, lead and

other) in Rivers Tom, Ob', in the city of Novosibirsk, in the upper zone of the Bratsk reservoir in some rivers of Yakutia was reliably detected by chemical methods. It was also confirmed by the fact of increased, and in some cases, high levels of these elements in fish in these reservoirs [13, 14, 15, 16].

There is very little data on the content of cadmium in the body of Yakutia freshwater fish. Meanwhile, this data is not only of theoretical but also of practical importance, since the toxicity of cadmium is independent from the form of its compounds, as one can observe in the case of lead and mercury compounds, "soluble" metal chemical forms (i.e., those which pass through a filter with a pore size of 0.45 microns) are equally toxic [14].

Our studies have shown that the highest level of cadmium was found in the liver of large perch in the summer period with age from 4 + to 6 + years, from the river Vilyuy and was 0.411 ± 0.290 mg / kg of cadmium in the organ green weight. This amount exceeds the MPL 2.1 times. In the liver of perch, in the same population, caught in winter, cadmium content was almost the same – 0.399 ± 0.282 mg / kg. In the same population of perch, but small species under the age of 2 + years, in summer cadmium's concentration in the liver was 0.165 mg / kg and in the winter time - 0.079 mg / kg of the organ green weight. Apparently, because of the change of feeding in the winter period, in small immature species some trend towards reduction of cadmium in the liver was observed.

Cadmium is distributed in tissues and organs in the perch from the river Vilyuy in the following order: liver – gills – muscle – gut - bone.

On this basis, it can be assumed that the main "gateway" of cadmium emission to perch organism is gills.

In guppies (*Poecilia reticulata*), which during 7 weeks ate worms - pipe makers (*Tubifex*), containing 20 mg / kg cadmium, showed no accumulation of toxic element [1]. In another group of fish, kept within that period in the water, contained 70-100 mg Cd / l, accumulated about 9 mg of Cd / kg (on the green weight) and, within this group there was no difference between the fish, which were fed with clean and cadmium-containing worms [1].

This again suggests the idea that the intake of cadmium compounds by fish is carried out through the gills, which is confirmed by the results of field trials (Table. 2).

Cadmium content in muscle tissue of perch from the river Vilyuy was within the MPL, and this fish is relatively safe when used for food. It is necessary to draw attention to the fact that the individuals in this group identified a significant excess of the MPLs in muscle tissue, which is 0.411 mg / kg (Table. 2). For this reason, one needs to expose the study of adult perch from the river Vilyuy and to prevent the use in food fish products containing cadmium above the MPL.

Based on these data, cadmium does not accumulate in the gut of perch. In the investigated fish we couldn't release intestines from the content because of the methodological difficulties of this operation. In the intestine of small perch specimens under the age of 2 + years small amount of cadmium contains. Thus, in summer their amounts are 0.095 mg / kg, in winter - 0.036 mg / kg; in large species in the summer - 0.118 mg / kg, in the winter - 0.116 mg / kg. As can be seen from the data, there are no significant differences in the content of cadmium in perch in different periods of the year.

Weis P. (1988) [20] considers that the process of elimination of the compounds of cadmium and mercury from the body goes through the intestines of fish. In our studies in Amginskiy area (p. Amga) fish (Table. 3) MPL exceeding of cadmium were not detected.

In muscle tissue of pike from the river Chroma (Table. 4) only in adult species cadmium was equal to 0.285 mg / kg in the summer and 0.164 mg / kg in the winter, which is close to the MPL. In the liver of the same pike MPL was much larger and composed in the summer 0.454 mg / kg, in the winter - 0.462 mg / kg, which exceeds the value 1.5 - 1.6 times. In the gills of adult fish in the summer it was 0.313 mg / kg, which exceeds the MPL 1.04 times.

In chir populations of the river Chroma only in the liver of adult fish exceeding MPLs in winter equal to 0.375 mg / kg were found, which exceeds the MPL value 1.6 times.

In perch from the Kolyma River (Table. 5) cadmium was in much smaller quantities in organs and tissues in comparison with the perch from the river Vilyuy. For example, if in the summer in large perch species of the river Vilyuy liver contained 0.411 mg / kg (Table. 2), then the fish population of the Kolyma river cadmium concentration was 0.251 mg / kg, in Indigirka population in large species in the liver was only 0.229 mg / kg of cadmium (Table. 6), i.e., the amount that may be within the maximum permissible level for freshwater fish.

Distribution of cadmium in the organs and tissues of the Kolyma, Indigirka perch populations (Table. 5, 6) is the same as in Vilui population (Table. 2). Perch in the rivers of the Kolyma and Indigirka, like other species of freshwater fish, showed a slight decrease of cadmium in the winter season.

In the body of the Verkhnekolymsky district carp cadmium levels were somewhat higher compared to Vilyui district carp. Thus, in large species aged 4 + to 6 + years old, caught in the summer in the lake Ozhogino (Verkhnekolymskiy district), the muscle tissue contained 0.108 mg / kg Cd, while the population of carp from the lake Dengkyude Vilyui district - 0.097 mg / kg. In the same situation were lake Dargalah Moma district, muscle tissue contained 0.093 mg / kg Cd, while the population of carp from the lake Ebe Vilyui district - 0.083 mg / kg. But these differences were not statistically significant because of the large error average.

These concentrations can be considered as the background content of cadmium in the body of the Yakutia lake carp, as these lakes are not subject to any local or any other human impact due to the remoteness from major population centers and the lack of flood waters from other polluted aquatic environments.

According to the degree of cadmium accumulation organs and tissues of Verkhnevilyuisk district carp are located in the following order: liver – gills – muscle – bone - intestine.

In roach from the River Vilyuy cadmium (Table. 2) is in the organs and tissues within the maximum permissible levels for freshwater fish. However, some large specimens established exceeding MPLs in the liver during the summer, reaching up to 0.3 mg / kg.

In Chukuchan fish Kolyma River Srednekolymsky region (Table. 5) the content of cadmium in the organs and tissues was within the maximum permissible levels for freshwater fish.

These data show that most of cadmium accumulates in adult perches, especially in the liver and gills (Table. 2-6). On this basis, one should limit the consumption of liver of perch 5 + - 7 + years of age, and possibly from younger species, and only after the toxicological studies.

Thus, in the literature data there is very little information about the content of cadmium in the body of Yakutia freshwater fish. Meanwhile, the field studies data carried out by us are not only of theoretical but also of practical importance, since the toxicity of cadmium is independent from the form of its compounds. Excess of cadmium in Yakutia freshwater fish is 1-2 MPC, often in polluted water, more often localizing in the gills and liver of the fish.

It should be noted that the main commercial product is a muscle tissue of the studied fish from different water reservoirs of Yakutia, which at present has no particular risk to human health because cadmium in muscle tissue is present in amounts not exceeding the maximum allowable levels.

No doubt, contaminated fish also affect human health. Thus, Yakutia freshwater fish must be intensively studied as a model for ecotoxicological research.

REFERENCES

1. Alabaster J. Lloyd R. Kriterii kachestva vody dlja presnovodnyh ryb [Water quality criteria for freshwater fish]. M.: Light and food prom., 1984, p. 333.
2. Akhmetova G.V. Monitoring sodержaniya tjazhelyh metallov v pochvah ostrova Kizhi [Monitoring of heavy metals in soils Kizhi] Jekologicheskie problemy Severnyh territorij i puti ih reshenija: materialy IV Vseros. nauch. konf. s mezhdunar. uchastiem, 2-5 oktjabrja 2012 g. [Ecological problems of the Northern Territories and their solutions: Proceedings of IV All-



Russia. scientific. conf. with int. participation, 2-5 October 2012]. Apatity, 2012, Part 2, pp. 13-15.

3. Belokon V.N. Formy nahozhdeniya tjazhelyh metallov v donnyh otlozhenijah Sasykskogo vodohranilishha [Forms of presence of heavy metals in sediments Sasykskogo reservoir] *Gidrobiologicheskij zhurnal* [Hydrobiological journal]. 1989, V.25, № 3, pp.83-88.

4. Guseva T.V. Molchanova J.P. Zaika E.A. Vinnychenko V.N. Averochkin E.M. *Gidrohimicheskie pokazateli sostojanija okruzhajushhej sredy* [Hydrochemical environment] *Gidrohimicheskie pokazateli sostojanija okruzhajushhej sredy: spravocnyye materialy / pod red. T.V. Gusevoj* [Hydrochemical environmental indicators: Reference / Ed. T.V. Guseva]. M.: Socio-Economic Union, 2000, p.148.

5. Kulebakina L.G. Pivovarova I.B. Nakoplenie i detoksikacija kadmija morskimi dvustvorchatymi molljuskami [Cadmium accumulation and detoxification of marine bivalves] *Tez. dokl. V Vsesojuz. konf. po vodn. toksikologii* [Proc. of reports. V All-Union conf. by aq. toxicology]. Odessa, 1988, pp. 89 - 90.

6. Lapshina T.P. Khomenko A.N. Perechen' prioritetnyh zagryaznjajushhih veshhestv i pokazatelej kachestva vody, rekomenduemyj dlja kontrolja zagryaznennosti prirodnyh i stochnyh vod [The list of priority pollutants and water quality parameters recommended for pollution control and natural wastewater] *Gidrohimicheskie materialy* [Hydrochemical materials]. 1990, V. 19, pp.115-125.

7. Linnik P.N. Iskra I.V. Opređenje svobodnyh i svjazannyh ionov kadmija v prirodnyh vodah metodom inversionnoj vol'tampermetrii [Determination of free and bound cadmium ions in natural waters by stripping voltammetry] *Gidrobiologicheskij zhurnal* [Hydrobiological journal]. 1993, V.29, № 5, pp. 96 -103.

8. Matei V.E. Izmenenie ul'trastruktury kletok zhabernogo jepitelija tiljapii pri dejstvii na ryb kadmija [Change cell ultrastructure of the gill epithelium of tilapia fish when exposed to cadmium] *Citologija* [Cytology]. 1993, V. 35, № 6/7, pp. 34-41.

9. Moiseenko T.I. Dauvalter V.A. Lukin A.A. [et al.] *Antropogennye modifikacii jekosistemy ozera Imandra* [Anthropogenic modification of the lake ecosystem Imandra]. M.: Nauka, 2002, p. 403.

10. Moore J.W. Ramomurti S. *Tjazhelye metally v prirodnyh vodah. Kontrol' i ocenka vlijanija* [Heavy metals in natural waters. Monitoring and evaluation of impact]. M.: World, 1987, p.286.

11. Nickanorov A.M. Zhulidov A. Biomonitoring metallov presnovodnyh jekosistem [Biomonitoring of metals in freshwater ecosystems]. L., 1991, p. 309.
12. Nyukkanov A.N. Kontaminirovannost' reki Vil'juj rtut'ju, svincom i kadmiem [Of contamination of rivers Vilyuy mercury, lead and cadmium] Pit'evaja i stochnye vody - problemy ochistki i ispol'zovanija: mater. mezhd. nauch.- prakt. konf. [Drinking and waste water - problems and cleaning isporlzovaniya: mater. Intl. scientific- pract. conf.]. Penza, 1997, pp. 43-44.
13. Nyukkanov A.N. Soderzhanie soedinenij rtuti, svinca i kadmija v rybah iz presnovodnyh vodoemov Jakutii: avtoref. diss. ...kand.biol.nauk [Content of compounds of mercury, lead and cadmium in fish from freshwater Yakutia: avtoref. dis. ...kand.biol.nauk]. Pokrov, 1996, p. 20.
14. Nyukkanov A.N. Nakoplenie kadmija u ryb v vodoemah bassejna reki Vil'juj [Accumulation of cadmium in fish ponds in the basin Vilyuy] [Veterinary Medicine]. 2003, № 12, pp. 46.
15. Popov P.A. Sostojanie i metodicheskie aspekty ocenki jekologicheskogo statusa vodoemov Sibiri metodami ihtioindikatsii [State and methodological aspects of the evaluation of the ecological status of water bodies Siberia methods ihtioindikatsii] Problemy gidrobiologii Sibiri [Problems of Hydrobiology Siberia]. Tomsk: glider, 2005, pp. 202-207.
16. Yurakova T.V. Petelin A.P. Struktura ihtiocenozov pritokov Nizhnej Tomi [The structure of the fish community of Lower tributaries Tom] Sovremennye problemy gidrobiologii Sibiri [Modern problems of Hydrobiology Siberia]. Tomsk, 2001, pp. 105-106.
17. Nriagu J.O. Global inventory of natural and anthropogenic emissions of trace metals to the atmosphere / J.O. Nriagu // Nature 279. - 1979. - P. 409-411.
18. Thornton J.D. Trace metal and strong acid composition of rain and snow in northern Minnesota / J.D. Thornton, S.J. Eisenreich, J.W. Hunger, G. Gerham // Atmospheric Pollutants in natural water. - Michigan, 1981.- P. 261-284.
19. Venugopal B. Luckey T.D. Metal toxicity in mammals. Chemical toxicity of metals and metalloids / B. Venugopal, T.D. Luckey // NY: Plenum Press. - New York, 1978/ - vol. 2. - 101 p.
20. Depuration of heavy metals by the Killifish, fundulus heteroclitus / P. Weis // Aquat. Toxicol. - 1988. - № 3.- P. 225-226.

Authors:

Matvei Matveevich Tyaptirgyanov - PhD, assistant professor of BGF NEFU named after M.K.Ammosov, Yakutsk, Russian Federation;

Victoria Matveevna Tyaptirgyanova – PhD, MD, deputy chief medical officer FBUZ "Center for Hygiene and Epidemiology in the Sakha Republic (Yakutia) », e-mail: vtyap@mail.ru, Yakutsk, Russian Federation.

Table 1

Isolation of cadmium from natural sources (thousand tons per year)

Natural source	Values range	Mean value
Soil particles carried by the wind	0.01 – 0.04	0.21
Sea salt aerosols	0 – 0.11	0.06
Volcanoes	0.14 – 1.5	0.82
Forest fires	0 – 0.22	0.11
Continental biogenic particles	0 - 0.83	0.15
Continental biogenic volatile substances	0 – 0.8	0.04
Marine biogenic sources	0 – 0.1	0.05
Total emission	0.15 – 2.6	1.3

Table 2

**Accumulation and distribution of cadmium in the organs and tissues of Viliuisk
district
freshwater fish**

Study period	Age of fish	Muscles	Liver	Intestine	Gills	Skeleton
Pike (<i>Esox lucius</i>)						
Summer	Up to 2+	0.006±0.004	0.061±0.043	0.007±0.005	0.031±0.022	0.048±0.034
	From 4+ up to 6+	0.015±0.011	0.032±0.0023	0.021±0.015	0.126±0.089	0.057±0.040
Winter	Up to 2+	0.004±0.003	0.041±0.029	0.003±0.002	0.017±0.012	0.031±0.022
	from 4+ up to 6+	0.009±0.006	0.038±0.027	0.027±0.019	0.103±0.073	0.112±0.079
Roach (<i>Rutilus rutilus</i>)						
Summer	Up to 2+	0.096±0.068	0.102±0.072	0.081±0.057	0.107±0.076	0.083±0.059
	from 4+ up to 6+	0.178±0.0126	0.189±0.134	0.125±0.088	0.141±0.100	0.131±0.093
Winter	Up to 2+	0.062±0.044	0.097±0.068	0.039±0.028	0.094±0.066	0.051±0.036
	from 4+ up to 6+	0.091±0.064	0.172±0.123	0.078±0.055	0.144±0.102	0.096±0.068
Perch (<i>Perca fluviatilis</i>)						
Summer	Up to 2+	0.111±0.078	0.165±0.117	0.095±0.067	0.127±0.090	0.091±0.064
	from 4+ up to 6+	0.162±0.114	0.411±0.290	0.118±0.083	0.316±0.223	0.107±0.076
Winter	Up to 2+	0.052±0.037	0.079±0.056	0.036±0.025	0.072±0.051	0.062±0.044
	from 4+ up to 6+	0.094±0.066	0.399±0.282	0.116±0.082	0.215±0.152	0.131±0.093

Table 3

**Accumulation and distribution of cadmium in the organs and tissues of Amginskij
district
freshwater fish**

Study period	Age of fish	Muscles	Liver	Intestine	Gills	Skeleton
Pike (<i>Esox lucius</i>)						
Summer	Up to 2+	<0,01	0,012±0,008	<0,01	<0,01	0,012±0,008
	From 4+ up to 6+	<0,01	0,014±0,010	<0,01	<0,01	0,013±0,009
Winter	Up to 2+	<0,01	0,010±0,007	<0,01	<0,01	0,010±0,007
	from 4+ up to 6+	<0,01	0,011±0,008	<0,01	<0,01	0,011±0,008
Roach (<i>Rutilus rutilus</i>)						
Summer	Up to 2+	<0,01	0,019±0,013	<0,01	<0,01	<0,01
	from 4+ up to 6+	<0,01	0,016±0,011	<0,01	<0,01	0,013±0,009
Winter	Up to 2+	<0,01	<0,01	<0,01	<0,01	<0,01
	from 4+ up to 6+	<0,01	0,011±0,008	<0,01	<0,01	0,012±0,008
Perch (<i>Perca fluviatilis</i>)						
Summer	Up to 2+	<0,01	0,013±0,009	<0,01	<0,01	0,012±0,008
	from 4+ up to 6+	<0,01	0,015±0,011	<0,01	<0,01	0,013±0,009
Winter	Up to 2+	<0,01	0,011±0,008	<0,01	<0,01	0,011±0,008
	from 4+ up to 6+	<0,01	0,013±0,009	<0,01	<0,01	0,011±0,008

Table 4

**Accumulation and distribution of cadmium in the organs and tissues of pike and chir
in the reservoir of Chroma River (Allaihovskij district, August – October 2006, n = 10)**

Study period	Age of fish	Muscles	Liver	Intestine	Gills	Skeleton
Pike (<i>Esox lucius</i>)						
Summer	Up to 2+	0,170±0,120	0,209±0,148	0,095±0,067	0,199±0,141	0,081±0,057
	From 4+ up to 6+	0,285±0,201	0,454±0,321	0,137±0,097	0,313±0,221	0,097±0,068
Winter	Up to 2+	0,097±0,068	0,108±0,076	0,044±0,031	0,137±0,097	0,047±0,033
	from 4+ up to 6+	0,164±0,116	0,462±0,326	0,082±0,058	0,284±0,201	0,132±0,093
Chir (<i>Coregonus nasus</i>)						
Summer	Up to 2+	0,094±0,070	0,102±0,072	0,096±0,068	0,114±0,081	0,113±0,080
	from 6+ up to 8+	0,241±0,170	0,298±0,211	0,231±0,163	0,201±0,142	0,163±0,115
Winter	Up to 2+	0,074±0,052	0,123±0,087	0,062±0,044	0,102±0,072	0,063±0,044
	from 6+ up to 8+	0,128±0,090	0,375±0,265	0,116±0,082	0,237±0,167	0,137±0,097

Table 5

**Accumulation and distribution of cadmium in the organs and tissues of
Srednekolymskij district freshwater fish**

Study period	Age of fish	Muscles	Liver	Intestine	Gills	Skeleton
<i>Dace (Leuciscus leuciscus)</i>						
Summer	Up to 2+	0,082±0,058	0,116±0,082	0,051±0,036	0,095±0,067	0,081±0,057
	From 4+ up to 6+	0,104±0,073	0,146±0,103	0,073±0,052	0,104±0,073	0,093±0,066
Winter	Up to 2+	0,053±0,037	0,083±0,066	0,027±0,019	0,072±0,051	0,063±0,044
	From 4+ up to 6+	0,089±0,063	0,107±0,076	0,053±0,037	0,081±0,057	0,079±0,056
<i>Chukuchan (Catostomus catostomus)</i>						
Summer	Up to 3+	0,081±0,057	0,092±0,065	0,089±0,063	0,088±0,062	0,061±0,043
	from 6+ up to 8+	0,127±0,090	0,197±0,139	0,092±0,065	0,129±0,092	0,123±0,087
Winter	Up to 3+	0,073±0,052	0,094±0,066	0,058±0,041	0,072±0,051	0,064±0,045
	from 6+ up to 8+	0,089±0,063	0,167±0,118	0,053±0,037	0,116±0,082	0,097±0,068
<i>Perch (Perca fluviatilis)</i>						
Summer	Up to 2+	0,131±0,093	0,157±0,111	0,092±0,065	0,031±0,022	0,082±0,058
	From 4+ up to 6+	0,256±0,181	0,251±0,177	0,201±0,142	0,199±0,141	0,112±0,079
Winter	Up to 2+	0,093±0,066	0,106±0,075	0,046±0,032	0,091±0,064	0,087±0,061
	From 4+ up to 6+	0,122±0,086	0,203±0,143	0,059±0,042	0,121±0,085	0,065±0,046

Table 6

**Accumulation and distribution of cadmium in the organs and tissues of Allaihovskij
district freshwater fish**

Study period	Age of fish	Muscles	Liver	Intestine	Gills	Skeleton
<i>Pike (Esox lucius)</i>						
Summer	Up to 2+	0,143±0,101	0,156±0,110	0,103±0,073	0,034±0,024	0,066±0,047
	From 4+ up to 6+	0,302±0,213	0,323±0,222	0,198±0,140	0,207±0,146	0,126±0,089
Winter	Up to 2+	0,089±0,063	0,187±0,134	0,054±0,038	0,091±0,064	0,080±0,056
	From 4+ up to 6+	0,243±0,172	0,288±0,203	0,057±0,040	0,097±0,068	0,063±0,044
<i>Dace (Leuciscus leuciscus)</i>						
Summer	Up to 2+	0,063±0,044	0,087±0,061	0,051±0,036	0,073±0,052	0,069±0,049
	From 4+ up to 6+	0,102±0,072	0,143±0,101	0,089±0,063	0,121±0,085	0,094±0,070
Winter	Up to 2+	0,056±0,040	0,089±0,063	0,041±0,029	0,079±0,056	0,064±0,045
	From 4+ up to 6+	0,086±0,061	0,116±0,082	0,062±0,044	0,095±0,067	0,087±0,061
<i>Perch (Perca fluviatilis)</i>						
Summer	Up to 2+	0,132±0,093	0,151±0,107	0,091±0,064	0,046±0,036	0,071±0,050
	From 4+ up to 6+	0,208±0,147	0,229±0,162	0,186±0,131	0,267±0,189	0,131±0,093
Winter	Up to 2+	0,091±0,064	0,102±0,072	0,063±0,044	0,093±0,066	0,097±0,068
	From 4+ up to 6+	0,149±0,105	0,208±0,147	0,067±0,047	0,165±0,117	0,102±0,072

Assessment of the Distribution of Heavy Metals in Meat Foods of Central Yakutia Inhabitants

Grigoryeva A. A., Mironova G. E.

ABSTRACT

This article presents the results of studies assessing the distribution of toxic elements (heavy metals) in the organs and tissues of cattle. So as a special role in human nutrition belongs to the micronutrients involved in the metabolism of the body and often defining health state. It was revealed that the concentration of lead, cadmium, mercury and arsenic in the body of surveyed animals was distributed in descending order: kidney > liver > muscle tissue, and did not exceed the MAC (maximum allowable concentration).

Keywords: heavy metals, muscle tissue, liver, kidneys, concentration, cattle.

INTRODUCTION

The problem of pollution environment and this disturbance in nature is very important. The main threat to environmental pollution is heavy metals.

The study distribution and accumulation of heavy metals in the organism of agricultural animals is important due to the fact that the food of Yakut people associated with the use of considerable quantities of food of animals [11].

The Far North is considered to be one of high-risk areas for the occurrence of many diseases. The great exposure to the organism of Northern people of the development of certain diseases is determined by climate-geographical position. In the northern conditions the cold climate requires a large consumption of energy by the body to sustain life. The products of animals (meat, butter, milk, fish) available and widely spread that contribute to the formation of special type of food Northern people so that is protein-lipid type. Proteins and fats of animals as the source of nutrition and energy are the basis of adaptation to the organism to the severe climatic conditions of the North [1,2].

The aim of work was to estimate the distribution of heavy metals (lead, mercury, cadmium and arsenic) in liver, kidney and muscle tissue of cattle.

MATERIALS AND METHODS

The samples of muscle liver and kidney were taken for research during the slaughter of cattle in Techtur and Nemugu villages of Changalassky region (The Central Yakutia). The selection of these villages was due to the fact that they were located near the federal highway Yakutsk – Nerungri. The content of heavy metals in the samples was determined to atomic

absorption spectrometry «MGA-915»: the level of lead and cadmium in accordance with GOST 30178-96, mercury – GOST 26927 and arsenic – GOST 26930-86 [5, 6, 7].

RESULTS AND DISCUSSION

According to our data the concentration heavy metals (HM) in the examined samples of muscle liver and kidney did not exceed the MPC (maximum permissible concentration) (Table.1).

Table. 1

The concentration HM in muscle tissue and the body of cattle (mg/kg)

Microelements		Muscle tissue	Liver	Kidney
Pb	MPC	0,5	0,6	1,0
	M±m	0,0610±0,0020	0,3400±0,0040	0,6400±0,0160
Cd	MPC	0,05	0,3	1,0
	M±m	0,0020±0,0001	0,0180±0,0001	0,0180±0,0002
Hg	MPC	0,03	0,1	0,2
	M±m	0,0220±0,0020	0,0260±0,0003	0,0220±0,0002
As	MPC	0,1	1,0	1,0
	M±m	0,0790±0,0010	0,0850±0,0010	0,0900±0,0030

From the table. 1 it can be seen that the contents of the lead in the muscle tissue was varied in the range from 0,025 mg / kg to 0,094 mg / kg, cadmium – 0,002 mg / kg to 0,004 mg / kg, of mercury - from 0,012 mg / kg to 0,030 mg / kg, arsenic – 0,06 mg / kg to 0,11 mg / kg. Average values of HM in muscle tissue distributed in descending order: As> Pb> Hg> Cd.

The concentration lead in the liver ranged from 0,20 mg / kg to 0,48 mg / kg, cadmium - 0,010 mg / kg to 0, 016 mg / kg, of mercury - from 0,024 mg / kg to 0,028 mg / kg, arsenic – 0,07 mg / kg to 0,10 mg / kg.

The level of lead in kidney of cattle ranged from 0,24 mg / kg to 0,93 mg / kg, cadmium - from 0,015 mg / kg to 0,021 mg / kg, of mercury - from 0,019 mg / kg to 0,029 mg / kg, arsenic - from 0,03 mg / kg to 0,13 mg / kg.

The concentration of metals in the liver and kidney of cattle can be arranged in the following descending sequence: Pb> As> Hg> Cd.

The content of mercury as in the blood and in the organs of the animals was surveyed actually identical. The concentrations mercury tended to increase in order of increasing muscle< liver < kidney. The middle meaning of cadmium in the liver and kidneys of cattle were 9 times higher than in the muscle tissue.

The concentration in the kidney, Cd was the same as in the liver and the content of Pb in 1.8 times higher than in the liver.

Our results show that HM in organism of animals accumulate in parenchymal organs. It is known that HM comes to animals with forage herbs. The rangeland of soil contamination lound up with anthropogenic load. The main pollutants of the environment in the area are Changelassky region are cement factory, thermal power plant (TPP), and automobile transport.

It is known that 54% of mercury emissions account for coal combustion; 86% of lead emitted into the atmosphere from automobile transport. A certain amount of heavy metals in the environment and delivers agriculture where pesticides are applied and mineral fertilizers, particularly superphosphate contain significant amounts of chromium, cadmium, to cobalt, copper, nickel, vanadium and zinc [3,8].

Yakutia is in continuous permafrost. Its influence is penalized cycle of many substances, including heavy metals (HM), which accumulate in the soil and the food chain may soil - plants - animals ingested that contribute to the development of many diseases [4].

Accumulation of heavy metals in parenchymal organs associated with the circulatory system. Heavy metals are received fodder grasses organism cattle digested in the gastrointestinal tract and via the portal vein to the liver, where there are major metabolic processes and disposal of heavy metals, one of the inducible metallothionein proteins. The accumulation of heavy metals in bovine kidney associated with their excretory functions [10].

Our data indicate that the level of heavy metals in the tissues of cattle Changelassky region area does not exceed the maximum allowable concentrations and fully meets requirements Sanitary 2.3.2.1078 - 01 [9].

CONCLUSION

So, heavy metals, trapped with herbage crops are distributed in the body of cattle lopsided. The lowest concentrations of heavy metals (lead, cadmium, mercury and arsenic) was found in muscle tissue, and the highest - in the kidney. Our results indicate that the concentration of lead, arsenic, mercury and cadmium in the body of animals surveyed distributed in descending order: kidney> liver> muscle.

REFERENCES

1. Aghajanian N. A. Ermakova N.V. Jekologicheskij portret cheloveka na Severe [Environmental portrait of a man in the North]. Moscow, "Kruk", 1997, 208 p.
2. Bezrodnykh A. A. Safonova S. L. Voprosy racional'nogo pitaniya prakticheski zdorovykh ljudej i bol'nyh nekotorymi zabolevanijami zheludochno-kishechnogo trakta v uslovijah

Krajnego Severa [Questions of nutrition of healthy individuals and patients with certain diseases of the gastrointestinal tract in the Far North] Yakutsk: Jakutpoligrafizdat, 1999, 176 p.

3. Gabysheva J. A. Tjzhelye metally v biologicheskikh ob#ektah raznyh prirodno-klimaticheskikh territorij Jakutii [Heavy metals in biological objects of different climatic areas of Yakutia]: avtoref. dis... kand. biol. nauk [Author. dis ... cand. biol. Sciences]. Novosibirsk, 2001, 21 p.

4. Gavrilova M. K. Klimat Central'noj Jakutii [Climate of Central Yakutia]. Yakutsk: Jakut. kn. izd-vo , 1973, 120 p.

5. Gigienicheskie trebovaniya bezopasnosti i pishhevoj cennosti pishhevyyh produktov. SanPiN 2.3.2.1078-01, utverzhd. Glavnym gosudarstvennym sanitarnym vrachom RF 06.11.2001 g., s 1 ijulja 2002 g. [Hygienic safety and nutritional value of foods. SanPin 2.3.2.1078-01 arguing. Chief state sanitary doctor of Russia 06.11.2001, p 1 July 2002] Sobr. zakonodatel'stva Ros. Federacii [Coll. Ros legislation. Federation], 2000, № 31, St. 3295, P. 180.

6. Donnik I. M. Bolshakov V.N. Problemy polucheniya kachestvennyh produktov zhivotnovodstva v rajonah tehnogenogo zagrjazneniya [Problems in obtaining high-quality animal products in the areas of technogenic pollution]. Nauchnye osnovy profilaktiki i lecheniya boleznej zhivotnyh [J Scientific basis for prevention and treatment of animal diseases], 2005, P. 433-442.

7. Shkuratova I. A. Sokolova O. V. Ryaposova M.V. Donnik I.M. [et al.]. Ocenka bioresursnogo potenciala vysokoproduktivnyh korov pri raznyh tehnologijah soderzhanija [Rating of potential bioresource of high yielding cows at different technologies content] Agrarnyj vestnik, 2012, № 1, P. 33.

8. Syr'e i produkty pishhevye. Atomno-absorbcionnyj metod opredeleniya toksichnyh jelementov [Raw materials and food. Atomic absorption method for the determination of toxic elements]: GOST 30178-96, 2010, Intr. 26 - 03 – 1997, Moscow: Standartinform, 2010, 33 p.

9. Syr'e i produkty pishhevye. Metody opredeleniya rtuti: [Raw materials and food. Methods for determination of mercury]: GOST 26927-86, 2010, Intr. 12/01/1986, Moscow: Standartinform, 2010, 15 p.

10. Syr'e i produkty pishhevye. Metod opredeleniya mysh'jaka [Raw materials and food. Method for the determination of arsenic]: GOST 26930-86, 2010, Intr. 01-01-1987, Moscow: Standartinform, 2010, 6 p.

11. T. I. Bokova, K. Ja. Motovilov, V. G. Guglja, A. P. Bulatov, N. A. Shkil'. Jekologo-tehnologicheskie aspekty povedeniya tjzhelyh metallov v sisteme pochva - rastenie - zhivotnoe - produkt pitaniya cheloveka [Ecological and technological aspects of the behavior of heavy metals



in the soil - plant - animal - human food]. Rossijskaja akademija sel'skhozjajstvennyh nauk, Sibirskoe otделение, Sibirskij nauchno-issledovatel'skij i proektno-tehnologicheskij institut pererabotki sel'skhozjajstvennoj produkcii [Russian Academy of Agricultural Sciences, Siberian Branch, Siberian Research and Design Institute of agricultural products processing]. Novosibirsk: GNU SibNIPTIP, 2004, 204 p.

The authors

Grigoryeva A. A., graduate student NEFU named after M.K. Ammosov, Yakutsk, Russia, e-mail: nastiagrigoryeva@mail.ru;

Mironova G. E., Doctor of Biology, prof. NEFU named after M.K. Ammosov, Yakutsk, Russia, e-mail: mirogalin@mail.ru.

Questions of Adaptation of First-Graders to School (THE LITERATURE REVIEW)

T.V. Potupchik, L.S. Evert, O.I. Zajtseva, E.S. Panicheva, E.V. Miroshnichenko

ABSTRACT

The article presents the literature review on adaptation of children to process of school training, criteria and clinico-functional features of adaptable processes in children, ways of prediction the course of adaptation in children to training at school are described in the article, features of cerebral blood circulation and a vegetative homeostasis in children of primary school age are presented.

Keywords: adaptation, first-graders, prediction, adaptive processes, vegetative homeostasis.

INTRODUCTION

The problem of health protection of children and teenagers at the present time is one of the most difficult and actual. The results of numerous researches estimating the state of health in children of preschool and school age inspire serious fears [7, 15, 19, 27, 45]. Against negative changes of ecological conditions, social problems and economic instability we can see the increasing number of children with weakened health, these children enter the school. Such children have difficulty in adaptation to educational activity, development of skills of training, ability to concentrate their attention and to solve educational tasks. Such a condition of an organism reduces the efficiency of the most advanced pedagogical technologies and considerably complicates realization of the program of development of the person [2,32].

The increased number of first-graders with the combined pathology is noted. In disease structure there is a considerable part of diseases of central nervous system, cardiovascular and endocrine systems. The majority of children have subclinical form of diseases that complicates the diagnostics and conducting the adequate treatment. Special attention is required by health of children studying in innovative educational institutions, working with developing educational programs [9, 34]. In the conditions of modern school programs these children can develop disadaptive stress reactions which can influence their somatic condition and progress level. The basic cause for such state of health, according to the majority of researchers, is high academic load [16, 36].

Deterioration of a state of health of schoolboys in recent years defines the necessity of dispensing of academic load according to functional opportunities of the organism, and also

working out of health complexes for prevention and health protection, based on exact estimations of the condition of the organism of each child. The special place in working out of these complexes is occupied by donozological diagnostics of deviations of health, directed to revealing of initial signs of pathology of the leading systems of the organism [17, 21]. The beginning of regular training at school is one of crisis stages in development of the child; it results in serious changes in a way of life and demands great efforts of functioning of all systems of the organism [12].

I. Concept of adaptation

The definition of health as an ability of an organism to adapt for environment conditions gives a key place to the theory of adaptation in the study of health and illnesses. In biology the process of adaptation is an adaptation of a structure and organism functions to existence conditions. The signs and properties which appear to be the most favourable for living beings with the help of which the organism gets the ability to exist in a concrete life environment are formed during the period of adaptation. Adaptation of an organism to conditions of environment can have different character and affect all parts of organization and life activity of the person [1,4].

Reserve possibilities of an organism should be sufficient to support the basic vital constants in normal limits. Adaptation to new conditions occurs due to mobilization of functional reserves and demands certain effort of regulatory systems. In case of change of the environment the organism should change some constants of its functions. There is the reorganization of homeostasis adequate to concrete conditions, it forms the basis of adaptation [6]. These changes occur, first of all, in systems of breath and blood circulation which are responsible for maintenance of organs and tissues with oxygen and nutrients. Therefore adaptive changes of regulatory mechanisms are more likely to appear in the course of regulation of cardiorespiratory system [18, 20].

According to the theory of general adaptive syndrome by Hans Selye (1961), there are three phases of course reactions of adaptation. The first phase – is "emergency" - develops at the very beginning of the action both physiological, and the pathogenic factor or the changed conditions of the environment. Thus blood circulation and breath systems are the first to react. These reactions are controlled by the central nervous system with wide involving of hormonal factors, in particular hormones of brain substance of adrenal glands (catecholamines), which is accompanied by hypertonicity of sympathetic system.

The second phase – is transitional to steady adaptation. It is characterized by the reduction of the general excitability of the central nervous system, the formation of the



functional systems providing management of adaptation to resultant new conditions. The intensity of hormonal shifts decreases, the number of systems and organs which originally were not involved in reaction is gradually increasing. After the transitional phase comes the third phase - the phase of steady adaptation or resistance. It is actually adaptation – and it is characterized by new level of activity of tissue, cellular, membrane elements, reconstructed due to time activation of auxiliary systems which thus can practically function in an initial mode, whereas tissue processes become more active, providing a homeostasis adequate to new conditions of existence. The basic features of this phase are: mobilization of power resources; the raised synthesis of structural and fermentative proteins; mobilization of immune systems.

Nowadays interaction between the organism and the environment is carried out so fast that nature and a human being have no time to adapt mutually, so there is an ecological balance disruption. The transition area between a norm and pathology represents not a homogeneous third condition, but a series of the alternative conditions differing according to the degree of adaptation of an organism to conditions of the environment [2].

II. Criteria of adaptive processes in children

The occurrence of functional and organic changes is preceded by the borderline cases characterized by the decrease of adaptable possibilities of a child's organism to changing conditions of life environment. They appear in the form of numerous signs of discomfort and stress, showing the trouble which is not revealed by usual methods of research [4]. That's why vital importance is given to the search of authentic information criteria, allowing to reveal risk group of children concerning the decrease in level of health to occurrence of organic changes with working out of the differentiated correction.

The important criterion reflecting the course of adaptive process to school is the level of physical development. It is proved, that disharmonious physical development is a prognostic adverse criterion of a course of adaptation of children to school [8, 9]. So, according to V.L.Gritsinskaya (2003) the most difficult adaptive process to regular training at school takes place in children with micro-and macro- somatotypes, as well as in first-graders at whom during the initial stage of training high values of «sthenia index» (above 1, 25), adaptive indicator (above 1,9), decrease in body weight and-or occurrence of disharmony of correlation between length and weight of a body appear.

E.D. Basmanova with co-authors (2009) specifies that as a sensitive indicator of a favorable course of adaptation in first-graders has positive dynamics of physical development in children. A.A. Kuzmina et al. (2006) consider that the deficiency of body weight is the most

frequent variant of deviation in anthropometrical indicators at children of the first year of training at school. At 52,6-71,0 % of the first-graders who have begun their studies at school at 6,5 years at the end of the academic year the prevalence of deviations in physical development [9] was marked.

The difficult mechanism of adaptation of an organism of the child to various levels of the anthropogenous load, directed to preservation of a functional condition and working capacity in inadequate conditions, due to reorganization of energetic, structural and informational levels, forces to consider the central nervous system to be the basic centre of formation of programs of adaptation. The basic mechanism defining the character of adaptation of a human body is the vegetative department of the central nervous system reflecting an integrated condition of somatic functions. Autonomic imbalance is the factor predetermining both the possibility of occurrence, and severity of somatic diseases. The most convenient and informative method of research of a condition of vegetative influences is the analysis of variability of heart rhythm because it is known, that nervous and humoral regulation of heart work changes much earlier, than energetic, metabolic and haemodynamic changes[5,22,31].

The effector system realizing this or that response of the organism, is the cardiovascular system which most sensitively reacts to rather insignificant adverse influences as it possesses a role of the indicator of adaptive reactions of the organism. That's why the revealing of initial deviations will promote in time correction of negative influence of factors of environment. Arterial pressure is one of the major indicators of central haemodynamics. Under the influence of intellectual and physical activities certain changes in level of arterial pressure are observed. Excessively intense educational activity at schools, according to a number of authors, is one of the reasons of arterial hypertension in children [18,20].

Adaptation is directly connected with nonspecific resistance and reactance, i.e. with that background which, finally, defines the risk of development of diseases and health level. The immune system, being one of the major homeostatic organism systems, participates practically in all adaptive processes and is a part of the protective mechanism of the organism. Active participation of the immune system in many vital processes of an organism leads to the fact that disorders of immunoreactivity cause functional and structural variety of appearance of pathologies of the person [1,15].

The circle of healthy functioning includes adaptable reactions of the organism which do not cause disorders in its activity and make norm of adaptation. Disorders in physical development of schoolboys, the increasing number of dysfunctions of cardiovascular and

vegetative nervous system, disease growth indicates, that adaptable mechanisms of children work intensively [4,18,19].



III. Clinic-functional features of adaptive processes in children

Process of growth and development of the organism of the child is in the sphere of interest for teachers, psychologists, physiologists and medical workers. Focused attention involves the development of children during the crisis periods of life during which time formation and development of functional and morphological possibilities and functions occurs more intensively, than during the stable age periods [14,15]. Pupils of primary school age demand special attention to themselves as incompleteness of morphological and functional development, lability of physiological processes promote the fact that during this period the child extremely sharply reacts to revolting factors of the environment. In spite of the fact that conditions of school and academic loads are far from extreme, the process of adaptation to these microsocial conditions with influence of adverse climatic and ecological conditions of the living region can have the character of the expressed stressful reaction [16].

According to the literature, adaptation of the child to new social conditions, along with development of a difficult kind of activity - training, is accompanied by considerable pressure of the central nervous system, demands high energetic expenses that leads to functional damage of a state of health of children: immunity decreases, loading on regulatory systems increases, the metabolism, the central and peripheral blood circulation change. As a result there are various changes characterized by the decrease of functionality of an organism and first of all of its regulatory systems which level of pressure reflects the degree of adaptation to environment conditions. Therefore there can be asymptomatic forms of a pathology with the long latent period in children, - premorbid conditions which can serve as the base to occurrence of numerous diseases [6,17].

Features of an age stage of 6-7 years appear in changes in all spheres. High functional pressure which tests an organism of the first-grader, is defined by the fact that intellectual and emotional loads are accompanied by long static pressure connected with preservation of a certain pose of the child at work in a class. The period of adaptation at first-graders is characterized by low and unstable level of working capacity, very high level of pressure cardiovascular, sympathoadrenal systems. Discrepancy of requirements and possibilities of the child leads to adverse changes of the central nervous system, to sharp falling of educational activity, to decrease in working capacity and the expressed exhaustion [19, 23, 34, 38].

Physiological and hygienic researches of last years show, that in many respects the ability of the child to adaptation is defined by the structurally functional organization of a brain [10, 25]. It is established that the basis of successful adaptation of the child to educational loadings and to realization cognitive activity is a certain level of a maturity of functional

structures of brain and adequate character of its activity various cortical-subcortical, cortical-stem regulatory systems [25]. Researches of children of 7-8 years has shown, that at this age under condition of conformity of a functional condition regulatory structures to age norm are generated neurophysiological mechanisms of selective modulation of cortical activity, providing selective adjustment of brain structures according to the cognitive problem. Specificity of the functional organization of the cortex at any selective attention in children of 7-8 years consists in absence of interhemispheric distinctions and domination of specific modular (left hemisphere) type of functional interaction of cortical zones in both hemispheres. Comparison of the data received during the research of children, shows relative immaturity of mechanisms of any attention at the training initial stage. Duration of formation of regulatory systems at younger school age and their role in the organization cognitive activity is confirmed in neuropsychological and psychometric researches [10,19,20,41,42].

Development of internal brake action in children of younger school age is at the initial formation stage, it differs by insufficient flexibility and durability, the nervous system of children is not ready to maintain long psychoemotional loadings and pressure. Discrepancy of social requirements and conditions of training of children somatophysical abilities of a growing organism leads to formation of neurotic reactions, frustration of a motility in the form of a hyperdynamic syndrome, reactions of the active protest or the phobic disorders the frequency of which depends on a functional maturity of an organism of the child and a condition of its health. Neurotic frustration in children can be shown by the various disorders which do not have organic nature, disorders of cardiovascular, respiratory, digestive and secretory systems [14, 26, 30, 37].

Children of younger school age have intensive changes of cardiovascular system: the weight and volumes of heart cavities increase, the histologic structure of heart and vessels is differentiated. The most general reaction to stressful influence from cardiovascular system is the increase in frequency of heart contractions, change of structure of its variability and reductions of indicators of haemodynamics connected with frequency of heart contractions. The beginning of regular training is accompanied by low adaptive possibilities, decrease in functional reserves of the cardiovascular system. Deviations of vegetative regulation underlie the formation of functional deviations in primary school age [20, 35, 43, 44]. We can attribute to peculiarities of formation of health in children during different age periods the expressed increase of prevalence of functional deviations and a chronic pathology; we can mention sharp reduction of quantity of absolutely healthy children. The decrease of immune protection more often appears in the form of sharp respiratory diseases. The most expressed growth of disease according to many authors is marked at school age [8, 15].

In the period of adaptation to training it is necessary to consider specific features of the schoolboy. One of the most perspective variants of the account of specific features of an organism of the child for today is constitutional approach. The system portrait of children of three basic constitutional types (centrovert, extrovert and introvert) is based on characteristics of the morphological, vegetative and mental organization of the child and is defined by the following signs. Centroverted children usually have digestive or macrosomatic types of a constitution, average indexes of power, speed qualities and strength. The psychological portrait is characterized by emotional stability, average indexes of aggression, social activity, all-around cleverness, communicative skills [3]. During the research of condition of vegetative nervous system eutonia appears.

The characteristic features of extrovert children are the mesosomatic type of a constitution, the tendency to brachyrania, advancing of biological age in relation to passport, high speed and power indicators and decrease of strength. Features of psychological development of these children are high indicators of figurative thinking at decrease in indicators of logic, memory, attention, discipline. Explosive hysterical character and inflated self-esteem are combined with a leadership position. Sympathicotonia with hypersympathicotonia vegetative reactance is characteristic for them. Introvert children are characterized by asthenic type of a constitution with the tendency to weight deficiency, they have dolichocephalic skull. The motor organization is characterized by low indicators of speed, force and strength. High indicators of memory, attention, logical thinking, and discipline are characteristic for them, but, at the same time, there is a tendency to lower self-esteem, bad mood, phobic anxiety reactions. In children of given constitutional type initial vagotonia with asympathicotonic reactance prevails [10, 42, 46].

Thus, the adaptive period is accompanied by various changes in a functional condition of children: factors of local protection decrease, tension of hypothalamo-pituitary-adrenal, sympathoadrenal and vegetative nervous systems is marked. One of the features of children's organism is heterochronicity of formation and maturing of its separate physiological systems and functions that affects the formation of readiness of the child to training. The success of primary stage of adaptation to school predetermines the general positive result of the adaptation of the child. Transformations to a children's organism occur throughout the first year of training, therefore it is so important to trace features of physical development, dynamics of physiological and psychophysical indicators during this period.

IV. Predicting the course of adaptation in children to training at school

Basic principle of modern medicine is prior development of a preventive direction. The important section in order to prevent the failure of adaptation is to predict the character of the

process of adaptation before the child enters the school, because about 70 % of children in school have different deviations in behaviour (appetite disorders, sleep disorders, disorders of emotional condition, etc.) before entering the school. Predicting the adaptation allows to estimate adaptable possibilities of the child before entering the school and gives the chance to define, how will proceed adaptation of the child during educational process in the first class [11,15,38]. The prognostic stage provides allocation of children with risk of unfavorable course of adaptation. This stage is carried out in children's preschool educational institution for one year and directly before entering the school. The established risk factors of an unfavorable course of adaptation of children to training at school give the chance to carry out stable work for preventive measures.

The most known way of definition of the prediction of adaptation of children to school is based on questioning the parents and drawing up prognostic tables in which the burdened factors of the biological and social anamnesis are presented. The factors of perinatal pathology include gestoses during the pregnancy, obstructed labour which are often accompanied by hypoxia of the brain in child and displays perinatal defeat of central nervous system. Diseases of the first year of life negatively affect maturing of a brain of the child [39].

Development of the child is defined by character of his living environment. Living in incomplete families, remarriage of parents, long separation from parents, severe diseases or death of parents affect the development of the child. The big influence on development of the child has deprivation in a family - loss or restriction of satisfaction of the vital requirements of the child. Disorders of the child's mind are often marked in problem families in which relations between the child and the parents are broken, accompanied with quarrels, conflicts, alcoholism or drug abuse, immoral behaviour of parents. Deprivation in secured family is a substitution of care and attention to the child by other persons (tutors, nurses, grandmothers and grandfathers). Deficiency of attention to the child in a family when even well-groomed, full-fed, carefully dressed child can appear internally lonely, psychologically neglected because nobody is interested in his mood, feelings, and interests. It can also affect mental health of schoolboys [13,29].

The primary school age is the beginning of formation of motivation of the study on which its further destiny during all school age in many respects depends. A number of authors notice, that lowered motivation to training causes regular stay of children in a condition of the psychic tension underlying deep mental and physiological disorders [14, 15, 23].

V. Features of cerebral blood circulation and a vegetative homeostasis in children of primary school age

The estimation of a vegetative tone is one of the basic criteria characterizing features of a functional condition of an organism. Disturbance of vegetative regulation is the factor predetermining possibility of occurrence of somatic diseases. Current activity of sympathetic and parasympathetic departments is the result of multiplanimetric and multilevel reaction of system of regulation by blood circulation changing in time the parameters for achievement of the optimum adaptive answer which reflects adaptable reaction of a complete organism. Adaptable reactions are individual and are realized in different persons with various degree of participation of functional systems. Activation of sympathetic nervous system specifies vegetative disbalance owing to desadaptation [22].

The results of researches have shown that functionality of heart and independent mechanisms of regulation of its activity in children of primary school age are imperfect, adaptive possibilities of heart are lowered, and tension of mechanisms of adaptation is high. Thus tension is most expressed degree in boys, than in girls. In first-graders with prevalence of a sympathetic link of regulation tension of adaptive systems is marked. At the same time in a number of first-graders the expressed overstrain of the device of the central regulation is noticed. It testifies insufficiency of adaptive mechanisms which can be shown by certain changes in a state of health of children. First-graders with the expressed parasympathetic influence on heart function can have initial stages of exhaustion which is found out much earlier, than visible decrease in working capacity. Optimum tension of systems of regulation of heart function can be considered as a condition, characteristic for satisfactory adaptation of an organism of children to influence of the environment [28]. Simultaneously it is established, that the basis of successful adaptation of children to educational loads and realization of the cognitive activity is certain level of a maturity of functional structures of a brain and adequate character of its various cortical-subcortical, cortical-stem regulatory systems [25].

According to the number of authors the majority of children with various types of vegetative dysfunction have the residual effect of natal damages in the form of pathology from cervical department of a backbone, disturbances in vertebro-bazillar system. The condition of hypoxia of brain is accompanied by disturbance of interhemispheric relations and promotes the formation of liquor hypertension in the field of the third ventricle in the location of structures of limbic-reticular complex, that further promotes the formation of syndromes of hypothalamic insufficiency, intracranial hypertension, psychosomatic diseases, including diseases of cardiovascular system. Among the acquired factors provoking the development of vegetative disorders, many authors name the superfluous psychoemotional tension in children, connected with adaptation to school and intellectual overfatigue [4, 32].

The analysis of activity of cardiovascular system in children of primary school age depending on features of a functional condition of brain represents special interest and is necessary for understanding the realization of disadaptive disorders, working out methods of their prevention, predicting and effective therapy [18, 20, 25, 28,35]. It is known, that in comparison with other organs the brain possesses a hypersensitivity to the lack of oxygen and nutrients. The brain is protected from decreasing of arterial pressure and hypoxia by a number of physiological mechanisms regulating both general, and cerebral haemodynamics, the basic of which is the reflex mechanism with participation the sinocarotid zone, aorta's depressor and cardiovascular centre in the medulla, being in a direct connection and under the influence of hypothalamo-mesencephal and subcortical vasomotor centres.

The collateral arterial blood supply of a brain, important for maintenance and normal blood-flow, plays especially considerable role in compensation of blood circulation in case of block of one of brain arteries. The great value in maintenance of constant pressure in brain vessels has such a local adaptive mechanism, as presence of double innervation vessels (vasodilating and vasoconstrictive nerves). The activity vasomotor brain centres is connected not only with nervous, but also with humoral influences: increase of level of oxygen slows it down. Last year it was reported about the existence of autoregulation system of the brain blood circulation, which has the direct influence of fluctuations of intravascular pressure upon a tone of non-striated muscles of brain vessels (reduction or their relaxation) therefore, despite considerable fluctuations of the general arterial pressure, cerebral blood flow is supported at constant level [10,25,33,35].

Thus, brain blood circulation is provided by reflex mechanisms, regulated by various levels of nervous system. The leading factor in the mechanism of defeat of a brain is hypoxia. Physiological researches show, that every minute in a brain arrives about 15% of the blood which is thrown out by heart for this period and containing 20 % of consumed oxygen. Therefore owing to even short-term vascular spasms the exchange processes in brain substance are broken, thereby influencing the functioning of neurons. Hypoxia causes activity changes of pituitary-adrenal systems which can cause the further disorders of regulation of a vascular tone and a blood flow.

In pathogenesis of neurologic frustration in case of disturbances of brain haemodynamics the considerable role is played by venous blood circulation. The venous hypertension, difficulty of venous outflow from the skull cavity can arise as a reaction to hypoxia in case of brain ischemia, and also in case of hemorrhages. The difficulty of venous outflow leads to the development of intracranial hypertension that in its turn can break arterial blood

circulation, and thus promote the formation of one more vicious circle in pathogenesis of neurologic frustration. At children's age the most frequent reason of paroxysmally coming frustration of brain blood circulation is vegetovascular dystonia with angiospastic disturbances. It is observed more often in girls; sometimes it is genetically caused and appears in the form of periodic attacks of headaches, dizziness, nausea, faints. The occurrence of these conditions is characteristic at excitement, overfatigue, in a stuffy room, at sudden change of position of a body, emotional lability, unstable arterial pressure [10, 25, 33, 44].

CONCLUSION:

Thus, the analysis of literary data testifies the necessity of the further studying of features of a course of adaptation period in children of the first year of training, including the use of the complex approach including stages of preschool prediction of adaptation. The literature data confirm actuality of the further studying of psychophysical features, a clinic-functional condition with use of functional methods of the research defining the condition of mechanisms of regulation of a vegetative homeostasis, the condition of cerebral blood circulation in dynamics during the first year of training at school.

References:

1. Agadzhanyan N.A. Adaptatsionnaya meditsina i zdorov'e [Adaptation Medicine and Health] Vestn. Ural'skoy med. Nauki [Vestn. Ural honey. science]. 2005, № 2, P. 10-18.
2. Meshkov N.A., Ivanov S.I., Val'tseva E.A. [et al.] Adaptatsionnoe sostoyanie detskogo organizma kak indikator neblagopriyatnogo vliyaniya okruzhayushchey sredy [Adaptive state the child's body as an indicator of the adverse effects of environmental] Gigiena i sanitariya [Hygiene and Sanitation]. 2007, № 5, P. 52-53.
3. Ayzenk G.Yu. Struktura lichnosti [Personality structure] SPb.: Yuventa; M.: KSP+ [St. Petersburg : Juventas, M.: SPC +]. 1999, 464 p.
4. Apanasenko G.L., Popova L.A. Meditsinskaya valeologiya [Medical valueology] Rostov n/D : Feniks [Rostov n/D. : Phoenix]. 2000, P. 248.
5. Baevskiy R.M., Ivanov G.G. Variabel'nost' serdechnogo ritma: teoreticheskie aspekty i vozmozhnosti klinicheskogo primeneniya [Heart rate variability: theoretical aspects and clinical applications] Ul'trazvukovaya i funktsional'naya diagnostika [Ultrasonic and functional diagnostics]. 2001, № 3, P. 108-127.
6. Baevskiy R.M. Kontsepsiya fiziologicheskoy normy i kriterii zdorov'ya [Ultrasonic and functional diagnostics] Ros. fiziol. Zhurn [Rus. Physiol. journal]. 2003, № 4, P. 473-487.

7. Baranov A.A., Il'in A.G. Aktual'nye problemy sokhraneniya i ukrepleniya zdorov'ya detey v Rossiyskoy Federatsii [Actual problems of preserving and strengthening the health of children in the Russian Federation] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2011, № 4, P. 7-12.
8. Baranov A.A., Kuchma V.R., Sukhareva L.M. Otsenka sostoyaniya zdorov'ya detey. Novye podkhody k profilakticheskoy i ozdorovitel'noy rabote v obrazovatel'nykh uchrezhdeniyakh [Evaluation of children's health. New approaches to prevention and health improvement work in educational institutions]. M.: GEOTAR–Media [M. : GEOTAR Media], 2008, 432 p.
9. Basmanova E.D., Perevozchikova N.K. Osobennosti fizicheskogo razvitiya detey v shkolakh raznogo tipa [Features of physical development of children in schools of different types] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 1, P. 53-56.
10. Bezrukikh M.M., Machinskaya R.I., Farber D.A. Strukturno-funktsional'naya organizatsiya razvivayushchegosya mozga i formirovanie poznavatel'noy deyatel'nosti v ontogeneze rebenka [Structural and functional organization of the developing brain and the formation of cognitive activity in ontogenesis child] Fiziologiya cheloveka [Human Physiology]. 2009, Vol. 35, № 6, P. 10-24.
11. Berezina N.O., Nikitina M.A., Khramtsov P.I. Kharakteristika funktsional'nykh vozmozhnostey organizma sovremennykh doskol'nikov [Feature functionality of an organism modern preschool] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2011, № 3, P. 39-42.
12. Bernatskaya N.A., Savchenko N.N. Fiziologo–psikhologicheskie aspekty adaptatsii detey k shkol'nomu obucheniyu [Physiological - psychological aspects of children's adaptation to school] Byulleten' sibirskoy meditsiny [Bulletin of Siberian Medicine]. 2005, Vol. 4, Pril.1, 156 p.
13. Bryazgunov I.P., Kasatikova E.V. Neposedlivyy rebenok, ili Vse o giperaktivnykh detyakh [Restless child, or hyperactive children of all types]. M.: Psikhoterapiya, 2008, 208 p.
14. Goncharova G.A. Osobennosti nervno-psikhicheskikh narusheniy u mladshikh shkol'nikov v dinamike obucheniya [Features neuropsychiatric disorders in primary school children in the dynamics of training] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 23-27.
15. Gordiets A.V. Sostoyanie zdorov'ya pervoklassnikov i osobennosti ikh adaptatsii k shkol'nomu obucheniyu [Health status of first-graders and features of their adaptation to schooling] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2010, № 6, P. 49-52.



16. Gurov V.A. Vliyanie tekhnologicheskogo komponenta obrazovatel'noy sredy na protsess psikhofiziologicheskogo razvitiya mladshikh shkol'nikov [Effect of the technology component of the educational environment on the process of psycho-physiological development of younger students]. Krasnoyarsk, 2008, P. 25-28.
17. Denisov L.A., Berseneva A.P., Baevskiy R.M. [et al.] Donozologicheskiy podkhod v otsenke zabolevaemosti i smernosti naseleniya [Donozologicheskimi approach in the evaluation of morbidity and mortality] Gigiena i sanitariya [Hygiene and Sanitation]. 2009, № 6, P. 77-80.
18. Zvezdina I.V., Zhigareva N.S., Agapova L.A. Funktsional'noe sostoyanie serdechno-sosudistoy sistemy detey v dinamike obucheniya v nachal'noy shkole [Functional state of the cardiovascular system in the dynamics of children in primary school] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 19-23.
19. Ivanova I.V., Chernaya N.L., Senyagina E.I. Sostoyanie zdorov'ya i sotsial'no-psikhologicheskie osobennosti uchashchikhsya shkol raznogo tipa [Health and socio-psychological characteristics of students at schools of different types] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2010, № 2, P. 53-55.
20. Koroleva N.V., Bugun O.V., Kolesnikov S.I. [et al.] Izmenenie sostoyaniya serdechno-sosudistoy sistemy v zavisimosti ot kharaktera funktsional'noy aktivnosti golovnogogo mozga u detey kak otrazhenie shkol'noy dizadaptatsii [Changing the state of the cardiovascular system, depending on the nature of the functional activity of the brain in children as a reflection of the school disadaptive] Pediatriya [Pediatrics]. 2011, Vol. 90, № 1, P. 121-125.
21. Rakhmanin Yu.A., Ushakov I.B., Sokolova N.V. [et al.] Kompleksnyy podkhod k gigienicheskoy otsenke kachestva zhizni uchashchikhsya [Integrated approach to the assessment of the sanitary quality of life for students] Gigiena i sanitariya [Hygiene and Sanitation]. 2010, № 2, P. 67-70.
22. Kuznetsova O.V., Son'kin V.D. Vegetativnyy tonus v zven'yakh respiratorno - gemodinamicheskoy sistemy u detey mladshego shkol'nogo vozrasta [Autonomic tone in respiratory links - hemodynamic system in children of primary school age] Fiziologiya cheloveka [Human Physiology]. 2009, Vol. 35, № 6, P. 94-102.
23. Kuindzhi N.N. Funktsional'naya gotovnost' rebenka k shkole: retrospektiva i aktual'nost' [Functional child's readiness for school: retrospective and relevance] Vestnik RAMN [Bulletin of the Academy of Medical Sciences]. 2009, № 5, P. 33-36.

24. Kuchma V.R., Skoblina N.A. Fizicheskoe razvitie mladshikh shkol'nikov i faktory, ego opredelyayushchie [Physical development of younger students and the factors determining his] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 14-19.
25. Machinskaya R.I., Sokolova L.S., Krupskaya E.V. Formirovanie funktsional'noy organizatsii kory bol'shikh polushariy v pokoe u detey mladshogo shkol'nogo vozrasta s razlichnoy stepen'yu zrelosti regul'yatornykh sistem mozga [Formation of the functional organization of the cerebral cortex alone in primary school children with varying degrees of maturity of the regulatory systems of the brain] Fiziologiya cheloveka [Human Physiology]. 2007, Vol. 33, № 2, P. 5-15.
26. Sukhareva L.M., Nadezhdin D.S., Kuzenkova L.M. [et al.] Osobennosti psikhicheskikh funktsiy u detey mladshogo shkol'nogo vozrasta s izmeneniyami psikhonevrologicheskogo statusa [Features of mental functions in school-age children with psycho-neurological status changes] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 28-34.
27. Zvezdina I.V., Sukhareva L.M., Zhigareva L.M. [et al.] Osobennosti formirovaniya zdorov'ya mladshikh shkol'nikov v dinamike obucheniya [Features of formation of health of younger students in the dynamics of training] Ros. pediatri. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 8-11.
28. Sharapov A.N., Bezobraznova V.N., Dogadkina S.B. [et al.] Osobennosti funktsional'nogo sostoyaniya miokarda i mozgovogo krovoobrashcheniya detey 7-10 let s raznymi variantami avtonomnoy nervnoy regul'yatsii serdechnogo ritma [Features of the functional state of the myocardium and cerebral circulation of children 7-10 years with different versions of the autonomic regulation of heart rate] Fiziologiya cheloveka [Human Physiology]. 2009, Vol. 35, № 6, P. 76-84.
29. Politika O.I. Deti s sindromom defitsita vnimaniya i giperaktivnost'yu [Children with attention deficit hyperactivity disorder and] S-Ptb. : Rech' [C-PTB. : Speech]. 2008, 208 p.
30. Polyashova N.V., Solov'ev A.G., Novikova I.A. Psikhofiziologicheskie osobennosti mladshikh shkol'nikov v dinamike obucheniya [Psychophysiological features of younger schoolboys in the dynamics of training] Byul. sib. Meditsiny [Bul. sib. Medicine]. 2010, № 1, P. 148-154.
31. Pokhachevskiy A.L. Izuchenie variabel'nosti ritma serdtsa pri nagruzochnom testirovanii [The study of heart rate variability during the exercise testing] Kardiologiya [Cardiology]. 2010, № 1, P. 29-35.



32. Stepanova M.I., Sazanyuk Z.I., Polenova M.A. [et al.] Profilaktika narusheniy zdorov'ya shkol'nikov v protsesse obucheniya [Prevention of health problems in students learning] Ros. pediater. Zhurn [Rus. pediatrician. journal.]. 2011, № 3, P. 46-49.
33. Sabir'yanov A.R., Sabir'yanova E.S. Vozrastnye osobennosti variabel'nosti pokazateley tsentral'nogo krovoobrashcheniya u detey mladshogo i srednego shkol'nogo vozrasta [Age features central circulatory variability indices in young children and secondary school age] Ros. pediater. Zhurn [Rus. pediatrician. journal.]. 2005, № 6, P. 4-7.
34. Mutalov A.G., Shiryaeva G.P., Vakhitova G.A. [et al.] Sostoyanie zdorov'ya i psikhofiziologicheskie osobennosti uchashchikhsya novykh vidov uchebnykh zavedeniy [Health and physiological characteristics of students new types of institutions] Vopr. sovremennoy pediatrii [Issues. modern pediatrics]. 2007, № 6, P. 122-126.
35. Koroleva N.V., Bugun O.V., Kolesnikov S.I. [et al.] Sostoyanie serdechno-sosudistoy sistemy u detey s razlichnym kharakterom funktsional'noy aktivnosti mozga v period obucheniya v nachal'noy shkole [The cardiovascular system in children with different nature of the functional activity of the brain during the period of primary school] Ros. pediater. Zhurnal [Rus. pediatrician. magazine]. 2010, № 2, P. 16-20.
36. Kuchma V.R., Stepanova M.I., Ulanova S.A. [et al.] Sokhranenie zdorov'ya shkol'nikov putem optimizatsii ikh obucheniya [Maintaining the health of schoolchildren by optimizing their learning] Ros. pediater. Zhurn [Rus. pediatrician. journal.]. 2011, № 3, P. 42-45.
37. Sukhareva L.M., Nadezhdin D.S., Kuzenkova L.M. Osobennosti psikhicheskikh funktsiy u detey mladshogo shkol'nogo vozrasta s izmeneniyami psikhonevrologicheskogo statusa [Features mental functions in school-age children with psycho-neurological status changes] Ros. pediater. Zhurn [Rus. pediatrician. journal.]. 2009, № 2, P. 28-34.
38. Tepper E.A., Grishkevich N.Yu. Vozrast rebenka i gotovnost' k nachalu sistematicheskogo shkol'nogo obucheniya [Child age and readiness to start a systematic schooling] Sib. med. Obozrenie [Sib. med. Review]. 2011, № 1, P. 12-16.
39. Tokar' O.V., Zimareva T.T., Lipay N.E. Psikhologo-pedagogicheskoe soprovozhdenie giperaktivnykh doshkol'nikov [Psychological and educational support hyperactive preschoolers]. M. : Flinta [M.: Flinta]. 2009, 152 p.
40. Fokina N.A., Pochivalov A.V., Ivannikov A.I. Rezul'taty otsenki sostoyaniya zdorov'ya mladshikh shkol'nikov obshcheobrazovatel'noy shkoly. Sistemnyy analiz i upravlenie v biomeditsinskikh sistemakh [The results of health assessment junior secondary school students. System analysis and control in biomedical systems]. Voronezh : Izd-vo Voronezh. gos. tekhn. un-ta [Voronezh : Univ. Voronezh. Reg. those. University Press]. 2009, Vol. 8, P. 913-917.

41. Age-related trends in Stroop and conflicting motor response task findings. Nichelli F., Scala G., Vago C. [et al.] *Child Neuropsychology*, 2005, Vol. 11, № 5, P. 431.
42. Activation and inhibition of bimanual movements in school-aged children. Barral J., De Pretto M., Debu B. [et al.] *Fiziologiya cheloveka*, 2010, Vol. 36, № 1, P. 56-66.
43. Assessment of Functional Capacity in Clinical and Research Settings: A Scientific Statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing. Balady J., Collins E., Fletcher G. [et al.] *Circulation*, 2007, Vol. 116, P. 329-343.
44. Braunwald's heart disease: a textbook of cardiovascular medicine. Libby P., Zipes D. P., Man D. L. [et al.] Town: Elsevier Sciences, 2008, 2304 p.
45. First Announcement 14-th Congress of European Union for School and Medicine 6-9 June 2007, Tampere, Finland, 2007.

The authors:

Potupchik Tat'yana Vital'evna, Candidate of Medical Science, senior teacher of the department of pharmacology with courses of clinical pharmacology, pharmaceutical technology and a course of postgraduate education, the State Budget Educational Institution of Higher Vocational Training "Krasnoyarsk State Medical University named after professor V.F. Vojno-Jasenetsky" of the Ministry of Public Health of the Russian Federation, 660022, Krasnoyarsk, Partizana Zheleznyaka 3r, mobile phone: 8-923-294-72-04, e-mail: potupchik_tatyana@mail.ru;

Evert Lidiya Semenovna, Doctor of Medical Science, head of the clinical department of cardiac arrhythmias and syncope, Federal State Budget Institution "Scientific research Institute of medical problems of the North", Siberian Branch of the Russian Academy of Medical Sciences, 660022, Krasnoyarsk, Partizana Zheleznyaka 3r, mobile phone: 8-950-436-6532, e-mail: lidiya_evert@mail.ru;

Zaytseva Ol'ga Isaevna, Doctor of Medical Science, head of the Laboratory of Clinical membranology and immunochemical studies, Federal State Budget Institution "Scientific research Institute of medical problems of the North", Siberian Branch of the Russian Academy of Medical Sciences, 660022, Krasnoyarsk, Partizana Zheleznyaka 3r, mobile phone: 8-913-561-2348; e-mail: 1081959@mail.ru;

Panicheva Elena Sergeevna, Candidate of Medical Science, the assistant clinical department of therapeutic stomatology, State Budget Educational Institution of the Higher Vocational Training "Krasnoyarsk State Medical University named after professor V.F. Vojno-Jasenetsky" of the Ministry of Public Health of the Russian Federation, 660022, Krasnoyarsk, Partizana Zheleznyaka 3r, mobile phone: 8913-590-0348, e-mail: lana_evert@mail.ru;

Miroshnichenko Elena Vital'evna, the post-graduate student of the department of pedagogical psychology, Federal State Budget Educational Institution of the Higher Vocational Training “Krasnoyarsk State Pedagogical University named after V.P. Astafyev”, 660049, Krasnoyarsk, Ada Lebedeva Str., mobile phone: 8-902-940-87-17; e-mail: miroadvokat@mail.ru.

The Study of Defects of Medical Documentation in Formulation and Confirmation of Diagnosis in Patients with Injuries of Ligaments

Lyadova M. V.

ABSTRACT

Any medical specialist in trauma, employed as a forensic medical expert, has to deal with crimes against life, health, freedom and dignity, responsibility for which is provided by the criminal code of Russian Federation. The most frequent kind of a forensic medical examination is an examination of victims to determine the severity of the injury. The examiner should assess the data from medical documents critically, as the duration of treatment of the victim may be caused not only by the nature of the injury, but also by the number of accompanying diseases. The analysis of the experts' reports in the amount of 237 examples which were submitted to the expert - traumatologist for the period from September till December 2013 at the Department of forensic medical examination of bodily injury of the Department examination of the victims, defendants and other persons of the state health budget Institution of Moscow Bureau of forensic medical examination of the Health Department of Moscow» was done. All these examinations were under the question about the diagnosis determined that required of the additional consultation of the trauma specialist to confirm or disprove the diagnosis in determining the extent of damage to health of a patient. As the analysis of the damage revealed, the most part (that is about 205 cases (86.3%)) was the damage of the ligaments of various localization. The detailed analysis of expertise of the damage of acrobaleno-clavicle joint, knee joint, and ankle joint was done. The main mistakes in the formulation of diagnosis were revealed, the ways of their elimination were defined, and the data in the literature with the description of the main characteristics of the diagnosis of the ligaments damage of the localizations specified were researched. The analysis of the defects in the medical records done by doctors-traumatologists in formulation and confirmation of diagnosis of patients with damaged ligaments acrobaleno-clavicle, knee and ankle joints for the determining of the severity of injury showed the following: there was no the one approach (algorithm) to the documentation of bodily injuries by the clinical doctors and no standards in their description and researching of capsular ligament joints. All this requires more closely interaction between forensic service and practical health care in the elaboration of appropriate standards for evaluation of patients with this pathology.

Keywords: medical examination, capsule ligaments, damage to health.

Any medical specialist in trauma, employed as a forensic medical expert, has to deal with crimes against life, health, freedom and dignity, responsibility for which is provided by the criminal code of Russian Federation. The most frequent kind of a forensic medical examination is an examination of victims to determine the severity of the injury. During the forensic medical examination of real patients about the severity of the bodily injuries, the expert-traumatologist is obliged to answer the following questions: what kind of injury; the duration of treatment is caused by this trauma or not?

But it is necessary to underline that the expert must assess the value of the datas from medical records critically, because of other factors (such as related diseases) can cause the duration of treatment except of the trauma itself. But on the other side, there are cases when the patient refuses to get a sick leave and wish to go to work ahead of treatment time. In any case it is important to assess the duration of disease and its severity on the base of real facts.

The analysis of the experts' reports in the amount of 237 examples which were submitted to the expert - traumatologist for the period from September till December 2013 at the Department of forensic medical examination of bodily injury of the Department examination of the victims, defendants and other persons of the state health budget Institution of Moscow Bureau of forensic medical examination of the Health Department of Moscow» was done. All these examinations were under the question about the diagnosis determined that required of the additional consultation of the trauma specialist to confirm or disprove the diagnosis in determining the extent of damage to health of a patient. As a result of the investigation of the injuries 'reasons, it was found the following: among all examinations under the research 151 cases were caused by traffic accident (among these ones 114 – as pedestrians, 37 – as drivers); 56 cases – criminal accidents; 30 – others (fallings, industrial accidents). The analysis of the injuries' types the most part of them (205 cases that is 86, 3 %) is the damages of ligaments in different places (table 1).

The expert evaluation showed the multiple defects in medical records and description of trauma. For example, in 138 cases there is no description of bodily damages (bruises, bruises, bruises, wounds). In 8 cases the diagnosis “trauma of acrobaleno-clavicle articulation” was not confirmed by facts. In two cases it was formulated as the partial injury without details (stretch, tear, partial break). As it is known, there are six types of damage of acrobaleno-clavicle articulation: 1) stretching; 2) breaking clavicle-acromial ligaments, but coracoid-clavicle ligaments are not damaged, there is a subluxation collarbone; 3) the gap clavicle-acromial and coracoid-clavicle ligaments, full dislocated collarbone; 4) complete dislocation with back offset through the trapezius muscle; 5) complete dislocation with increasing distance between the

coracoid process shoulders and collarbone in 2-3 times; 6) full bottom dislocated collarbone, under the acromion or under the coracoid process [7]. The diagnosis “breaking of clavicle-acromial ligaments” was defined in 6 cases (code MKB-10-S43.1), while there was no description of bodily damages in 4 cases. Although this kind of trauma occurs because of direct (hitting the shoulder area) and indirect (impact in the area of the elbow joint is shown hand) impacts. So, any kind of bodily damages may be in the localizations defined. As it was indicated in 6 cases, the symptom of «keys» was positive; in 2 cases this symptom was negative. Other symptoms, confirmed this diagnosis, are not described. Yes, it is true, that the symptom of “keys” for such type of damage is very typical. It lies in the fact that under pressure with a finger on, the distal end of the clavicle he shifted down, and at the termination of pressure returns to its former place. However, there is so called the test of the crossed hands», described G.P. Kotelnikov, when the patient is asked to relax the muscles of the shoulder girdle, and then to maximally bring arms, crossing them. This shovel is shifted to the middle line and the acromion pushes her up. This test is helpful when the symptom of “keys” is not clear [3]. From other examination methods only radiographs in standard anteroposterior projection were carried out in all cases. When describing roentgenograms in 4 cases specified at increasing the joint space ASC, which is highly dubious. So, according to various sources, the size acrobaleno-clavicle articulation is about 19 x 9 mm on average and the width of the joint space of 1 to 3 mm [5]. From the anatomy point there are three forms of joint with different angles of the joints surfaces. While in 21 % of cases articular surfaces of discongruity [9]. In radiography in anteroposterior projection it is difficult to see the bottom edge of the collarbone and acromion, so radiographs in this projection to diagnose injuries ACU are not informative. It is better to perform x-rays anteroposterior projection with tilt tube 10^0 - 15^0 up [8]. But the most informative are x-rays with the load when the patient takes in both hands some burden 3-5 kg and it is performed images ACU in direct projection on both sides. The increase of the distance between the lower edge of the collar bone and the top edge of the coracoid process before and after exercise to 25^0 - 30^0 compared with healthy hand indicates on the full gap of the clavicle-beaked ligaments [4].

In the analysis of expertise with injury of the ankle joint (30 cases) the diagnosis was confirmed in only 4 of them. The distribution of the diagnosis's in the medical records are the following: injury of the ankle joint (code MKB-10 S 90.0) - 7 out of 30 (23.6%), the sprained ankle (S 93.4) - 12 (40.0%), ligaments ankle (S 93.2) - 2 cases (6.6%), partial damage to the ligaments of the lower leg joint (cipher) - 2 cases (6.6%), damage to the ligaments of the ankle joint (cipher) - 2 (6.6%), distortion of ankle joint ligaments (cipher no) - 1 (3.3%), the outer ankle fracture (S82.6) - 3 cases (10.0%), post-traumatic arthritis (M 13.9) - 1 case (3.3%).

However, the description bodily injury in an ankle was absent in 18 cases (60.0%). In all cases radiography in standard front and rear projection was carried out. In neither case was not performed an ultrasound or MRI to confirm the diagnosis that would ensure the accuracy of diagnosis of injuries of the ankle joint ligaments according to the literature in 90 % of cases [6]. In 24 cases (80%) the diagnosis was defined on the fact of complaints of the patient on the pain without adequate medical and clinical evidences. The stability of the external part of the ankle joint is provided anterior talofibular ligament (ATFL), the length of which 12.0 cm in width 5.0 cm gap which occurs primarily when povertyline foot inside, because what is it to break occurs most frequently. Then the heel-peroneal ligament (CFL), which has great strength, comes. The most durable among the ligaments of the external part is back talofibular (PTFL) with a diameter of up to 9.0 mm at length to 9.0 mm. The gap of this link is due to exceeding the permissible load on the rotation and the varus deformity of the talus. This ligament may break or come off during involving a zone of rupture of the joint capsule [5].

The computed tomography (CT) was made in one case, which identified the outer ankle fracture that was qualified as a secondary harm. A heavy injury was defined in one case; the diagnosis was confirmed by x-ray and CT diagnostics: broken both ankles with damage tibiofibular of SYNDESMOS.

The diagnosis of damage of the ligaments of the knee joint occurs quite frequently (49 cases of 237 21.9%). Mainly 94% of patients were affected during a traffic accident: 85.7% - pedestrians, 8.3% - drivers and passengers; in 6% the damage to the ligaments of the knee joint was caused by criminal injury in accordance with medical documentation. On the diagnosis MKB -10 distributions was as follows (table 2). As the table shows, the diagnosis was confirmed only in 13 cases (25 %). The reasons are the following: in 21 cases there was no any expert-traumatologist's description of bodily damages. It must be underlined that MRI diagnostics for patients with the damage of knee ligaments was done more often (27 cases out of 52) than for patients with the damage of ligaments in other places. However, in the week after the injury study was conducted in 10 cases out of 27 (37.0%), in other cases - a month or more after injury. In 23 cases (44.2%) on medical documentation diagnosed with a bruised knee. But the examination of this diagnosis was only in 9 cases (39.1%): first, the presence of physical injuries in 9 cases (100%), clinically description of the symptom of «ballotation» patellar with subsequent arthrocentesis with obtaining blood - 7 cases (77.8%), MRI diagnostics - 5 cases (55.5%), ultrasound - 4 cases (44.4%). Of course, it is necessary to note the fact that diagnosis in acute period of injuries considerably is complicated because of the pain and associated hyper muscles with restriction of movement in the joint. According to literary data the correct

diagnosis is done in only 23.0% of cases [1]. While clarifying the circumstances of the injury is important. Thus, the gap internal lateral ligament happens when allocating shins with simultaneous external rotation, with severe (full rupture) additional blow to the outer surface of the lower third of the thigh or knee. During the inspection of the limb is the presence of bruising and excoriation. According to the literature the hemarthrosis in damaging of medial ligaments is found in 37% of cases. Moreover, according to some authors, the more volume hemarthrosis is than the damage heavier [2].

The deformation of the joint in the form valgus or varus deformity shows the complete rupture of the relevant collateral ligaments. This symptom is described in only 2 out of 9 cases (22.2%). In 17 cases gonarthrosis more than 2 degrees was diagnosed, which also caused the erroneous diagnosis of damage to ligaments, because it is accompanied by pain syndrome. However, the diagnosis of posttraumatic gonarthrosis installed on medical documents in 4 cases (7.8%) less than 3 months after injury, on the basis of x-ray performed within the first 24 hours after the injury, in General, is a gross mistake by trauma.

Thus the analysis of the revealed defects in medical records done by doctors-traumatologists in the formulation and confirmation of diagnosis for patients with damaged ligaments acrobaleo-clavicle, knee and ankle joints when determining the severity of injury showed the following: there is no one approach (algorithm) in description of bodily injuries by clinical doctors, no uniform standards of research of capsular ligament joints. All this requires more closely interaction between forensic service and practical health care in the elaboration of appropriate standards for evaluation of patients with this pathology.

Table 1.

The distribution of the patients with the injuries of ligaments by the localization of damages in accordance with the medical expertise records

The place of damage	Number of cases	The treatment period over 21 days	Without harm to health	Insignificant damage	Medieval damage	Hard harm	Difficult to estimate
Acrobaleno-clavicle articulation	8	8	8	0	0	0	0
Knee joint	52	46	37	9	3	1	2
Chest	9	6	7	2	0	0	0
Wounds of various localization	18	15	1	10	5	2	0
Muscles	8	8	4	1	3	0	0
The cervical spine	10	10	9	1	0	0	0
Lumbar spine	9	9	7	1	1	0	0
Hip joint	9	7	8	0	1	0	0
Coccyx	3	3	3	0	0	0	0
Shoulder joint	19	0	16	1	1	0	1
Ankle joint	30	28	24	2	1	1	2
Stop	13	12	9	3	1	0	0
Wrist joint, hand	9	7	7	0	2	0	0
Hematoma of various localization	26	20	4	19	3	0	0
Arthritis of various localization	11	11	11	0	0	0	0
Crash-syndrome	3	3	3	0	0	0	0
Total	237	199	158	49	21	4	5

Table 2.

The distribution of the patients with the injuries of ligaments of knee joint by the localization of damages in accordance with the medical expertise records

The diagnosis	Code MKB-10	The number of patients	Defined harm			Without harm
			Insign.	Med.	Hard	
Bruise, hemarthrosis of knee joint	S 80.0	9	5	0	0	4

Bruise of knee joint	S 80.0	14	4	0	0	10
Gap of internal literal ligament	S 83.4	9	0	2	0	7
Gap of knee joint's ligaments	M 23.8	3	0	0	0	3
Meniscus tear	S83.2	4	0	1	0	3
Gap of PKS	S83.5	4	0	0	0	3
Posttraumatic knee joint synovitis		2	0	0	0	0
post-traumatic arthrosis of the knee joint		2	0	0	0	2
Dislocation of the patella	S83.0	1	0	0	0	1
Stretching of the ligaments of knee joint		4	0	0	0	4
Injury of condilis lateralis	S82.1	1	0	0	1	0
Total		52	9	3	1	37

REFERENCES

1. Girshin S.G. Lazishvili G.D. Dubrov V.Je. Povrezhdenija i zabolevanija myshc, suhozhilij i svjazok (klinicheskij opyt i obzor literatury) [Injuries and diseases of the muscles, tendons and ligaments (clinical experience and literature review)] Moscow: IPK Dom knigi, 2013, 496 p.
2. Girshin S.G. Lazishvili G.D. Kolennyj sustav (povrezhdenija i bolevye sindromy) [The knee joint (damage and pain syndromes)] Moscow: NCSSH im. A.N.Bakuleva RAMN, 2007, 352 p.
3. Kotel'nikov G.P. Stukolov V.S., Tchernov A.P. Hirurgicheskoe lechenie akromial'nyh vyvihov kljuchicy [Surgical treatment of acromioclavicular dislocations] Mater mezhdunar. kongressa: «Travmatologija i ortopedija: svoevremennost' i budushhee» [Materials of International Congress: «Traumatology and orthopaedics: present and future»] Moscow, 2003, pp. 246-247.
4. Bearden J. Acromioclavicular dislocation: method of treatment/ J. Bearden, J.Hughson, Whatley W. J. //Sports Med. – 1973. - Vol 1. – P. 5-17.



5. Bosworth B.M. Complete acromioclavicular dislocation. / N. Engl. J. Med. - 1949.- Vol. 241. - P. 221-225.
6. Muchle C. Collateral ligaments of the ankle: high resolution MR imaging with a local gradient coil and anatomic correlation in cadavers Radiographics / C.Muchle, L.R. Frank, T. Rand, [et al.]. - 1999. - Vol. 19. -P.673-677.
7. Rockwood C. J. Disorders of the AC joint. The shoulder / C.J Rockwood., F Matsen, G.Williams, D. Young. / Vol.1. - Philadelphia W.B.
8. Vastamaki M. Pectoralis minor transfer in serratus anterior paralysis / M. Vastamaki //Acta. Orthop. Scand. 1984 Vol. 55. - P. 132-137.
9. Zanca P. Shoulder pain: involvement of the AC joint: an analysis of 1000 cases AJR / P.Zanca, J. Roentgenol. – 1971. - Vol. 112, P 493-506.

The author:

Lyadova Maria Vasilievna, Candidate of Medical Sciences, doctor traumatologist-orthopedist of the medical ambulance, the state hospital No 1 named after Pirogov N.I., assistant of the traumatological and orthopedically surgery's Department of Russian Medical University named after Pirogov N.I (the chief of the Department – MD, Prof. Skorogliadov A.V., 117 049, Moscow, Leninskiy Prospect, 10, phone: 8 (903) 722-11-67, e-mail: mariadoc1@mail.ru.

Features of Rehabilitation in Pediatric Tuberculosis Sanatorium in the North

Starostin V.P., Nezgovorova A.M., Pestereva M.I.

The article is devoted to rehabilitation features in the children's sanatorium in the Far North conditions.

Since the opening of the national children's sanatorium great importance was attached to physical methods of treatment that enhances the immune status of the child's body: physiotherapy, physical exercises therapy, massage, herbal medicine and clinical nutrition management.

Years of experience of sanatorium functioning in various regions of Russia has shown that with proper organization treatment of tuberculosis patients in local health centers is effective in all climate zones. Tuberculosis is one of those diseases for which the course is associated with meteorological conditions. Natural conditions, especially the weather, influence through the nervous system reactivity and compensatory adaptability of the patient.

Treatment measures in the Far North are complicated by local sharply continental climate, prolonged for five or six months in the winter with very low temperatures.

The main directions of our sanatorium rehabilitation work are rational clinical nutrition, physical therapy, physiotherapy, massage, herbal medicine. Chemotherapy is the antibacterial treatment aimed at reducing the virulence of microorganisms and at the same time reducing the body's defenses. Rational clinical nutrition takes into account changes in metabolism, coming under the influence of the pathological process and under the influence of drugs. The success of treatment depends on the properly selected set of non-drug chemotherapy and means to enhance the body's resistance.

CONCLUSIONS:

1. Complex use of physical therapy, exercise therapy, massage, and herbal medicine is an important part of the restoration of the physical, mental, immune status of children, along with a specific treatment.
2. In the rehabilitation of children in tuberculosis sanatorium in the Far North is necessary to create the optimal motor mode, taking into account the duration of induced physical inactivity in the winter, with better food.
3. Summer time should be used as efficiently as possible; planning practically on days summer healthcare company.



4. Methods of Nordic walking has been successfully tested in many countries, can be used in children's sanatorium, because it is simple and effective means for the recovery of the respiratory, musculoskeletal and cardiovascular systems.

5. Taking into account local climatic conditions it is necessary to develop specific standards of rehabilitation of children in tuberculosis sanatoriums in the Far North.

The authors:

Starostin V. P., chief physician of the sanatorium, Honored Doctor of Sakha (Yakutia) Republic, Excellent Health worker of the Russian Federation and the Republic Sakha (Yakutia);

Nezgovorova A.M., physiotherapist, head of the department of rehabilitation, Excellent Health worker of the Russian Federation;

Pestereva M.I., doctor of physiotherapy.

Items of Optimizing the Structure of the Population Nutrition and Improving the Quality and Safety of Food Production in the Republic Sakha (Yakutia)

U.M. Lebedeva, A.N. Rumyantseva, K.M. Stepanov, M.E. Ignatieva, I.Y. Egorov, M.V. Kornilova, N.B. Borisova

ABSTRACT

The article presents the results of long-term monitoring studies on dietary nutrition and dietary habits of different population groups and the analysis of the control of the conformity of the quality and safety of food products, according to the legislation of the Russian Federation, the legislation of the Customs Union and the standardized methods used in population-based epidemiological studies. The authors justify necessity of optimizing the structure of the population nutrition and improving the quality of food and the level of its security. They consider the complex of the factors influencing the increasing interest of the food industry to ensure the safety of their products.

Objective: a comprehensive assessment of actual nutrition and dietary habits, as well as the analysis of the quality and safety of primary and food products in the Republic Sakha (Yakutia).

Research Materials. Actual nutrition of the population of the Republic was estimated based on study data obtained from random stratified by sex and age samples of the population aged 25-64 years (560 people). Frequency method and the daily, memory recalling, method («24 h-recall») were used. Statistical processing and analysis were performed using the statistical program SPSS.

Research results. According to the results of scientific research Nutrition Center Health Research Institute NEFU named after M.K. Ammosov actual nutrition of the population in dynamics over the last ten years can be described as unsatisfactory.

Conclusion. The energy value of the ration for a 10-year period decreased by 2012 on 11% and amounted to an average 1885.7 kcal. The greatest reduction in caloric occurred in an industrial area (1.797 kcal), the lowest - in the Arctic (2020 kcal). The average daily intake of protein, fats and carbohydrates for a 10-year period did not change significantly, remaining well below the recommended physiological norms. A significant deficit in potassium, magnesium, calcium, iron, vitamins B1, B2, C, PP, retinol remains.

Keywords: monitoring, diet and consumption of food caloric value, the quality of food products and food safety, sanitary-chemical, microbiological, parasitological, radiological indicators.

INTRODUCTION

Rational healthy nutrition is one of the main factors that determine the health of the nation, ensuring normal growth and development of children, life extension, and disease prevention.

It is very important to know, why the foods we decide to eat today affect our health not just today, but many years later in our lives.

Priority issues of nutrition science in Russia today become assessment of nutrition and nutritional status of children and adults; its impact on health, the rationalization of nutrition. The results of large-scale epidemiological studies have established the most important violations of status: the excessive consumption of animal fats and the lack of polyunsaturated fatty acids, high-grade (animal) protein, most of vitamins, minerals (calcium, iron), trace elements (iodine, fluorine, selenium, zinc) and dietary fibers [1, 4].

The Russian Federation has adopted a number of basic legal acts aimed at ensuring the country's system of healthy eating, including: the laws "On sanitary and epidemiological welfare of population", "On Consumer Rights Protection", "On the quality and food safety", "On basis of health protection of the Russian Federation". Presidential Decree from November 17, 2008 № 1662-r approved the Concept of Long-Term Socio-Economic Development of the Russian Federation for the period up to 2020, one of the ways to implement the task of improving the health care system is the creation of a culture of healthy eating. Legislation acts are supported by a number of regulations of the Government of the Russian Federation, such as the Food Security Doctrine of the Russian Federation, the State Policy of the Russian Federation in the field of healthy nutrition for the period up to 2020 and plans to implement them.

National legislation is improved in terms of harmonization with international documents in the field of healthy nutrition, such as the WHO Global Strategy for Food Safety, "Global Strategy on Diet, Physical Activity and Health", set of recommendations on the marketing of foods and non-alcoholic beverages for children, European strategy for the Prevention and Control of Noncommunicable Diseases and others.

Within the framework of the WTO accession Russian Federation accepted an obligation that all sanitary measures will be developed in the Russian Federation, and the competent authorities of the Customs Union, in accordance with the WTO Agreement and, in particular, the Agreement on Sanitary and Phytosanitary Measures. Particular importance in connection with Russia's WTO accession is given to rapprochement of Russia and the Customs Union with foreign requirements under the Codex Alimentarius [2].

Objective: a comprehensive assessment of actual nutrition and dietary habits, as well as the analysis of the quality and safety of primary and food products in the Republic Sakha (Yakutia).

STUDY MATERIALS

Actual nutrition of the population of the Republic was estimated based on study data obtained from random stratified by sex and age samples of the population aged 25-64 years (560 people). Frequency method and the daily, memory recalling, method («24 h-recall») were used. Statistical processing and analysis were performed using the statistical program SPSS.

Sectoral annual reporting statistical form №18 «Information on the health status of a subject of the Russian Federation" for 2007-2013, Statistical compilation "Socio-economic status of the RS (Y)" for 2000-2011, Government reports 2007-2013.

STUDY RESULTS

According to the results of scientific research Nutrition Center Health Research Institute NEFU named after M.K. Ammosov actual nutrition of the population in dynamics over the last ten years can be described as unsatisfactory. Regardless of the various population groups inadequate intake of foods containing animal protein and excessive consumption of sugar-containing products were identified. We determined a low energy value of diets in comparison with physiological norms, defined increased carbohydrates contribution in dietary energy. We also revealed a low provision of rations by almost all studied vitamins and minerals, almost 100% lack of some micronutrients was observed.

11 groups of products, according to the questionnaire on the frequency of consumption of certain foods, were under study [3, 4].

Among the products consumed daily or 3-6 times a week, sausages were 61%, meat – 71, milk – 32, fish - 37, potatoes - 38, other vegetables – 34, fruits - 14, cereals and pasta - 43, bread and bakery products - 94, sweets - 19%.

In studying the rations there were differences in the daily caloric capacity among the respondents according to gender and ethnicity. Daily energy intake for men was 2308, women - 1801.3 kcal ($p < 0.05$). Caloric value of the indigenous population ration was significantly higher than that of non-indigenous (1787.1 and 2129.2 kcal, respectively, $p < 0.05$).

The highest caloric diet was observed in the Arctic and industrial districts, low – in the agricultural ones. It should be noted that the energy intake of the inhabitants of the republic is below the recommended standards (2500 kcal).

According to the norms of physiological needs nutrients and energy for different groups of the population of Russia (Ministry of Health, Moscow, 2008) for the northern regions are established energy needs of the population up to 10-15%, as compared to other climatic zones. In this case, we recommend the following ratios of the nutrients on calorie: protein - 15%, fat - 35 and carbohydrates - 50%.

On average, the share of the Republic of proteins and fats in the diet is less than the recommended standards, and the proportion of carbohydrates in all districts exceeds the required 50%, especially in the agricultural (up 65.1%), the republic's population consumes on average 64 grams of protein per day (75 g in the norm), which is below the recommended values by 16%.

On average population of the country consumes 72 g fat (83 g in the norm). In the industrial, Arctic and agricultural districts fat intake was 312, 345, 339 g day, respectively, while the contribution of fat in the dietary energy in these areas exceeds the recommended 50% and compounds 58; 61.5; 58%, respectively.

It is revealed that on average the population consumes 113.5 grams of meat and meat products per day; the annual consumption on an average is 41.4 kg. The recommended rate per capita in Russia is 83 kg / year. Thus, the consumption of meat and meat products of the country's population is twice lower the recommended standards.

Consumption of fish and fish products in the country is substantially lower (3-fold) of the existing norms of consumption (8.6 kg / year, compared with 23.7 kg / year). For the consumption of vegetable oil figures for the whole country is closer to the norm, but there are districts where consumption is 23 g / day versus the recommended 37.3 g / day.

According to the norms of good nutrition in the average adult needs to consume 404 kg / year of dairy products (milk equivalent). Population on average consumes 297.7 g / day, i.e. 108.7 kg / year per capita, which is almost 4 times lower than the recommended norm. In this case there are districts, where the difference is 6 or more times.

For the consumption of bread and bakery position is just the opposite, there are areas where the population consumes 453 grams per day versus 239 g recommended. It is clear that the population makes up for the lack of the main products at the expense of grain products (pasta, cereals, bread).

For the consumption of potatoes indicators for all districts is below the norm in 3 or more times.

Studying the dynamics of consumption of micronutrients and vitamins showed that the consumption of iron in all the districts is scarce, in total in the Republic 11.8 to 14 mg per day. For calcium in all districts consumption is also significantly lower than normal (1.200 mg), in some areas in 2 or more times. Phosphorus consumption on average in the Republic amounted to 893.9 mg per day (in the norm 1000 mg), the content of potassium - 2039.3 mg versus 3.500 mg (the norm). Magnesium intake was also below the recommended numbers (220.5 vs. 400 mg per day).

For the consumption of vitamins it is also noted a significant deficit in all major types, so the deficit on vitamin C is more than 50%.

For vitamins B1, B2, PP and retinol a significant deficit (40-50% of the recommended norm) is also noted [3, 4].

Rospotrebnadzor of the Republic Sakha (Yakutia) conducted monitoring of the nutritional status of the population, control of the conformity of the quality and food safety requirements of the legislation of the Russian Federation, the legislation of the Customs Union [2].

Proportion of samples of food raw materials and food products that do not meet hygienic standards for the analyzed indicators, in total for the whole country exceeds the national average 2.3 times, accounting for 11.5% (Russia - 4.8%), in the dynamics of 7 years reduction of proportion of non-standard samples on sanitary and chemical indices in 9 times, microbiological - at 10.8%. Increase in the proportion of food samples that do not meet the requirements for parasitological indicators (6.2%) is marked. It should be noted that in 2013 the number of samples for chemical indicators, as well as the number of non-standard, does not include research on the physical, chemical and organoleptic characteristics (Table. 1).

Over the period 2007-2013 excess of permissible levels of radioactive substances was not found, in the whole for 7 years 2447 samples were studied (2013- 454, 2012- 378, 2011- 276, 2010- 394, 2009-310, 2008 - 279, 2007-356) [2].

In 2013, there has been a significant improvement in the quality of the investigated food and food raw materials for chemical indicators compared to 2007 in all categories, exceeding the hygienic standards was met for index "nitrate" in the following product groups: "potato", "fruit and berries "(Table 2).

In order to oversee the biosafety of food raw materials and food products for microbiological indicators for the period 2007-2013 174731 samples were investigated; annually more than 20 thousand samples were investigated. In 2013 21.60 samples were studied, the proportion of samples that do not meet the hygiene requirements was 11.5%, compared with the 2007 figure was reduced by 1.4% (2012 - 11.8%; 2011- 12. 9, 2010- 12.1, 2009-13.0, 2008-12.2, 2007 - 12.9%). The share of imported products that do not meet the requirements of hygienic standards, for 7 years is leveled from 6 to 1.4% (4.2 times).

A high percentage of non-standard samples are occurring in milk, dairy products, " meat and meat products», «bird and poultry products", "fish and non-fish species and products produced from them", "culinary", "bakery", "pastry", "flour, cereal products", "fruit and vegetables", "vegetables, dining greens ", "alcoholic beverages and beer", "mineral water", "food supplements."

It should be noted that the proportion of samples that do not meet the requirements of hygienic standards for a product group "meat and meat products" decreased by 1.5 times, "poultry and poultry products", "fish and non-fish species and the products produced from them" - 1.3 times [2].

In 2013, the number of samples tested for parasitological indices exceeds the number of samples in 2007 to 41.8% (in 2013 – 770, in 2007-543). According to studies, the proportion of samples that do not meet hygienic standards at the level of 2007: in 2013 - 1.7, in 2012 - 1.8, in 2011- 2.5, 2010- 2.3, 2009-1.4, 2008 -0.7, 2007 - 1.6%. In 2013 13 non-standard samples were found, including the following product groups: "meat and meat products" - 1 sample (1.4%), "fish and non-fish species and the products produced from them" - 3 (1.2 %), "fruit and vegetables" - 6 (1.8%), "fruit, berries" - 2 samples (2.9%).

Control over the safety of food raw materials and food products from genetically modified sources is carried out within the framework of the implementation of the Resolution of the Chief State Sanitary Doctor of the Russian Federation from December 31, 2004 N 13 "On strengthening the supervision of foods derived from genetically modified ingredients."

Since 2008, on the basis of the virology laboratory FBUZ "Center for Hygiene and Epidemiology in the Republic Sakha (Yakutia)" research on the identification of genetically modified sources have been conducted. In 2013 77 samples of meat, dairy, fruit and vegetable products, canned food, cereals were studied, the content of genetically modified sources above the permissible requirements have not been identified (in 2012 - 80 samples, in 2011 - 133 samples), the presence of GMOs in the period 2008 -2013 years was not established [2].

In 2013, on the results of surveillance activities of the Rospotrebnadzor Dpt. of the Republic Sakha (Yakutia) 911 batches of food raw materials and food of 16.648.93 kg were rejected and disposed, which exceeded almost 2 times the number of rejected batches in 2012 (in 2008 in the Republic 531 batches were rejected, with a total weight of 15.380 kg).

All in all, for the period 2008-2013 3646 batches of food were withdrawn from circulation, totally more than 100 tons (100.032.968 kg), the major parties in the categories of "meat and meat products", "poultry and poultry products", "milk and milk products", "fish and fish products" "bakery and confectionery", "soft drinks", "alcohol", "canned", "baby food."

CONCLUSION

The energy value of the diet for a 10-year period decreased to 2012 by 11% and amounted to an average of 1885.7 kcal. The greatest reduction in caloric occurred in an industrial area (1797 kcal), the lowest - in the Arctic (2020 kcal). The average daily intake of protein, fats and carbohydrates for a 10-year period did not change significantly, remaining well below the



recommended physiological norms. A significant deficit in potassium, magnesium, calcium, iron, vitamins B1, B2, C, PP, retinol remains.

According to the Rospotrebnadzor Dpt. Republic Sakha (Yakutia) it was revealed that the proportion of samples of food raw materials and food products that do not meet hygienic standards for the analyzed indicators on the whole in the Republic exceeded the national average 2.3 times, accounting 11.5% (RF - 4.8%). In the dynamics of 7 years decline in the share of non-standard samples on sanitary and chemical (9 times), microbiological (10.8%) indicators was demonstrated. Increase in the proportion of food samples that do not meet the requirements for parasitological indicators (6.2%) was marked.

Table 1

**Indicators of samples of food raw materials and food products, do not comply with
sanitary and epidemiological requirements**

Indicators	2007		2008		2009		2010	
	samples	proportion, %	samples	proportion, %	samples	proportion, %	samples	proportion, %
Sanitary-chemical	1567	5.5	839	4.1	761	5.1	758	4.8
Parasitological	9	1.6	2	0.7	5	1.4	7	2.3
Microbiological	4884	12.9	3564	12.2	2701	13.0	2721	12.1
Indicators	2011		2012		2013		Growth rate in 2013 (to 2007), %	
	samples	proportion, %	samples	proportion, %	samples	proportion, %		
							In number	In proportion
Sanitary-chemical	783	5.5	551	3.9	9	0.6	-99.4	-89
Parasitological	10	2.5	12	1.8	13	1.7	+44.4	+6.25
Microbiological	2677	12.9	2766	11.8	2434	11.5	-50.1	-10.8

Table 2

**Proportion of samples of food raw materials and food products that do not meet
hygienic standards for sanitary-chemical indicators**

Food raw materials and food products	The proportion of food samples that do not meet the requirements of hygienic standards						
	2007	2008	2009	2010	2011	2012	2013
Total	5,4	4,1	5,1	4,8	5,5	3,9	0,6
imported	5,1	1,2	2,7	3,5	1,4	4,9	0
Vegetables, greens dining / fruits and vegetables	1,7	0	0	1,4	3,3	2,4	0,8
imported	0,5	0		1,3	0	2,7	0
imported	0	0		1,4	1,8	5	2,3
imported	0	0		0	0	0	0
Fruits and berries	4,0	1	1,7	3,3	4,3	0	2,5
imported	4,0	0	0,6	0	7,1	0	0

References

1. Egorov I.Ja., Protod'jakonov A.P., Chernjavskij V.F. [et al.] Bezopasnost', jetnotradicionnye podhody i sovremennaja nauchnaja obosnovannost' korrekcii pitaniya severjan [Safety, ethnotraditional approaches and modern scientific validity of correction of food of northerners] Aktual'nye problemy reproduktivnogo zdorov'ja v uslovijah antropogennogo zagrjaznenija: Mat.mezhd.simp. [Actual problems of reproductive health in the conditions of anthropogenous pollution: Proc. Int.Simp.]. Kazan', 2001, P. 148-149.

2. Gosudarstvennye doklady «O sanitarno-jepidemiologicheskoj obstanovke v Respublike Saha (Jakutija) »za 2007-2013 gg. [The state reports "About a sanitary and epidemiologic situation in the Republic of Sakha (Yakutia)" for 2007-2013].

3. Lebedeva U.M., Dohunaeva A.M., Zaharova L.S., Stepanov K.M. Jepidemiologicheskaja ocenka fakticheskogo pitaniya i pishhevyh privyчек sredi razlichnyh grupp naselenija Respubliki Saha (Jakutija) [Epidemiological assessment of the actual food and food habits among various groups of the population of the Republic of Sakha (Yakutia)] Pitanie i zdorov'e: sb. statej Mezhdunarodnogo kongressa; Mezhdunarodnoj konferencii detskih dietologov i gastrojenterologov [Food and health: coll. of articles of the International congress; The International conference of children's nutritionists and gastroenterologists]. Moscow: Izdat. dom Dinastija, 2013, 124 p. <http://www.congress-pitanie.ru/Tezis2013.pdf>

4. Lebedeva U.M., Stepanov K.M., Samsonova M.I. [et al.] Nauchno-metodicheskoe i innovacionnoe obespechenie optimizacii pitaniya naselenija Respubliki Saha (Jakutija) [Scientific and methodical and innovative ensuring optimization of food of the population of the Republic of Sakha (Yakutia)]. Voprosy pitaniya, 2014, № 3, P. 25-27.

Authors:

Lebedeva Uliana M. - MD, PhD, Head of the Center for therapeutic and preventive nutrition Health Research Institute NEFU named after M.K. Ammosov, Ch. out of staff nutritionist MOH Republic Sakha (Yakutia), a member of the Scientific Board of Medical Nutrition RAMS, ulev@bk.ru; Yakutsk, Russia;

Office of the Federal Service for Supervision of Consumer Rights Protection and Human Welfare in the Sakha Republic (Yakutia):

Rumyantseva Anna N. - Ch. Specialist-Expert, yakutia@14.rospotrebnadzor.ru; Ignatieva Margarita E. - Head, Kornilova Margarita V. - Head of Department, yakutia@14.rospotrebnadzor.ru; Borisova Natalia B. - deputy Head of Department; Yakutsk, Russia;

Stepanov Konstantin M. – PhD (agriculture). Senior researcher Research Institute of Health NEFU named after M.K. Ammosov, stenko07@mail.ru; Egorov Ivan Ya. - deputy Ch.

doctor FGUZ Center for Hygiene and Epidemiology in the Republic Sakha (Yakutia), Chairman of the Commission on Health of the Public Chamber of Sakha (Yakutia) and the Public Council under the Ministry of Health of the RS (Y), yakutia@14.rospotrebnadzor.ru, Yakutsk, Russia.

Differential diagnostic criteria of normal and abnormal as a result of tuberculous process intrathoracic lymph nodes

L.P. Shepeleva

ABSTRACT

Comparative analysis of radiological patterns of normal and abnormal, as a result of tuberculous process, intrathoracic lymph nodes using the approach of computer tomography showed criteria used to diagnose primary tuberculosis in children and adolescent: quantity, groups and sizes of visualized intrathoracic lymph nodes. The results of study of tuberculous changes in lymph nodes due to age parameters are provided.

Keywords: computed tomography, intrathoracic lymph nodes, tuberculosis of intrathoracic lymph nodes, children and adolescents.

Nowadays, one of the main problems of phtisiopediatry is lack of consensus on CT visualization of normal lymph nodes and the criteria of norm that would help to determine pathological changes in the nodes. Some authors believe that in connection with incorrect interpretation of enlarged lymph nodes computed tomography (CT) often aids the hyper diagnosis of tuberculosis (Y.V. Mikhailova, I.M. Son, E.I. Skachkova, S.N. Sterlikov, 2009) [8]. Level of hyper diagnosis of child tuberculosis, in some cases, can reach 70% (F.E. Gegeyeva, 2006) [3]. When diagnosing primary tuberculosis in children subjective criteria are frequently implemented. For example, when CT scanning of a child infected with tuberculous microbacteria (TMB) shows intrapulmonar nodes it is considered to be an evidence of local form, regardless of their size or age of the child. Although it is known that use of CT helps to visualize minimal intrathoracic lymph nodes (IPLN), both connected with tuberculosis and not. Both Russian and foreign authors have not come to one conclusion on this matter. According to Y.V. Lazareva (2002), intrathoracic lymphadenopathy in tuberculosis can be divided into: severe lymphadenopathy with lymph nodes size over 10mm or mass of nodes; minor adenopathy with lymph node size ranging 5-10mm; micro adenopathy with lymph node size less than 5mm [6].

B.I. Ishenko (2001) and A.A. Starshinova (2013) take 0.5cm as a relative value unit for lymph nodes [4,11]. Authors Y.V. Vaganov, L.G. Zemko (2002) consider mediastinal lymph nodes to be pathologically changed if they are over 8mm or smaller but in groups [2]. H. Geldmacher, C. Taube (2002) recommend to view all the detected lymph nodes over 1cm as [querulous](#) [13]. Y.V. Matushkina (2008), W.H. Boom (1996), N.W. Schluger (1998), R.F. Yen (2008) do not exclude the possibility of tuberculous lesion in non-enlarged lymph nodes not detected by CT [7,12,14,15].

The problem of determining the age morphology of lymphatic system still carries important theoretical and practical meaning. The research on this matter has been conducted by L.I.Rassokhina-Volkova (1958-64), G.T.Krasovskiy (1963), I.P. Parfenova (1960) et al [10,5,9]. They have determined that lobed nodes appear significantly more often during childhood, they are also more florid. Slightly more of them occur in fetuses and infants. Most nodes of larger size appear in children of 2-11 years of age. With aging, the quantity and size of lymph nodes lessen, and each of remaining nodes has larger territory of flow. According to A.A. Akhmedzyanov (1976), people of mature age the capsule of lymph nodes is more closely attached to surrounding tissue [1]. Thus, currently there is still no consensus on the "norm" and "pathology" on size criterion of the lymph node.

Goal of research. To study criteria of differential diagnostics of normal (non-changed with pathological process) and tuberculosis affected intrathoracic lymph nodes using computed tomography.

MATERIALS AND METHODS OF RESEARCH

In order to differentiate abnormal due to tuberculous process lymph nodes from normal lymph nodes, two study groups were created:

Group 1 - 99 children with tuberculosis of intrathoracic lymph nodes (TITLN) in active phase of tuberculous process;

Group 2 (control group) - 105 healthy children and adolescent, non-infected with micro bacteria of tuberculosis.

All children from Group 1 were infected with tuberculous micro bacteria: 10 children (10.1%) had weakly positive (5-9mm) TB skin test with 2TU, 28 (28.3%) showed reaction of mild intensity (10-14mm), 21 (21.2%) - intensified, and 40 (40.4%) showed hyperergic results. From this group only 34 children received DST, 10 children had doubtful and negative results (29.4), one had mild reaction (2.9%), 5 children (14.7%) had severe reaction, 18 (53.0%) were hyperergic. In total 70 (70.75) children had contact with tuberculous patient.

All children from Group 2 also underwent TB skin test with 2TU. All 105 children had tuberculin-negative results from the day of birth up to the moment of CT scanning. 68 children (64.8%) underwent DST: results were also negative. 45 (42.9%) of children from this group frequently had catarrhal diseases of lungs: ARVI, catarrhal tonsillitis, acute bronchitis and pneumonia. On the moment of CT scanning there is no cases of acute or acute exacerbation of chronic inflammatory disease, all children were practically healthy.

All children were scanned with Siemens Somatom Emotion Duo CT scanner, with a slice of 3mm for children and 5mm for adolescent, and intervals of slices 2.5mm.

RESULTS

Given groups were comparatively evaluated on the localization, quantity and size of the intrathoracic lymph nodes.

Research showed that children with tuberculosis of intrathoracic lymph nodes (Group 1) had lesions of 1-6 anatomical groups of lymph nodes and more. Among 99 children with active form of tuberculosis of intrathoracic lymph nodes 40 (40.3%) had lesions of 1-2 groups of lymph nodes, i.e. there was occurrence of minor forms of tuberculosis of ITLN (fig.1).

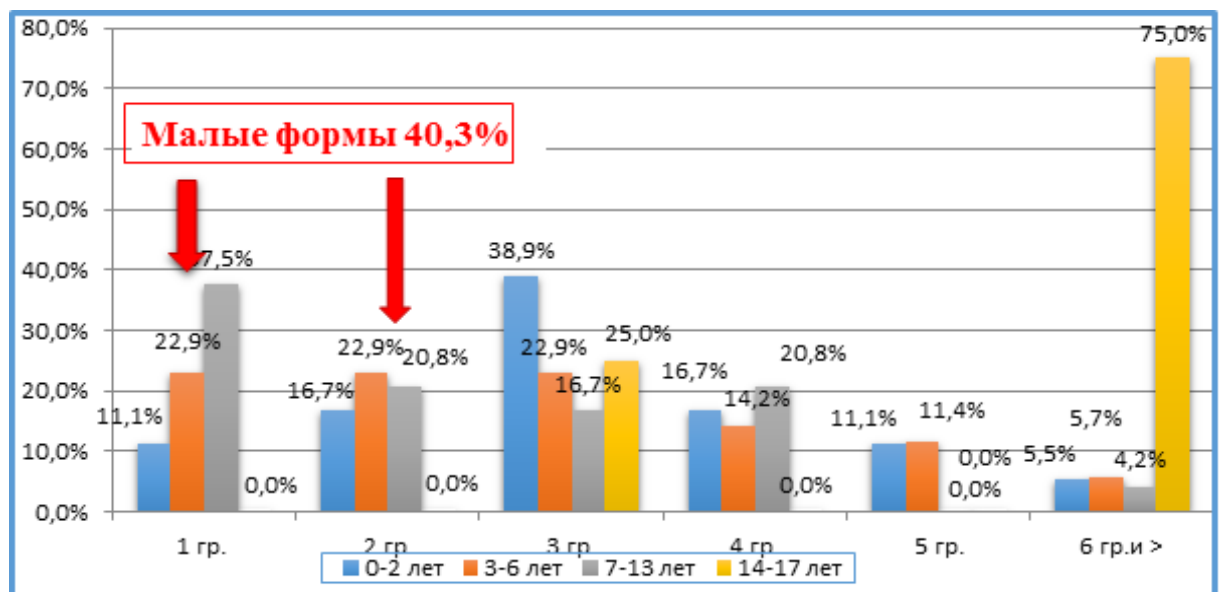


Figure 1. Prevalence rate of lesions of intrathoracic lymph nodes during TITLN.

In addition to the above, it was determined that prevalence of tuberculous lesion with a range of many groups of lymph nodes depends on age peculiarities (table 1).

Table 1

Distribution of quantities of lymph nodes during TITLN depending on age of patients

Quantity of lymph node groups	0-2 y.o.(n=36)		3-6 y.o. (n=35)		7-13 y.o. (n=24)		14-17 y.o. (n=4)		Total	
	bs.	%	bs.	%	bs.	%	bs.	%	bs.	%
0	-	-	-	-	-	-	-	-	-	-
1	4	11,1	8	22,9	9	37,5	-	-	2	2,2
2	6	16,7	8	22,9	5	20,8	-	-	1	1,1
3	14*	38,9	8**	22,9	4***	16,7	1****	25	7	7,3
4	6*	16,7	5**	14,2	5***	20,8	-	-	1	1,1
5	4*	11,1	4**	11,4	-	-	-	-	8	8,8
6	2*	5,5	2**	5,7	1***	4,2	3****	7,5	8	8,8
Total	36	100	35	100	24	100	4	100	9	100

Note: lesion of 3 and more lymph node groups": * and *** p=0,036, ** and **** p=0,022, *** and **** p=0,007.

lesion up to 2 lymph node groups: * and *** p=0,008, **** and ** p=0,022, **** and *** p=0,007.

Involvement in the specific tuberculous process of 3 and more groups of lymph nodes with their increased enlargement was more frequently indicated in young children (26 children among 36, 72.2%). Children of older age (pres-school and school age) showed lesion of up to 2 groups of lymph nodes (16 children among 35 - 45.8% and 14 of 24 children - 58.3% accordingly), i.e. more frequently there was indicated a minor form of bronchadenitis (45.8% and 27.8%, p=0,008; 45,8% и 58,3%, p = 0,000; 58,3% и 45,8%, p=0,05; 58,3% и 0%, p=0,022; 27,8% и 0%,

$p=0,007$). 100% of adolescents showed wide-spread primary tuberculous process with lesion of 3-6 and more groups of lymph nodes.

Most frequently tuberculosis affected bronchopulmonary (23.2% and 22.2%), bifurcational (14.7%) and retrocaval (14.7%) groups of lymph nodes (table 2).

Table2

Groups of affected lymph nodes during tuberculosis of intrathoracic lymph nodes in different age groups of children and adolescents

Groups of lymph nodes	0-2 y.o.		3-6 y.o.		7-13 y.o.		14-17 y.o.		Total	
	Aбс	%	Aбс	%	Aбс	%	Aбс	%	Aбс.	%
Bronchopulmonaryright	28	26,7	24	24,0	13	18,3	3	17,6	68*	23,2
Bronchopulmonary left	24	22,9	24	24,0	14	19,7	3	17,6	65*	22,2
Bifucational	17	16,2	11	11,0	13	18,3	2	11,8	43*	14,7
Retrocaval	15	14,3	14	14,0	10	14,1	4	23,6	43	14,7
Paravasal	6	5,7	13	13,0	6	8,4	3	17,6	28	9,6
Paratracheal	7	6,7	7	7,0	4	5,7	1	5,9	19	6,5
Para-aortic	5	4,7	3	3,0	5	7,1	1	5,9	14	4,8
Subcarinal.	2	1,9	3	3,0	3	4,2	-	-	8	2,7
Aortic window	-	-	-	-	3	4,2	-	-	3**	1,0
Perioesophageal	1	0,9	1	1,0	-	-	-	-	2**	0,6
Total:	105	100	100	100	71	100	17	100	293	100

Note: in comparison * and ** $p<0,01$

Enlargement of lymph nodes rarely was seen in perioesophageal group (0.6%) and aortal window (1.0%).

In current conditions infiltrative bronchadenitis was detected in majority of cases (79.7%) and tumor-like was seen less frequently (20.3%, $p=0.000$). Enlargement of lymph nodes of the hilu, led to its widening. The hilum's structure was disrupted, its contours became uneven, wavy, and there was indication of intensification and deformation of periapical picture due to thickening of interlobular interstitium in adjacent lung tissue.

In TITLN sizes of visible nodes varied from 0.5 to 1.6cm and more ($M\pm m = 0,93\pm 0,24$). The analysis of correlation between size of tuberculous lymph nodes and age of the patient

showed lack of statistically significant differences of average cross size of lymph nodes in studies age groups.

Isolated tuberculous lesion of lymph nodes of the hilum without involvement into pathological process of mediastinal nodes was rarely detected (23.6%). Use of CT angiography allowed to clearly distinguish enlarged lymph nodes from large mediastinal and hilum vessels. At that, the radiopaque was accumulated in the capsule of infected lymph node, limiting thyroid necrotic masses inside the capsule.

Analysis of CT presentation of Group 2 showed that among 82.8% children and adolescents quantity of visible lymph nodes varied from 0 to 2, with no difference in age parameters ($\chi^2=13,045$, $p=0,788$). At that, 22.9% children showed no lymph nodes. 17.2% of healthy children in CT scanning showed 3-6 groups of lymph nodes, and majority of lymph nodes was detected in adolescents (13.9%)

Frequency analysis of different localizations of lymph nodes in non-infected children showed that no matter the age, the most frequently detected groups are: retrocaval (27.6%), para-aortic (22.7%), paravasal (20.0%) ($\chi^2=7,041$, $p=0,989$) (table 3).

Table3

Groups of lymph nodes in infected and non-infected children

Groups of lymph nodes	0-2 y.o.		3-6 y.o.		7-13 y.o.		14-17 y.o.		Total	
	Abs.	%	Abs	%	Abs	%	Abs	%	Abs.	%
Bronchopulmonary right.	-	-	-	-	-	-	-	-	-	-
Bronchopulmonary left	-	-	-	-	-	-	-	-	-	-
Bifucational	3	10,0	7	14,3	3	10,7	6	15,7	19	13,1
Subcarinal.	3	10,0	2	4,1	1	3,6	4	10,5	10	6,9
Paravasal	6	20,0	9	18,3	5	17,9	9	23,8	29	20,0*
Paratracheal	1	3,3	4	8,2	3	10,7	3	7,9	11	7,6
Para-aortic	7	23,3	12	24,5	8	28,6	6	15,7	33	22,7*
Retrocaval	9	30,1	14	28,6	7	25,0	10	26,4	40	27,6*
Aortic window	1	3,3	1	2,0	1	3,5	0	0,0	3	2,1
Total:	30	100	49	100	28	100	38	100	145	100

Note: * $\chi^2=7,041$, $p=0,989$

Lymph nodes in children and adolescents started showing from 0.3cm and their sizes were no more that 0.8cm. In one group no more than 2-3 lymph nodes were determined; they were not in conglomerates, homogenous structure, clear contours, smooth, perilymphatic fatty tissue unchanged.

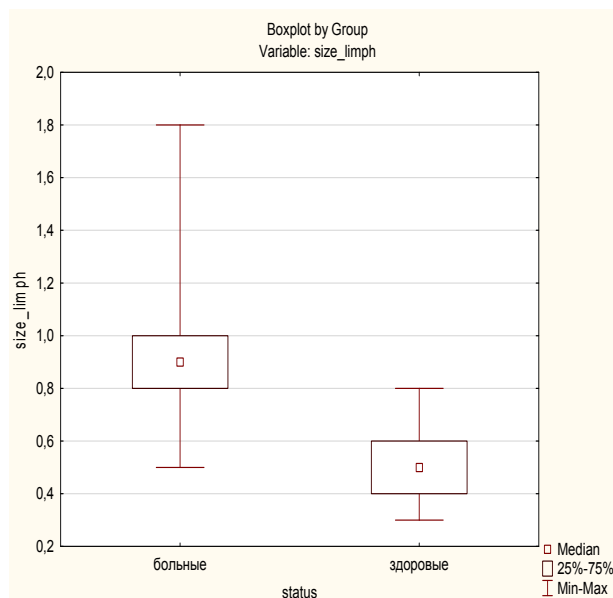


Figure 2. Comparative analysis of sizes of lymph nodes in infected and non-infected children

Thus, infected and non-infected children have significant differences in size of visible lymph nodes ($p=0,000$) (fig.2).

RESULTS

Comparative analysis of CT picture of normal (in non-infected with TMB) and abnormal, changed with tuberculous process lymph nodes showed existence of specific criteria, distinguishing given conditions in differential diagnostics. Quantity of visible groups of lymph nodes in non-infected children usually stays under 2, when during TITLN 3 or more groups are affected. Average cross size of lymph nodes in TITLN usually exceeds 0.90cm ($M \pm m = 0,93 \pm 0,24$), and non-infected children have lymph nodes with size of 0.50cm ($M \pm m = 0,51 \pm 0,13$). At that, upper line of norm of ITLN is 0.8cm. Frequency of occurrence of different groups of lymph nodes also varies: normally retrocaval, para-aortal and paravasal groups prevail, in TITLN bronchopulmonary, bifucational and retrocaval groups occur more frequently. Sizes of lymph nodes depend on age peculiarities.

REFERENCES

1. Akhmedzyanov A.A. Lymphogenic system in vaccination and tuberculous processes. - Irkutsk: Eastern-Siberian book publishe, 1977. – 132 p.
2. Vaganov Y.V. Complex radiodiagnostics in systemic lesion of mediastinal lymph nodes / Y.V. Vaganov, L.G. Zemko // New technology on medicine: diagnostics, treatment, rehabilitation: materials of scientific workshop. - Minks, 2002. - p. 89-92.
3. Gegeyeva F.E. Clinical radiological diagnostics of "minor" forms of tuberculosis of intrapulmonary lymph nodes in children: autoref. diss. ... Candidate of Medicine. - M., 2006. – 20 p.
4. Ishenko B.I. Radiodiagnostics for thoracic surgeons / B.I. Ishenko, L.N. Bisenkov, I.E. Turin. - St. Petersburg.: Dean, 2001. - 133p.
5. Krasovskiy G.T. Materials on age anatomy of lymphatic apparatus of mesostenium. Collected works of Sverdlovskiy Medical Institute. - 1962. - #37. - 215.
6. Lazareva Y.V. Computer tomography in diagnostics of tuberculosis of respiratory organs: autoref. diss. ... M.D. – M., 2002. – 34 p.
7. Matushkina Y.V. Матушкина Ю. В. Spiral computer tomography in diagnostics of lesion of intrapulmonary lymph nodes during lung tuberculosis: autoref. diss. ... Cand.Med. - St. Petersburg. 2008. - 24p.
8. Mikhailova Y.V., Son I.M., Skachkova E.I., Sterlikov S.N. Spread of tuberculosis among children and adolescent in the Russian Federation (analysis of official statistics data). Problems of tuberculosis.– 2009. – # 1. –5-10.
9. Parfenova I.P. Lymphatic system of a lung in normal state and during tuberculosis (radiological anatomical study). M.: Medgiz. 1960. - 150p.
10. Rassokhina L.I. Age-related changes of intraorganic lymphatic system of the lung. Works of the III Scientific Workshop on age morphology, physiology and biochemistry: ed. A.A. Markosyan. - M. : Ed. of Ped. Academy of RSFSR, 1959. - 551-556.
11. Starshinova A.A. Tuberculosis in children from family pocket of infection (daignostics, clinical development and prevention): diss. ... M.D.. - St. Petersburg, 2013. - 250p.
12. Boom W. H. The role of T-cell subsets in Mycobacterium tuberculosis infection. J. Infect. Dis. – 1996. – Vol. 5. – P. 73-81.
13. Geldmacher H. Assessment of lymph node tuberculosis in northern Germany / H. Geldmacher, C. Taube, C. Kroeger [et al.] // Chest. – 2002. – Vol. 121. – P. 1177-1182.
14. Schluger N. W., Rom W. N. The host immune response to tuberculosis. Crit. CareMed. – 1998. – Vol. 157, N. 3. – P. 679-691.

15. Yen R. F., Chen K. C., Lee J. M. 18F-FDG PET for the lymph node staging of non-small cell lung cancer in a tuberculosis-endemic country: is dual time point imaging worth the effort? Eur. J. Nucl. Med. Mol. Imaging. – 2008. – Vol. 35, N. 7. – P. 1305-1315.

The author:

Larisa Petrovna Shepeleva - Head of the Radiologic Diagnostics Department, 'Phthisiatry' Research & Practice Center, Cand.Sc. (Medicine), 677015, Sakha Republic (Yakutia), Yakutsk, 93 Petr Alexeev St.

Contacts: Larisa Shepeleva, tel. 350325, fax 475080, e-mail shepeleva1p@mail.ru.