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"When a child is sick"

Chronicle of Events





Pavlova T.Yu., Douglas N. I.
Republic Sakha (Yakutia) women's health

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Maternal and child health care - a special branch of health care as it is largely determines the future of the nation, therefore, is an important concern of the state. Health problems of women of reproductive age remain constant in importance. Maternal and perinatal mortality is a major integrated indicator of not only the services of maternal and child health and health care in general, but social well-being of society.



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Neurospecific enolase marker of hypoxic - ischemic brain damage in newborns

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Summary: Authors presents results of neuron-specific enolase (NSE) determination in neonates with hypoxic-ischemic brain disorders. Examination showed correlation of NSE serum level and severity of brain disorders and the gestational age in neonates. As well as high probability of infectious-inflammatory diseases in newborns with a high level of NSE.

Key words: neonates, hypoxic-ischemic brain disorders, neuron-specific enolase (NSE)

Introduction: according to the special medical research at the present time the prevalence of neurological diseases in newborn children in Russia amounts to 50-60 per 1000 live births, and the share of perinatal lesions of the central nervous system (CNS) accounts for up to 70% of cases, in the 60-65% of childhood disability due to a lesion of the brain in the perinatal period [1]. In the economically developed countries hypoxic - ischemic lesions of the central nervous system occupy one of the first places in the structure of perinatal mortality, yielding only intrauterine developmental defects [4]. The degree of severity of hypoxic - ischemic lesions of the central nervous system of the newborn is not possible to identify by the methods of clinical and instrumental examination, prognosis of its course and outcome also difficult.

The pathogenesis of chronic neurodegenerative process, which is determining the course and outcome of perinatal hypoxic-ischemic lesions of the central nervous system, remains mostly unknown. Some of researchers believe that after the primary lesion of the nervous tissue of an inclusion in the pathological process of autoimmune mechanisms [2,3], which is accompanied by a violation of the resistance of the blood-brain barrier (BBB). Prospective markers of pathological processes and brain injuries for in vivo assessment of the state of the central nervous system are biochemical, immunochemical methods to analyse the changes in the metabolism in the brain tissue, accompanied by the appearance in blood serum specific for brain chemicals [6]. Neurospecific proteins (NSP) do not detected in biological fluids in normally and fall in blood system only when the violation of the permeability of BBB. The determination of the NSP in the blood serum and cerebrospinal fluid today is recognized as one of the most promising methods of studying of the permeability of BBB[3].



Neurospecific proteins (NSP) are structural components of cells of the nervous tissue, performing specific functions of the central nervous system (the enzyme, receptor, regulatory, transport, etc.). Due to the fact that the NSP are synthesized by cells of nervous tissue, do not come into contact with by immunocompetent cells, they immunotolerant and in the norm there are no blood in immunogenic concentrations. Aetiological various injuries of the nervous tissues (hypoxia-ischemia, injury, infection) cause the same type of complex violations in the form of changes in permeability of the blood-brain barrier with a goal in the blood of the NSPs, with high antigenicity [7]. Contact NSP with by immunocompetent cells of the blood can lead to result the power of immune response, particular in relation to the corresponding protein, leading to the emergence in the blood of antibodies. Antibodies to the NSP, in turn, can pass through the damaged blood-brain barrier and contact with antigens in brain tissue, where with the mediation of the factors of the complement will be started not specific acute phase reactions, leading to autoimmune inflammation and cytotoxic edema [7].

Neurospecific enolase (NSE) - protein differentiated neurons, catalyzing the transformation of 2-phosphoglycerate in phosphoenolpyruvate. *енолпируват*. NSE - this is a key enzyme of glycolysis in neurons. At the present time the NSE is considered as one of the most specific markers damage neurons and serves as an indicator to identify their degree of differentiation [3,11,12].

Materials and method: the method of random sampling carried out a randomized study of the level of the NSE in 25 newborns, of which 13 children were born in the period of gestation 38-40 weeks (I group) and 12 premature infants born at term 35-37 weeks of gestation (II group). All newborns, included in our study, received treatment in the Department of neonatal resuscitation in the form of respiratory support by artificial pulmonary ventilation, the beginning of the artificial lung ventilation for all the children had not later than 12 hours after birth. The basis for the transfer of the child on the respiratory support by artificial pulmonary ventilation served as a clinical-laboratory complex of cerebral ischemia severe degree, the growth of respiratory failure and severe. The degree of severity of hypoxic-ischemic brain lesions were evaluated in accordance with the classification of RASPM.

All newborn carried out determination of the level of neurospecific enolase (NSE) on 3-5 day life by immunoenzyme analysis according to the standard Protocol with the use of a set of reagents for immunoenzyme analysis for determining the concentration of the NSE in the blood serum "NSE - IFA - BEST" by company VEKTOR-BEST, on the basis of immunological laboratory of Perinatal centre, Khabarovsk. Material for the immunoenzyme analysis was the venous blood in the amount of 0.5 ml, taken from a survey of children. To a reference value



neurospecific enolase in the serum of the blood of the newborn accepted value of 3.65 ± 2.0 ng/ml, some have full term newborns without hypoxic - ischemic brain lesions [6].

Statistical processing of the material carried out generally accepted methods of descriptive statistics. Reliable indicators were considered to be at $p < 0,05$.

Results and discussion: as a result of the conducted research it was established that the increase of the level of the NSE was observed in 100% of newborns. In group I (доношенные newborns) the level of NSE, the majority (62%) amounted to 8.6 ± 2.7 nm/ml, and in 38% of cases - $42,5 \pm 13.6$ nm/ml. The increased number of the NSE was observed in children exposed asphyxia during birth, with the development of the hereinafter in this group of infectious-inflammatory complications - to pneumonia. In the group of premature births increased levels of the enzyme dominated (70%, a 42.4 ± 9.5 nm/ml). In this group in the dynamics of the neonatal period, all newborns have marked the realization of infectious-inflammatory diseases, such as pneumonia, meningitis. In children with perinatal lesions of the nervous system changes of immunological indices connected with violation of the regulation of immunogenesis and the influence of hypoxia on the state of the immune system [10], possible increase of the level of NSE may be a criterion for evaluating the implementation of the infectious-inflammatory diseases of the newborn, post-hypoxic-ischemic brain that requires further study.

Conclusion: the obtained data shows that among premature newborns with hypoxic - ischemic brain damage the average content of NSE significantly exceeds the indicators of full term newborns. In this case, the heavier defeat of the brain in newborn infants, the higher the level of the NSE in the blood serum. In the focus groups noted the stable correlation between clinical indicators that characterize the severity of the disease, and disorders of the higher nervous activity. In newborns with hypoxic - ischemic lesion of the central nervous system of the NSE in the blood system can serve as a criterion of severity of perinatal injuries and, together with other indicators, determining the tactics of the therapy, assess the timing of the withdrawal of respiratory support artificial pulmonary ventilation, to identify violation of the permeability of BBB, determine the outcome in children with perinatal hypoxic - ischemic lesion of the central nervous system.

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**ROLE REGIONAL ALLERGOCENTER WITH THE DAY HOSPITAL IN TREATMENT
OF CHILDREN WITH ALLERGIC DISEASES**

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The resume: frequency of calls of the first help and emergency hospitalization at children with an aggravation of allergic diseases on base of allergocentre with a day hospital of large industrial region of St.-Petersburg is analyzed.

Keywords: allergocenter, a day hospital, allergic diseases, calls of fast medical help, emergency hospitalization.

Summary: Analyzed the frequency of calls to emergency medical care and hospitalisation in children with exacerbation of allergic diseases based on allegrocentre with day care hospital of a large industrial area of Saint-Petersburg.

Key words: allergocentre, day care hospital, allergic diseases, calls to emergency medical care, hospitalization.

Introduction. Last decades in our country the big attention to introduction, both high medical technologies and new forms of activity of establishments of public health services also is abroad paid. New social and economic conditions: change of principles of financing, introduction of medical insurance, rise in price of treatment, especially stationary, necessity of application at polyclinic level of modern methods of diagnostics and the treatment, not keeping within frameworks of the out-patient help; refusal of some patients of hospitalization - was created by preconditions for wide introduction of hospital replacing technologies (the medical centres, day hospitals) with wide application of medicamentous and not medicamentous treatment [2,4,5,6]

Creation of the medical centres of regenerative treatment with a day hospital is a way of economic and effective, professional service of patients since allows to concentrate the specialised equipment and to introduce modern technologies, to provide continuity in diagnostics, treatment and rehabilitation of patients [6]. The out-patient centres with a day hospital allow to reduce duration of hospitalization, and also to release cots of hospitals for heavier patients.



At the present stage of medicine for treatment of allergic diseases medical products and though medicamentous treatment allows to supervise highly effectively symptoms of allergic illnesses are more often used, it is necessary to pay all attention to the actions directed on the prevention of aggravations, urgent conditions, reduction of frequency and expressiveness of symptoms of allergic pathology and increase in the periods of remission. Preventive maintenance should be directed also on decrease in influence of risk factors and reduction of requirement for medicamentous therapy.

Till now use of not medicamentous methods of treatment, and also their combination to medicamentous therapy have not been confirmed by clinical researches. Application of various methods of treatment at allergic pathology demands scientific studying for the purpose of an estimation of efficiency concerning variety of indicators. Especially it concerns many not medicamentous methods of the therapy which efficiency not always can be spent according to modern requirements of demonstrative medicine in a variant of blind platsebo-supervised researches.

The purpose. To estimate efficiency of rendering of medical aid to children with allergic diseases in the conditions of a day hospital.

Materials and methods. For an estimation of an overall performance of a day hospital in the Moscow administrative area the analysis of frequency of calls of the first help and requirement for emergency hospitalization in connection with an aggravation of allergic diseases at children receiving various variants of treatment is carried out: complex (medicamentous and not medicamentous) therapy, only the medicamentous basic therapy, receiving treatment only in the period of an aggravation of the basic disease. Calls of the first help and emergency hospitalization of children were analyzed during 2007-2010

Center structure. The centre is included into structure allergic services of St.-Petersburg. On диспансерном the account in the Center there are children of the Moscow administrative area from 0 till 18 years with БА, an allergic rhinitis, pollinosis, atopic diseases and other allergic diseases. In 2007 - 2443 children, in 2008 - 2438, in 2009 - 2519, in 2010 - 2596. The Center structure is presented in drawing 1.

To patients in a day hospital render the urgent help in the period of an aggravation of allergic diseases, and also complex preventive medicamentous and not medicamentous therapy.

For the purpose of training of medical workers doctors of the Center 2 times a year conduct lectures for doctors in children's polyclinics of area and for parents under the program

allergic school. In area it is organized specialized allergic a kindergarten № 35.

For the analysis of an overall performance of the centre with day hospital children of the Moscow area consisting on the account in the centre, have been divided into 4 groups:

I group. Children receiving complex medicamentous and not medicamentous therapy in the conditions of a day hospital (2007 - 642, 2008 - 697, 2009 - 710, 2010 - 732 children);

II group. Children receiving only medicamentous therapy (2007 - 710, 2008 - 995, 2009 - 998, 2010 - 920 children);

III group. Children consisting on the account in the Center, but aggravations addressing only in the period and aggravations receiving therapy (2007 - 532, 2008 - 513, 2009 - 571, 2010 - 652 children);

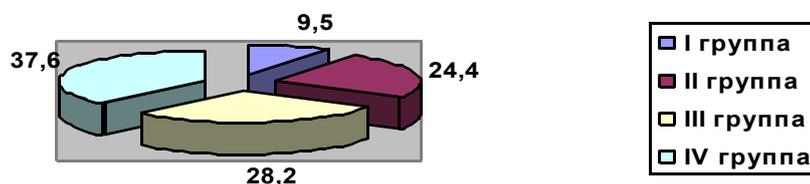
IV group. Children who are on the account in other medical institutions (2007 - 459, 2008 - 133, 2009 - 140, 2010 - 192 children).

For an estimation of efficiency of rendering of medical aid contemporary records of branch of the children's first help of the Moscow administrative area during 2007-2010 Criterion of selection are analyzed: the basic diagnosis - allergic disease agrees МКБ-10. Analyzed documents: magazines of registration of calls, backs of alarm coupons, reports of children's polyclinics, out-patient cards and cards of the patients observed in the Center. In 4 compared groups defined: quantity of calls of first aid and requirement for hospitalization.

Drawing 2

Relative density of calls of the first help to children of the Moscow area in connection with an aggravation of allergic diseases

(An average index in % for 2007-2010гг.)



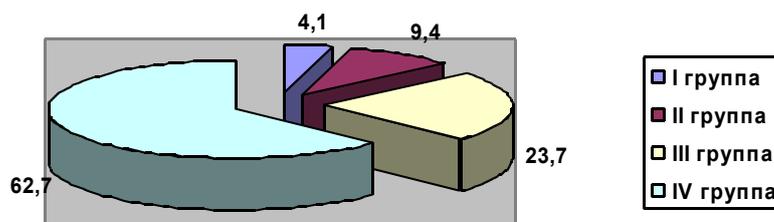
From drawing 2 follows, that the least quantity of calls of the children's first help occurs to children receiving complex therapy in a day hospital and, consisting on the account in the Center (I group). In 2010 the number of departure of brigades of first aid in 3,6 times was more rare in comparison with 2008. The greatest quantity of calls to children of IV group. On the average during

2007-2010 more than half of calls were to children who are not observed in the Center (IV group) in spite of the fact that it is the smallest group in area. In IV group the greatest relative density of calls of the first help in group is observed also: on the average for four years of 72,2 % of patients of the given group demanded rendering of the first help. In I group relative density of calls - 5,3 % ($p_{IV-I} \leq 0,001$).

Frequency of calls of the first aid which has demanded hospitalisation is presented in drawing 3.

Drawing 3

Relative density of emergency hospitalization to children of the Moscow area with an aggravation of allergic diseases
(An average index in % for 2007 - 2010)



From drawing 3 follows, that the least quantity of hospitalization at patients of I group ($p_{IV-I} \leq 0,001$). In 2010 emergency hospitalization was not necessary for any child receiving complex treatment in the conditions of a day hospital. Children I and II groups are hospitalized in 8 times less often, than children III and IV groups.

The conclusion: the Presented results testify that children with an aggravation of the allergic diseases less often, regularly receiving complex therapy in the conditions of a day hospital, essentially require the help (calls of the first help, hospitalization). Aggravations at these patients proceed easier, therapy of an aggravation demands smaller volume of medical products.

It does necessary to recommend hospital technologies to introduction in wide medical practice not only in large cities, but also in the regional centres of the Russian Federation.



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Physical development of children up to 3 years in the Republic of Sakha (Yakutia)

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Introduction. State of physical and sexual development of children is one of the characteristics of the components of health. Monitor the dynamic changes of anthropometric indicators of the growing organism is necessary to identify the individual characteristics of its development. Level of physical development of children is largely dependent on the environmental, social and ethnic factors in the population studied. In the Republic of Sakha (Yakutia), the problem of growth and development highlighted. But regional standards should be updated every 5-10 years. In this connection we carried out this work to justify the need for a modern regional standards for children under 3 years.

Purpose of the study. Assess the physical development of children under 3 years of various ethnic groups living in the Republic of Sakha (Yakutia).

Materials and methods. To study the physical development of children under 3 years of living in the republic of Sakha (Yakutia), the data of anthropometric indicators. Total 11 675 children studied.

Results and discussion. Growth in boys Sakha from 0 to 6 months higher than children of Russian and native. In this age group differences in the growth of irrelevant. Birth weight of native boys is higher than that of Sakha and Russian. On 2 month weight boys Sakha grows to 6 months more than the Russian and native boys.

From 7 to 12 months, the growth of Russian boys above the Sakha and native.

Weight of boys between 7 and 12 months, has the distinction of. So that the weight of boys of Sakha is higher than that of Russian and native boys. In the age group of 1 to 3 years the growth of Russian boys is higher than that of sakha and native. Body weight in this age group is



significantly higher in boys Sakha.

At birth and growth of indigenous girls Sakha no significant differences. Birth weight in girls of different ethnic groups did not differ. To 6 months weight native girls is higher than the Russian and Sakha. In the age group from 7 to 12 months the weight of russian girls is higher than Sakha and native girls. Weight of native girls above.

From 1 to 3 years, the highest increase is seen in russian girls. The lowest growth among native girls. Weight of girls Sakha from 1 to 3 years higher than the russian and native.

Findings. Almost all the groups analyzed above, the growth of russian children. Same body weight of children Sakha and native higher than the Russian. Thus, the results are the basis for the development of regional standards for physical development, taking into account ethnicity.



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ACTUAL DIET OF CHILDREN WITH PATHOLOGY OF ORGANS OF SIGHT IN THE CONDITIONS OF PRESCHOOL INSTITUTIONS

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Resume. We have carried out a study of actual diet among 240 children with pathology of organs of sight in the conditions of a preschool institution in Yakutsk. The received data on menu-apportionment point out the lack of fish, dairy produce (milk, sour dairy produce, curd, cheese), fresh fruit, low content of calcium, magnesium and vitamin E. The results of the study can substantiate the necessity to correct the nutrition of children with pathology of organs of sights in a preschool institution.

Keywords: children of under school age, pathology of organs of sight, basic nutrients, vitamins and trace elements.

Introduction. A rational diet is of a great importance in a preschool age, when main physiological, metabolic, immunologic mechanisms are being formed, which will determine the health of a human during all his further entire life [2, 3, 8]. Physiological peculiarities of children of under school age is characterized by high rate of growth, intensive movement activity, structural and functional reconstruction of some organs. Due to this fact an organism of a child experiences a great demand in nutrients, minerals and vitamins. Thus, organization of correct nutrition in a preschool institution is a very urgent problem under the modern circumstances [5].

The investigations of scientists-ophthalmologists, pediatricians, hygienists demonstrate an important role of a vitamin insufficiency (vitamins A, B, C, E) and a deficiency of some microelements (zinc, calcium and potassium) in the development of eye diseases and their complicated course among children. Unbalanced diet with high content of carbohydrates weakens connective tissue of organs of sight, bringing on the weakness of sclera, which results in sight disorders (myopia, hypermetropia, astigmatism). The diet of children with a sight pathology must be rich in dairy and vegetable diet, enriched with vitamin and mineral complexes, prevailingly with liposoluble vitamins A, E and carotenoids (lutein, zeaxantine) and flavonoids, which provide an active functioning of a sight system, raises the sharpness of sight, improves the condition of eye vessels [1, 9].

The aim of the study. To study the actual diet of children with a pathology of sight organs



in the conditions of a preschool institution.

Materials and methods of study. We have studied 240 children with different eye pathologies (retinal degeneration, optic atrophy, congenital nystagmus, congenital aphakia, optic nerve hypoplasia, hypermetropia, amblyopia, myopia) at the age of 3-7 years, who constantly attended specialized preschool educational kindergarten № 11 “Snowdrop” in Yakutsk. There were 116 boys and 124 girls among them.

The investigation of the actual diet was carried out by menu-apportions. The calculation of an average daily consumption of energy, nutrients, minerals and microelements was carried out with the use of the data of the reference book “The chemical content of the Russian food products” under edition of I.M. Skurikhin, V.A. Tutelyan and the standard program Microsoft Excel.

In order to compare the actual diet of children with the norms of physiological needs “The requirements of SanPin 2.4.1.2660-10, addendum 6” of 2010, the methodological recommendations MD 2.3.1.2432-08 of Rospotrebnadzor of the RF dated 18.12.2008 “The norms of physiological needs in energy and nutrients for different groups of the population of the RF” were used. The statistical development was carried out with the use of a standard packet Microsoft Excel, as well as the packets of the applied statistical programs SPSS 16.0.

The results of the study. In a specialized kindergarten № 11 “The snowdrop” the menu-apportions for the children with sight pathologies is usually composed in accordance with the SanPiN 2.4.1.2660-10 requirements of 2010 with four meals a day. The norms of the food products are usually prescribed in accordance with Order of the Board of Education of Yakutsk № 01-11/97 dated 22.04.2008, besides 105 roubles a day per child for 10,4 hours of stay is an actual daily expense in a preschool institution.

The analysis of 20-days menu-apportions of the children in the preschool institution showed the lack of the repetition of the same dishes during 10 days. Such products like meat, milk, butter and oil, bread, cereals, sugar, potatoes are all included in a daily menu. Fish, sour dairy products (kefir, bifacil, curds), fresh vegetables are all included once or twice a week, and fresh fruit, cheese – once a week. The average daily set of products in a menu showed the lack of fresh fish (30 g at the norm of 45 g), sour dairy products and curds (40 ml a day at the norm of 150 ml), milk (350 g at the norm of 420 g), fresh vegetables (actual 200-250 g at the norm of 400 g, fruit (20 f at the norm of 60 g), natural juice, berries drinks (155 g at the norm of 200-250 g); and the excess consumption of the preserved products (tomatoes, cucumbers, salads), cacao and oil.

Breakfast usually consists of a hot meal (milk porridge and soup, mashed potatoes with sausages, rice and fruit plov), cheese sandwiches, and curd puddings, flat cakes with jam, sweet



coffee, coffee and cacao once or twice a week.

For lunch children usually have vegetable salads (mainly from preserved cucumbers, potatoes, cabbages, carrots, beetroot and fresh vegetables once a week), meat soups, soups from fresh fish once a week; for the second course they usually have meat or fishballs, cutlets, puddings, meatrolls, zrazy, boiled or stewes goulyash (meat), once in ten days they have liver pancakes, cereals and pasta for garnish, and once or twice a week they have stewed vegetables. To improve the taste of food they use dry seasonings (parsley, dill, onions). As for the third course they are served with stewed dry fruit, berries juice, kissel, assorti-stewed fruit, juice, frozen fruit and berries drinks.

As for 5 o'clock tea children are fed with rolls, curd-tarts or jam-tarts, sausages in dough, biscuits, wafers, honey-cakes, sweets, milk and sour milk products. As for fruit, like apples, bananas, plums and tangerines, they are introduced in a menu only once a week.

Dinner usually consists of buck-wheat, oatmeal, millet porridges, curd puddings, curd fritters, omelets, semolina tarts, baked pies with meat, potatoes, fish cutlets with mashed potatoes, tea with honey.

Actual consumption of nutrients and energy is shown in Table 1. As it is seen in the table, the content of albumen in a child's ration in average is equal to – 59,8 g (the norm is 54 g), $p=0,002$; fats – 61,2 g (the norm is 60 g), $p=0,460$ g; carbohydrates – 228 g (261 g), $p=0,000$ per day, i.e. the excess quantity of albumen and insufficient quantity of carbohydrates can be noticed in the ration of children's diet, calorie content is within the norms.

The average content of some vitamins, minerals and microelements in the ration of children in a preschool institution is demonstrated in Table (2). As seen from the table, the content of calcium ($p=0,000$) and vitamins C ($p=0,001$) is actually lower than the norm; the content of sodium ($p=0,001$), potassium ($p=0,000$), magnium ($p=0,001$), and vitamin E ($p=0,000$) is surely higher. The level of iron ($p=0,010$), phosphorus ($p=0,008$) and vitamin A ($p=0,773$), B ($p=0,043$) corresponds to the age standards.

Conclusion:

The received data point at the insufficiency of fresh fish; milk and dairy products, curd and cheese, fresh vegetables and fruit in the daily average ration of diet of children. The fact is evident by the low content of calcium (by 34% lower than the norm), vitamin C (by 23% lower than the norm), carbohydrates (by 12% lower than the norm). The excessive content of sodium, potassium, magnesium and vitamin E has been revealed due to the excessive consumption of salty and preserved food, cacao and oil. The results of the investigation can substantiate the necessity to



correct the diet of children with sight pathologies in a preschool educational institution.

Table 1. Actual consumption of main nutrients and energy of children with sight pathologies in a preschool educational institution.

	n	M± m	σ	Norm	p
Albumen (g)	20	59,8±1,62	7,27	54	0,002
Fats (g)	20	61,2±1,27	7,58	60	0,460
Carbohydrates (g)	20	228,5±4,9	22,2	261	0,000
Energy (ccal)	20	1777,7±30,9	138,6	1800	0,481



Table 2. Average content of some vitamins, minerals and microelements in a diet of children with sight pathologies in a preschool educational institution.

	Norms	Actually (average meaning) M± m	σ	p
Sodium, mg	700	881±17,31	121,42	0,001
Potassium, mg	600	806±15,62	98,36	0,000
Calcium, mg	900	594,4±35,07	156,86	0,000
Magnesium, mg	200	248,4±12,41	55,52	0,001
Phosphorus, mg	800	893,0±31,15	139,30	0,008
Iron, mg	10	11±0,18	0,95	0,010
Vitamin A, mcg.	500	568±23,1	104,73	0,773
Vitamin C, mg	50	38,7±1,2	5,43	0,001
Vitamin E, mg	7,0	11,9±0,32	0,14	0,000
Vitamin B, mg	1,0	0,8±5,2	23,26	0,043

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MOLECULAR-GENETIC TYPING AND STUDYING OF ANTIBIOTIC SENSITIVITY OF THE P.AERUGINOSA NOSOCOMIAL STRAINS IN MULTI-TYPE CLINIC

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The article presents the results of molecular genetic typing and studying of resistance to antibiotics of *Pseudomonas aeruginosa* nosocomial strains, isolated from the clinical samples of the patients who were hospitalized in different units of Republican Hospital №2 – Center of Emergency Medical Care in period of 2010-2011. Clonal spread of multidrug-resistant (XDR) metal-beta-lactamase-producing *P.aeruginosa* strains ST235 (VIM-2) were revealed.

Key words: *Pseudomonas aeruginosa*, nosocomial infections, antimicrobial resistance, sensitivity to antibiotics, metal- β -lactamase

Abstract. Nosocomial infections are a serious problem in modern medicine and have significant impact on prognosis and outcome of disease. One of the most serious pathogens of nosocomial infections complicating course of many chronic inflammatory diseases is *Pseudomonas aeruginosa* (*P.aeruginosa*). The special features of this organism are rapid formation and high level of resistance to many wide range antibiotics, which is usually prescribed for empirical treatment of nosocomial infections [2].

P.aeruginosa characterized by different mechanisms of resistance – reducing of cell wall permeability to antibiotics (lower OprD protein expression), active excretion of antibiotic from the cells (activation of efflux systems), production of individual serine β -lactamases with Carbapenem activity. However, most clinical and epidemiological importance production of metal-b-lactamase (M β L) has. Metal-b-lactamase IMP and VIM hydrolyzes all b-lactams in practice, including Carbapenems, except Aztreonam.

Therefore, effective treatment of infections caused by *P.aeruginosa* remains a complex clinical problem and requires adequate microbiological control and compulsory studying of their sensitivity in vitro [3].

Objective. The object of our investigation was to determine the antibiotic resistance levels,



prevalence of metal- β -lactamase and genetic typing of *P.aeruginosa* strains, isolated from multi-type clinic patients.

Materials and methods.

During two years (2010-2011), the 662 isolates of *P.aeruginosa*, isolated from clinical materials of patients from different units of Republican Hospital №2 – Center of Emergency Medical Care (unit of urgent surgery, unit of purulent surgery, resuscitation and intensive care unit, burns unit, emergency department, unit of patients with stroke, intensive care unit for patients with stroke, neurosurgery unit), were studied.

Identification and re-identification of the strains by the conventional methods according to the documents regulating work of bacteriological laboratories were performed. Also we used a biochemical microtest MICROLATEST, API system test (bioMerieux, France).

Study was conducted within project "National program for monitoring spread of the Gram-negative microorganism strains producing metal- β -lactamase in Russia (METAL)" together with Scientific Research Institute of Antimicrobial Chemotherapy of Smolensk State Medical Academy of Russian Ministry of Health, Interregional Association of Clinical Microbiology and Antimicrobial Chemotherapy, Scientific Methodological Center of Antimicrobial Resistance.

Sensitivity to the 15 antimicrobial drugs by disc-diffusion method on Mueller-Hinton medium according to methodical instructions 4.2.1890-04 was determined. Quality control was performed using the control strains of *P.aeruginosa* ATCC 27853, *E. coli* ATCC 25922. Interpretation of results was carried out in accordance with guidelines and criteria of CLSI / NCCLS (2010-2011).

Phenotypic screening of products of metal- β -lactamase (M β L) by double disc method with EDTA for the all Carbapenem resistant strains was performed [4].

To detect genes M β L VIM and IMP types we used multiplex polymerase chain reaction in real time (28 multiresistant clinical isolates of *P.aeruginosa*).

Identification of the amplification fragments of the bla_{VIM} and bla_{IMP} genes was carried out by determining their melting point (~ 80°C for bla_{IMP} and ~ 85°C for bla_{VIM}) in the presence of intercalating fluorescent dye SYBR Green I. In addition, the melting curves of the experimental samples were compared with the melting curves of the positive control strains.

To evaluate structure of the integrons, carrying the genes M β L, RFLP (restriction fragment length polymorphism) method was used. The variable sections of the class I integrons was amplified using the primers to 5' (intI1) and 3' (qacE Δ 1 or tniC/Tn5090) conservative sequences of



the integrons in pairs with the internal primers to the bla_{VIM} genes and was subjected to restriction by the endonuclease TaqI. Obtained restriction profiles of the PCR fragments were compared with corresponding profiles of the known M β L-encoding integrons, used as controls.

Epidemiological typing of the Carbapenem resistant isolates of *P.aeruginosa*, using multiple-locus variable number tandem repeat analysis (MLVA), was performed. Number of tandem repeats in the six VNTR-loci (VNTR - Variable Number Tandem Repeat, tandem repeats with variable number of the links) was estimated. Amplification of the six VNTR-loci was performed using multiplex PCR (2 separate reactions for each isolate). Analysis of the size of amplification products of the six VNTR-loci was carried out by capillary electrophoresis with fluorescence detection (a fragment analysis) on an automatic sequencer ABI-310 Genetic Analyzer (Applied Biosystems). Cluster analysis of MLVA profiles was performed by software package Bionumerics v.6.6 (Applied Maths) using categorical values of the lengths of the VNTR-loci and algorithm for the construction dendrograms of minimum distance (Minimum Spanning Tree) [4].

Input, processing and statistical analysis was performed using computer program Microsoft Excel (version 7.0. for Windows 2000) and software WHONET 5.6.

Results and discussion.

Greatest number of the *P.aeruginosa* strains – 42,8% (283 isolates), was revealed in the patients treated at burns unit. Share of the identified *P.aeruginosa* strains in other hospital departments was as follows: resuscitation and intensive care unit – 24,4% (162), unit of purulent surgery – 15,5% (102), neurosurgery unit – 8,1% (54), unit of urgent surgery – 2,9% (19), intensive care unit for patients with stroke – 2,4% (16), unit of patients with stroke – 2,2% (15) and emergency department – 1,7% (11).

The clinical isolates of *P.aeruginosa* (n=662) with high frequency were isolated from the wound discharge – 428 (64,6%), than in descending order from the tracheal aspirate – 91 (13,8%), bronchial wash-water – 81 (12,2%), sputum – 42 (6,4%), pleural fluid – 20 (3%) (Fig. 1).

Using the "Double disk with EDTA" method in the 662 strains, M β L production was detected in the 223 (33,6%) Carbapenem resistant strains of *P.aeruginosa* from the 7 different units of Republican Hospital №2 – Center of Emergency Medical Care.

At the next stage of work we have conducted molecular genetic study of the 28 Carbapenem resistant strains of *P.aeruginosa*. In the all 28 isolates the presence of VIM-type M β L was confirmed by PCR analysis.

Method of RFLP (restriction fragment length polymorphism) established identity of structure of the integrons carrying the gene M β L in these isolates and in the VIM-2-encoding



integron with the set of genetic cassettes: *aacA7-bla_{VIM-2}-dhfrB5-aacC-A5* (GenBank Acc. No. DQ52233) (Fig. 2), previously described in the strains of *P.aeruginosa* from the U.S. [6], Russia [7] and Norway [8].

Typing of *P.aeruginosa* by multiple tandem repeats analysis (MLVA) revealed that the all 28 MBL-positive strains of *P.aeruginosa* are related and belong to single clonal complex (CC235) (Fig. 3). This common sequence-type 235 (ST235) is epidemic now. It was detected in hospitals of 27 cities of Russia, Belarus and Kazakhstan (project "National program for monitoring spread of the Gram-negative microorganism strains producing metal- β -lactamase in Russia (METAL)")

Determination of sensibility of the MBL-producing *P.aeruginosa* isolates showed that the isolates are characterized by high levels of resistance (100%) to the all tested antimicrobial drugs: Piperacillin, Piperacillin-Tazobactam, Ceftazidime, Cefepime, Cefoperazone-Sulbactam, Aztreonam, Imipenem, Meropenem, Doripenem, Gentamicin, Netilmicin, Amikacin, Ciprofloxacin, Levofloxacin, Phosphomycin. The sensitivity of isolates identified only to Colistin and Polymyxin B.

Conclusions:

1. In multi-type clinic "Republican Hospital №2 – Center of Emergency Medical Care" clonal spread of the super-resistant (XDR) strains of *P.aeruginosa* ST235 (VIM-2) were detected.
2. Spread of antibiotic poly-resistance among the isolates of *P.aeruginosa* in clinical departments of "Republican Hospital №2 – Center of Emergency Medical Care" is conditioned by one of most common mechanism of antibiotic resistance associated with metal- β -lactamase production.
3. The MBL-producing isolates of *P.aeruginosa* were detected in the all clinical materials and practically in all units of multi-type clinic of the Republic of Sakha (Yakutia).
4. Revealing the MBL-producing strains and the dangerous epidemic clones of *P.aeruginosa* requires the development of infection control measures aimed at early detection and limitation of circulation the MBL-producing isolates of *P.aeruginosa* in hospital departments and other medical institutions, introduction of permanent monitoring of antibiotic resistance, epidemiological tagging of the Carbapenem resistant isolates.



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FUNCTIONAL STATE OF CELLS OF BRONCHOALVEOLAR LAVAGE FLUID OF PATIENTS WITH BRONCHIAL ASTHMA OF VARYING SEVERITY

The cellular composition of the oxidation-state of metabolic function and cytokine-producing activity of cells of bronchoalveolar (BAL) fluid of patients to clarify the mechanisms that determine the severity of the clinical course of bronchial asthma (BA) was studied.

The increased number of neutrophils in BAL fluid of patients with asthma as the worsening of the disease was marked. Also it was found that with the worsening of the severity of BAL fluid cells of asthmatic patients secrete more Th2 cytokines profile. The authors substantiated the fact that these changes in the functional state of pulmonary cells are the basis of the mechanisms that determine the severity of the clinical course of asthma.

Keywords: bronchial asthma, bronchoalveolar lavage, neutrophil, macrophage, active oxygen metabolites, cytokines.

Introduction.

Respiratory diseases are the leading place in the overall morbidity of the population of the Russian Federation, which determines not only their medical significance, but also the social burden on the economy of any country in the world.

As you know, the most important factors in the onset and progression-trivial bronchial asthma (BA) are the changes in immune regulation, among which the leading role belongs to the IgE-mediated allergic reactions [1], which, of course, depend on the functional state of the effector cells of inflammation and allergy [7].

Currently in clinical practice for diagnosis and treatment of patients with asthma are widely used methods of bronchoscopy, with the result that it became possible to carry out morphological study of bronchial biopsies to obtain pulmonary cells and study their structural and functional status [5]. In our view, in contrast to the evaluation of cytologic features of sputum, bronchoscopic method and further cytological and morphological study of the biological material is obtained in the course of its holding, allows us to understand the true picture of pathological processes occurring in the airways and lung tissue. At the same time it is worth noting that the sputum is often used in



pediatric patients because it is noninvasive, has no side effects and contraindications [11, 13, 16].

Thus, the present study examined the cellular composition, oxidative-metabolic function and cytokine-producing activity of cells of bronchoalveolar lavage fluid of patients to clarify the mechanisms that determine the severity of the clinical course of asthma.

Material and methods.

We examined 18 patients with mixed form of bronchial asthma (allergic and infectious-dependent) who were hospitalized in pulmonology department of Amur Region Hospital (Blagoveshchensk). Age of patients ranged from 18 to 68 years (mean age $43 \pm 2,8$ years). Among the examined patients, 10 were diagnosed as moderately of BA (I group), and 8 - severe severity (II group).

This paper has been used to study the bronchoalveolar lavage (BAL) fluid cells of patients with asthma received in the course of therapeutic and diagnostic bronchoscopy performed by standard methods [12]. BAL fluid was centrifuged at 1000 rev/min for 10 min to obtain a suspension of lung cells. For differential cell counting BAL fluid smear cell sediment was fixed in formalin vapor and stained by the Romanovsky-Giemsa.

BAL fluid cells were cultured in the number of 10^6 /ml in RPMI-1640 added 10% fetal calf serum, gentamicin 80 μ g / ml, 2 mM L-glutamine, 5×10^{-5} mM mercaptoethanol. To stimulate the cells of the BAL fluid in parallel wells were added LPS E. coli in a concentration of 0.5 mg / ml. The content of immunoregulatory cytokines IL-1 β , IL-4 and TNF- α in the conditioned culture medium of cells BAL fluid was assessed after 24 hours of incubation with a commercial ELISA test systems ("Protein contour", St. Petersburg), according to the protocol productivity shipment.

To assess the oxidative-metabolic function (OMF) BAL fluid cells of patients with BA was assessed by luminol-dependent chemiluminescence (CL) [4]. In this case, BAL fluid cells are used immediately after their selection. Measuring the intensity of the CL response BAL fluid cells was performed using biochemiluminometer "SKIF-0306M" (SKTB "Nauka", Krasnoyarsk, Russia). As the luminophor was used purified preparation of luminol (5-amino-2, 3 - digidrotalazindion-1, 4) («Serva», USA). To assess the reactivity of the BAL fluid cells using a yeast polysaccharide zymosan (Zymosan A, «Sigma», USA) at a concentration of 5 mg / ml. Registration of the intensity of CL emission BAL fluid cells was performed after 3 min for 30 min. Results are expressed as CL studies combined spontaneous (sp-CL) and zymosan-induced (Z-CL) CL response of cells BAL fluid: sp-Isum and Z-CL-Isum = imp/10³ BAL cells / 30 min, where n - number of pulses emitted by BAL fluid cells within 30 minutes of study. To assess the reactivity of the BAL fluid cells was calculated stimulation index (IS) using the formula: $IS = sp-CL / Z-CL$, conv. units.



Statistical analysis was carried out of the material licensed software package Excel 7,0 and Statistica 5,0, using the arithmetic mean, the average error, t-test. Results were considered significant at $p < 0,05$.

Results and discussion.

The results of calculation of the relative numbers of BAL fluid cells have shown that patients with severe asthma severity (II group), the number of pulmonary macrophages (PMf) was smaller, and neutrophils (Nph) - more than in patients with moderate disease severity (I group). The relative number of eosinophils and lymphocytes in BAL fluid of patients in both comparison groups was approximately equal. At the same time, patients of group II the number of other cellular elements (bronchial epithelial cells, basophil and mast cells, etc.) was greater than in patients in group I (Table 1).

In patients with severe asthma severity (II group), spontaneous CL response of cells BAL fluid was higher than in patients with moderate disease severity (I group) ($p < 0,05$). However, the additional stimulation of cells BAL fluid zymosan A their Z-CL response was weaker than that of patients in group I (Table 2).

Thus, in patients with severe asthma severity found increased BAL fluid cells of OMF. However, the reactivity of the BAL fluid cells of patients in this group was significantly lower than patients in group I (Table 2).

According to D.N. Mayansky [7], the key effector cell of acute inflammation is the Nph. Hence, judging by the increase in the relative abundance of Hph in the BAL fluid in patients with severe asthma severity has an intense inflammatory process caused by the increase in the functional state of Nph and PMf. Our results showed that the BAL fluid cells of patients with severe asthma the severity actively generate reactive oxygen metabolites (ROM), as evidenced by the data of sp-CL response. As you know, in the etiopathogenesis of bronchopulmonary system, including allergic nature, play an important role on the one hand, microcirculatory disorders, on the other - the activation of Nph and macrophages, generating ROM. ROM-generated Nph and macrophages have a direct toxic effect on cells of the microenvironment [14]. Probably, the increase in desquamated epithelial cells of the BAL fluid of patients with severe asthma severity (II group) due to the effect of the damaging effect of ROM, produced by Nph and hard PMf. In addition, ROM may activate mast cells that are actively begin to secrete biologically active substances, such as biogenic amines - histamine, serotonin, which have a pronounced constrictor action that aggravates the clinical course of BA [3].

The content of pro-inflammatory cytokine IL-1 β in the conditioned cell culture medium



BAL fluid of patients with comparison groups were about equal. At the same time, the conditioned cell culture medium BAL fluid of patients with asthma, severe gravity of the content of TNF- α was significantly lower than in patients with moderate disease severity (I group) ($p < 0,05$). However, in the conditioned cell culture medium BAL fluid of patients with asthma, severe gravity of the contents of an anti-inflammatory cytokine IL-4, by contrast, was significantly higher than in patients with moderate disease severity (I group) ($p < 0,01$) (Table 3).

Stimulation of BAL fluid cells of asthmatic patients of both groups of LPS E. coli resulted in the increase of cytokine-producing activity. In the conditioned culture medium BAL fluid of patients with asthma, stimulated by LPS E. coli increased levels of both pro- (IL-1 β and TNF- α), and anti-inflammatory (IL-4) cytokines. Thus, upon stimulation of cells BAL fluid LPS E. coli in patients with moderate severity of asthma (I group) in the conditioned cell culture medium concentrations of proinflammatory cytokines IL-1 β and TNF- α increased, respectively, 2.99 and 3.4 times ($p < 0,001$). At the same time in patients with severe asthma severity of the content of proinflammatory cytokines IL-1 β and TNF- α in the conditioned cell culture medium BAL fluid increased at 1,6 ($p < 0,01$) and 2,2 ($p < 0,001$) times respectively (Table 3).

For cell stimulation BAL fluid LPS E. coli in patients with moderate severity of asthma (I group) in the conditioned cell culture medium concentrations of anti-inflammatory cytokine IL-4 increased 1.9-fold ($p < 0,01$), whereas in patients with severe gravity - in 3.1 times ($p < 0,001$).

Thus, BAL fluid cells of patients with moderate severity of asthma actively produced the proinflammatory cytokines, including TNF- α , and in patients with severe gravity - IL-4. In addition, it was found that the BAL fluid cells of patients with severe asthma severity, according to the results of LPS-induced cytokine-producing activity, preconditioned to enhance Th2-cytokine profile (IL-4).

The key to determining the development of asthma is a violation of the ratio of Th1-and Th2-cytokine profile associated with the lack of Th1-response due to decreased production of IL-12 by macrophages with a decrease in the level of IFN- γ and increase activity Th2-cells in the form of increasing production of IL -4, IL-10, IL-13 [15].

During an asthmatic inflammatory cells that control the production of antibodies, produce regulatory factors that lead to the production of antibodies mainly class IgE (IL-4, IL-13), which attract eosinophils to the site of inflammation and promote their subsequent activation of IL-5, GM-CSF, G-CSF . These cells are called Th2 lymphocytes and their secreted biologically active regulatory proteins (IL-4, IL-13, IL-5) - Th2 cytokine profile [2, 8]. Drawn into the inflammatory mast cells and eosinophils also secrete cytokines, Th2 profile, inducing Th2 lymphocytes. This creates a vicious cycle that supports the characteristic inflammation of the airway wall.



Inflammatory changes associated with bronchial hyperreactivity - a typical sign of the functional asthma [6, 10].

In summary, the results of the study suggest that the allergic inflammation of the respiratory system, including asthma, is one of the variants of chronic inflammation [7, 9], which is based on mononuclear infiltration, and major effector cells are phagocytic cells - monocytes / macrophages and lymphocytes, that implement its functionality enhancement products ROM, pro- and anti-inflammatory mediators, etc. [7] However, the increase in BAL fluid Nph in patients with asthma as the worsening of disease severity may reflect the activation of inflammation in the airways and lung interstitium. At the same time set the activation of BAL fluid cells OMF, which is also indicative of inflammatory activity with increasing destructive processes. In addition, it was found that as the worsening of the severity of BAL fluid cells of asthmatic patients secrete more Th2 cytokines profile. All these changes are likely to underlie the mechanisms that determine the severity of the clinical course of asthma.

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Table 1.

The cellular composition of BAL fluid of patients with asthma of varying severity

Cellular composition, %	Group of patients with asthma	
	I	II
PMf	74,3±4,7	63,2±3,1*
Nph	11,2±3,3	23,3±3,3*
Eosinophils	1,5±0,5	1,7±0,4
Lymphocytes	11,8±0,3	10,6±0,06
Other cellular elements	1,1±0,5	2,1±0,1*

Note: * - significant difference from those of patients in group I. In other cellular elements including single bronchial epithelial cells, basophils and mast cells, etc.

Table 2.

The total CL response of cells BAL fluid and their reactivity (IS) in patients with asthma of varying severity

Groups	CL response, imp/10 ³ cells BAL/30 min		IS, conv. units
	Spontaneous	Z-induced	
I	6,7±1,2	16,4±2,7 ^x	2,4±0,1
II	9,8±1,6*	11,3±1,9	1,13±0,05*

Note: * - significant difference from those of patients in group I and ^x – compared with those of the spontaneous CL response of cells in the corresponding group.

Table 3.

Cytokine-producing activity of cells in BAL fluid of patients with asthma of varying severity

Cytokines, pg/ml	Groups	Cytokine-producing activity of cells	
		Spontaneous	LPS- induced
IL-1 β	I	75,3±2,4	225,7±15,2 ^x
	II	67,5±4,3	111,2±9,3* ^x
TNF- α	I	99,5±5,8	337,4±23,5 ^x
	II	65,3±7,4*	145,8±11,4* ^x
IL-4	I	63,8±5,8	124,4±9,8
	II	109,2±9,7*	342,4±33,3* ^x

Note: * - significant difference from those of patients in group I and ^x – compared with those of the spontaneous production of cytokines in the corresponding group.

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Prevalence of dyspepsia symptoms among the elderly and senile population of Yakutsk

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Summary: A high spread of dyspepsia symptoms have been revealed among elderly population in Yakutsk. Reliable differences of dyspepsia symptoms have been noted according to sexual and ethnic indications.

Keywords: dyspepsia, elderly and senile age, indigenous and non-indigenous population, town inhabitants.

Introduction: According to epidemiological studies dyspepsia symptoms widely spread among a population and 20-40% of them suffer of it. Half of adult population have gastroenterological symptoms, major part of these symptoms are functional, without morphological substratum (Agreus L et al). Sickness of digestion organs inflict significant economic damage to a society (Grigoriev P.Y, V.I.Ivashkin, V.A.Isakov, V.M.Nechev).

Some disturbance of dyspepsia is equally wide-spread among young and elderly population (Talley N.J, Locke G.R, Hague M et al), however geographical and ethnic differences exist. The problem of gastrointestinal disorder of elderly population in the conditions of the North is actual because it is not investigated enough.

Aim and objectives of the research: to investigate spread, gender and ethnic indications of gastrointestinal symptoms among elderly, more elderly and the most elderly population of Yakutsk.

Materials and methods: the research has been carried according to scientific programme "Epidemiology of some chronic non-infectious diseases and risks of elderly population in Yakutsk". The object of investigation was the population of Yakutsk at the age of 60 and senior. The sample of patients has been developed on the base of the list of Yakutsk inhabitants for organizing this research. The sample was done by method of casual numbers with the help of a computer programme. The sample consists of 1394 respondents (200 – masculine, 200 – female in each age group of 60-89 years old and 194 people of the most elderly population). So the sample included 7,6% from the whole number of elderly population in Yakutsk.

775 people were investigated (response 71,6%). 290 people were included into the database for analysis of dyspepsia. Patients were divided into age groups (60-69, 70-79, 80-89 and more than 90 years old). Also according to gender indication they were divided into masculine, female. Two



race-ethnic groups were indicated: indigenous and non-indigenous.

The research has been held in Republican hospital and Geriatric center of the Republican hospital 3 in Yakutsk. People of 80 and senior, some patients of 60 and senior who could not be transported were examined by visiting them at their permanent houses. The most elderly population (90 and senior) was examined in Geriatric center of Republican hospital 3. The research was approved by Ethical Committee of Yakutsk scientific center of the Siberian Branch of the Russian Academy of Medical Sciences (protocol 2, November 2006). All respondents signed the informational agreement of participation in the research. 556 respondents were selected for diagnosing gastrointestinal symptoms by standard questionnaire (57 questions).

According to the Rome III process, 2006 dyspepsia is diagnosed as “dyspepsia symptoms caused by food (meal-induced dyspeptic symptoms (DS) or postprandial distress – syndrome (PDS) or epigastric pain syndrome (EPS) – syndrome of epigastric pain or epigastric pain syndrome (SEP). The symptoms of the disease should be more than 3 months from the beginning and not less than 6 months before diagnosing”.

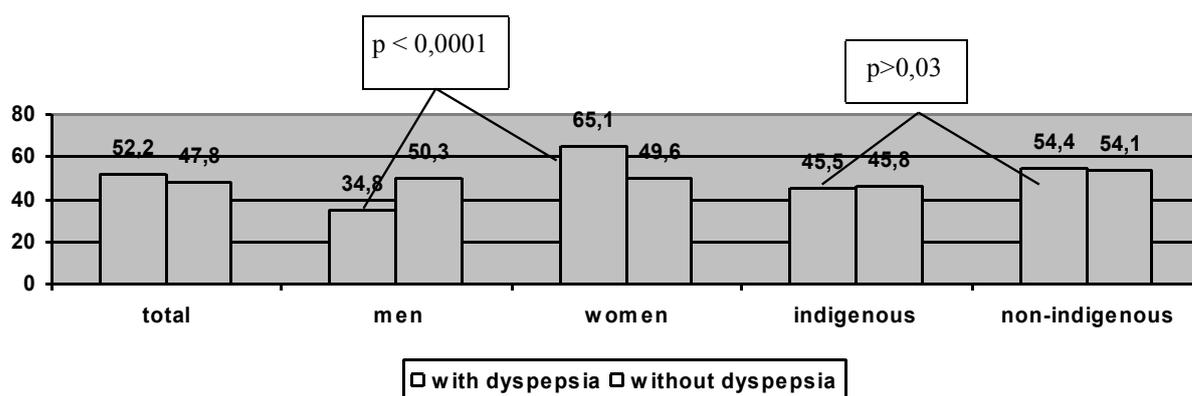
Table 1. Characteristic of examined respondents by sexual, age and ethnic indications

Age	n	%	masculine		female		indigenous		Non-indigenous	
			n	%	n	%	n	%	n	%
60-69 years	182	32,7	81	34,4	101	31,4	66	25,9	116	38,4
70-79 years	184	33,1	83	35,3	101	31,4	90	35,4	94	31,1
80-89 years	129	23,2	56	23,8	73	22,7	69	27,1	60	19,8
90 < years	61	11,0	15	6,3	46	14,3	29	11,4	32	10,5
n	556	100	235	42,2	321	57,7	254	45,7	302	54,3

Characteristic of examined respondents by sexual, age and ethnic indications is given in Table 1. Women and non-indigenous people dominate in the group of respondents ($p < 0,0001$), men and indigenous are the less number, but this is not connected with special selection. It corresponds to general trend of population. Non-indigenous group formed 54,3% of indigenous one, who have been 45,7% ($p = 0,004$). Two age groups have dominated among female: 60-69 and 70-79 years (31,4%). The age group of 70-79 males was the most in number among masculine (35,3%). Women dominated in the group of the most elderly group (14,3%) against males (6,3%, $p = 0,0001$). The group of the most elderly of 90 years and senior was less in number against the other age groups. So everyone from the most elderly population was included in the research (61 people).

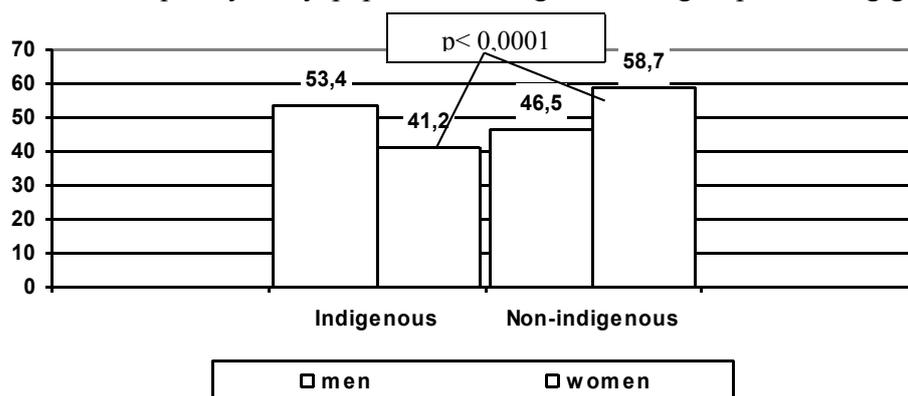
Results of investigation: 52,2% (290 people) of all examined respondents were diagnosed of dyspepsia symptoms.

Picture 1. Spread of dyspepsia according to sexual and ethnic groups



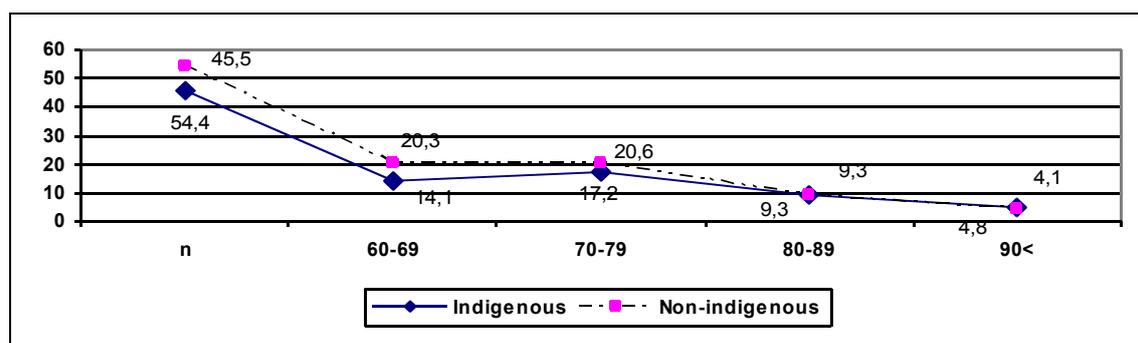
Statistically significant results according to gender are revealed among population of 60 and senior: women – 65,1% (189 people) and men – 34,8% (101 people) ($p < 0,0001$). Statistically significant results according to ethnic indication are revealed: non-indigenous – 54,4% (158 people) and indigenous – 45,5% (132 people) ($p > 0,03$), (pic.1).

Picture 2. Frequency of dyspepsia according to ethnic group including gender



As it is shown in Picture 2, dyspepsia is more often revealed for certain among non-indigenous women (111 people) than indigenous female (78 people) (41,2% and 58,7%, $p < 0,0001$). The clean data were not received among males, indigenous – 53,4% (54 people) and non-indigenous – 46,5% (47 people).

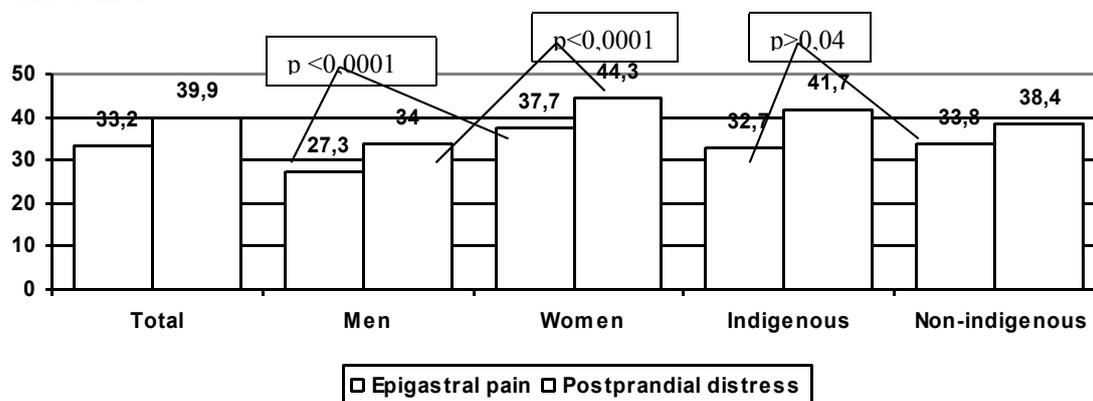
Picture 3. Frequency of dyspepsia according to ethnic group including age



As it is shown in Pic.3 the reduction of frequency of dyspepsia symptoms is revealed in age

group of 60-90 years among non-indigenous from 20,3% to 4,1%, $p < 0,0001$ and among indigenous from 14,1% to 4,8%, $p < 0,03$.

Picture 4. Frequency of epigastric pains and postprandial disorder among Yakusk population aged 60 and senior



As it is shown in Pic.4, frequency of epigastric pains forms 33,2% (185 people). It was noticed that epigastric pains statistically significant for women – 37,7%, for men – 27,3%, $p < 0,0001$, for indigenous – 32,7%, non-indigenous – 33,0%, $p < 0,04$.

There are statistically significant results according to ethnic indication, non-indigenous women – 36,5% to 28,7% males, $p < 0,0001$, indigenous women – 39,3% to 26,0% of males, $p = 0,03$.

Postprandial disorder was noted for 39,9% (222 people) respondents. Statistically significant results were revealed according to gender: women 44,3%, males – 34,0%, $p < 0,0001$, Statistically significant results were not noted according to ethnic indication: indigenous – 47,7%, non-indigenous – 52,3%.

Statistically significant differences were revealed according to non-indigenous women – 41,7% and non-indigenous men – 32,4%, $p < 0,0001$, indigenous women – 48,0% and indigenous men – 35,4%, $p = 0,02$.

Table 2. Frequency of dyspepsia symptoms according to age groups

Age	Number		Men		Women		Indigenous		Non-indigenous	
	EP	PD	EP	PD	EP	PD	EP	PD	EP	PD
60-69 years	76	85	39,0	35,0	42,1	40,1	32,5	34,9	48,0	41,3
70-79 years	61	89	35,9	45,0	31,4	37,3	43,3	38,6	24,5	41,3
80-89 years	29	34	18,7	15,0	14,0	15,5	13,2	18,8	17,6	12,0
90 < years	19	14	6,2	5,0	12,4	7,0	10,8	7,5	9,8	5,1
n	185	222	27,3	34,0	37,7	34,0	32,7	41,7	33,8	38,4

As it is shown in Tab.2 the frequency of epigastric pains are decreasing according to age 60-90 years: women from 42,1% to 12,4% and men from 39,0% to 6,2%. Decreasing of epigastric



pains according to age is observed with indigenous elderly population from 43,3% to 10,8% and non-indigenous population from 48,0% to 9,8%.

Postprandial disorders are decreasing from age of 60 to 90 with women from 45,0% to 5,0%, with men from 40,1% to 7,0%. Also postprandial disorder is decreasing according to age with indigenous elderly population from 38,6% to 7,5% and non-indigenous population from 41,3% to 5,1%.

It is seen from Tab.3 and Tab.4 that decreasing of epigastric pains are observed according to age. Statistically significant differences has been revealed with women suffering of strong, night, famine, and frequent, impulsive, pains after meal and after 2 hours. Epigastric pains decreases after taking a meal, belching (eructation), and acceptance of antiacid. Strong, periodical, famine, pains just after meal are experimentally proved with non-indigenous population in compare with indigenous one.

Table 3. Characteristic of upper abdominal pains on ethnic and gender groups

symptom	n=185		Indigenou s (n= 83)		Non- indigenous (n=102)		Men (n=64)		Women (n=121)		P i-n	PM-w
	n	%	n	%	n	%	n	%	n	%		
Strong pains	44	19,2	17	7,4	27	11,7	7	3,0	37	16,1	0,03	0,0001
Night pains	66	28,8	29	12,6	37	16,1	15	6,5	51	22,2	0,1	0,0001
Periodical pains	45	19,6	14	6,1	31	13,5	15	6,5	30	13,1	0,0001	0,002
Famine pains	60	26,6	24	10,4	36	15,7	20	8,7	40	17,4	0,03	0,0001
Pains just after meal (within 30 min)	55	24,0	22	9,6	33	14,4	19	8,2	36	15,7	0,03	0,001
Pains after 30 min-2 hours after meal	79	34,4	39	17,0	40	17,4	24	10,4	55	24,0	0,8	0,0001
Pains are over after meal	55	24,0	24	10,4	31	13,5	21	9,1	34	14,8	0,1	0,01
Pains are relieved	26	11,3	8	3,4	18	7,8	7	3,0	19	8,2	0,007	0,001



after accepting antiacids												
Pains are relieved by belching (eructation)	44	19,2	24	10,4	20	8,7	11	4,8	33	14,4	0,3	0,0001
Pains become stronger after meal	54	23,5	30	13,1	24	10,4	20	8,7	34	14,8	0,2	0,008
Pains increase after alcohol	22	9,6	14	6,1	8	3,4	10	4,3	12	5,2	0,07	0,5
Impulsive pains	64	27,9	29	12,6	35	15,2	20	8,7	44	19,2	0,2	0

Table 4. Characteristic of upper abdominal pains on age

symptome	n=185		60-69 years		70-79 years		80-89 years		90 years <	
	n	%	n	%	n	%	n	%	n	%
Strong pains	44	19,2	20	8,7	16	6,9	3	1,3	5	2,1
Night pains	66	28,8	28	12,2	21	9,1	11	4,8	6	2,6
Periodical pains	45	19,6	26	11,3	12	5,2	3	1,3	4	1,7
Famine pains	60	26,6	29	12,6	20	8,7	7	3,0	4	1,7
Pains just after meal (within 30 min)	55	24,0	22	9,6	21	9,1	5	2,1	7	3,0
Pains after 30 min-2 hours after meal	79	34,4	30	13,1	26	11,3	14	6,1	9	3,9
Pains are over after meal	55	24,0	22	9,6	22	9,6	6	2,6	5	2,1
Pains are relieved after accepting antiacids	26	11,3	16	6,9	7	3,0	1	0,4	2	0,8
Pains are relieved by belching (eructation)	44	19,2	14	6,1	20	8,7	6	2,6	4	1,7
Pains become stronger after meal	54	23,5	19	8,2	21	9,1	8	3,4	6	2,6
Pains increase after alcohol	22	9,6	8	3,4	8	3,4	4	1,7	2	0,8
Impulsive pains	64	27,9	25	10,9	25	10,9	13	5,6	1	0,4

Conclusion:

According to investigation data high spreading of dyspepsia symptoms is indicated among



elderly, more elderly population (52,2%), and also among indigenous (45,5%) and non-indigenous (54,4%) population of Yakutsk. Epigastric pain, postprandial distress experimentally approves to be more frequently with women (37,7% and 44,3%), epigastric pain is noted with non-indigenous people of Yakutia (33,8%). Dyspepsia is decreasing according to age.

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Partial segmental anesthesia in elderly patients

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In given article the comparative characteristic of application of two kinds neuroaxials blockade is resulted: symmetric spinal anaesthesia and unilateral spinal anaesthesia at operations on a ground floor of a belly cavity at patients of the senior age groups. It is proved that at use of unilateral spinal anaesthesia stability of indicators of haemodynamics, smaller requirement in infusion therapy and sympathetic support is marked.

Keywords: neuroaxial blockade, unilateral spinal anesthesia, bupivacaine.

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Clinical and ethological characteristics of patients with paranoid schizophrenia at the outcome of the disease

The paper carried ethological study of the structure of non-verbal behavior of patients with paranoid schizophrenia in relation to the evolutionary strategy of human behavior. Material study of 100 patients. A relationship between the clinical types of defect states, behaviors, according to the four evolutionary models of human behavior (egoistic, altruistic, cooperative, agonist).

Keywords: schizophrenia, outcome, defect, ethology, behavior of patients.

Introduction. The use of ethological methods in psychiatry are increasingly important in the study of schizophrenia. Of great interest is the possible relationship between genetic and physiological bases of behavioral responses and mechanisms of pathogenesis of schizophrenia. Study the relationship of individual symptoms, syndromes, some forms of schizophrenia and ethology of behavior. Since the formation of catatonic syndrome is associated with "vital physiological response of the body, forming a phylogenetically ancient part of the repertoire of specific adaptation mechanisms" [2]. So "touch" emotional hunger in conjunction with the violation of an instinctive ability to recognize danger and respond flexibly and adaptively to environmental change shapes paranoid symptoms or causes the shell to hide in his own "I" (autism) [7]. These violations of instinctive activity can lead to mental disorders, "the brain itself begins to fill the vacuum, having hallucinations," [7].

Sociobiological model of behavior says about human resource constraints and the adaptive capabilities of human beings in fast-paced environment, which contributes to failure of adaptation and mental disorders, respectively. [5] In connection with what the founder of ethology, Tinbergen [9] in his Nobel lecture emphasizes the importance of ethological approaches in the study of mental disorders in humans. The main tasks of ethological psychiatry [2,3,9] are - 1. study the types and structure of non-verbal behavior for the diagnosis and prognosis 2. identifying the causes of individual behavior, management behavior, and 3. study of the evolution of the pathological behavior in phylo-ontogenetic istoriogeneze.



The object of ethological studies [9,10] are as instinctive behaviors, as well as conditional reflex associated with the long process of learning (communication, social traditions, professional activity). Behavior is organized in a hierarchical manner, so that the system behavior [3] distinguish several levels of integration - it's elementary motor acts, postures and movements, sequences of related poses and movements, groups, represented by complexes of chains and operations. On the basis of these principles in its research Samokhvalov V.P. [10] developed a glossary of non-verbal human behavior, which includes the elementary units of behavior, both simple and complex systems.

In reducing the data from various researchers (Samokhvalov V.P., Korobov A.A., M.A. Derjaguin, Khrennikov O.V., Mayburd E., Fedorenko N.A., etc.) [10] isolated phenomena of behavior that is clearly correlated with the schizophrenic defect. These include the position of subordination in which the head down, hands wound up back, reducing shoulder posture of the embryo. It was found that patients with schizophrenia at least look into the eyes of the interlocutor, usually to the side, down significantly more often dominated by the proboscis and components half proboscis, open mouth with a shift in the direction of the lips, drooping mouth corners. With all the deficit symptoms of schizophrenia were observed, dull or leaden eyes, such components as a single "clawed foot", restriction of the brush, "the hand of an obstetrician." For simple and complex systems of behavior in schizophrenic patients, researchers noted the stereotyped activity stereotyped rocking (yaktatsii), stereotyped manipulation, stereotypes feet and posture, for example, people with schizophrenia, unlike healthy active gesticulating fingers, the so-called "playing with his fingers" [10].

In the future, conducting his research in the direction of sociobiology schizophrenia Gilburd O.A., Balashov P.P. [1] found that "schizophrenia is subject to typological quaternionic general evolutionary patterns of the quaternary structure of the system of mutual symbolic and semantic transcoding and broadcasting with the rules of universal grammar of the Quaternary." It was concluded that the polymorphism of schizophrenia is a layered, systematic and evidence of its integrity and unity of the nosology. So, spending, environmental sociobiological behavior analysis 88 patients with schizophrenia catatonic showed that the content of their nonverbal repertoire is translated into the semantics of agonal evolutionarily stable strategy of behavior, for 97 patients with simple schizophrenia was found that "the content of their nonverbal repertoire is translated into the semantics of selfish evolutionary stable strategy of behavior. " As a result of socio-biological-ethological analysis of the behavior of 295 patients with paranoid schizophrenia, it was concluded that the "evolutionary teleological raison d'etre of paranoid schizophrenia in the human community"



is the "conservation and presentation of semiotically gominizirovannoy altruistic evolutionarily stable strategy of behavior."

The purpose of this study was to examine the nonverbal behaviors of patients suffering from paranoid schizophrenia at the end of the disease.

The objectives of the study were: 1) to examine non-verbal behavior of patients with paranoid schizophrenia in the final state in accordance with the clinical types of defects. 2) Identify the relationship between evolutionary models of human behavior and the clinical picture of the initial states.

Materials and Methods. Using a glossary of non-verbal human behavior, we have examined 100 patients of psychiatric hospitals for over 10 years, suffering from paranoid schizophrenia and "recorded" the attending physician in the category of "chronically ill" and have a stable mental state more than 5 years, without the expressed productive symptoms. For statistical processing of the material used the program Statistica 6.0.

All patients were disabled 2 groups. No statement more than a year in hospital were 68 patients in this group of patients were completely lost social connections, housing. Among them there was the greatest number of disabled - this is 20 patients. In the medical-labor workshops are 25 patients, 34 patients, only occasionally involved in the work within the department, the rest of the day spent in inaction. Nine patients were not included in the occupational therapy due to severe defect and needed to monitor the behavior and compliance with sanitary requirements, the clinical picture in these patients were observed phenomenon of secondary catatonia. The clinical picture of this group of patients was diverse (dominated by the state and the residual apathy and abulia, hallucinatory-paranoid symptoms, psychopathic personality disorder, paraphrenic syndromes). Among the reasons for prolonged hospitalization was dominated by social issues - in 70.4% of cases, negative attitude to discharge (a type of endogenous dependent hospitalism) [4] - 16.4%, from 13.2% of patients discharged impeded mental state and the full disadaptation in society. Of the surveyed patients, 32 patients were discharged from hospital with a periodicity of 3-6 months to 1-2 weeks. In these cases, the patients remained intact social networks. But the relationship with his family were often formal, cold. Hospital discharge provoked doctors.

At hospital discharge in 90% of patients stopped taking medication, and in rare cases alcoholized, which contributed to the continuation of re-hospitalization and inpatient treatment. This group of patients differed little from the previous group. The only difference was that all patients in varying degrees, included in occupational therapy (within the department, medical-labor workshops, external objects, cleaning of territory, working in the kitchen, bakery, potato fields,



etc.). Only 10 patients in spite of the pronounced defect, were discharged for 2-6 months during the year from a psychiatric hospital. For these patients was characterized by the presence of strong social ties (hyper custody mothers, wives, daughters, sisters). The relationship of the type "mother-child relationship." Such patients are often helped at home on the farm (washing floors, dishes, taking out the trash, could make their own purchases, etc.), they were characterized protective adaptive response - "hiding under the care" [6]. Interestingly, when the death of "guardian", these patients quickly maladjusted and joined the first group of patients. The clinical picture is dominated by disorders apathy and abulia, asthenia, in 3 cases remained not expressed hallucinatory disorders.

The results. It was found four types of clinical conditions. All the data were reliable direct correlation (at $p < 0.05$). The first is characterized syndrome of apathy and abulia. This group accounts for 45% of patients. The clinic was determined in these cases emotional and volitional decline, impoverishment of the emotions, reduced volitional activity, extreme passivity, isolation, restriction of social contacts, and four patients had severe symptoms of asthenia. The behavior is dominated by the components of energy conservation: dull eyes, gipomimiya, facial expressions of indifference, stupidity, misunderstanding, lack of contact eyes, dirtiness of the body, unfixed hand gestures removal, stereotypy, which corresponds egoistic model of human behavior. According to Gilburdt [1], this model corresponds to a simple form of schizophrenia.

The second group of patients at the clinic found against apatoabulia, paranoid (30%) or hallucinatory inclusion (10%) as a residual (residual) symptoms. The behavior of dominant positions to Raden, the Pharaoh, Napoleon's opinion on the sides, compressed lips, asymmetry of the face, squinting eyes or stare into the face, hands fixation on his knee, thigh, gestures, treatment focus, increasing leverage. These behaviors are determined by "altruistic behavior strategy," and complies with the paranoid form of schizophrenia [1]. The third group (6%) patients revealed marked changes in the personal sphere, the clinical picture in these cases is determined by the psychopathic behavior in the form of motor excitation, disinhibition of instincts, ridiculous behavior, mannerisms, and corresponds to the "cooperative evolution strategy of human behavior." Such a strategy of behavior is typical for hebephrenic schizophrenia [1].

The fourth group (9%) is characterized by signs of catatonia secondary and paraphrenic symptoms. They are characterized by extreme autism, stereotypical, disruptiveness of speech, social and personal helplessness, combined with affective flashes, fragmentary hallucinations. The appearance and behavior of these patients presented with horizontal wrinkles on the forehead, grin, half grin, torso forward, chaotic movement of the territory, unblinking scrutiny, the lack of fixation,



chewing, proboscis, masklike face, grimaces suffering, smiles, playing with his fingers, stereotypes. These clinical and "ethological markers" corresponding to "agonistic strategy evolutionary model of human behavior" and the catatonic form of schizophrenia [1].

In general appearance of patients with the initial state of paranoid schizophrenia is very similar. Are typical gestures, postures, subordination, oppression, look closer, dim-flashing is not directed at his companion (down, sideways) in mimicry of the lips released proboscis extension of the lower lip forward, there is a minimal fix hands. Motility of the head is characterized by rocking movements of the sternocleidomastoid and immobility in the torso, shoulders, pronounced stereotypy, especially stereotyped rocking and "playing with your fingers." At the same time grooming (preening) are rare.

Talk. The results of these studies suggest that paranoid schizophrenia at the end of the disease can be represented by all four evolutionary models of human behavior (selfish, altruistic, cooperative, agonist), each of which is characteristic of the behavior of the main forms of schizophrenia patients [1]. These clinical observations and ethological analysis of the behavior of patients suggest the unity of the pathogenesis, genetic conditionality of some form of schizophrenia. But this statement does not reveal the etiology of schizophrenia, only helps to understand the external manifestations and pathogenesis, confirming the concept of nosological unity of schizophrenia, its forms, options and allow the formation of adequate therapy and rehabilitation programs.

Conclusions:

1. Schizophrenia is a common nosology, regardless of the shape and course of illness.
2. Among patients with long-term clinical course of paranoid schizophrenia on the background of continuous use of antipsychotics separated defect apatoabulia. In this regard, for patients with initial-state energy-saving strategy dominated behavior.
3. Depending on the clinical picture of the defect, paranoid schizophrenia is represented by all four models of human behavior (selfish, altruistic, cooperative, agonist)
4. A proper understanding of nonverbal signs will not only adequate interpretation, but will also promote the "appropriate use of their own pantomimic opportunity" to increase "social competence of patients and building their adaptive behavior" [8].

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Cytoarchitectonics of mucous membrane's diffuse lymphatic tissue of larynx of the deceased from common hypothermia in the Republic of Sakha (Yakutia).

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By methods of microscope research cytoarchitectonics of mucous membrane's diffuse lymphatic tissue of larynx of the deceased from common hypothermia and alcohol intoxication was learned. It was revealed that some changes in cellular composition of mucous membrane's diffuse lymphatic tissue of larynx at mortally hypothermia – decreasing of T- and B- lymphocytes and plasmacytes and increasing of the number of destructively changed ctlls and macrophages, that let us confirm in suppression of local immunity of the deceased from natural low temperature in the territory of the Republic of Sakha (Yakutia).

Key words: diffuse lymphatic tissue, common hypothermia of organism, cold factor, lymphocytes, plasmacytes, macrophages, destructively changed cells.

Introduction. Learning of cold factor on man's organism in modern conditions is rather actual. Accumulated literature data convincingly testify the oppressive action of hypothermia on cellular and humeral immune answer about changes in man's organism at one time deep influence of cold. [1,4,7].

In realization of protective reaction of organism the main role is given to lymphoid tissue of larynx of hollow organs. By M.P. Sapin's terminology this tissue does the function of "watching post" on the way of introduction of genetically strange substances. [3,9,10].

Thus one of the perspective directions researching of acute and chronic influence of cold factor on man's organism is researching of immune structure of respiratory system specifically of larynx which is the primary part of respiratory ducts and one of the first is influenced by low temperature.

Given research work is the first complex morphological research of reactivity of lymphoid structure of larynx at the influence of natural low temperature in conditions of the Republic of



Sakha (Yakutia).

The aim of researching: Learning of cytoarchitectonics of mucous membrane's diffuse lymphatic tissue of larynx of the deceased from common hypothermia in the Republic of Sakha (Yakutia) (morphological researching).

Achieving of the aim is provided by solving the following tasks:

- Learning of mucous membrane's diffuse lymphatic tissue of larynx of the deceased in summer from incompatible with life mechanical trauma not having pathology in their respiratory system during their life in conditions of the Republic of Sakha (Yakutia).
- Learning of morphology of diffuse lymphatic tissue of mucous membrane of larynx of people who died from organism's hypothermia in winter in conditions of the Republic of Sakha (Yakutia).
- Learning of morphology of diffuse lymphatic tissue of mucous membrane of larynx of people who died from alcohol intoxication in winter in conditions of the Republic of Sakha (Yakutia).
- To give comparative value of mucous membrane's diffuse lymphatic tissue of larynx of people who died in summer from common hypothermia of organism and alcohol intoxication.

Materials and methods of researching: Taking of material is carried out in different time of the year on the base of State Budget Establishment "Forensic Medical Expert Bureau" the Republic of Sakha (Yakutia). The object of researching was mucous membrane's diffuse lymphatic tissue of all parts of larynx taken from 48 died men from 20 till 68 age. All bodies of the deceased were divided into 3 groups:

The 1st group – people died in summer from incompatible with life mechanical trauma not having pathology in their respiratory system during their life (control group);



The 2nd group - people died in winter from common hypothermia;

The 3rd group - people died in winter from alcohol intoxication.

Pieces of mucous membrane of larynx were taken from the part entry, of left and right ventricle's and under throat field. The material was fixed in 10 % neutral solution of formalin, put paraffin Histomix. Cutting of paraffin blocks was done by microtome Leica HL 1210, the thickness of the microscopic section is 0,3-0,5 mkm. The microscopic sections for wide path histological research were colored by gemotoxilin and eosin. Cytoarchitectonics lymphoid structure was learned by the use of light microscope Leica DMD under oil immersion at increasing 90 times with the use of 25 ocular C.B.Stefanov's morph metrical screen. (1974) [8]. Counting of screens (area $S= 0,016 \text{ mm}^2$) was done in blood epithelia, in diffuse lymphoid tissue of own tablet of the mucous membrane of larynx and under mucous layer. At analysis of histological preparations little, middle and big lymphocytes mature and immature plasmatic cells, macrophages, thick cells, eosinofils, neutrofil, phibroblasts, cells in the state of mythos, destructively changed cells were taken into consideration. Each histological microscopic section was seen in five fields of vision. At counting cells in focal point of the screen were fixed. Received data were written in the tables. Statistic analysis of the taken data is in ms Excel 2007.

Immunophenotyping T-, B-lymphocytes and macrophages (CD3+, CD20+, CD68+) were carried out with the use of vision PolyVue Mous/Rabbit HRP Kit (producer Diagnostic BioSystems, the USA) in accordance with the instructions of firm-producer. Antigen's decamouflaging was fulfilled during 2 minutes in citrate buffer (pH 6,0). Primary antibodies (CD20+, CD3+, CD68+) were incubated at temperature 37°C during one hour. The result of reaction were visional by diaminobenzidin [2,5,6]. Microscopy was made in the passing through light by microscope Leica DMD under oil immersion at increasing the microscope 90 times. Taking picture of micro preparations was done by microscope Leica.

Results and discussion. Results of our research showed that lymphoid structure of larynx in summer time were performed by diffuse lymphatic tissue which is found in mucous membrane of all parts of organs mainly in subepithelian layer, besides single lymphoid cells are met in epithelia's, in mucous membrane and adventices and by gathering of lymphoid cells – lymphoid knots which are situated in the field of over larynx, ventricles and in the front wall of vocal chords field. At learning histological preparations of larynx of people, died from common hypothermia of organism, we established that mortal hypothermia calls a number of structural changes of lymphoid tissues in comparison with control. So it is marked that substantial decreasing of percentile content of lymphoid tissues of mucous membrane in the beginning of larynx: lymphocytes 20%,



plasmacytes 2 % less in comparison with summer period. At the same time the content of thoraxes destructively changed is increased at 13% in comparison with control and alcohol intoxication (picture 1).

Such a picture is watched in of mucous membrane of larynx's ventricle. Number of lymphocytes in comparison with control group is decreased at 21 %, plasmatic cells at 3 %. Per cent content of destructively changed cells is increased at 6% (picture 2).

In vocal chords of larynx we also watch considerable suppression of immunity. Per cent content of lymphocytes is decreased at 21%, plasmatic cells at 2 %, per cent correlation of destructive cells is increased at 13%, macrophages at 7% in comparison with control group (picture 3).

The value of immune status index of people who died from common hypothermia, in comparison with control group has revealed the decreasing of T- cellular (CD3+), B-cellular (CD20+) and considerable activation of macrophage cellular population (CD68+) (picture 4).

Thus, the number of T-lymphocytes (CD3+) in mucous membrane of the right ventricle of people who died from common hypothermia is decreased at 16%, number of B- lymphocytes (CD20+) is decreased at 18% in comparison with control group. The number of macrophage cellular population (CD68+) is increased at 11% (photo 1,2).

Conclusions. Thus we found out reliable differences in index of researched group's thorax content of diffuse lymphoid tissue of larynx's mucous membrane.

According to the results of our data people died from common hypotermia of organism considerable decreasing of T- and B-lymphocytes, plasmocytes, and increasing the number of destructively changed cells and macrophages is marked in comparison with control and alcohol intoxication that let us confirm in suppression of thorax immunities at mortal hypothermia in conditions of the Republic of Sakha (Yakutia).

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Study of the degree of calcification of the coronary arteries after cardiovascular interventions in patients of different ethnic groups of Yakutia

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The authors analyzed the results of complex examination of patients' of native and non-native nationality of Yakutia with diseases of the cardiovascular system for definition of atherosclerotic coronary artery lesions using tomography techniques (CT of the heart). It was revealed that the degree of calcification of the coronary arteries has no significant differences between native and non-native patients with CHD.

The inclusion of CT coronary heart disease in the algorithm of outpatient examination patients with suspected coronary artery disease will reduce the number of invasive angiography, and provides important prognostic information to clinicians.

Keywords: calcium index, RCT, quantity, calcium volume, atherosclerosis, native, non-native.

Results of complex observation of 189 native, non-native inhabitants of Yakutia have been analyzed to define atherosclerosis affection of coronary arteries with the help of tomographic method heart as a result of X-ray computed tomography average age in the 1st group is 55,1±0,6, in the second group 57,5±0,7 of (D=0,03). Most of the patients (71,9%) are men. Involving RCT of coronary arteries into algorithm of ambulatory monitoring patients with supposed IHD will let cut down interventional procedures (ischemic heart) give important prognosing information to clinical physicians.

Introduction

Standard methods to define risk development of cardio-vascular disease complications are based on finding out and evaluating traditional risk factor, such as sex, age, smoking, artery hypertension, high level of blood cholesterol, diabetes, overweight (T.A. Romanova, 2011). Some climatic, physico-geographical, ethnic factors play a certain role in Yakutia. According to the traditional factors most cases of cardio-vascular disease complications are observed in patients with low or middle risk ("prophylaxis paradox" V.S. Sinitsina, D.A. Voronov, C.P. Morosov 2006). It proves that traditional risk factors don't identify patients with a pre-clinic atherosclerosis coronary artery diagnosis because of limited prognosing value of traditional risk factors of ischemic heart disease development. One of these methods is diagnosing calcinosis amount in coronary artery as a marker of atherosclerosis defect of coronary artery with the help of tomography method (V.E. Sinitsin 2010).

There are several works studying peculiarities of coronary atherosclerosis, its connections with traditional and new risk factors, for ex. significance of calcium index amount measured by tomography methods of native and non-native inhabitants in Yakutia (A.N. Romanova, N.V. Makharova, T.Yu.Tomskaya and et.al., 2005). These obtained results will be able to optimize medical-prophylactic ways concerning ischemic heart disease.

Research objective: studying coronary artery calcinosis (as a result of RCT) in patients suffering from IHD and AH.

Material and methods.

189 patients of native and non-native inhabitants of Yakutia were observed. They suffered from



IHD, stenocardia tension (I-IV by Canadian classification, 1972), infarction myocardium in anamnesis together with hypertension disease. Research was done on the base of Clinical-consulting department (CCD) of RH#1-NCM, Yakutsk.

The patients were selected according to the recommendations of European cardiologist's society, 2008.

10. Patients with IHD to find out changes of coronary artery (and also as a diagnosing test of ambulatory patients till 65 years old having atypical pains in the chest, doubtful results of leading tests or traditional coronary risk factors without IHD diagnosis).
11. Patients after surgical IHD treatment to find out a coronary artery state and permeability of venous and artery coronary shunts.

Period of selected material is 2008-2011, Research program included: anamnesis studying, anthropometric research, objective observation, electrocardiographic, echocardiographic observation of heart (Echocardiographic computed tomography of heart and main vasculars (RCT), apparatus Acuson -128/XP-10 HDI-3000 (USA) was used. Final diastolic, final systolic sizes, the thick of ventricular septum, the thick of back of LV were carried out in the M-regime on the level of MC chord on wall of parasternal access along long heart axis. The following points were analysed: final – diastolic size (FDS), final – systolic size (FSS), the thick of ventricular (TVS), the thick of back part of left ventricle (TBPLV).

LV hypertrophy was diagnosed in the extension of VS and BPLV at the end of diastoly more than 1,1 sm myocardium mass of the left ventricle and its hypertrophy were determined by “Penn-cube” formula Devereux R.B., Reichek N., Echocardiographic determination of left ventricular mass in man. Circulation: 55:613 – 618. LVM=1,04 TVS+TBPLV+FDS – 13,6 (Devereux R.B., Reichek N. Echocardiographic determination of left ventricular mass in man. Circulation: 55:613 – 618. 1977).

RCT of heart and main vasculars was done by apparatus Siemens Medical Solutions. Computed Tomography standartised datum of coronary artery calcinosis is calcium index (Agatston index) helping to diagnose risk development of IHD and coronary complications. Clinical significance singles out four diapasons of calcium index (CI9.0 lowest, 1-10-low, 11-100-moderate, 101-400-highest).

Standard mathematical methods were used to work out statistic data, including correlative analysis, using SPSS program (version 19.0). statistichypothesisists Stewardent, x-Pirson, F-Fisher were used as a value criterion. Data are $M \pm m$, where M is an average value of quantity, m is an average mistake of quantity. A dispersion analysis or non-parameteric criteria were used to value differences of groups. Differences were considered to be significant in $p < 0,05$.

Factors value of coronary artery calcinosis of native and non-native inhabitants in Yakutia.

Analyzed results of complex observation of 189 patients are divided into 2 groups: 1 – native inhabitants (the yakut) – 94 people; 2 – non-native (the russian) – 95 people.

An average age of patients: 1 gr. – $55,1 \pm 0,6$; 2 gr. – $57,5 \pm 0,7$ ($p = 0,03$). Most of the observed patients (71,9%) were men. Before observation 141 patients (74,6%) were supposed to have diagnosis of IHD on the base of anamnesis data and traditional instrumental methods, IHD was confirmed in 162 patients (85,7%) (Table 1).

Complains of pains, contrained feeling in the chest while being loaded had 80 patients (39%). 9 patients (4,4%) had stenocardia in rest (spontaneous). 15 patients (7,3%) complained of chest pain in load and rest. 116 patients (56,6%) complained of short breath in morement. Heart intermissions were observed in 60% of patients. 9 patients didn't have clinical IHD symptoms. The reasons of their observation were: 3 of them had artery hypertension and heart intermission during ECG in rest, 4 patients – during daily monitoring, 2 had dislipidaemia in blood plasma, 1 – tumour in the heart, 1 – combination of artery hypertension and heart intermission in daily monitoring.

43 patients (21%) had infarction myocardium, 8 of them had twice, 1-3 times. 5 patients had breach of blood circulation of brain. Artery hypertension was most the frequent risk factor (89,4%). 69



patients (36,5%) suffered from diabetes, 42 patients smoked (20.5%), heredity was burdened with cardio-vascular diseases in 64 patients (31,2%), 115 (60,8%) patients had overweight, 72 patients (35,1%) had dislipideamia, 7 patients had sharp and non-sharp myocardium, 3 of them were examined because of supposed myocardium.

189 patients were examined by ECG method in rest. echoCG-180-RCT of coronary artery – 189, coronary angiography – 98 (51,8%), myocardium scintigraphy – 97 (51,3%).

Comparative characteristic of risk factors of native and non-native patients in Yakutia.

	Group 1 (n 94)	Group 2 (n 95)	P
Age, year (M+m)	55,1±0,6	57,5±0,7	0,03
Sex, m/f	52,2 (71) /43,4 (23)	56,6 (30)/47,8 (65)	0,278
Kettle index (kg/sm ²)	28,9±0,5	31,6±0,5	0,0001
Diabetes	33 (31)	40 (38)	0,488
Artery hypertension	86,2 (81)	92,7 (88)	0,150
Overweight	47,9 (45)	73,7 (70)	0,0004
IHD	84,8 (78)	90,5 (86)	0,233
LVM	245,75±9,4	287,54±12,5	0,008
ILVM	148,17±5,5	169,75±7,5	0,018
Average CI	306,0±66,2	418,4±74,8	0,262
Average V	251,5±52,5	309,4±55,9	0,451

Average CI datum of native patients 306±66,2, V-251,5±52,5 is lower than of non-native patients where CI 418,4±74,8, V-309,4±55,9 ($p>0,0001$), these data are confirmed by previous research (Makharova N.V., 2010).

Determination of calcinosis level of different ethnic groups living in Yakutia suffering from IHD (by Agatston).

Spread and seriousness of coronary atherosclerosis in compared groups were observed together with determination of coronary calcium score. Calcium index (CI) according to A.S. Agatston method in age group of 40-49 with IHD is 178,43±27,92 in patients without IHD – 18, 14±3,64, $d<0,001$. All the patients are divided into 5 groups by calcium score depending on CI volume according to the recommendations of Mayo clinic specialist (Rumberger Y.A., at al, 1999).

Table 2.

Patients dividing by sex and nationality (women, men, native and non-native and calcinosis scoring)

Score of calcinosis (CI)		%	0	1-10	11-100	101-400	> 400
Native women	n=23	43,4	28,3	3,8*	3,8*	5,7	1,9
Non-native women	n=30	56,6	24,5	11,3*	15,1*	3,8	1,9
Native men	n=71	52,2	20,6**	5,1	8,1**	6,6**	11,8**
Non-native men	n=65	47,8	10,3**	5,1	6,6**	9,6**	16,2**
Number of patients	n=189	189	70	22	30	27	40
Total (%=)		100,0	37	11,6 1	15,9	14,3	21,2

Notes: *-d (1-2) 0,05 – real significance of n and n-, women

**-d (1-2) 0,05 – n-n-n men

Calcinosis score in analysis by sex CI of native women, men is lower, but there are some peculiarities. Among non-native patients a number of women with CI 11-110 is more than among native ones, the some is among men. Frequency of CI more than 400, is the same in native and non-



native women. Real significance between native and non-native patients by nationality is $d=0,043$ (Manna-Witney criteria), difference between men and women by nationality is $d=0,025$ (Table 2).

Real statistical datum by nationality is $d=0,043$ (Manna-Witney criteria), by age CI is $d=0,025$.

Early diagnosis of IHD with known risk factors helps to work out treatment strategy. The most known risk factor of cardio-vascular diseases is artery hypertension. Most researchers marked the frequency of coronary calcinosis in patients with high AT (V.S. Sinitsyn, D.A. Voronov, S.P. Morosov, 2006). Possible interconnection of coronary atherosclerosis, calconosis and artery hypertension is complicated and not researched up to the end (Doyle A.E., 1990, Schiffmand A., Lange S. et al, 1992).

Out of total number of women $n=53$, combination of IHD and AH is $n=49$ (92,5%), without AH $n=4$ (7,5%), 9 men with IHD and AH $n=113$ (59,8%), without AH $n=23$ (12,2%) (Table 3).

Native men and women with IHD and AH are more than non-native ones.

Table 3.

Dividing of men and women by stages of AH

Stage AH	1 group (n=94)	2 group (n=95)		
Sex	1(1,0)	7(7,4)	8(8,5)	0(0)
1 stage	16(17)*	43(45,7)**	59(62,8)***	17(17,9)*
2 stage	4(4,3)*	11(11,7)**	15(15,9)***	11(11,6)*
3 stage	2(2,1)	10(10,6)***	12(12,8)	2(2,1)
Total without AH	23(24,5)	71(75,5)	94(100)	30(31,6)
Total patients	21(22,3)** *	61(64,9)***	82(87,2)	28(29,5)***
With AH	1(1,0)	7(7,4)	8(8,5)	0(0)

Notes: *-d (1-2) 0,05 real information by sex

** -d (1-2) 0,05 comparative data of both groups be sex

there are no significant differences between 1 and 2 groups of men, 1 stage of AH, but there are differences with and without AH in total number, with AH $d=0,022$ ($d=0,019$) by non-parametric method. AH is associated with age of both ethnic groups $d=0,0001$.

Frequent increase of AH connected with age in non-native men is marked (Klimova T.M., 2001, Yanchenko O.V., 2002, Romanova A.N., 2007). Average CI meaning and amount of IHD with and without AH.

Average meaning of observed patients CI (native and non-native) with AH is much more higher than in patients not suffering from AH. received data are trustworthy.

Average CI of 1 group patients (native) with AH $n=81$ is $279,4 \pm 65,9$, without AH $n=88$, CI is $409,9 \pm 75,8$, without AH $n=7$ CI is $296,2 \pm 84,0$ $d=0,686$ (picture).

In comparing of average meanings CI of non-native patients is much more higher than average CI and data, but it's not trustworthy. According to some data combination of IHD and AH leads to calcinosis increase of coronary arteries, though achieved statistic results are not trustworthy which confirm results of Chertzog and coauthors (2004) Lau and elat (2005). participation of AH in atherogenesis is possible and it makes worse atherosclerosis process due to artery wall (Doyle A.E., 1990, Schiffand A., Lange S. et al 1992).

it is noticed that calcinosis presence is connected with hypertension duration where as ... level doesn't influence (Megnien J.I., Simon A., Lemaricy M. 1996).

A lot of research data meta-analysis that CI is an independent risk factor of coronary atherosclerosis complications and IHD. In this case a relative risk of cardio-vascular complications is higher than of standard risk factors of IHD (V.E. Sinitsyn, 2010).

In observed women group with IHD native nationality – 23,7%, non-native – 31,2%, men of native nationality – 75,6%, non-native – 68,8%.

Table 4.



	1st group (n=94)		2nd group (n=95)		
	women, total)	men, total)	women, total)	men, total)	
I FC (n=21)		5(5,3)	14(14,9)*	19(20,2)***	2(2,1)
II FC (n=65)		8(8,5)	23(24,5)	31(33)	12(12,6)
III FC (n=76)		5(5,3)**	25(26,6)**	30(31,9)***	11(11,6)**
Absence of IHD (n=21)		5(5,3)	9(9,6)***	14(14,9)	5(5,3)

Note: Patients of IV FC are not registered in the given research.

- * d=0,05 difference of I FC stenocardia between native and non-native men
- ** d=0,05 difference of III FC stenocardia between men and women of native and non-native patients
- *** d=0,05 difference between men of native and non-native patients without IHD

Real significance is determined between men and women with IHD, d=0,004 in non-native patients, in native ones with IHD by sex with IHD, d=0,013.

Carried out analysis confirmed stenocardia FC that II stenocardia FC is a little more in non-native men (33,8% and 35,9%), III stenocardia FC prevails in non-native men and women (37,9%, 57,8% accordingly).

Table 5.

Significance of CI, V in native and non-native patients with and without IHD.

Nosology	Native (n=94)	Non-native (n=95)		
IHD	CI		V	
With IHD	317,4±70,5*	260,7±57,2*	441,3±79,3** _*	340,2±60,8*
Without IHD	12,5±8,5*	11,1±7,2*	21,8±19,3**	18,9±16,3**
Total	306,0±66,2	251,5±52,5	418,4±74,8	309,4±55,9

Note: * d=0,05 significant difference between native patients with IHD and without it

*d=0,05 significant difference between non-native patients with and without IHD

There is no trust in comparing native and non-native patients with IHD a worthy significance of patients with and without IHD of CI is d=0,004, of Vd=0,013, trust is observed in native and non-native patients in total. Patients suffering from IHD got statistically significant data in native patients (n=80), CI-317 70,5 and in non-native (n=86 with IHD, CI – 441,3 79,3. Absence of IHD in native (n=14) CI-12,5 8,5, in non-native (n=9) CI – 21.8 19,3 (Table 5).

Thus, patients suffering from IHD have a big average CI, V and trustfully significant differences than patients not suffering from IHD, native and non-native patients.

Conclusions:

1. Average CI, V of patients with IHD and AH in both groups is much more higher than of patients not suffering from AH. In comparing of average CI, V of native and non-native patients with AH, quantitative significance is higher in non-native patients, but received results are not worthy statistically.
2. Patients suffering from IHD have larger average CI than patients without IHD. This fact is kept in native and non-native patients.
3. Calcinosi score of coronary artery hasn't any worthy differences in native and non-native patients with IHD.

Practical recommendations.

1. RCT of coronary arteries is shown to patients: without coronary symptoms but with risk factor of IHD; pains in the chest, but with negative and doubtful results of stress-tests; before operation by ballonangioplasty and stenting or shunting.
2. CtT-angiography is not shown to patients with CI 400 in artery. It's better to carry out



invasive CAG to determine tactics of myocardium revascularization.

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Paroxysmal disorders of consciousness among aviation professionals

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The article presents the clinical observations of episodes of loss of consciousness among aviation professionals representing a threat to safety. Results of complex examination showed features of clinical manifestations, the results of instrumental findings identified the predominant etiologic factors provoking paroxysms of loss of consciousness.

Keywords: aviation professionals, seizure, syncope, paroxysmal bioelectrical activity of the brain without the unconsciousness clinic, flights safety.



Mutation analysis in the *COL1A1* gene in osteogenesis imperfecta patients from the Republic of Sakha (Yakutia)

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Summary

DNA sequencing of 51 exons and exon-intron junctions in *COL1A1* gene in patients with osteogenesis imperfecta from Yakutia was performed. Two different mutations: mutations shifting the reading frame c.3540_3541insC (p.Gly1181AlafsX38) was identified in a patient Yakut ethnicity and splicing site mutation c.4005 +1 G> T in patient Russian ethnic origin. Mutation c.3540_3541insC (p.Gly1181AlafsX38) hasn't been described early. Mutations lead to a clinical 1 type of osteogenesis imperfecta, identified in heterozygous state and are unique to each family.

Keywords: osteogenesis imperfecta, collagen type 1, mutations.

Introduction

Osteogenesis imperfecta (OI) is a systemic disease of connective tissue, characterized by a wide spectrum of clinical manifestations, the main of which is the high bone fragility. Nowadays there are eight genes responsible for the development of 11 types of OI. The genetic defect which cause the development of OI type 5, hasn't been identified yet. OI type 1 is the most common form of the disease, which occurs in 60-80% of patients and is characterized phenotypically by blue



sclerae and minimal bone abnormality [5, 18, 20]. This form of the disease is characterized, as a rule, by the decrease of collagen type I due to frameshift mutations, stop codons or splicing mutations in the genes of collagen type 1 - the main structural protein of bone tissue. The molecule of collagen type I is constructed of 3 polypeptide α -chains: two $\alpha 1$ (I) and one $\alpha 2$ (I) chain. Each strand contains approximately 1,000 amino acids [3, 23]. The *COL1A1* gene encoding the alpha 1 chain is located on chromosome 17q21.31-q22, and contains 51 exons. Its length is 18 kb [6, 19]. At present time more than 200 mutations in the *COL1A1* gene are revealed in OI patients: insertions, deletions, nucleotide substitutions, splicing and nonsense mutations [23]. Mutations are different in their types and location and result in insufficient amount of protein by reducing of normal collagen secretion in quantitative mutations or in formation of abnormal collagen in qualitative mutations [4]. The majority of identified mutations are missense mutations, which account for more than 70% of all the changes; frameshift mutations are less common; deletions, duplications, and insertions are rare. [4, 13]. The spectrum of mutations in the collagen type 1 gene is described by many researchers in American and European populations [4, 14, 16, 21]. There are several studies of OI patients from Asia [7, 9, 10]. It is shown that the expression profile and the spectrum of mutations for each population depend on the ethnic origin [9].

The high genetic homogeneity of indigenous population of Yakutia due to high levels of isolation (low frequency of interethnic marriages) let refer the population to "ideal" in point of the possibility to identify specific genes and mutations of hereditary diseases and to map genes of complex diseases [1, 2]. In such populations with a traditional way of life existing for a long time in relative isolation, the new allele comes from outside by the founder of population («founder effect»), or arises de novo. Taking into consideration these facts, we studied nucleotide sequence changes in the *COL1A1* gene in osteogenesis imperfecta patients from the Republic of Sakha (Yakutia) to determine «founder effect» mutations, and analyzed correlations of the identified mutations with the form and type of inheritance of OI.

Material and methods

We used DNA samples of 15 patients with clinical diagnosis "osteogenesis imperfecta" from 12 families from the Republic of Sakha (Yakutia), registered in the medical and genetic counseling of "Republic hospital № 1 - National Medical Center." Genomic DNA was isolated from peripheral blood lymphocytes by phenol-chloroform extraction, Mathew, 1984 [11]. The search of changes in the nucleotide sequence of the *COL1A1* gene was performed by single-strand DNA conformational polymorphism analysis (SSCP) using the method proposed by Orita M., et al. with alkaline and thermal denaturation [12]. We used primer pairs flanking the exons and adjacent intron region



which were previously described [8]. After denaturation, the samples were applied on 8% polyacrylamide gel (PAAG). Gel electrophoresis of 20 cm long, 1 mm thick was held at room temperature at a voltage of 100V for 20 - 40 hours. The gel was stained in 0.09% silver nitrate (AgNO₃) within 25 minutes. Analysis of samples was carried out by the presence or absence of additional bands in comparison with the control DNA. Determination of the nucleotide sequence in samples with altered mobility of single-stranded DNA was performed using an automatic sequenator ABI PRISM model 310 («Applied Biosystems») with the use of fluorescent labeling kit DYEnamic™ ET, according to the protocol of the manufacturer («Amersham Pharmacia Biotech» DYEnamic™ ET Terminator Cycle Sequencing Kit .) For the nucleotide sequence analyses MegAlign software package from DNASTar Inc (1993-2002) and BioEdit v.5.0.9. (1997 - 2001) were used.

The impact of newly identified substitutions on the probability of occurrence / loss of splice sites was performed using the program «Splice Prediction using Consensus Sequences» (WebGene): <http://www.itba.mi.cnr.it/webgene>.

Results and discussion

The molecular-genetic study was performed in 15 patients from 12 families, 10 of them were of Yakut ethnic origin, one family – of Russian- and one – of Even ethnic origin. The main method we used was SSCP, the main advantages of which are simplicity and high sensitivity [12]. However, there are also some disadvantages of SSCP method – low sensitivity, if the analyzed fragment exceed 400 bp and a long duration of the electrophoretic separation of the amplification products. However, the method is widely used by many researchers to search for polymorphic DNA sites. Exons with the length of more than 400 bp were directly sequenced. DNA samples with altered mobility of single-stranded DNA were followed by sequencing.

The *COL1A1* gene encoding the alpha 1 chain of type I collagen contains 51 exons and consists of 38 kb. Currently, about 200 mutations are found in OI patients in different populations of the world [<https://oi.gene.le.ac.uk/>]. Despite the large number of detected mutations in the *COL1A1* gene, each population is characterized by a spectrum consisting of a small number of mutations, ranging from 6 in patients from Brazil to 14 in patients of Jews origin from Israel [4, 8, 15, 16, 17]. In patients from Lithuania 11 types of mutations, in Americans – 10, in Japanese – 9, in Chinese – 8 were revealed [4, 7, 10, 22]. In addition, each researcher finds previously undescribed mutations, as well as known mutations. Most of the mutations resulting in OI development are unique and reflect the high variability of the *COL1A1* gene.

We analyzed 51 exons and adjacent intronic regions of *COL1A1* gene in OI patients and



found two types of altered single-strand DNA mobility in exons 49 and 50 of the *COL1A1* gene in two unrelated patients from Sakha Republic.

Subsequent sequencing of the sample with an altered mobility of single-stranded DNA allowed to detect previously unreported mutation c.3540_3541insC (p.Gly1181AlafsX38) in exon 49 of *COL1A1* gene in OI patient of Yakut ethnic origin (Fig. 1). The proband has deafness and blue sclera and such associated diseases, as residual encephalopathy, cerebroasthenic syndrome, neuropathy, and myotonic syndrome. This mutation hasn't been revealed in parents, suggesting that the mutation is de novo.

Analysis of samples with altered mobility of single-stranded DNA in the 50th exon of *COL1A1* gene allowed to identify the splicing mutation c.4005 +1 G> T in a family of Russian ethnic origin (Fig. 2). The patient has blue sclera, multiple fractures of arms and legs, ribs, vertebral compression fracture and dentinogenesis imperfecta. The patient also had concomitant diseases: [uranostaphyloschisis](#), residual encephalopathy and [pollinosis](#). Unfortunately, the proband's parents were not available for DNA analysis, however, the pedigree analysis suggests an autosomal dominant inheritance of the disease from his father. This mutation was previously described only by Italian researchers [<https://oi.gene.le.ac.uk>].

According to the literature data, frameshift and splicing mutations often lead to OI type 1 with mild disease form [24], which is consistent with our data. Both patients from Yakutia with mutations s.4005 +1 G> T and c.3540_3541insC (p.Gly1181AlafsX38) in the *COL1A1* gene has OI type 1 with concomitant diseases.

We haven't found *COL1A1* gene mutations caused by «founder effect» in OI patients from the Republic of Sakha (Yakutia). Our results are in consistent with those of scientists from Israel, who also conducted the analysis of mutations in the *COL1A1* gene in 65 OI patients of Jewish origin to identify «founder effect». They identified 14 different mutations (missense, nonsense, frameshift and splicing mutations), but all the detected mutations were unique for each family and were scattered throughout the gene [16]. It is possible that OI is not characterized by «founder effect» mutations, even in relatively isolated populations.

Conclusions

Thus, two types of mutations were identified in 16.7% of OI families from Yakutia: frameshift and splicing mutations, which are quantitative and lead to the decrease of normal collagen level due to the instability of abnormal RNA resulting in mild clinical manifestations of the disease. These mutations were identified in the heterozygous state and were unique for each family. Mutation c.3540_3541insC (p.Gly1181AlafsX38) in the *COL1A1* gene hasn't been described



previously. Families with the mutations detected are informative for prenatal DNA diagnostics. Our research has contributed significantly to the understanding of molecular-genetic features of the disease and to gene-phenotype correlations in Osteogenesis Imperfecta. The results of this work can also be a theoretical and methodological basis for the development and optimization of molecular-genetic diagnostics of such complicated diseases as Osteogenesis Imperfecta.

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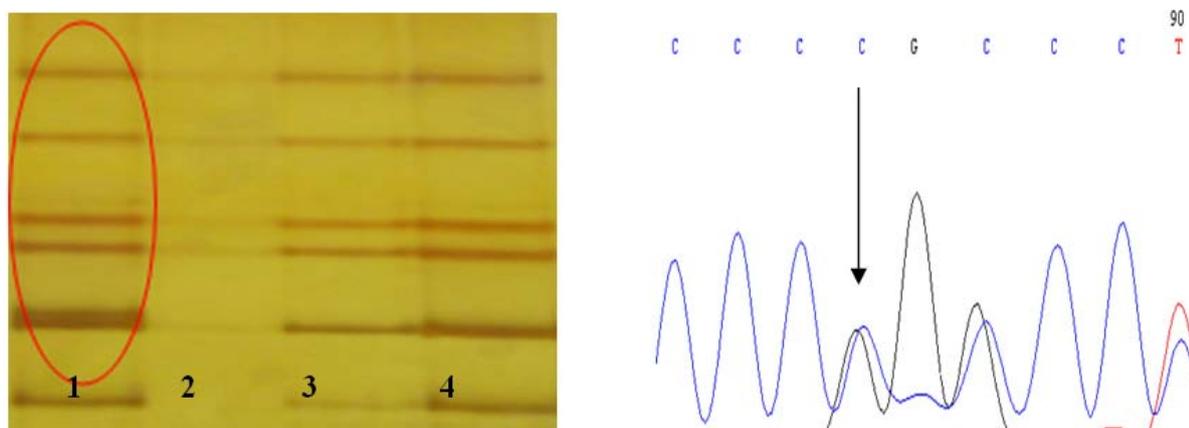


Fig. 1. Identification of c.3540_3541insC (p.Gly1181AlafsX38) mutation in *COL1A1* gene in OI patient of Yakut ethnic origin.

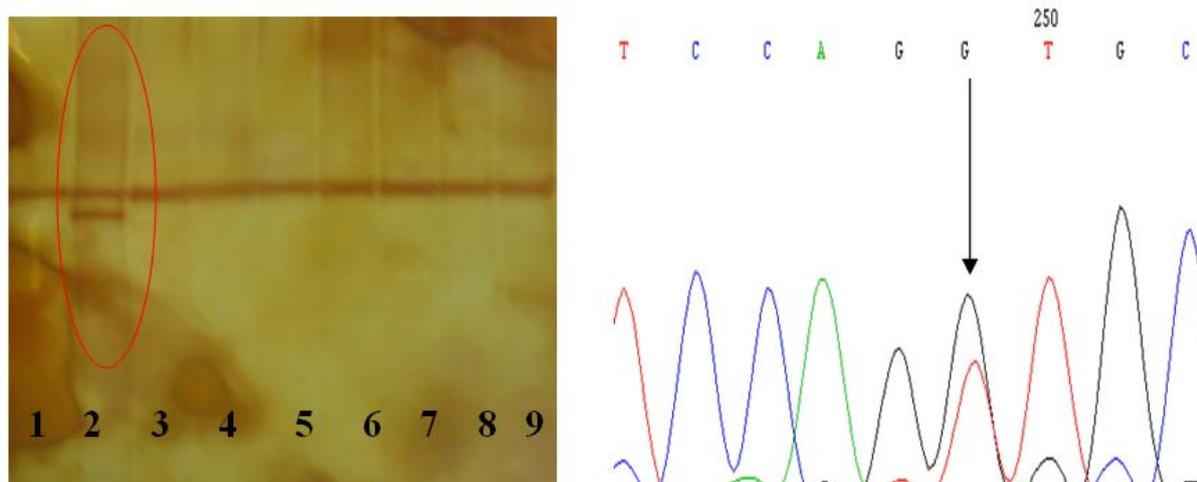


Fig 2. Identification of c.4005+1G>T mutation in *COL1A1* gene in OI patient of Russian ethnic



origin.



P.M. Ivanov, M.I. Tomskiy, P.D. Karataev

Dynamics and prognosis of kidneys malignant tumors in Yakutia

The results of the analysis of 1365 cases of kidney cancer of Republic Sakha (Yakutia) population for 1991-2010 are presented. In Yakutia, the incidence of male and female kidney cancer in the all age groups had a marked tendency to grow and is prognosed to have in both populations almost threefold increase compared to the original figures.

Keywords: Yakutia, kidney cancer, incidence, prognosis.

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The analysis of patients with malignant neoplasms of the female genitals registered in YAROD

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Efficiency of treatment and quality of life of patients at a gynecologic cancer immediately depend on timely diagnostics and treatment. Authors carry out the analysis of a contingent of the female genitals sick of malignant neoplasms consisting on the dispensary account in Yakutsk republican oncologic dispensary (YROD) for detailed studying of indicators of survival rate depending on a stage and spent treatment.

Keywords: the contingent analysis, a cancer of female genitals, treatment.

Introduction. The data which describe a condition of the oncologic help a sick cancer of female genitals in RS (Y) is unfavourable. It is caused by depression of morphological verification of diagnoses on the basic onco-gynecologic localizations that is bound to disadvantages of the organization of diagnostic process and low oncologic vigilance of doctors of the general medical network. Low detectability on routine inspections becomes perceptible, level of neglect is still high and as consequence - the one-year lethality is high. There is a series of unresolved problems, first of all improvement of quality of the organization of prophylactic medical examination of the women consisting on the dispensary account after treatment.

The purpose. To analyse a contingent of the female genitals sick of malignant neoplasms consisting on the dispensary account in Yakutsk a republican oncologic dispensary on the extremity of 2009.

Materials and methods. By us are subjected the analysis of data about 1326 patients consisting on the dispensary account in YROD on the extremity of 2009 concerning a gynecologic cancer. From them 681 necks of a uterus sick by a cancer, 327 – a hysterocarcinoma and 318 – a cancer of ovaries.

Results and their discussion. Frequency of a lesion a cancer of genitals among city and agricultural population was not identical. So, the share sick of a cancer of a neck of a uterus among city dwellers has made 63,6 % (433 patients), rural – 36,4 % (248). Similar distribution isn't also at a hysterocarcinoma and ovaries (city patients – 64,2 and 63,2 %, rural – 35,8 and 36,8 % accordingly).

The parity of persons of a radical and alien contingent has made at a cancer of a neck of a uterus 1,0:2,2, a hysterocarcinoma – 1,0:5,4 and an ovary cancer - 1,0:1,7.

Among sick of a cancer of a neck of a uterus authentically high indicators aren't in age group of 40-49 years (37,2±1,9 %) irrespective of their ethnic accessory and the place of residence. The share of patients with malignant tumors of a body of the womb and ovaries in the general population was high at the age of 40-49 (37,0±2,7 and 28,3±2,5 % accordingly) and 50-59 years (34,9±2,6 and 27,0±2,5 %). At the analysis of age structure sick the hysterocarcinoma and a cancer of an ovary depending on the place of residence and a nationality tap some differences. So, at the age of 50-59 years high frequency of a hysterocarcinoma is taped at natives (41,3±6,9 %), living mainly in village (52,2±4,6), and ovary cancer – at aboriginals (29,6±4,3 %) city district



(29,4±3,2).

The remote results of treatment are the basic criterion which can indirectly give the chance to judge level of the specialized help in region.

We carry out the analysis of survival rate of organs of genitals sick of a cancer depending on a kind of treatment and a process stage.

According to the spent analysis at 50,4 % sick a cancer of a neck of a uterus a leading kind of therapy was operative treatment in a combination to radial therapy (the combined method). From them the most part of patients with I and II stages - 37,3 and 50,4 %. Only operative treatment was received by 11,9 % of patients: with a carcinoma in situ - 35,8, with I–II stages – 64,2 %. Combined-radial therapy as an independent method is spent 35,8 % basically by the patient with II (53,7 %) and III (32,8) stages. It is necessary to notice that 5 necks of a uterus sick by a cancer with 0-I-II a stage have refused the offered treatment for the various reasons.

Now according to the literature at hysterocarcinoma I-II of stages the combined treatment – operation with the subsequent radial therapy is more often applied. At III stage at a postoperative stage treatment is used chemo-hormonotherapy. At IV stage of a cancer of endometrium taking into account the general condition of the patient, the data of inspection, features of diffusion of tumoral process probably application radial and-or chemo-hormonotherapy.

Among patients, in conformity to the standard standards of treatment of a hysterocarcinoma of the given localization, the basic method of treatment was combined (48,6 %).

At I stage of a hysterocarcinoma in 37,7 % operative treatment, in 44,3 % - the combined treatment was applied only. At II stage at the majority sick the hysterocarcinoma applied the combined treatment (71,6 %). Complex treatment (operation and chemo-hormonotherapy treatment) was carried out at 93,5 % of patients with III stage of a cancer of endometrium. Patients with the remote metastasises (IV stage) received chemo-hormonotherapy and an expected treatment.

The standard of treatment of a cancer of an ovary, according to clinical references of the European society of medical oncology (ESMO), National institute of a cancer (NCI), FIGO, the operative measure with procedure full surgical staging and carrying out non-adjuvant and-or adjuvant chemotherapies is.

According to the analysis of 87,4 % sick of an ovary cancer have received the combined treatment, 7,2 % - only operative (cI by a stage), 4,1 % the patient with widespread process it is spent medicinal and 1,3 % - symptomatic therapy (III-IV stages).

The life expectancy analysis has shown that from 1326 necks sick by a cancer, a body of the womb and ovaries from the moment of an establishment of the diagnosis till 3th years live 408 (30,8 %), 3-5 years – 237 (17,9), 5 and more years of 212(16,0andmore) 10 years – 469 (35,4 %).

So, from among consisting on the account concerning a cancer of a neck of a uterus of five years' survival rate it was possible to achieve from 14,1 % (96 patients), including after radial treatment there live 41,7 % (40), combined – 38,5 (37) and after operative – 19,8 % of patients (19).

Further the analysis has shown that necks of a uterus sick of a cancer after treatment live 10 years and more in 39,2 % of cases (267 patients), from them after surgical treatment – 11,6 % (31), radial therapy – 38,2 % (102) and after combined - 50,2 (134).

Apparently on fig. 22 of 44 (6,5 %) women with a carcinoma insitu 5 and more years live 8 (18,2 %), and more than 10 years – 18 (40,9 %). In group of patients with I and II stages the five years' and 10-year-old survival rate has made accordingly 24, and 43,9 % and 17,2 and 35,9 %. From 113 patients with III AB a stage similar terms live 21,2 and 31,9 %.

The analysis of life expectancy of patients PTM shows that from among sick of a hysterocarcinoma from the moment of statement on the account of 5 and more years live 61 (18,7 %), and more than 10 years – 78 (23,9 %).

According to the analysis 159 (48,6 %) patients have received the combined treatment (operation with radial therapy), from them 5 and more years live 26 (16,4 %), 10 and more years –



48 (30,2). Operative treatment, as an independent method, patients with I stage of cancer process (21,1 %) received, from which 5 and more years live 19 (27,5 %), and more than 10 years – 8 (11,6 %). Complex therapy is spent to 53 patients (15,6 %), at the given group of patients 5 and the 10-year-old survival rate has made 15,1 %.

Indicators of survival rate at sick of a hysterocarcinoma depending on a disease stage look as follows. In group of patients with I and II stages 5 and the 10-year-old survival rate has made accordingly 56,7 and 50,6 %; 31,3 and 41,4 %. At III stage of 5 years also are more live – 8 (11,9 %), and more than 10 years – 6 (6,9 %).

From 318 ovaries sick by a malignant neoplasm 5 and 10 summer survival rate is registered at 17,3 and 39,0 % accordingly.

On our material the combined treatment have received: from 55 patients who have lived 5 and more years - 50 (90,9 %), and from 124, 10 years which have lived more - 111 (89,5 %). From 23 women who have finished treatment with use only of an operative measure, 5 and more years have lived 3 (13,0 %), and more than 10 years – 13 (56,5). In group of the patients who have received medicinal therapy as the independent method, from 13 women of five years' survival rate was possible to achieve only from 1st patient that has made 7,7 %, and more than 10 years were lived by anybody.

As of the extremity of 2009, from 101 (31,8 %) patients with ovary cancer I stage of 5 and more years live 16 (15,8 %), and more than 10 years – 47 (46,5).

In group of patients with II stage (77 persons) noted factors corresponded 20,8 and 46,8 %. At III stage from 119 patients of 5 and more years are live 23 (19,3 %), and more than 10 years – 41 (34,4).

The conclusion. Thus, the analysis of the remote results of treatment of a cancer of genitals carried out by us has taped presence set of the unresolved problems bound first of all with quality of the organization of treatment-and-prophylactic work in republic and as consequence, low detectability of early stages and high neglect.

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TERRITORIAL FEATURES OF INCIDENCE AND PREVALENCE OF ALCOHOL AND DRUG ABUSE IN THE KOSTROMA REGION

By I. P. Pochitayeva, A. P. Golubeva

Introduction

Over the past 20 years after the collapse of the Soviet Union, abuse of psychoactive substances (PS) has become one of the most serious social and economic problems facing all societal groups, families and causing growing concerns since this problem adversely affects the demographic situation in Russia and poses a real threat to its national security [9]. Even though chronic alcoholism has reduced over the past three years, its share in all substance dependence disorders in different constituent entities of the Russian Federation ranges from 75% to 90%. It is known that detectability of PS addicts, especially drug addicts, remains low. For instance, according to data from the Ministry of Health and Social Development of the Russian Federation, the ratio of people who have drug problems and seek medical advice to the actual number of drug addicts is 1:7 [5]. The number of drug users in Russia, according to sociological surveys, exceeds the official statistical figure 8–10 times and (according to data from the Federal Drug Control Service of the Russian Federation) accounts for nearly 2% of the national population. Users of opiates, including heroin, account for 90% of drug addicts.

In Russia, the trends in drug and alcohol abuse prevalence have pronounced regional differences [9, 8, 4, 1, and 6]. In these regions, action for prevention and control of alcohol and drug abuse should be organized taking into account social, hygienic, economic, and geographical regional specific features primarily in order to prevent early deaths among people of active working age and develop purposeful preventive measures.

Research materials and methods

With a population of 688,000 and urban residents accounting for 70%, the Kostroma Region is located in the center of the European part of Russia and is part of the Central Federal District of the Russian Federation.

The economic and geographic location (on main traffic arteries) of the cities of Kostroma, Sharya, Volgorechensk, Buy, and Nerekhta and their high economic potential necessitate high-priority and prompt measures on the part of drug control authorities.

Caused by a continuing phase of economic instability that arose in 2009–2010, the social and



economic labor situation is characterized by high unemployment levels.

We compared drug situations in the Kostroma Region, Russia [9], the Republic of Sakha (Yakutia) [6], the Novosibirsk Region [2], and the Kabardino-Balkarian Republic [4].

We studied substance dependence disorders for the 1999–2011 period and the territorial features of incidence of substance dependence disorders by evaluating and analyzing statistical data (reports and overviews) for 13 years of observation, interviews with young people and alcohol and drug addicts, and addiction relapse risk factors.

Results and discussion

Over the past years of observations (2009–2011) in the Kostroma Region, mental and behavior disorders caused by PS abuse varied as follows: primary incidence – from 239.3 to 211.6 and prevalence – from 3,098 to 2,872.5 per 100,000 residents, or about 3.0% of the total population (the Russian Federation – 2.3%). The equalization of time series over 13 years of observations made it possible to identify a trend toward increasing primary incidence and prevalence with low average annual rates with an increase of 1.82% and 1.56% respectively.

Primary incidence and prevalence of substance dependence disorders vary substantially across the constituent entities of the Russian Federation.

In the Kostroma Region, for example, the number of registered drug addicts (185.6 per 100,000 residents) is 2.2 times higher than in the Republic of Sakha (Yakutia) [6], 2–3 times lower than in the Novosibirsk Region [2], while primary incidence is 19% higher than in the Kabardino-Balkarian Republic [8]. Different causes of drug abuse were identified in Yakutsk and Neryungri, the Republic of Sakha (Yakutia) [6].

We studied the territorial features of primary incidence and prevalence of substance dependence disorders in the Kostroma Region (Table 1).

The analysis of data shown in Table 1 makes it possible to conclude that the highest levels of prevalence of substance dependence disorders occur in 4 districts: the Manturovo, Sudislavl, Ponazyrevo, and Krasnoselsky districts. For example, the Manturovo District ranks first for primary incidence and prevalence of chronic alcoholism, while the highest levels of primary incidence and prevalence of drug addiction can be observed in Kostroma and the Kostroma and Nerekhta districts.

The data related to the trends in and territorial features of substance dependence disorders in the



Kostroma Region population require detailed and in-depth research to identify relevant underlying factors that can be combined in two large groups: risk factors for disease occurrence and recurrence and factors related to provision and quality of public medical aid.

Of the total number of patients registered in the Kostroma Region, most registered patients were people with chronic alcoholism and alcoholic psychoses and alcohol users with deleterious consequences (86.1%), in the Russian Federation – 82.2%. Drug addicts and abusers accounted for 13.1% (the Russian Federation – 17.3%), while patients with toxicomania and those who abuse non-narcotic PS account for 0.8% (the Russian Federation – 1.1%) (Figure 1).

Therefore, of all substance dependence disorders in the Kostroma Region, special emphasis was placed on alcoholic disorders.

The highest levels of alcoholism with psychoses were observed in the Manturovo, Pyshchug, and Susanino districts respectively. In these districts, primary incidence of alcoholism is nearly 2–3 times higher than the average regional level (Figure 2).

For instance, primary incidence of chronic alcoholism with psychoses and alcoholic psychoses exceeded the regional level 2.8 times in the Manturovo District, 2.2 times in the Pyshchug District, and 2.1 times in the Susanino District.

Fundamental analyses of risk factors related to incidence of chronic alcoholism in the above-mentioned and other problems districts of the Kostroma Region identified a connection with considerable violations in moral, ethical, intellectual, and domestic spheres; violations of labor status; and vulnerable family status—these districts were characterized by frequent criminal offences, criminal records, prevalence of craniocerebral injuries, and organic diseases of the central nervous system.

The Kostroma Region's territorial entities showed the same rank distribution of chronic alcoholism prevalence indicators.

Questionnaire surveys among chronic alcohol addicts showed dependence of relevant indicators on age-sex structure, social status, family traditions, and friend-related social environment.

In the Manturovo District, most people are engaged in heavy manual labor (harvesting timber). In addition, a special commandant's office, special penitentiary institutions, and a large biochemical integrated plant has operated in this district since the 1990s. At present, after deinstitutionalization people stay and work in this district, forming specific social risk groups.

The Pyshchug District is characterized by ruined villages, predominant middle- and old-aged



population, unemployment, and low living standards.

The Susanino District is well-known for its widespread moonshining practices with oftentimes low-quality alcoholic products.

Medical aid appealability and, primarily, availability of drug therapists and psychiatrists play an essential role in registration of alcohol addicts. No incidence of chronic alcoholism was registered in the Kologriv and Neya district, where no drug therapists were available, with no diagnostic procedures for alcoholic disorders put in place.

In Russia, due to increased individual stress levels (measured using the Rider test), i.e. decreasing income level, personal threat, apprehensiveness, domestic conflicts and frustration, as well as the absence of institutions for compulsory medical treatment, low-quality alcoholic products cause a high prevalence of such chronic alcoholism-related complications as alcoholic psychoses. In this respect, the worst situation can be observed in the Pyshchug, Susanino, and Manturovo districts (Figure 3).

Analyses of primary incidence (39.7 per 100,000 people) of alcoholic psychoses in the territorial entities of the Kostroma Region made it possible to identify a connection between incidence of chronic alcoholism and factors determining efficiency of psychosis prevention. For example, incidence of primary psychoses exceeded the average regional level 4 times in the Pyshchug District, 3 times in the Susanino District, and 2.7 times in the Manturovo District, which is indicative of inefficient preventive measures for alcoholic psychoses.

In different territorial entities of the Kostroma Region, differences in drug addiction levels can be explained by a combined effect of social, biological, and economic factors, population density, communications levels, and levels of preventive measures. In terms of drug addiction prevalence, the worst situation can be observed in the City of Kostroma and in the Kostroma and Nerekhta districts. Most people who sought narcological medical advice were opium addicts; according to anamnestic data, 90% of them were people who used Desomorphine, a cheap and easily available drug made of polyvalent codeine-containing drugs available at pharmacies. Desomorphine abuse caused a considerable increase in heavy complications and a rise in mortality among drug addicts. Patients aged 20–39 and 18–19 account for 98.2% and 1.8% respectively. Most patients (83.3% in 2010) were men, while women accounted for only 16.7%. In this connection, the number of female patients has increased from 14.3% to 16.7% over the past.

Conclusion

In the territorial entities of the Kostroma Region, incidence and prevalence of chronic



alcoholism and drug addiction are caused by a combined effect of the following factors: addiction incidence and relapse risks and the organization of narcological aid.

In the territorial entities of the Kostroma Region, the main problem of incidence of substance dependence disorders is prevalence of alcoholic disorders, including chronic alcoholism.

For the purposeful prevention of substance dependence disorders, adequate organization of narcological aid (personnel, diagnostic, and financial resources) should be put in place in specific territorial entities, while taking into consideration the most relevant specific disorder risk factors: population structure in terms of age, sex, social status, education and employment levels, and family and local traditions.

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Summary

We present an evaluation and analysis of the changes in and territorial features of substance dependence disorders in the Kostroma Region, based on the 1999–2011 statistical materials that describe the structure and levels of primary incidence and prevalence. We determined the specific features of territorial differences in chronic alcoholism and drug addiction indicators. In addition, we determined their connection with disorder risk factors. No dependence was determined for chronic alcoholism levels on drug addiction indicators. For purposeful prevention of substance dependence disorders in specific districts, it is necessary to study specific disorder and relapse risk factors and the organization of narcological aid.

Key words: substance dependence disorders, chronic alcoholism, psychoses, drug addiction, territorial entities, Kostroma Region.

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Table 1

Primary incidence and prevalence of substance dependence disorders in specific territorial entities of the Kostroma Region in 2010 (in indicator ranks per 100,000 people)

No.	District	Primary incidence			Prevalence		
		Total	Chronic alcoholism	Drug abuse	Total	Chronic alcoholism	Drug abuse
1	Kostroma	9	12	3	7	6	1
2	Volgorechensk	12	13	7	25	25	7
3	Antropovo District	19	20	-	26	26	-
4	Buy District	17	18	-	23	24	11
5	Vokhma District	24	24	-	21	21	12
6	Galich District	13	11	-	16	16	-
7	Kadyi District	5	5	-	13	13	-
8	Kologriv District	-	-	-	20	20	-
9	Kostroma District	7	9	4	8	8	2
10	Krasnoselsky District	8	6	9	5	5	6
11	Makaryev District	15	14	-	22	22	-
12	Manturovo District	2	1	8	1	1	8
13	Mezha District	20	21	-	10	10	-
14	Neya District	-	-	-	18	18	-
15	Nerekhta District	6	8	2	9	9	3
16	Oktyabrsky District	18	19	-	19	19	-
17	Ostrovsky District	21	22	-	2	2	10
18	Pavino District	16	16	-	24	23	-
19	Parfenyevo District	11	10	6	14	14	9
20	Ponazyrevo	23	15	-	4	4	-
21	Pyshchug District	1	2	-	11	11	-
22	Soligalich District	22	23	-	6	6	-
23	Sudislavl District	3	4	1	3	3	6
24	Susanino District	4	3	-	17	17	-
25	Chukhloma District	10	7	-	12	12	-
26	Sharya District	14	17	5	15	15	4
	Total for the Region	242.8	113.7	19.9	3,052.1	2,374.5	166

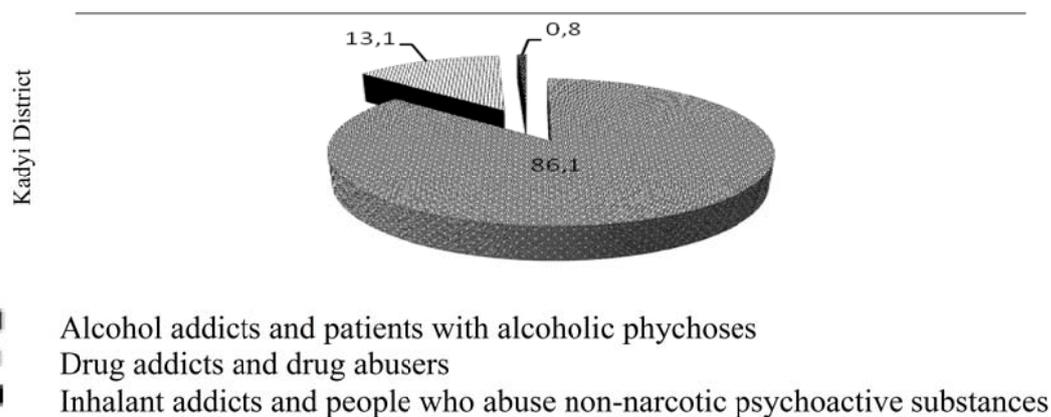


Figure 1. Structure of patients with substance dependence disorders in the Kostroma Region by disorder group (% of the total)

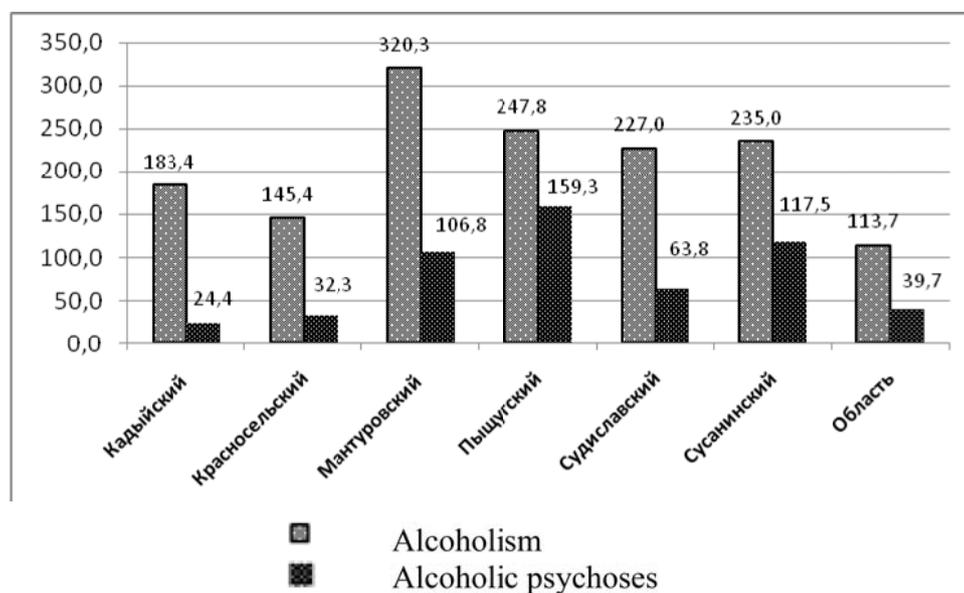


Figure 2. Primary incidence of chronic alcoholism and alcoholic psychoses in 6 districts where relevant indicators exceed the average regional data

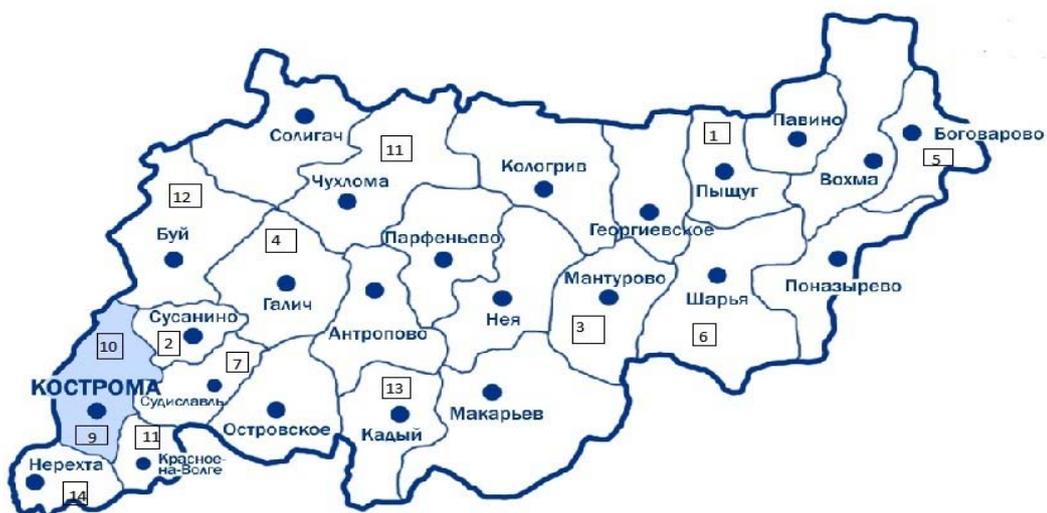


Figure 3. Incidence of alcoholic psychoses in different territorial entities of the Kostroma Region in 2010 (in ranks)



Diagnosis of inflammatory breast cancer

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Abstract. Diagnosis of edematous changes in the breast without clearly identifiable tumor is a challenging task. Differential diagnosis should include cancer and mastitis of various etiologies. The results of breast ultrasound, mammography, computed tomography and magnetic resonance imaging can be uninformative. Thorough examination of regional lymph nodes must be performed: presence of metastases in them, combined with clinical changes in the breast, confirms diffuse breast cancer. Any suspicious areas are subject to a biopsy. Echographic determined asymmetrical thickening of the skin over 3mm pathological evidence of edema.

Keywords: inflammatory breast cancer; ultrasound diagnostic, x-ray mammography, CT, MRI, multipoint vacuum– assisted biopsy.

Introduction. The breast cancer takes the first place among malignant tumors at women in Russia and European countries [5].

There are nodal and edematous forms of breast cancer. The development and clinical manifestations of inflammatory breast cancer are different from nodular breast cancer. Inflammatory breast cancer is characterized as a diffuse growing tumor mass, and it is difficult to prescribe anticancer therapy. At inflammatory breast cancer is an edematous affection with skin changes like “[peau d'orange](#)” and palpable lesion in the breast without clear boundaries. On a cut the inflammatory breast cancer looks like white-yellow thick strands or infiltrate which occupies the most part of breast or all it entirely [2].

Features of clinical manifestation of “diffuse” breast cancer with mastitis symptoms can lead to diagnostic errors and delay to initiation of treatment. This is extremely dangerous for patients with this form of breast cancer. For the diagnosis of inflammatory breast cancer we usually use medical imaging techniques: US, digital x-ray mammography, CT, MRI, biopsy under X-ray or ultrasound



guidance.

Each method of diagnostics has the restrictions of visualization the tumors connected with properties of a breast tissue and character of a tumor. It is considered that mammography is more informative method it patients older than 40 years, because of the fatty tissue and involutive process in breasts. Young women have high-density tissue hyperplasia of the glandular component and fabric, so the lesion could be occult in the breast tissue and using of X-ray mammography in these cases is reduced. In this situation, ultrasound is more informative [6].

CT in comparison with US and mammography in patients with inflammatory breast cancer allows detecting tumors in space under a breast and evaluating a degree of distribution of a tumor on a chest wall and skin changes in a breast, increasing in size of affected breast compared with the other. Using mammography is more precisely in cases when we need to appreciate the structure of breast tissue surrounding a tumor and vascularity of a breast. CT concedes mammography in detection preclinical breast cancer forms, therefore CT do not use in cases of nonpalpable breast cancer [10,11,12]. The MRI has high indicators of sensitivity (100 %) and specificity (90 %). MRI carry out on a system with intensity of a magnetic field of 1,0 Tl. The typical MRI examination produces after intravenous introduction of a contrast preparation. The patient put on a stomach; breast put in mammographic «coil» and creates a necessary compression of gland.

The diagnosis of breast cancer setting up after detection a lesion which drawing intensively and diffuse amplifies within two minutes after introduction of a contrast agent [9]. Specific signs of the inflammatory form of a breast cancer are not present [6].

Unlike other imaging techniques such as US, biopsy performance under MRI-guidance is technically more difficult and is applied in small numbers of clinics. This method is much more expensive and difficult.

At research “diffuse” breast cancer difficulties directed by the diagnosis because of bad visualization of volume formations. It extends the period of inspection and detains the beginning of necessary treatment. The increasing in number of out-patient visitings promotes additional financial expenses of medical institution.

Materials and methods.

The study involved 22 patients who applied to Herzen Moscow Institute of Cancer Research with complaints of discomfort and "feeling pressure" in the chest, as well as external changes of the breast. The age of all patients was 35-72 years (middle age was 51,4 years). Menstrual function was kept at 12 (54,5 %) patients, 10 (45,4 %) patients were in menopause.

At survey all patients had a typical clinical picture of edematous breast cancer: the breast

became larger, indurate and edematous. There were more expressed pigmentation and the strengthened venous drawing of a skin. All patients had a change in the skin, like an orange peel (peau d'orange), and in a half of cases (12 patients) it was combined with warmth and edema. Palpably we estimated lesion consistence and lesion was non-uniform, nodal formations was not defined. Some patients had a pain in the breast. In the beginning of inspection all patients were spent US and mammography. Results were negative in most cases, because volume formations in breast are not revealed. Metastases of a breast cancer are found out in half of patients (12 persons) in axillary lymph nodes. The diagnosis of a breast cancer was verified by using a fine needle aspiration biopsy under US-guidance. Accessory of a breast tumor was confirmed by immunophenotyping of metastasis cells and by additional surveys (repeated US, CT, biopsies of suspicious areas of the breast, looking at histological material under the microscope).

The patients without regional metastasis also made CT and MRI as an obligate part of medical inspection. At revealing of suspicious sites in these patients we spent repeated US, fine needle aspiration biopsy and large core biopsy or vacuum– assisted biopsy under US- guidance. Despite of precision and repeated biopsies we did not achieve the results in 5 patients. We applied to multipoint vacuum– assisted biopsy for removing samples of the breast tissue. Only 3 patients with red and edematous skin were being exposed to surgical biopsy of a skin for histologic research. Cancer cells are revealed only in 1 patient in this subgroup of patients. All patients established clinical diagnoses. A breast cancer was diagnosed in 20 patients (under the histologic form - ductal, lobular, ductal and lobular combination) and in 2 patients - a chronic mastitis. All diagnoses are confirmed by operation with histologic research and supervision not less than 1 year.

US- picture of “diffuse” breast cancer

In the B-mode the US- picture of inflammatory breast cancer is similar to the US- picture of a mastitis or fibrosis (picture 1).

Picture 1. US examination by using a linear transducer. The skin is thickened to 10 mm (1). Visible tissue section has a hypoechogenic heterogeneous structure similar to a tumor with irregular indistinct outlines. Histological research after biopsy identified fibrosis tissue.

All 22 patients had edematous skin. The skin thickness was varied from 3 to 10 mm. On the border of the skin and subcutaneous tissue revealed extensive lymphatic ducts and vessels as hypoechoic tubular structures from 1.2 mm to 2.6 mm. Breast tissue of increased echogenicity and heterogeneity, with significant attenuation of the echo signal. Adipose tissue in the affected breast is



hyperechoic compared to fatty tissue contralateral (healthy) breast. The described US semiotics was not very informative for differential diagnosis between “diffuse” form of breast cancer and a benign lesion. The detection of metastases in lymph nodes in the armpit we considered as an objective US criterion for breast cancer.

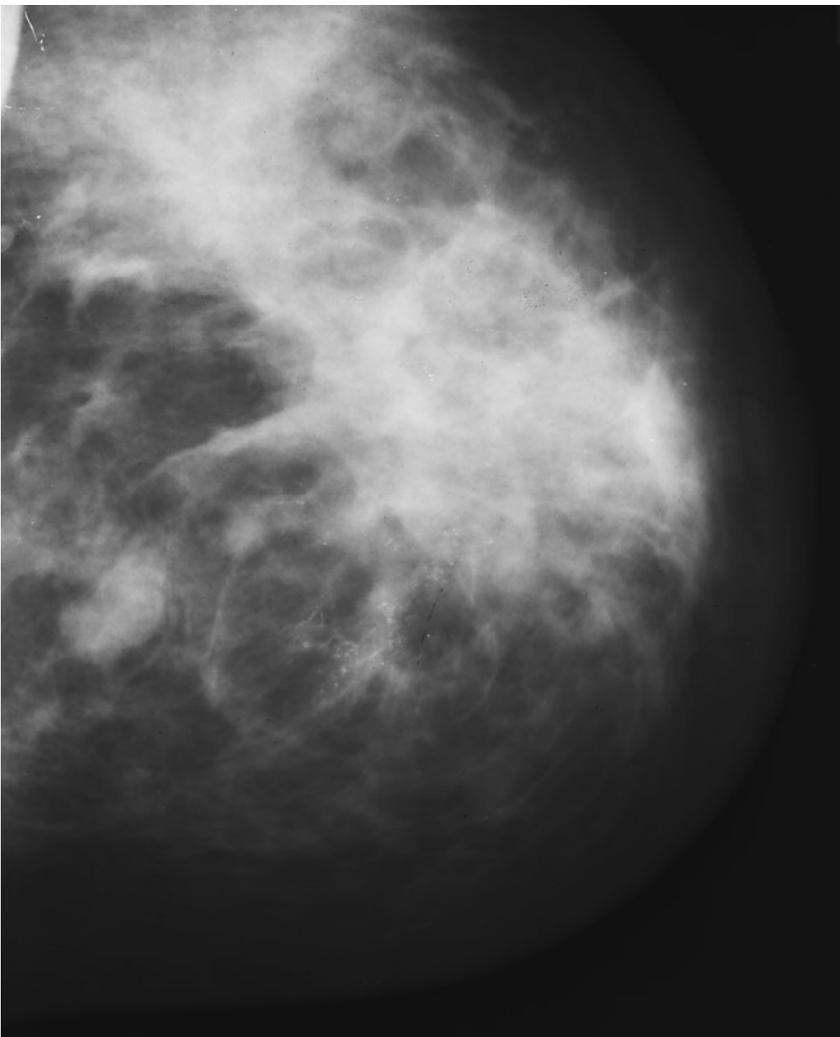
To evaluate the difficulties of differential diagnostic between “diffuse” forms of breast cancer and fibrosis we present the following observation.

Case report.

Patient M., 34 years old.

Diagnosis: cancer of the left breast stage IIIC, T4b N3 M0, inflammatory form (during the pregnancy). From the history: in October 2010, being at the 7th month of pregnancy of the third child she find her left breast increasing in size with a local lesion. The patient was being diagnosed a mastitis. In the immediate postpartum period the symptoms increased. Breasts were несимметричны. The left breast was red and swollen with hyperpigmentation on a skin. The patient was treated with herbal remedies and she has been prescribed to take Bromocriptine to suppress lactation as a recommendation of doctors who suspected mastitis. The treatment was not effective. The patient was suspected of breast cancer and she was sent to the Oncological Clinic. In a survey in Hertsen Moscow Oncological Research Institute we diagnosed breast cancer in the left breast - stage IIIb T4bN3M0, infiltrative-edematous form. On examination the left breast was edematous, increased in size (large than the other breast) with red skin, thickened areola and nipple retraction. Palpably at the boundary of the outer quadrants of the breast we defined a lesion without clear boundaries with [approximate](#) size of 3x3 cm. Also we found swollen [lymph nodes](#) in the armpit (1.5 cm in size).

The mammography picture: there was a lesion without clear borders about 8.0 cm in size in the outer parts. The differential diagnosis was between breast cancer and mastitis with fibrosis (picture 2).



Picture 2. Mammography picture of the left breast



(Pic. 3). The US- picture: edema of the skin and subcutaneous fatty tissue. The structure of the mammary glands was diffuse hyperechoic without clear boundaries. The skin was thickened to 10 mm. The nodulus or tumor were not visualized. Conclusion: infiltrative-edematous form of breast cancer.

CT scan showed a picture of a nodular tumor of the left breast, metastasis in lymph node in the left subclavian and axillary regions.

Histological examination of biopsy specimen revealed an infiltrative ductal carcinoma, lobular with the structures of cancer in situ. Receptor status: reaction with estrogen receptors was positive- 8 points, the progesterone receptors was negative - 0 points, reaction with Her2/neu receptors – 2 + (FISH amplification was not detected).



The patient carried out a comprehensive scheme of treatment: chemotherapy - surgery - radiotherapy - chemotherapy - hormone therapy. At follow-up examination one year after the operation revealed the generalization process (metastasis spread to the lungs and liver).

Conclusion.

Diagnosis of “diffuse” changes in the breast without clearly identifiable mass is a challenging task. Differential diagnosis should include breast cancer, fibrosis, fibroadenomatoid mastopathy and mastitis of various etiologies. The results of breast US, mammography, CT and MRI can be inconclusive. Thorough examination of regional lymph nodes must be performed: presence of metastases in them, combined with clinical changes in the breast, confirms “diffuse” form of breast cancer. Any suspicious areas are subject to a biopsy. In a clinical presentation suggestive on a “diffuse” form of a breast cancer, an accurate diagnosis should be sought in view of severe consequences of errors and delays in diagnosis. The most informative and effective method of detection skin thickness is US. US may show thickened skin in comparison with the skin of the other breast. Skin that thickened more than 3 mm is considered as a symptom of edema.

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The poll of TB institutions heads on key issues for improving TB care

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Summary: Analysis of the poll of antiphthisic institutions heads showed some problems of the organization of TB care in terms of national health care reform. The main ones are poor condition of buildings, low staffing levels of tuberculothapist, insufficient funding, lack of TB beds, low adherence to treatment of patients and incidence of tuberculosis, combined with HIV infection. Also the proposed measures to improve the effectiveness of TB services were studied.

Keywords: heads of TB institutions, questionnaires, problems of organization of TB care.

Introduction. According to research published in terms of modernization of national health care the so-called interstitial analysis of the effectiveness of the reforms with subsequent correction of the main directions of its further development is becoming increasingly important. At the same time an integral part of this analysis should be studying the views of managers of different levels and medical staff of various medical institutions including TB institutions.

In this regard, **the purpose of** our sociological study is to examine the views of heads of TB institutions on the main problems in organizing medical care for tuberculosis patients, and possible approaches to solving them.

Materials and methods. Questionnaires were conducted among the heads of regional and municipal TB institutions of the Irkutsk region. 74 heads of TB institutions were interviewed: 2 of them were the chief medical officers, 45 of them were department heads, and 9 of them were heads of branches of government health care - Irkutsk TB dispensary, and 18 heads of municipal antiphthisic institutions.

Results and discussion. The analysis revealed the following: the majority of respondents were at the age of 50 and older (59.5%), then comes the group at the age of 40 to 49 (23.0%), and the last respondents were at the age of 30 to 39 years (17.6%). The majority of respondents had overall medical experience about 25.7 years, the experience of working in a tuberculosis dispensary



- 21.9 years and experience as a manager - 7 years.

Most (87.8%) managers have graduated from medical faculty and 12.2% of pediatric faculty. A significant proportion (75.7%) of managers were certified in the specialty "Phthiology", at the same time one-third (29.7%) of the doctors had a certificate in the specialty "organization of health care and public health". 77.0% of doctors had higher qualification category, and the first category had 23.0% of them. 70.3% of doctors had an experience in leadership positions, more than half (58.1%) of respondents had this experience for 10 years, a quarter (25.7%) - 10-15 years, 16.2% - up to 20 years.

The survey showed that in assessing the current situation in health care, including in the activities of TB services the negative opinion dominates among doctors. Thus, the issue of assessing the health situation, the majority (51.4%) of managers rated it as "critical", 41.9% of them described it as "uncertain", and the remainder (6.8%) indicated that the overall situation is "stable". At the same time, the assessment of this situation in TB service, a significant portion (83.9%) of managers have rated it as "critical", only 16.2% of them characterized it as "uncertain." In this situation, none of the respondents assessed the situation in Phthiology as "stable" or "optimistic."

According to opinion of the majority (95.9%) respondents the most important influence on the development of the epidemiological situation of tuberculosis the socio-economic factors exerted, the second place (64.9%) took the socio-cultural factors, the third place (70.3%) took the epidemiological situation with HIV infection, the fourth place (47.3%) took medical-organizational factors, the fifth place (90.5%) took political factors and the sixth (81.1%) - characteristics of a population of *Mycobacterium tuberculosis*.

The study of heads' opinion about the problems of tuberculosis institutions in the organization of TB care in present-day conditions showed that the most pressing problems are the unsatisfactory material and technical condition of buildings, low staffing levels of tuberculothapist, this opinion was held by all respondents.

The next most important problems identified by managers, are the lack of funding (noted by 89.2% of respondents), lack of drugs (70.3%), inability to use modern methods of diagnosis (66.2%), lack of TB beds (67.6%), antisocial behavior of patients (64.9%). More than half (55.4%) of respondents indicated the low staffing levels of nursing staff, 43.2% of them reported a problem of imperfect legal framework and outdated equipment, 27.0% of them reported lack of skills, 24.3% of respondents reported lack of medical and social work among the socially maladjusted contingent, 21.6% of them reported lack of proper linkages to other health facilities and lack of TB alertness among other doctors.

All respondents reported some changes in TB facilities in recent years, in particular the increase of medical documents, 64.9% of respondents reported an increase of volume and intensity of work, 60.8% of them noted the reduction in performance, 51.3% of them noted the worsening staff shortages, 23.0% of respondents reported lack of attention from the executive to the issues of tuberculosis, 8.1% of them noted the reduction of funding, 6.8% of them reported the difficulties of



interacting with other hospitals.

According to the opinion of the majority (74.3%) of the heads the current regulatory and legal framework governing the work of TB facilities does not meet modern requirements in the new socio-economic conditions. In particular, the following topics require extensive and detailed work on: all the respondents noted the issues of compulsory treatment of tuberculosis patients, issues of drug supply for treatment and prevention of tuberculosis among HIV-infected patients (97.3%), preventative work (83.8 %), social protection of patients and physicians (78.4%); regulation of doctors' loads (31.1%), interaction with departmental agencies (21.6%), organization and controlling the foci of tuberculosis infection (12.2% .)

The availability of tuberculothapist is not sufficient. The availability of nursing staff is better, as noted all the respondents. The majority (71.6%) of heads noted that the number of doctors in their institution does not meet the required standards, at the same time 83.8% of respondents reported that the number of nursing staff meets relevant staff standards.

Among the main causes of insufficient staffing, according to the opinion of all the respondents, is an occupational hazard. 78.4% of respondents noted the reluctance of young professionals to work in rural areas, 56.8% of doctors pointed to a low pay, 36.5% of them reported that there are no adequate conditions for work, 29.7% of them noted low prestige of the profession.

Heads' opinions on the staffing problems showed that almost all of them (97.3% of respondents) noted the need for executive agencies to develop some measures aimed at providing the staff with accommodation, subsidized mortgage lending and other measures of social protection. At the same time, 71.6% of respondents believe that one of the mechanisms of medical personnel staffing should be targeted at training them from the bench of the university. In 68.9% of cases it's a rise of wages, perhaps due to the introduction of targeted regional surcharges. In 44.6% of cases it's a development and introduction of incentive pay for health care workers, depending on their qualifications, workload, quality and efficiency of work, in 33.8% of cases it's an adaptation the organization of workers, the development of adaptive program, which could include the system of mentoring for young professionals, in 24.3% of cases it's the insurance of medical personnel in case of occupational disease and in 5.4% of cases it's the improvement of training and retraining of doctors and other medical staff.

When asked about the changes that occurred in the work of TB doctors in 91.9% of cases they noted an increase of different documentation, in 73.0% cases they indicated the need for getting greater professional knowledge, in 44.6% of cases they noted an increase in volume and intensity of work performed.

According to most respondents, the activities in the framework of the Priority National Project "Health" generally positively impact on the activities of health facilities of general health care for the early detection of tuberculosis among the population, in particular, in 94.6% of cases the respondents referred to the increased coverage of preventive examinations for tuberculosis, in 93.2% of cases they noted better equipment with X-ray for health facilities. But at the same time,



the impact on improving the quality of screening for tuberculosis, and improving the performance of the TB service did not note anybody from the respondents.

When asked about the proposals to improve the effectiveness of early detection of tuberculosis among the population, the respondents' opinions on the importance of these responses were as follows: in 89.2% of cases they referred to the need to strengthen monitoring of the diagnostic minimum for the early detection of tuberculosis by physicians of general medical health facilities, 85.1% of respondents noted the necessity of additional equipping health facilities of general health care with laboratory equipment, in 73.0% of cases they noted the need for increasing the responsibility of health facilities of general health for the early detection of tuberculosis among the population, in 68.9% of cases they referred to the need to use more widely the method of microscopy for the early detection of tuberculosis in health facilities of general health, in 64.9% of cases they referred to the need for the legal consolidation of the functions of TB control services for the early detection of TB in health facilities of general health, in 60.8% of cases they prefer the use of a differentiated approach to testing for tuberculosis (including the risk groups), in 47.3% of cases they want a large-scale programs to improve health literacy in the prevention and treatment of tuberculosis in order to improve medical treatment, in 9.5% of cases the respondents noted the need of increasing availability of doctors internists, general practitioners and pediatricians, in 4.1% of cases they referred to the need of mobile fluorographs for areas with low population density.

Overall, the poll of the heads showed that there is not only decrease of the effectiveness of early detection of tuberculosis among the population, but also there is reduced indication of TB services for the treatment and dispensary observation of patients with tuberculosis. Thus, the main reasons for reducing the effectiveness of a surveillance and treatment of patients with tuberculosis are: patients with antisocial behavior (noted in 86.5% of cases), lack of TB beds (67.6% of cases), inadequate supply of drugs for the treatment of comorbidity (in 66, 2%), lack of interaction with the AIDS center, mental and narcological health services (in 60.8% of cases), the defects in the organization of prevention work and survey of contact persons in hospitals were reported in 45.9% of cases, for defects in the TB doctors' work they reported in 37.8% of cases, about one-third of respondents (28.4%) reported the deficit of tuberculothapist, other specialists and lack of laboratory and diagnostic equipment (27.0%), in 20, 3% of cases it was noted the lack of interaction with departmental bodies and agencies.

All the respondents noted that the main reasons for reduction of the effectiveness of hospital treatment of tuberculosis patients are a violation of the treatment regimen of patients and premature discharge, in 70.3% of cases - lack of TB beds, in 56.8% of cases - the lack of provision of medicines for the treatment of concomitant pathology, in 47.3% of cases - an increase of TB patients, combined with HIV infection and clinical weighting structure breaker, in 29.7% of cases - the lack of laboratory equipment and diagnostic equipment, in 28.4% of cases - shortage of TB doctors.

All the heads made the following proposals to improve hospital care and outpatient treatment of TB patients: the development and implementation of measures to improve adherence to tuberculosis treatment, the organization of supervised treatment to outpatient treatment, restructuring and alignment with the need for hospital beds for TB services, improving sanitary condition of buildings, bringing the equipment of TB services in accordance with the standards, the



solution of the legal issues of compulsory treatment of TB patients.

Conclusion. Thus, a study of the opinions of the heads of TB facilities showed that there are many problems in the care of TB patients at this stage. The main ones are: poor material and technical condition of buildings, low staffing levels of tuberculothapist, insufficient funding, lack of drugs, the inability to use modern methods of diagnosis, lack of TB beds, and antisocial behavior of patients. According to most respondents, in addition to the above reasons the growth of tuberculosis combined with HIV infection and the need for better screening for tuberculosis also can be added.

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ANALYSIS OF ACCUTE INTESTINAL INFECTIONS MORBIDITY BY INTEGRAL INDICATOR IN THE REPUBLIC OF SAKHA (YAKUTIA)

Summary. The paper presents data of complex epidemiological analysis of acute intestinal infections in the Republic of Sakha (Yakutia) for the period from 2002 to 2011.

Keywords: acute intestinal infections, dysentery, morbidity, the epidemiological situation, the integral indicator.

Introduction. Infections of fecal-oral transmission hold a significant position among inflectional pathologies. With Russia annually witnessing 600-700 thousand people catching acute intestinal infections (AII), their number in the past decade (2002-2011) totaled to over six million people. The negative impact of these infections is even greater due to the fact that the infections hit primarily children, making up to 60% of the patients; and they also result in hundred-million-ruble-worth economic damage. The situation with acute intestinal infections is especially severe on the territory of the Siberian and Far-Eastern regions, regarded as the territories with a risk of the fecal-oral transmission occurrence [1, 4, 6, 7].

The recent years have also seen global transformation of the AII morbidity structure and changes in some epidemiological peculiarities of certain groups of acute intestinal infections. For example, the territories with established laboratory diagnostics of the rotavirus infection have seen transfer of the diseases which used to be registered as acute intestinal infections of **unknown** etiology (AIIUE) to the group of acute intestinal infections of **known** etiology (AIIKE). At the same time we must remember that the AII occurrence is extremely uneven, that is to say that there are territories with different incidence and the epidemiological situation, from region to region, can change from favorable to very unfavorable.

Given the above, **the present paper aims** at analyzing the epidemiological situation with acute intestinal infections on the territory of the Republic of Sakha (Yakutia).

Materials and Methods. We have analyzed the multiyear morbidity of shigellosis, AIIKE, AIIUE, as well as such integral indicator as total AII (shigellosis + AIIKE + AIIUE) for the past ten years (2002 – 2011).

The morbidity data was processed statistically with the use of common parametrical and



non-parametrical statistical criteria with preliminary testing of the dynamic rows for normalcy of distribution [3, 4]. We also used integral epidemiological indicators. The algorithm of their calculation is called the method of “occupied cells sum” [2, 8, 9], which selects the list of territories and indicators for comparison. Each of the indicators is ranged (from minimum to maximum) for a certain period of time, then they are summed up giving the integral indicator (II) as a sum of a certain indicator or object cells.

At the final stage of the method, the illustrative coefficient (K_i in %) is calculated with the following formula:

$$K_i = \left(1 - \frac{S_x - S_p}{S_x - S_y} \right) \times 100$$

where S_x - the worst sum of cells; S_p - the sum of cells for a certain object; S_y - the best sum of cells. The worst sum of cells (S_x) is determined by the formula: $S_x = x \times n_1$, where x – is the number of members from the dynamic row selected fro ranging; n_1 – is the number of indicators selected for analysis. The best sum of cells (S_y) corresponds to the number of indicators selected for analysis or the number of the years of monitoring.

Results and discussion. Table 1 illustrates main indicators of the multiyear dynamics of acute intestinal infection morbidity in the Republic of Sakha (Yakutia) (RS(Y) and the Russian Federation (RF).

Table 1

**Indicators of the multiyear dynamics of acute intestinal infection morbidity
in 2002 – 2010**

Types of AII	Territory	\bar{M}	$\pm m$	Criterion t	Regression equation ($Y=ax+b$)**	Rate of increase
Shigellosis	Russian Federation	29.7	4.6	115.2 $P < 0.01$	$-5.5x + 60.0$	-24.1
	Republic of Sakha (Yakutia)	\uparrow *56.3	17.2		$-12.2x + 123.5$	-38.7
AIIKE	Russian Federation	113.0	6.6	127.2 $P < 0.01$	$7.6x + 71.1$	8.4
	Republic of Sakha (Yakutia)	\downarrow *78.6	10.7		$5.8x + 46.8$	9.3
AIIUE	Russian Federation	324.5	10.6	18.9 $P < 0.01$	$9.6x + 271.7$	3.3
	Republic of Sakha (Yakutia)	\downarrow *315.7	28.4		$14.4x + 236.7$	5.4
Total AII	Russian Federation	467.2	14.6	33.4 $P < 0.01$	$11.71x + 402.8$	2.9
	Republic of Sakha (Yakutia)	\downarrow *450.5	37.6		$7.9x + 407.0$	2.0

Notes: * \uparrow lower, \downarrow higher in comparison with the RF data;

** $Y=ax+b$, where Y – a theoretical indicator of a dynamic row, a – a regression coefficient, x – an index number of a dynamic row, b – the starting level of a dynamic row.

The comparative analysis of the data shows that out of all kinds of the inflectional pathology for the studied period, the shigellosis morbidity statistically significantly ($p < 0.01$) exceeded the all-Russian level. For all the other compared kinds of inflectional pathologies, the inflectional morbidity in Yakutia was considerably lower than in the RF. At the same time, analyzing the long-term dynamics of morbidity one may conclude that the only AII kind that showed any significant ($p < 0.01$) reducing pattern is bacterial dysentery, both in the Russian Federation and in Yakutia. And this trend was more obvious in the republic than in the entire RF, which is proven by the presented regression equations and rates of growth, describing the process of decrease in shigellosis morbidity for both the territories (see Table 1).

Over this long period, the rest of the inflectional pathology forms (AIIKE, AIIUE and total AII) showed a considerable trend for growth, both in the entire Russian Federation and Yakutia, in particular.

Analyzing the average multiyear morbidity rate for the studied AII forms by their errors, one may conclude that the long-term dynamics of the inflectional pathology epidemic process in the



Republic of Sakha (Yakutia) is characterized by greater instability than the RF data, which is seen in the relation between the minimum and maximum figures in the studied morbidity dynamic rows:

Shigellosis	RF – 1 to 5.2;	RS(Y) – 1 to 9.8;
AIIKE	RF – 1 to 1.7;	RS(Y) – 1 to 4.4;
AIIUE	RF – 1 to 1.4;	PC (Я) – 1 to 2.3;
Total AII	RF – 1 to 1.3;	RS(Y) – 1 to 2.1.

The study of the morbidity structure $\sum All$ showed that in general, for the monitored period, it is as follows: shigellosis accounted for 12.6 ± 2.8 %, AIIKE 17.4 ± 1.6 % and AIIUE 70.0 ± 3.2 %. At the same time, the structure of the studied inflectional pathology forms considerably changed over the past 10 years. For example, while in 2002 shigellosis accounted for 30.1% in $\sum All$, in 2011 this parameter fell to 3.7%; the share of AIIKE increased from 13.1 % to 27.2 %; AIIUE – from 56.7 to 69.1%, respectively for the same years. This change in the morbidity structure results, first of all, from extremely intensive decrease in bacterial dysentery morbidity rate (see Table 1).

Therefore, we have established that the epidemiological situation in the Sakha Republic (Yakutia) is more serious than in the Russian Federation.

Next we studied in detail epidemiological peculiarities of intestinal infections in children and adults in the RS(Y). We found out that the largest share falls on children under 14 years, making 69.6 ± 1.1 %; with the children population share ranging from 61.3 % to 76.8 %.

For the monitored period (2002-2011), both in adults and children, the dominant acute intestinal infections were those of the unknown etiology, making 77.8 ± 1.6 % and 66.5 ± 2.3 % , respectively. The average multiyear figure of AIIUE morbidity exceeded the one for AIIKE in adults by 10.1 times and for dysentery by 2.5 times, and in children – by 3.1 and 5.9 times, respectively ($p < 0.01$). In the long term, the statistically significant increase in occurrence of acute intestinal infections of unknown and known etiology was found in children only ($p < 0.01$, $p = 0.05$). At the same time, both in children and adults there was a significant decrease in shigellosis morbidity ($p < 0.05$), with this process being more intense in adults than in children (Table 2).

The studied period showed some changes in the structure of the studied inflectional pathology forms. For example, in 2002 shigellosis in the age group under 14 years accounted for 18.1% in $\sum All$, and in 2011 this figure dropped to 2.4 %; AIIKE share increased from 10.7 % to 25.8 %; and AIIUE share – from 32.5 % to 44.7 % , respectively for the same years. In adults, shigellosis share in $\sum All$ decreased from 12.1 % in 2002 to 1.3 % in 2011; whereas the share of AII of known and unknown etiology did not change significantly.

Table 2

**Multiyear dynamics of acute intestinal infections morbidity
in different age groups in the Republic of Sakha (Yakutia)
for the period 2002 – 2010**

Inflectional pathology	Age group	\bar{M}	$\pm m$	Share (%)	Regression equation ($Y=ax+b$)*	Rate of increase	Trend
Shigellosis	children	154.1	43.1	64.6	$-31.8x + 323.7$	-36.2	$P < 0.5$
	adults	26.1	9.5	35.4	$-6.3x + 60.9$	-168.8	$P < 0.5$
AIIKE	children	300.3	50.6	86.5	$33.7x + 114.8$	16.4	$P = 0.5$
	adults	13.8	1.1	13.5	$-0.8x + 18.0$	-6.3	$P > 0.5$
AIIUE	children	915.4	99.7	65.9	$73.1x + 513.9$	10.3	$P < 0.1$
	adults	139.6	9.6	34.1	$0.6x + 136.0$	0.5	$P > 0.5$
Total AII	children	1369.8	139.5	69.3	$77.8x + 941.8$	6.9	$P > 0.5$
	adults	179.5	19.9	30.7	$-6.449 + 214.9$	-3.9	$P > 0.5$

Notes: * $Y=ax+b$, where Y – a theoretical indicator of a dynamic row, a – a regression coefficient, x – an index number of a dynamic row, b – the starting level of a dynamic row.

The lowest shigellosis morbidity rate in RS(Y) adults was 6.8 ‰ (2007), the highest – 99.3 ‰ (2002). In children under 14 years, over the studied period, dysentery morbidity rate decreased by 7.8 times, with the lowest figure registered also in 2007 (26.9 ‰), and the highest – in 2002 (445.4 ‰). The share of children under 14 years in shigellosis morbidity, over the studied period, was $64.6 \pm 1.9\%$ (Fig. 1).

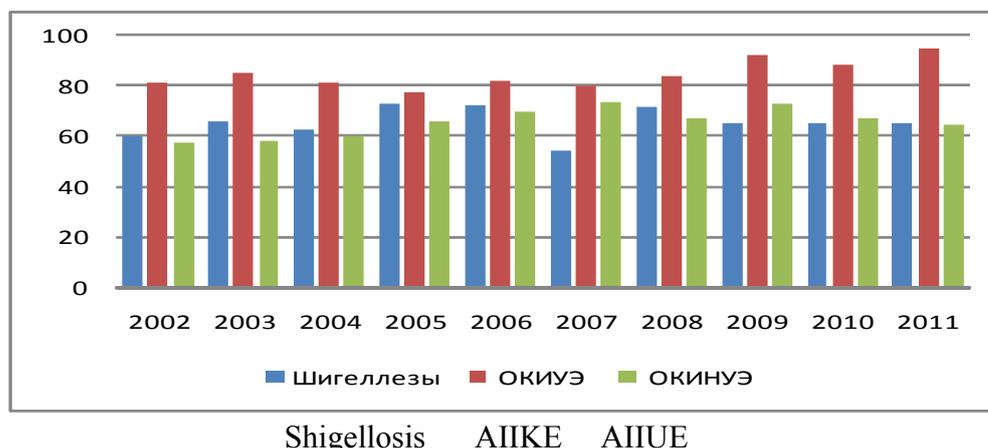


Figure 1. Share of children under 14 years in AIIKE, AIIUE and shigellosis patients in the Republic of Sakha (Yakutia) (%).

Over the monitored period, the rate of AIIKE morbidity in children increased by 2.3 times, reaching the maximum in 2011 (606.7 ‰). In adults, the figures decreased from 20.0 ‰ in 2002 to 8.9 ‰ in 2011; however, this trend failed to show any statistically significant values ($p > 0.05$). The shares of children under 14 years in AIIKE morbidity structure for the studied period was above 77.7 %, and, on average, made $86.5 \pm 1.8\%$ (See Fig. 2).



The morbidity rate for intestinal infections of unknown etiology in adults ranged widely from 107.5⁰/₀₀₀₀ (2006) to 206.5⁰/₀₀₀₀ (2010). In children under 14 years, AIIUE morbidity for the period 2002-2011 increased by 1.3 times ($p < 0.01$), reaching its maximum in 2010– 1521.9⁰/₀₀₀₀. The adult population did not follow this pattern ($p > 0.05$). The major share in AIIUE patients for the studied period fell on children under 14 years ($65.9 \pm 1.7\%$) (See Fig. 1).

Analyzing the morbidity rate for the AII total, we note that while this figure increased in children, the adult population demonstrated the trend for decrease, which, however, failed to be statistically significant ($p > 0.05$).

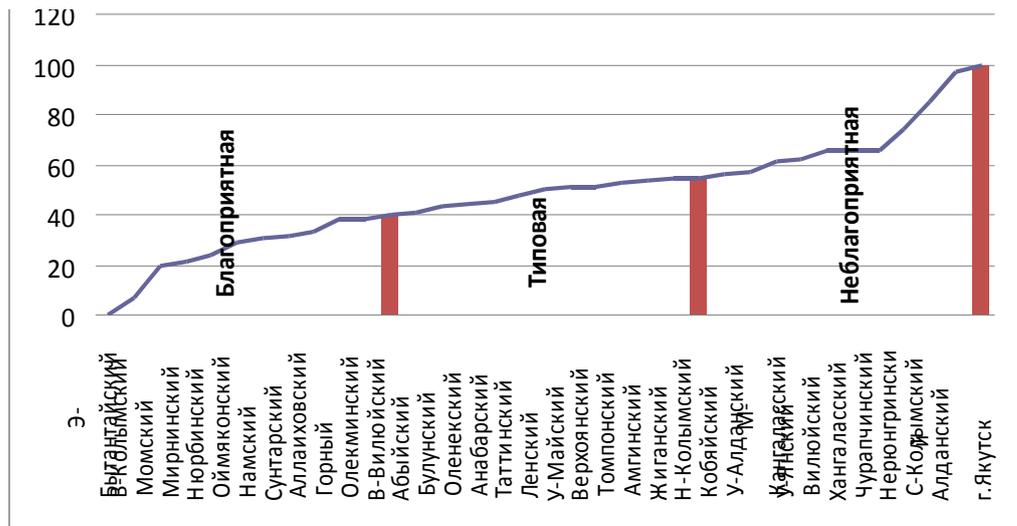
The next stage in our research was the comprehensive analysis of the epidemiological situation with acute intestinal infections in regions of the Republic of Sakha (Yakutia). Here we used the method of integral analysis “by the occupied cells sum”.

The analysis covered morbidity rates for shigellosis, AIIKE and AIIUE in adults and children under 14 years in ten years (2002 – 2011) for each administrative unit of the republic. For calculation of the integral indicators, we analyzed all the 35 administrative units.

The analysis done makes it possible to divide the republic into three categories of the epidemiological situation, namely:

14. favorable;
15. typical;
16. unfavorable;

Then, the AII epidemiological situation in the regions of the RS(Y) in adults and children is as follows (Figures.2, 3).



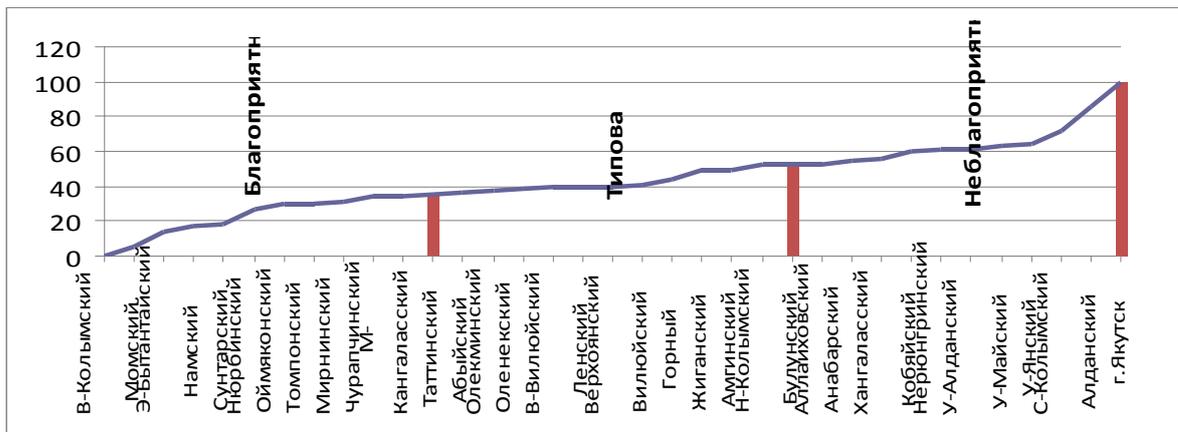
E-Bytantaisky
V-Kolymsky
Momsky
Mirninsky
Nyurbinsky
Oimyakonsky
Namsky
Suntarsky
Allaikhovskiy
Gorny
Olyokminsky
V-Vilyuisky
Abyisky
Bulunsky
Olenyoksky
Anabarsky
Tattinsky
Lensky
U-Maisky
Vekhoyansky
Tomponsky
Amginsky
Zhigansky
N-Kolymsky
Kobyaisky
U-Aldansky
M-Kangalassky
U-Yansky
Vilyuisky
Khangalassky



Churapchinsky
Neryungrinsky
S-Kolymsky
Aldansky
Yakutsk City

Figure 2. Epidemiological situation with AII in adults for regions of the Republic of Sakha (Yakutia), given integral indicators (II).

The analysis of the epidemiological situation data with the use of integral indicators enabled detection of the territories with the worst situation with acute intestinal infections. Out of 35 regions of the republic of Sakha (Yakutia), 11 regions have an epidemiological situation which is considered unfavorable. In both the adult and children population, the worst epidemiological situation is observed in Aldansky and S-Kolymsky regions, and the city of Yakutsk, being the largest city of the republic. The most favorable situation is observed in V-Kolymsky, Momsky and E-Bytantaisky regions, both in adult and children.



V-Kolymsky
Momsky
E-Bytantaisky
Namsky
Suntarsky
Nyurbinsky
Oimyakonsky
Tomponsky
Mirninsky
Churapchinsky
M-Kangalassky
Tattinsky
Abyisky
Olyokminsky
Olenyoksky



V-Vilyuisky
Lensky
Vekhoyansky
Vilyuisky
Gorny
Zhigansky
Amginsky
N-Kolymsky
Bulunsky
Allaikhovsky
Anabarsky
Khangalassky
Kobyaisky
Neryungrinsky
U-Aldansky
U-Maisky
U-Yansky
S-Kolymsky
Aldansky
Yakutsk City

Figure 3. Epidemiological situation with AII in children for regions of the Republic of Sakha (Yakutia), given integral indicators (II).

Conclusion. Therefore, the analysis of AII morbidity in population of the Republic of Sakha (Yakutia) showed that over the period from 2002 to 2011, along with significant decrease in shigellosis morbidity, there was increase in AII of known and unknown etiology, which is in line with the all-Russian trend. Shigellosis morbidity in the Republic of Sakha (Yakutia) was registered at a statistically higher level compared to the similar data for the Russian Federation. Children under 14 years made the largest share of the patients, under the dominance of acute intestinal infections of unknown etiology. Dysentery morbidity tended to decrease, both in children and adult population. In children population, there was a trend for increase in acute intestinal infections morbidity, both of unknown and known etiology.

In addition, we detected the AKI risk territories in adults and children in the Republic of Sakha (Yakutia). It was established that the city of Yakutsk is a zone of epidemiological problems.

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EXPRESSION OF SUPERFICIAL MARKERS ON PERIPHERAL BLOOD LYMPHOCYTES IN IHD PATIENTS IN THE CONDITIONS OF YAKUTIA.

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Abstract

A research objective was an assessment of an expression of superficial markers of lymphocytes in patients with IHD of a various form depending on ethnicity. The received results of the comparative analysis depending on IHD form allow to confirm that destabilization of IHD is characterized by increase of an expression of CD19 + (B-lymphocytes), activation markers of CD25 + (a receptor to IL-2) and CD71 + (a transferrine receptor), and also molecules of intercellular adhesion of CD54 + (ICAM-1). At unstable angina in persons of native nationality signs of deficiency of the T-cellular link (T-lymphocytes, T-helper), and also significant increase of expression CD11b + (integrine) in comparison with persons of non-native nationality are revealed.

Keywords: atherosclerosis, stenocardia, immune system, activation antigens.

Introduction.

According to modern views, the atherosclerosis is considered as a number of consistently developing cellular and molecular infringements which can be described as chronic inflammatory disease [4]. The quantity increase monocyte - and granulocyte - trombocytting complexes, observed at patients with atherosclerosis, according to researchers, testifies to activation of inflammatory process in the damaged vein. At the development of cardiac infarction and an unstable stenocardia the intracoronary thrombosis developing on a place of rupture, damage of an atherosclerotic plaque or endothelium erosion [2]. A number of authors considers leukocyte - trombocyte aggregation and aggregation of leucocytes as a possible key link of development of sharp coronary syndromes [14]. Along with distinct spontaneous aggregation of trombocyte in vivo the literary data testifies about various changes and decrease aggregation of trombocytes blood plasma in vitro at patients with cardiac infarction during the sharp period [15]. Leukocyte – trombocyt adhesions on extracellular matrix and intercellular aggregation act as a ligand of molecula ICAM-1: α IIb / β 3 and β 1-bound интегрини, P-selektin - PSGL (P-selectin glycoprotein a ligand-1) and CD40 - CD40L [6].

At sharp coronary syndromes there is an activation of trombocytes, monocytes and granulocytes of peripheral blood. The quantity increase monocyte - and granulocyte - trombocyte the complexes, observed at patients with an atherosclerosis, according to many researchers, testifies to activation of inflammatory process in the amazed vessel [16, 9].



Participation T-lymphocyte in atherogenesis is caused by their role in an antigen recognition, clone expansion, initiate the cellular-mediated inflammatory answer and is confirmed by results immunological the researches showing an associatively of demonstration of clinical symptoms of an atherosclerosis and processes T-cellular activation [10]. It is shown the chronic T-cellular activation accompanied by increase of quantity lymphocyte which expressed activate antigens, it is observed not only in a damage zone, but also in peripheral blood and meets at patients various forms of an atherosclerosis [3, 12].

Believe that activation of T- lymphocyte and, most likely, CD4 +-T- helpers occurs in the T-zone of lymph nodes, whence the activated T-cells migrate in corresponding sites of a vascular wall [5]. The estimation of the immune status patients of atherosclerosis has allowed establishing at them essential disbalance immunological parameters, characterized by high activity humoral immunity interfaced to relative deficiency T-cellular link of immune system [1]. Quantitative changes circulating lymphocytes, expressing activating antigens can be reflexion activating processes in a zone of damage of a vessel

Interaction of blood cells with a vascular wall is the major component of immune protection of an organism, providing constant transvascular migration lymphocytes in tissue and lymph nodes with view of detection of alien antigens. Besides it, the expression in the conditions of damage of fabrics adhesion molecules on endothelium and inflammatory blood cells is to their initial stages recruiting in the centre of an inflammation and initiates a wide spectrum of changes, in the basic, protective character, but resulting at excessively long and intensive activation to additional development dystrophic and necrotic changes. [7]. Thereby, considering small number and discrepancy of the data about a functional condition lymphocytes at atherosclerosis, and also existing ethnic distinctions on growth of disease and death rate from cardiovascular diseases of native population at smaller expressiveness of an atherosclerosis of coronary arteries, than at nonnative Yakutia, considerable interest is represented by an estimation of an expression of superficial markers lymphocytes to peripheral blood at patients ischemic heart disease (IHD) of the various form (a stable and unstable stenocardia) depending on an ethnic accessory.

Materials and methods. Into research have entered 71 sick IHD (all men, middle age $54,6 \pm 7,1$ years). All patients have divided on two groups depending on form IHD: 1 group included 32 patients with the diagnosis stable stenocardia (middle age $53,75 \pm 1,29$ years); into 2 group have entered - 38 patients ИБС with an unstable stenocardia (branch of resuscitation and intensive therapy), middle age $58,56 \pm 1,61$ years. Subsequently these groups have separately been divided depending on an ethnic accessory: in 1 group of patients with a stable stenocardia of the person of



native (Yakuts) have made 13 men, nonnative - 19 men. In group of patients with an unstable stenocardia of the man of a native have made 22, nonnative - 16 persons.

For immunological researches used lymphocytes, allocated of peripheral blood of patients. Blood took away on an equal footing: in the morning, on an empty stomach, in volume 5 - 7 ml. Immunofenotyping of lymphocytes spent a method flowing cytometry (FACSCalibur, Becton Dickinson) with use monoclonal antibodies with a threefold label: CD3FITC + CD4RPE + CD45RPE-Cy5; CD3FITC + CD19-RPE + CD45RPE-Cy5; CD3FITC + CD8RPE + CD45RPE-Cy5; CD16FITC + CD19RPE + CD3RPE-Cy5; with one label CD25-RPE; CD11b-RPE; CD71-FITC; (Dako); CD54-RPE, CD95-RPE (Becton Dickinson), CD62L-FITC (Sorbent, St.-Petersburg). Relative maintenances of lymphocytes, expressive following markers are analysed: CD3 + - T-lymphocytes; CD4 + - T-helpers; CD8 + - cytotoxic T-lymphocytes; CD16 + - NK - killers; CD19 + - B - lymphocytes; CD11b + - α M - chain integrin; CD25 + - α - chain of receptor ИЛ-2; CD54 + - adhesion receptor ICAM - 1; CD62L + - adhesion molecule L-selectine; CD71 + - receptor transferrine; CD95 + - proapoptosis marker.

Results and discussion. The carried out analysis of the indicators characterizing structure of the basic subpopulations of peripheral blood of patients IHD, has revealed at sick of an unstable stenocardia significant increase of relative and absolute maintenance CD19 + in comparison sick of a stable stenocardia (tab. 1). Thus the greatest average value of relative and absolute maintenance CD19 + is marked at persons of native without significant distinctions (tab. 2). Comparison of parameters of the T-cellular link of immunity depending on forms IHD has no significant distinctions, and average values are in limits reference sizes. However, at comparison of indicators sick of an unstable stenocardia depending on an ethnic accessory has revealed that at native men signs of T-cellular deficiency, i.e. decrease in relative and absolute maintenance CD3 + and CD4 + (tab. 2) are observed. An estimation immunoregulate index (IRI), i.e. parity of number CD4 + and CD8 + (the norm 1,6 - 2,2) depending on form IHD has shown a tendency of distinctions ($p=0,06$). The least average value IRI is observed at persons of a radical nationality at an unstable stenocardia at the expense of expressed decrease CD4 + (T-helpers).

For an estimation of ability of cages of immune system to activation by us it is spent fenotyping "early" CD25 +, CD71 + and "late" CD95 + activation markers. CD25 + - receptors to IL-2 expressed mainly on activated T-helpers. The increase in their number arises at proliferation T-cells under the influence of T-cellular рострового growthing factor IL-2, and maintenance CD25 + positive cells above 15 % testifies to activation of immune system. Comparison of groups depending on form IHD has shown significant increase relative ($p=0,006$) and the absolute



maintenance ($p=0,01$) CD25 + at sick of an unstable stenocardia, than at sick of a stable stenocardia. Comparison depending on an ethnic accessory has not revealed significant distinctions, however in group sick the unstable stenocardia marks a tendency to increase of relative and absolute maintenance CD25 + positive cages ($p=0,09$) at persons of not radical nationality.

CD71 + (receptor of transferrine) is early activation marker of lymphocytes appears on leukocytes at their activation. It is found out on the majority of sharing cells. Increase of number CD71 + lymphocytes with high proliferate activity reflects processes of activation of immune system, occurrence of early predecessors, infringement of normal process of maturing immunocytes. The relative and absolute maintenance of lymphocytes with high proliferate activity, expressing CD71 +, at an unstable stenocardia has appeared significantly above, than at a stable stenocardia ($p=0,042$; $p=0,036$, accordingly). At comparison of groups depending on ethnic accessory significant distinctions are revealed at a stable stenocardia: at nonnative relative and absolute maintenance CD71 + has appeared above, than at native though values are in limits of referential sizes.

It is necessary to underline that there are fundamental distinctions between consequences apoptose of endothelium and inflammatory cells in a zone of damage of a vessel. CD95 + (Fas, APO-1) concerns family of receptors of the factor necrosis to a tumour/factor of growth of nerves, it is presented mainly on T-cells, in particular, on T-helper. The increase in number of cages with CD95 + - the receptors perceiving a signal of an induction apoptosis, can reflect as activation of immune system (CD95 + - a marker of "late" activation), well a readiness marker to apoptose. In our research average values of relative maintenance CD95 + in all investigated groups exceed referential sizes, and the greatest value is marked at sick of an unstable stenocardia. Statistically significant distinction on an ethnic accessory is established in group sick of an unstable stenocardia: at nonnative absolute quantity CD95 + significantly above, than at radical ($p=0,04$) though values is in limits of referential sizes. It is necessary to notice that strengthening apoptose of lymphocytes with participation CD95 + is connected with processes of nonspecific and defective activation immune cells, and also infringement of processes of their normal maturing. Thus, the results received by us according to ability of cages of immune system to activation testify that an expression «early and late» activate markers at an unstable stenocardia are raised, than at a stable stenocardia and are most expressed at persons of not radical nationality.

The expression adhesion molecules on endothelium and leukocytes is their initial stage recruitment in the inflammation centre that is accompanied by occurrence of a wide spectrum of the reactions having in the basis protective character, but resulting at excessive duration or intensity to



additional development dystrophic and necrosis changes. Such process is characteristic for a local inflammation in a wall of vessels which underlies atherosclerosis development. We define levels of an expression such adhesion molecules as CD54 + (ICAM-1) - a molecule of intercellular adhesion of 1 type, belonging to superfamily of antibodies; CD11b + - α M - a chain integrin CR3; and CD62L + - L - selectine.

The comparative analysis depending on form IHD has established significant increase at sick of an unstable stenocardia relative ($p=0,041$) and absolute ($p=0,01$) quantities CD54 + positive lymphocytes, than at sick of a stable stenocardia. It is necessary to notice that the expression of these molecules on endothelium vessels has constant character, but considerably amplifies at its stimulation proinflammatory cytokines and modified lipoproteins. On based leukocytes of peripheral blood CD54 + expressed it is weak, amplifies at activation T- lymphocytes, V- lymphocytes and monocytes and promotes their mutual adhesion with formation of large multicellular units. An expression as ICAM-1 and VCAM-1 according to authors [13] it was not marked in the intact arteries, it was found out only at activation endothelium proinflammatory медиаторами FNO - α , IL-1, interferon and was dependent on factor NF-kB.

CD11b + - α M the chain in a combination with β - a chain (CD18 +) forms specific to leukocytes integrin, designated as Mas-1 (macrophag receptor-1) or a receptor of inactivating complement CR3, expressed on myeloid cells and natural killers. We establish significant increase ($p=0,041$) relative maintenance CD11b + at a stable stenocardia, in comparison with sick of an unstable stenocardia. The comparative analysis depending on an ethnic accessory has revealed significantly high ($p=0,000$) indicators CD11b + at persons of a radical nationality sick of an unstable stenocardia.

CD62L + - L- selektin it is constant expressed on a tip [pseudopodia mononuclear](#) and provides an attachment lymphocyte to endothelium cell. At activation lymphocytes often there is "washing off" L - selectine that is accompanied by activation b2 - integrin complex (CD11/CD18) of lymphocytes and monocytes [11]. Loss of adhesive molecules from a surface of cages can be one of forms of negative regulation of an inflammation. In our research relative maintenance CD62L + at sick of an unstable stenocardia significantly more low ($p=0,001$), than at patients with a stable stenocardia, i.e. infringements of regulation L-selektin of the mediated adhesion at patients with an unstable stenocardia are most expressed. Thus, the estimation of molecules of adhesion at patients IHD has shown ambiguous changes on character. So at an unstable stenocardia expression CD54 + is raised and infringements L - selektine are expressed, to the mediated adhesion (decrease CD62L +). At a stable stenocardia the raised expression CD11b +. Ethnic distinctions are revealed in group



sick of an unstable stenocardia: at native maintenance CD11b + is significantly raised, than at persons of nonnative.

Such, in the image, the received results of the comparative analysis depending on form IHD allow to confirm, destabilization IHD is characterised by increase of expression CD19 + (B-lymphocytes), activate markers CD25 + (a receptor to IL-2) and CD71 + (a receptor transferrine), and also molecules of intercellular adhesion CD54 + (ICAM-1). At an unstable stenocardia at native signs of deficiency of the T-cellular link (T-lymphocyte, T-helper), and also significant increase of expression CD11b + (integrin) in comparison with nonnative.

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Expression of markers on lymphocytes at patients depending on form IHD

Table 1

Parametres	1- stable stenocardia (n=32)	2 - unstable stenocardia (n=38)	p... 1-2	
CD3+	%	71,96 ± 1,67	70,52 ± 1,63	
	abs.	1,37 ± 0,11	1,42 ± 0,11	
CD4+	%	40,72 ± 2,03	40,78 ± 1,55	
	abs.	0,80 ± 0,08	0,82 ± 0,07	
CD8+	%	23,28 ± 1,73	26,65 ± 1,29	
	abs.	0,43 ± 0,05	0,54 ± 0,05	
IRI (CD4+/CD8+)		2,22 ± 0,26	1,69 ± 0,12	
CD19+	%	7,28 ± 1,00	12,15 ± 1,37	0,006
	abs.	0,16 ± 0,03	0,23 ± ±0,03	0,006
CD16+	%	19,80 ± 1,64	16,50 ± 1,27	
	abs.	0,36 ± 0,04	0,33 ± 0,04	
CD25+	%	16,60 ± 1,89	24,13 ± 1,79	0,006
	abs.	0,30 ± 0,04	0,51 ± 0,06	0,011
CD54+	%	31,62 ± 3,32	39,97 ± 2,38	0,041
	abs.	0,61 ± 0,08	0,81 ± 0,07	0,01
CD62L+	%	49,68 ± 2,89	34,13 ± 3,42	0,001
	abs.	0,97 ± 0,11	0,67 ± 0,10	
CD95+	%	39,46 ± 3,98	45,45 ± 3,40	
	abs.	0,76 ± 0,11	0,99 ± 0,12	
CD11b+	%	41,25 ± 3,00	33,63 ± 2,17	0,042
	abs.	0,74 ± 0,06	0,65 ± 0,06	
CD71+	%	4,56 ± 0,53	10,26 ± 1,37	0,008
	abs.	0,10 ± 0,02	0,20 ± 0,09	0,036



Expression of markers лимфоцитов at patients ИБС in dependence
from an ethnic accessory

Table 2

Parameters	stable stenocardia		unstable stenocardia		<i>p...</i> 3-4		
	1 native n=13	2 nonnative n=19	<i>p...</i> 1-2	3 native n=22			
CD3+	%	72,61±2,39	71,52±2,34		67,47±1,95	75,42±1,82	0,006
	abs.	1,17±0,11	1,51±0,16		1,18±0,11	1,76±0,18	0,012
CD4+	%	37,69±3,09	42,78±2,65		36,86±1,56	45,85±2,42	0,002
	abs.	0,62±0,08	0,93±0,11		0,65±0,07	1,06±0,12	0,004
CD8+	%	25,84±2,72	21,52±2,21		26,78±1,85	26,92±1,78	
	abs.	0,42±0,05	0,45±0,07		0,45±0,05	0,65±0,09	
IRI (CD4+/CD8+)		1,72±0,26	2,55±0,37		1,57±0,16	1,81±0,15	
CD19+	%	7,07±1,37	7,42±1,42		13,21±2,17	10,35±0,97	
	abs.	0,12±0,03	0,19±0,06		0,22±0,05	0,24±0,04	
CD16+	%	22,92±2,50	17,55±2,08		18,61±1,70	13,92±1,62	
	abs.	0,37±0,06	0,34±0,04		0,34±0,06	0,31±0,04	
CD25+	%	14,66±2,61	17,89±2,65		20,91±2,52	27,40±2,47	
	abs.	0,24±0,04	0,35±0,06		0,41±0,09	0,62±0,08	
CD54+	%	32,69±5,93	30,89±3,99		41,95±3,12	37,35±3,89	
	abs.	0,51±0,11	0,68±0,11		0,73±0,08	0,95±0,15	
CD62L+	%	50,27±4,34	49,29±3,96		34,36±4,38	32,80±5,94	
	abs.	0,84±0,13	1,07±0,17		0,62±0,14	0,71±0,16	
CD95+	%	41,91±5,45	37,62±5,74		44,27±5,61	48,50±4,05	
	abs.	0,64±0,11	0,78±0,08		0,81±0,20	1,17±0,12	0,04
CD11b+	%	44,00±4,59	39,27±4,01		40,43±2,44	24,00±2,07	0,000
	abs.	0,69±0,08	0,78±0,08		0,71±0,09	0,56±0,07	



CD71+	%	3,28±0,61	5,55±0,66	0,03 <i>1</i>	12,30±1,95	6,93±1,61	
	abs.	0,05±0,01	0,15±0,03	0,03	0,21±0,04	0,19±0,44	

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UDC: 616.98: 578.827.1]. 036.2 - 084

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PAPILLOMAVIRUS INFECTION AND CERVICAL CANCER INCIDENCE IN PRE-VACCINATION AND THE INITIAL VACCINATION PERIODS IN THE REPUBLIC OF SAKHA (YAKUTIA)

Summary

The research aims at studying patterns and regional characteristics of morbidity and incidence of various papillomavirus infection and cervical cancer forms in the Republic of Sakha (Yakutia) in the pre-vaccination period and the first years of vaccination against this pathology. It is established that the studied periods do not show any significant differences or decreasing trend in anogenital (venereal) warts morbidity. The study revealed higher (by 1/6-2 times) incidence of high-risk HPV of type 16 in women, compared with men. There was no decrease in type 16 and 18 HPV incidence in 2008-2011 (the period of introducing low vaccination coverage), compared with the year 2007. There is a trend for increased CC morbidity in women aged 30-44 years.

Key words: human papillomavirus infection, cervical cancer, morbidity, prevalence, vaccination

Introduction

In the early 1980s researchers managed to identify types of human papillomavirus (HPV) directly responsible for development of the oncologic process [1, 5, 6]. Harald zur Hausen was the first to suppose that HPV causes cervical cancer (CC) [10]. Nowadays, cancer-risk HPV types are recognized to provoke CC etiopathogenesis; moreover, they are responsible for development of vulvar cancer (20%), vaginal cancer (80%), penile cancer (40%), and anal cancer (90%); there is research being done to study the influence of cancer-risk HPV types on development of guttural and buccal cancers. Out of over 100 HPV types known today, 15 types have the oncogenic potential, and 8 (16, 18, 45, 31, 33, 52, 58, 35) are involved in 90% of CC cases, with types 16 and 18 HPV occurring in up to 70% of cases. Type 6 and 11 HPV are responsible for development of genital condylomas (anogenital (venereal) warts) in 90% of cases [1]. Our country's professionals in different fields have worked out principles of the laboratory diagnostics, epidemiological monitoring and prevention of papillomavirus infection and malignant growths related to this infection [2, 3, 4]. The study of mechanisms of carcinogenesis, induced by high-risk human papillomavirus infection (HR HPV), as well as the introduction of vaccines for preventing the



infection, caused by human papillomavirus of 6, 11, 16 and 18, has created conditions for decreased externalia condylomatosis morbidity and potential decrease in CC [7, 8, 9]. Papillomavirus infection has a number of peculiarities: variety of the virus genotypes and cancerogenic activity, polymorphism of clinical manifestations, chronic forms, dominance of symptom-free infections, primarily sexual transmission – they all call for a specific epidemiological monitoring system, which is to be developed under vaccination against the disease.

The aim of the research was to study patterns and regional characteristics of the morbidity and incidence of various papillomavirus infection and cervical cancer forms in the Republic of Sakha (Yakutia) in the pre-vaccination period and the initial years of vaccination against this infection.

Materials and Research Methods

We used methods of clinical, laboratory and epidemiological diagnostics. We analyzed the anogenital (venereal) warts morbidity in the years 1999-2011, the data being taken from forms of the state statistical observation that, in accordance with order of the Ministry of Health of the Russian Federation, are filled in by all derma-venereologic institutions. Also, we compared the prevalence of HPV of types 16 and 18 in 2007 (pre-vaccination period) and 2008-2011 (the period of the initial vaccination against HPV infection) in the Republic of Sakha (Yakutia). Using materials of the Republic's Oncology Center, we examined the morbidity trends, CC prevalence and mortality from the disease in the female population of the republic in 2000-2011. For laboratory diagnosis of human papillomavirus infection, caused by HPV of types 16 and 18, there was used the method of polymerase chain reaction (PCR) in the real time format and a number of locally-produced reagents: AmpliSens HPV 16/18-FL, AmpliSens HR HPV screen-FL, permitted for the use in the Russian Federation in the due order. There was a survey of patients having addressed the National Skin and Venereal Diseases Clinic and the Republic's Hospital of the Republic of Sakha (Yakutia). The material for the study was scraping of the mucous membrane epithelium from the cervical canal and urethra, taken by a universal urethral probe or a cytobrush. Among the patients examined, there were ones infected with sexually transmitted diseases (gonorrhea, anogenital warts), other sexually transmitted infections, inflammatory diseases of the urinary tract lower parts, as well as ones surveyed for preventive reasons, the patients with active sexual life. The total number of examinees in 2007-2011 amounted to 16,298 males and females.

Results and Discussion

The anogenital (venereal) warts morbidity in the Republic of Sakha (Yakutia) is distributed



unevenly over the years; thus, we made calculations and comparison of the average three-year data in the pre-vaccination period and the initial vaccination period (Fig. 1). The research showed that in 1999-2007 the morbidity varied from 21.7 to 34.0 per 100,000 of the population. In 2008-2010, the indicator remained at the 2005-2007 level (21.4 per 100,000 people). In 2011 there was an increase in morbidity (26.0 per 100,000 people). It should be noted that the republic used only the bivalent vaccine against HPV of types 16 and 18. In 2008, 2009, 2010 and 2011, the number of vaccinated women aged 10-30 years was 65, 70, 60 and 100 people, respectively. Therefore, there is no reason to expect a decrease in the incidence of this HPV infection form, which is caused predominantly by HPV of types 6 and 11.

The prevalence of HR HPV of type 16 and 18 in the Republic of Sakha (Yakutia) in 2007 and 2008-2011 is presented in Table 1. The results showed that, in general, type 16 HPV was found in 10.1% of the patients examined, type 18 HPV was found 2.6 times as less often - 3.9%. In 2011, there was an increase in type 16 HPV prevalence, compared with the year 2007, but the differences were not statistically significant ($p > 0.05$).

The frequency of HR HPV detection in female patients was 1.6-2 times higher than in males (Fig. 2). These data should be considered when analyzing the cancer morbidity associated with HR HPV in men and women.

Important results were obtained in the study of the prevalence of types 16 and 18 HPV in different age groups of the female population. Even children, who become sexually active early, were infected with HR HPV (Fig. 3). The highest prevalence of type 16 HPV were found in women aged 15-19 and 20-29 years, which corresponds to the age structure of the CC patients in the recent years.

The problem with cervical cancer in the Republic of Sakha (Yakutia) is one of the most serious health problems. In 2010 – 2011, this pathology ranked third in the female cancer structure, having ranked fourth in the year 2000. Annually, the republic registers from 67 to 106 new cases of the disease. The morbidity tends to increase: the 2011 indicator was significantly higher compared with the year 2000 (20.4 and 13.9 per 100,000 of the female population, respectively). The CC prevalence and mortality of this disease are relatively high. Fig. 4 shows the results of the studying the cervical cancer morbidity in different age groups of the female population of the Republic of Sakha (Yakutia) in 2000 and 2011. There is a shift of the morbidity towards younger age groups, with the increased incidence rate in reproductive-age women aged 30-34 (by 1.3 times), 35-39 (by 2.7 times) and 40-44 years (by 3.2 times); and it is traditionally high in persons over 60 years.

Conclusion



The results showed a high relevance of human papillomavirus infection and cervical cancer in the Republic of Sakha (Yakutia). For the first time, the study established patterns of the epidemic processes caused by high and low cancer risk HPV, and regional characteristics of the infection in the pre-vaccination period and the initial stage of vaccination against this disease. We determined age and sex characteristics in the prevalence of HR HPV of type 16 and 18. There was established a relation between the high prevalence of HR HPV in women aged 15-29 years and the changed age structure of cervical cancer patients, in particular, the increase in morbidity in the age group 34-44 years, which corresponds to the published data, indicating the range of about 10 years between the moment of being infected with HR HPV and development of cervical cancer. In general, the results of the study show that the republic needs to establish the epidemiological monitoring system over human papillomavirus infection, and the present study outlines main principle thereof. The results of the study can contribute into development of the Regional Vaccination Calendar and Vaccination Financing Plan, with HPV vaccination being included therein.

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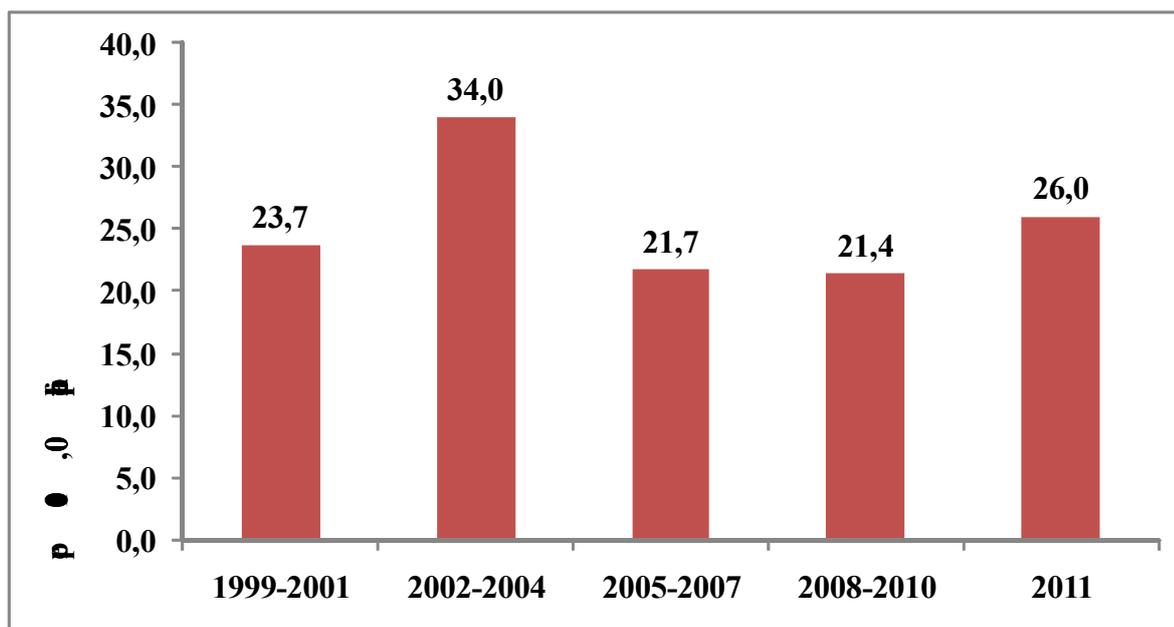


Fig. 1. Anogenital (venereal) warts morbidity (ICD-10 - A63.0) in the Republic of Sakha (Yakutia), 1999-2011.

Table 1.

Type 16 and 18 HPV detection rate in the Republic of Sakha (Yakutia) in 2007-2011.

Year	Number of the examined	HPV 16		HPV 18	
		Abs. number	% ± m	Abs. number	% ± m
2007	710	69	9.7 ± 1.1	35	4,9 ± 0,8
2008	2,234	182	8.2 ± 0.6	80	3,6 ± 0,4
2009	4,140	434	10.5 ± 0.5	149	3,6 ± 0,3
2010	3,376	322	9.5 ± 0.5	113	3,4 ± 0,3
2011	5,838	644	11.03 ± 0.4	256	4,4 ± 0,3
Total for 5 years	16,298	1,651	10.1 ± 0.2	633	3,9 ± 0,2

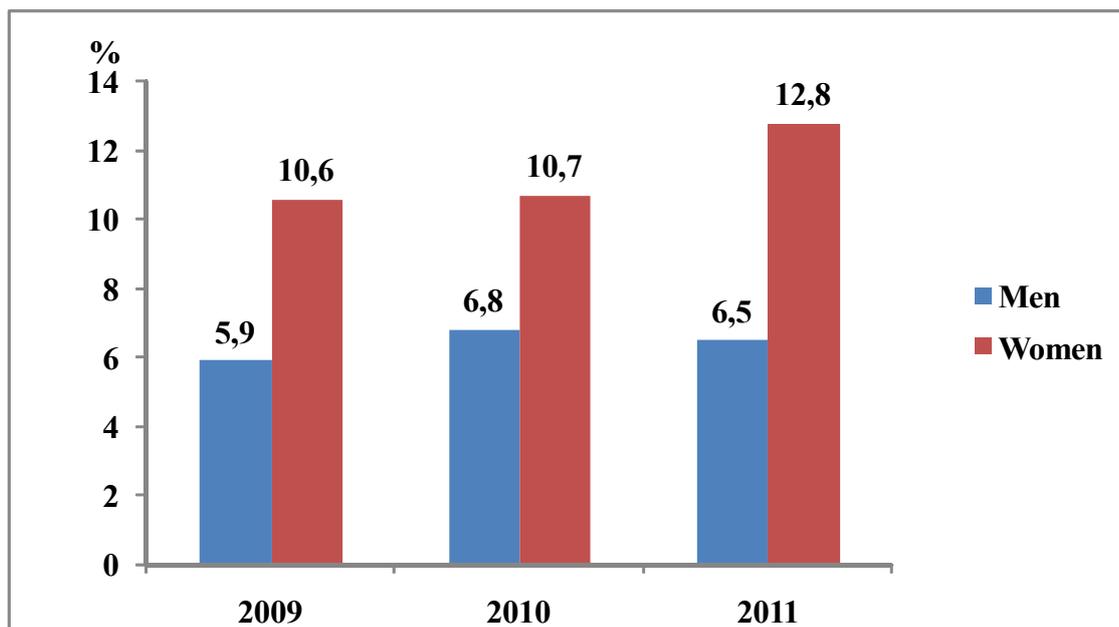


Fig. 2. Detection rate for high-risk HPV of type 16 in men and women in the Republic of Sakha (Yakutia) in 2009-2011 (per 100 examined people)

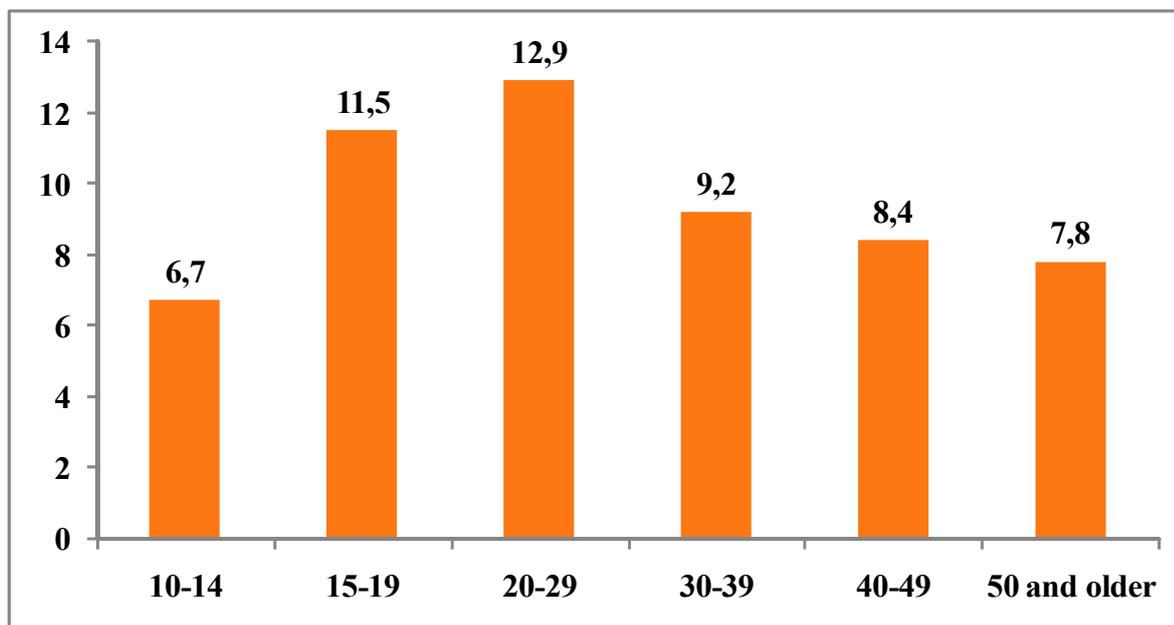


Fig. 3. Type 16 HPV incidence for various age groups of women in the Republic of Sakha (Yakutia) in 2007-2011 (per 100 examined people)

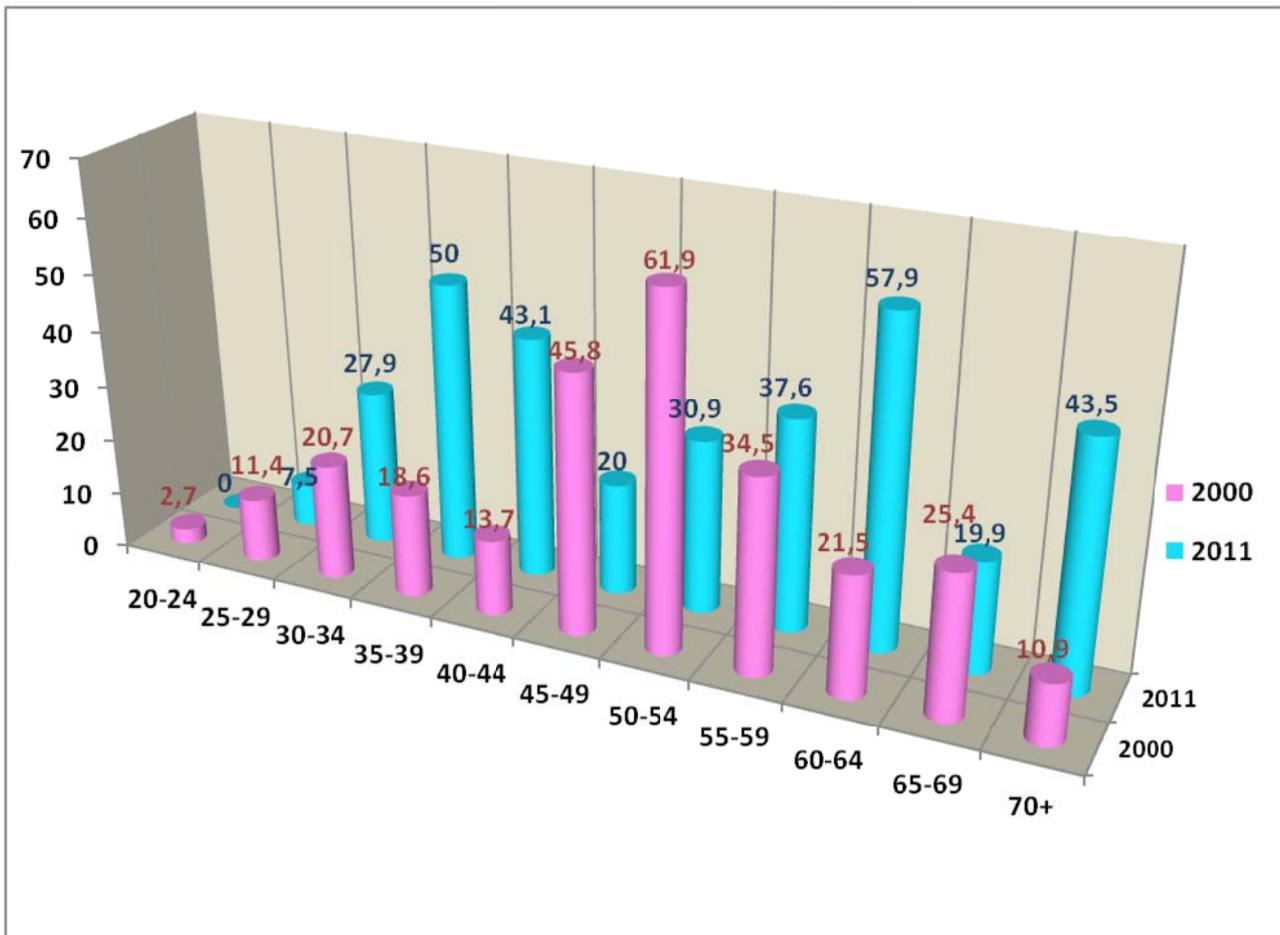


Fig. 4. CC morbidity in various age groups of the female population in the Republic of Sakha (Yakutia) in 2000 and 2011 (per 100,000)



UDK 543.32:616.1 (571.56)

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**The mineral composition of drinking water as one of the risk factors
for formation of the pathology of cardio - vascular system**

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Long-term laboratory study of drinking water to the level of calcium, magnesium, and hardness in different sources of water: the Lena River, lakes and ground water from wells was conducted. It was established that the low calcium and magnesium, and total hardness of water were recorded in the lake water. Analysis of statistical data on morbidity, mortality, and the infestation has revealed that the population, consuming low-mineralized, soft lake water, is more susceptible to diseases of the circulatory system, as evidenced by relatively high correlation coefficient between mortality from cardiovascular diseases and hardness of drinking water due to the presence of magnesium and calcium salts.

Keywords: drinking water, calcium, magnesium, water hardness, morbidity, mortality, and cardiovascular disease.

There are numerous risk factors for cardiovascular disease. Traditionally, most attention has been paid to factors such as diet, exercise, smoking, serum cholesterol, high blood pressure, diabetes, obesity, age and heredity. Changing of these variables where possible gives a positive effect on reducing the morbidity. At the same time to the risk of cardiovascular disease and mortality and other environmental factors, such as air pollution or drinking water hardness, which receive less attention, may play a role and can have a serious impact on the health of the population.

In recent years a theory according to which the water with low content of electrolytes, causing the stiffness contributes to the development of cardiovascular diseases. According to the results of epidemiological studies a statistically significant, though not very strong inverse correlation between the hardness of drinking water and the level of mortality from cardiovascular disease was revealed [2-4,6]. In foreign studies researchers have reported a correlation between the hardness of drinking water and risk of coronary heart disease - the harder the water, the lower the risk [9,10, 13].

Water hardness is determined by the content of calcium and magnesium. Most studies indicate that magnesium is the most heart protective, and some studies suggest that the most important factor is the ratio of magnesium and calcium. It seems that the high ratio is greater than a low one. Consistency of these findings in a number of studies suggests that the mineral content in the water is a risk factor for diseases of the cardiovascular system [7, 8].

However the relative importance of this factor in comparison with others (such as smoking, obesity, diet, and high pressure) remains unclear.

First in Japan they noticed the connection between the hardness of drinking water and cardiovascular disease, where most of the water sources have soft water with the acidic medium, the lower was the stiffness, and the higher was the incidence of strokes. In communities where water cleaning systems with devices that reduce water hardness were installed and mortality from diseases of the circulatory system increased on average by 20%, compared to those where from the water did not remove hardness salts. Excess calcium at magnesium deficiency, except calcification, can cause heart attacks, cardiac arrest in systole, headaches, premature aging, high blood pressure [11, 12].



In our Republic as a source of water supply are mainly surface water - rivers, lakes, and, to a lesser extent - the underground water.

It is known that in the surface waters all over the republic have lacks of the fluorine and iodine, as well as a reduced content of calcium and magnesium in drinking water is registered.

The results of the long-term studies show that the waters of the major rivers in general, satisfy the quality requirements of Class II sources in accordance with GOST 2761-84 "Sources of centralized drinking water supply" and can be used for drinking after cleaning and disinfection. These waters are low - and middle mineralized, on the chemical composition -calcium bicarbonate, with a satisfactory oxygen regime, poor nutrient components, moderately polluted. Pollutants are mainly oil (1 to 3 PDK) and phenols (3 to 5 PDK). A large part of the population living in areas without central water supply, used water, which is not conforming to the quality of drinking water. [5]

Total hardness - it is a natural property of water caused by the presence in the raw water of so-called hardness salts, i.e. of calcium and magnesium (sulfates, chlorides, carbonates, bicarbonates, etc.).

Water with a total hardness up to 3.5 mEq / L (10 °) is a soft, 3.5 to 7 mEq / L (10-20 °) - moderately hard, from 7 to 10 mEq / L (20-28 °) - tough and more than 10 mEq / L (28 °) - very tough.

Cardiovascular disease (CVD) remains the most pressing problem for medical science, healthcare, due to the high morbidity, permanent incapacity and mortality. In the Republic Sakha (Yakutia) in the past 15 years, mortality among working-age population from the CVD increased in 2.2 times (RF - 1.7 times). Identification of environmental CVD risk factors will disclose the nature of ongoing trends; identify ways and prospects for prevention.

The purpose of this study was to establish a link between the rigidity of calcium, magnesium in drinking water and the levels of morbidity and mortality from cardiovascular disease among the working population of the Republic Sakha (Yakutia).

The material for the study were the YARMIATS statistics data on morbidity and mortality from diseases of the circulatory system of the population of working age, the results of laboratory tests of drinking water FBUZ "TsGiE in RS (Y)" for the period 2005-2008 years on the content of calcium, magnesium, and total hardness by complexmetric determination.

For a comprehensive study of the influence of the mineral composition of drinking water on the incidence and mortality from cardiovascular disease have been identified three areas of the Republic: Megino-Kangalasskii, Churapcha and Khangalassky areas. Site selection was based on the fact that the population of each district uses drinking water from various water sources, respectively, and the mineral content of the water consumed is different. In Megino - Kangalassky area the source of drinking water is wells, in Churapcha - lake water, in Khangalassky – the Lena River.

For a more detailed study of the effects of calcium, magnesium, and hardness in drinking water on cardio - vascular system morbidity of population, living in the study area, in field conditions there has been a single comprehensive medical examination of the indigenous people of working age (312 people) in v. Maya of Megino-Kangalassky, v. Deering of Churapcha and v. Oktemtsy of Khangalassky areas. Comprehensive medical examination included: visiting a neurologist, cardiologist, ECG and biochemical blood cholesterol, triglycerides, VLDL, LDL, HDL, glucose.

Research results:

In analyzing the results of laboratory tests of drinking water received for 2005 to 2008, it was found that the most poor in calcium and magnesium were water lakes. In the drinking water of the Lena River and wells of v. Maya magnesium content was at the same level, and higher calcium content was in river water. The index of total hardness in all investigated water supplies is low.



Thus, in accordance with the Sanitary "Drinking Water" water in all three study water sources can be described as a soft and weak-mineralized (Table 1).

Assessing the impact of risk factors on population health was carried out under the incidence of diseases of the circulatory system and mortality from this class of diseases. Comparative analysis of average annual incidence rates for diseases of the circulatory system uptake in 2005-2008 in the study areas showed that the lowest level was observed in Khangalassky area, high – Churapcha (Table 2).

The average annual mortality rate of working age population from CVD for the observed period are presented in Table. 3. It can be seen that the greatest number of deaths rate from CVD was also observed in Churapcha area, which is in 14% higher than in areas where the river and underground water from wells is used.

Results of a comprehensive medical examination revealed that, among the surveyed population prevalence of diseases of the circulatory system accounted for 100 examined in v. Maya Megino-Kangalassky District - 24.5, v. Deering Churapcha - 81.6 and v. Oktemtsy Khangalassky - 51.2 (Table 4). The average age of the surveyed: in v. Maya - 38 years, v. Deering - 51, v. Oktemtsy - 48 years. By nationality 99% - the Yakuts.

Thus, a comparative analysis of morbidity and mortality from CVD, as well as the affection of the population of working age on the results of a one-time physical examination showed that the population, consuming low-mineralized, soft lake water, is more susceptible to diseases of the circulatory system.

During the correlation analysis between mortality from cardiovascular disease among the population of working age and mineral composition of drinking water in the country as a whole it was established the presence of reliable feedback stiffness ($r = -0,34$, $p \geq 0,05$), magnesium concentration ($r = -0,41$, $p \geq 0,01$) with mortality, which supports the hypothesis that a deficiency of nutrients such as calcium and magnesium is a risk factor for cardiovascular disease.

During the correlation analysis on the three study areas also were received relatively high correlations between mortality from cardio-vascular system diseases and the hardness of drinking water ($r = -0,96$) and magnesium content ($r = -0,94$).

Private correlation analysis showed a direct relationship between the incidence of high blood pressure, and calcium ($r = 0,93$), magnesium ($r = 0,94$), stiffness ($r = 0,917$). The obtained result confirms the hypothesis that the lack of these elements in drinking water is a risk factor for cardio-vascular system diseases.

The final stage of our study was to reveal the association between calcium and magnesium content and hardness in drinking water and blood biochemical parameters, for which a significant correlation with diseases of the cardiovascular system: LDL, cholesterol, glucose was determined.

Study of serum lipid spectrum in the working population, consuming drinking water from various water sources, showed that the biochemical parameters did not exceed the generally accepted normal values, but at the same time there were significant differences (Table 5).

A significant high level of serum glucose in Churapcha area residents compared with residents of Megino-Kangalassky was revealed. Levels of total cholesterol, LDL-C were significantly higher in people of Churapcha and Khangalassky areas compared with residents of Megino-Kangalassky. Because of the significantly lower HDL value atherogenic ratio was higher than normal among residents of Khangalassky district.

During the private correlation analysis statistically significant associations were not identified, but, sufficiently high correlation coefficients between the content of HDL cholesterol ($r = -0,92$), triglycerides ($r = 0,917$), and the hardness of drinking water were received. The results suggest the need for further research to establish the effect of micronutrient deficiencies of calcium and magnesium in drinking water on the blood biochemical composition and, therefore, the incidence of cardio-vascular diseases.

Correlation analysis between the obtained results of biochemical blood tests and the



incidence of cardio - vascular diseases of the population in the study area revealed the presence of significant inverse correlation ($p < 0,05$) between the incidence of cerebrovascular disease and blood glucose ($r = -0,99$), acute myocardial infarction morbidity and LDL ($r = -0,99$), cholesterol ($r = -0,99$), coronary heart disease and LDL ($r = -0,99$), glucose ($r = -0,99$).

Thus, the results obtained in the course of the study, allow establishing the fact that lack of calcium, magnesium, and low value of hardness in drinking water is one of the risk factors of cardio - vascular diseases in the population living in the area. Since to fill deficiency of specified elements in drinking water is not possible, it is necessary to continue the study to assess the adequacy of calcium and magnesium from food in order to develop a comprehensive program to solve this important issue.

The afore-cited lets us to consider as a well-founded previously extended suggestion about possible association between mortality from cardiovascular diseases and mineral composition of the water (calcium, magnesium, water hardness).

Attention to these environmental risk factors as the mineral composition of drinking water can lead to a significant reduction in the load on the health care system associated with cardiovascular diseases.

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Table 1

Mean annual rates of calcium, magnesium and total hardness in drinking water in the study area

District	Calcium	Magnesium	Total hardness
	MPC 100 mg / liter	MPC 50 mg / liter	MPC 7 mEq / L
Megino-Kangalasskii	17,3	24,0	2,9
Churapchinskii	7,3	18,5	2,4
Khangalasskii	34,0	32,4	3,8

Table 2

The average annual morbidity of diseases of the circulatory system among the adult population in 2005-2008 in the study area (on 1000 inhabitants)

Morbidity	Megino-Kangalasskii	Khangalasskii	Churapchinskii
Cardiovascular diseases	200,3	136,2	215,2
Including illnesses, characterized by high blood pressure	69,9	50,4	79,1
Coronary heart disease	56,6	28,9	29,1
Acute myocardial infarction	1,1	0,7	0,6
Cerebrovascular diseases	23,4	14,7	15,9
Other causes	49,3	41,5	90,5



Table 3

The average annual mortality rate of the population of working age from diseases of the circulatory system in the study area in 2005-2008 (on 1000 of corresponding age)

Mortality from CVD	Megino-Kangalasskii	Khangalasskii	Churapchinskii
All CVD	1,81	1,79	2,06
Including diseases, characterized by high blood pressure	0,03	0,03	-
Coronary heart disease	0,54	0,56	0,21
Acute myocardial infarction	0,08	0,18	0,08
Cerebrovascular diseases	0,62	0,5	0,62
Other causes	0,54	0,52	1,15

Table 4

Pathology of the blood circulatory system of the population inspected in three settlements (on 100 surveyed)

Indicators of pathology	v. Maya Megino-Kangalasskii	v. Deering Churapchinskii	v. Oktemtsy Khangalasskii	Total
Total CVD	24,5	81,6	51,2	53,7
Including diseases, characterized by high blood pressure	17,4	38,6	26,0	27,7
Cerebrovascular diseases	1,0	20,2	15,0	12,7
Other heart diseases	4,1	10,5	0,8	5,0
CHD	1,0	10,5	8,7	7,1



Table 5

Levels of biochemical parameters of blood serum at the inspected population
in the studied settlements (mmol / L)

Biochemical tests	Maya Megino-Kangalassky	Deering Churapchinskii	Oktemtsy Khangalasskii
Glucose	4,97±0,08 ⁺ p=0,000	4,92±0,09	4,23±0,06** p=0,000
Triglycerides	0,95±0,05	0,97±0,05	0,88±0,05
Cholesterol	5,41±0,09 ⁺ p=0,000	5,57±0,25	4,85±0,09** p=0,002
HDL cholesterol	1,44±0,03	1,31±0,04* p=0,041	1,45±0,04** p=0,017
LDL cholesterol	3,52±0,08 ⁺ p=0,000	3,61±0,09	2,98±0,08** p=0,000
VLDL	0,44±0,02	0,44±0,02	0,42±0,03
Atherogenic factor	2,84±0,09	3,24±0,13	2,5±0,09** p=0,001

Note: * Authenticity between Churapcha and Khangalassky districts,

+ authenticity between Churapcha and Megino-Kangalassky districts,

** authenticity between Khangalassky and Megino-Kangalassky districts.



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Regional features of reproductive health of women of the Russian federation

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Summary:

Analyzed literature proves the known fact that the state of women's reproductive health depends not only on their gynecologic and physical health, but also is characterized by regional specifics and depends on ecological and demographic situation of the region.

Keywords: population, morbidity, region, reproductive health, birthrate, reproduction.

Actuality:

The demographic situation in the Russian Federation is the critical, it is mostly caused by supermortality of the population of able-bodied age (in 2008 the mortality rate coefficient has made 16,1 died on 1000 population) and catastrophically low birth rate which is not providing simple reproduction (for maintenance of reproduction of the population the total indicator of birth rate should make 2,14, and in 2004 it has made only 1,34) (Arkhangelsky V. N., 2007). As a whole on the country excess of number of died over number of the born has made 1,3 times, and in 8 subjects of the Russian Federation it reached 2-2,5 times.

Long preservation of existing level of birth rate will lead to that each new generation of Russians will not exceed 60 % from number of previous (Kuznetsov V. N., Rybakovskij L.L., 2005). Considering extensive territory of our country, its climatic and geographical features, it is necessary to search for the decision of the given situation as a whole, but founding on and adapting them for features of region.

Introduction:

According to V.E.Radzinskogo and S.D.Semjatova (2005), reproductive and somatic health of women of Russia over the last 10 years has considerably worsened, moreover, less than 50 % of



children are born the healthy. Besides, the share of girls of 15-17 full years which can be considered as the nearest and most real reserve of reproduction of the population of the country, has appeared minimum as in structure of all female population (4,72 %), and among women of potentially reproductive age, that is 15-49 years (8,16 %) (Uvarova E.V., 2006).

Distribution of such epidemics as alcoholism, the narcotism and AIDS do not improve demographic indicators. Researches I.J.Chasnoff et al. (2005) have shown that 32,7 % of pregnant women take alcohol and narcotic substances. 21 % of women recognized alcohol intake until the moment of diagnostics of pregnancy, and 11 % of pregnant women continued its use even after have learnt about the pregnancy.

The Russian Federation remains one of the most unsuccessful regions of the Eastern Europe on prevalence of a HIV-infection. Over the last 10 years the number of again revealed cases of a HIV-infection has increased in 27 times, and among women – in 49 times (about 351 cases in 1996 to 17321 in 2006). Frequency of revealing of new cases of a HIV-infection at pregnant women has increased in the Russian Federation over the last 10 years in 190 times! (from 0,6 of 100 thousand tested in 1996 to 110,0 - in 2006) (Sadovnikova V. N and others, 2008).

The state of health of modern girls and girls does not inspire optimism. According to T.J.Fillipova (2006) gynecologic disease of girls from 0 till 14 years has grown from 28,4 ‰ to 65,5 ‰, from 15 till 17 years from 81,3 ‰ to 112,3 ‰. For last five years, according to data of the Health Ministry of the Russian Federation (2002), the general morbidity of children till 14 years has increased by 21,6 %, and teenagers – on 24,1 %; 65-70 % of girls-teenagers have various chronic somatic diseases, and at 112 ‰ of girls is revealed pathological disease of reproductive system (Uvarova E.V., 2006). Prevalence of gynecologic diseases among girls is high and averages in Russia of 12-15 % (Kokolina V. F, Mitin M. Ju, 2005). According to routine inspections of girls from 1 year till 15 years lead in 2003-2004, many infringements in a condition of reproductive system are found out in 29,1 % of girls (Ushakov G. A and others, 2006).

In S.J.Tsaturjan's work (2003) it is shown that formation of reproductive health of girls and the girls living in the Moscow megacity, occurs against deterioration of a socially-demographic situation, in particular - decrease in birth rate, increase of death rate, falling of a natural increase of the population, a low material prosperity, and also irrational reproductive and contraceptive behavior of teenagers. The similar tendency is traced and in Moscow Region.

Researches of a demographic situation in the Samara region (Antimonova M. Ju, 2007) have shown stability of resident population (2005г. – 3 258,7 thousand persons), a negative natural increase (2005г. – 6,2 on 1 000 population), regressive type of age structure of the population



(children – 16 %, older persons – 21 %), a low indicator of total factor of birth rate (2005г. – 1,01) and a low indicator of expected life expectancy (2005г. – 64,5 years). Somatic health of the population of the Samara region (2002г.) is characterized by high indicators of the general morbidity of children – 204 472,9 on 100 thousand children, children's physical inability – 202,8 on 10 thousand children, disease of malignant newplasms – 377,9 on 100 thousand population, low disease of an active tuberculosis – 53,5 on 100 thousand population. In area there was an adverse situation on disease of a HIV – 555, 2 on 100 thousand population. During 1998 – 2002 in the Samara region there was stably high an indicator of gynecologic disease of girls – teenagers 130,4 – 154,8 on 1 000 girls. The parity of childbearing to abortions makes 1,1; coverage of women of reproductive age contraception has grown from 38,7 to 44,8 %; there was a prevalence growth of extragenital diseases at pregnant women from 77,8 to 89,9 on 100 pregnant women, frequencies of an anemia of pregnant women from 42,2 to 47,5 %.

The analysis of morbidity and death rate of newborns in Kursk region over the last 10 years has shown growth of death rate of newborns practically twice (from 4,32 ‰ to 8,27 ‰). In area the increase practically in 3 times of disease of newborns takes place: from 66,28 ‰ to 205 ‰ with growth of a congenital pneumonia (Ivanov V. P and others, 2004). The similar researches lead in the next Oryol region, have shown that early neonatal death rate, on the contrary, has decreased twice, and morbidity of newborns has increased in 1,5 times (in Kursk region – in 3 times) (Pahomov S.P., 2006).

In Perm from 1990 for 2007 decrease in number of girls at the age from 0 till 14 years (on 60756 persons) and girls-teenagers from 15 till 18 years (on 4569 persons) is revealed. The situation is traced against increase in group of women at the age of 46-49 years (on 10899 persons) that testifies to ageing of women and is the adverse factor for reproduction of the population of Perm (Olina A.A. and others, 2008).

The similar adverse demographic situation is observed and in Republic of Sakha (Yakutia). Birth rate level made in 2002 in countryside 2,53 children, in city settlements - 1,56, against 2,23 population necessary for simple reproduction. In countryside the birth rate factor is for the present sufficient for simple replacement of generation of parents by children. For comparison across Russia the similar indicator has made 1,32, including in a number of regions of the Central Russia, where total factor of birth rate even more low - about 1,1 births on one woman. On 1/1/2006 in republic lived 488 184 female population, including women of reproductive age - 276 531, girls-teenagers - 28 111, girls - 103 320. Women of reproductive age, as a part of female population of the Republic, make 56,6 %, from them in city district live 67,1 %, in countryside – 32,9 %. The age and sexual structure of the population is one of its major characteristics. In the beginning of 2006,



number of women on 26,5 thousand exceeds number of men, men in population structure make 48,6 %, women - 51,4 %.

Not less important the permission of the questions connected with early reproductive losses is represented. The concept «reproductive losses» includes cases parent and перинатальной death rates, and also losses of products of conception owing to abortions and extra-uterine pregnancy (Manuhin I.B. and соавт., 1999).

In Russia against a severe problem of reproduction of the population in 2006 from the reasons connected with pregnancy and childbearing, 387 women have died. (Radzinsky V. E, Gordeev A.N., 2007; Tarasova L.P., 2008). The indicator of maternal mortality rate has essential distinctions in different federal districts – from 18,7 on 100 thousand born live in Northwest to 33,7 - in Uralsk. The Far East federal district is characterized by stably high indicator of maternal mortality rate (in 2005 – 34,4 % on 100 thousand born and 31,9 % - in 2006г.) (Jusupova A.N. and others, 2009). In structure of the reasons of maternal mortality rate in the Russian Federation, as well as in previous years, complications of pregnancy, sorts and the postnatal period (73,8 %), on the second place – death rate after abortion (19,6 %), on the third – after extra-uterine pregnancy prevailed. The increase in relative density of death rate of women after extra-uterine pregnancy - 4,7 % in 2005 and 6,7 % - in 2006 (Filippov O. S and others, 2008). The structure of maternal mortality rate on 33 % consists of the operated reasons while in the developed countries the reasons which difficultly give in to regulation (thrombembolia, extragenital diseases and narcosis complications) (Serov V. N, 2008) prevail.

According to E.M.Zelenina (2010), principal causes of maternal mortality in the Kemerovo region are a sepsis (28,3 %), extragenital diseases (24,8 %), bleedings (15,9 %), hypertensive frustration (13,1 %). Besides, O.G.Frolova's researches (2010) have shown that territories of the Russian Federation have essential distinctions in level of prenatal death rate and its reasons.

Despite decrease of absolute number of abortions in the last decade, they take the second place in structure of the reasons of maternal mortality rate. Total number of the registered abortions in 2005 has made 1 501594, or 37,8 on 1000 women of reproductive age (Frolova O. G, 2007). According to V.E.Radzinsky, I.N.Kostin (2007), one of the factors promoting it, that fact is that artificial abortion is a unique method of regulation of the birth rate, provided by system of obligatory medical insurance (OMC) (frequency of use of highly effective methods of contraception in 3 times more low, than in economically developed countries). During first 6 months from the beginning of sexual life of 28-46 % of young women interrupt pregnancy with a method of surgical abortion (Radzinsky V. E, Semjatov S.D., 2006). For comparison, in the USA the level of artificial



interruptions of pregnancy during 1996-2003 has made 8 %, and in China – 21 % (Sedgh G. et al., 2007).

According to S.P.Sinchihin (2008), in Russia only 25-40 % of women of genital age use modern methods of contraception, 60-75 % of women subject themselves to risk of undesirable pregnancy.

Abortion in the youth environment is a serious problem and the most significant reason of deterioration of reproductive health. In 2004 pregnancy at 161 200 girls-teenagers has ended with abortion, that is almost every tenth abortion (9,6 %) in the country is made at teenage age (Uvarova E.V., 2006).

So, M.B.Krasnikova, A.N.Dodonov (2009), having studied a current of childbearing after the first medical abortion in the teenage period, have shown that interruption threat is diagnosed for every second, gestos – at 62,5 %, an anemia – at 74,1 % of women. If from the moment of abortion before the present pregnancy has passed less than 6 months the risk of development of a pathological condition of a fetus increases in 2,8 times in comparison with longer interval (Kulavsky V. A, 2009).

L.V. Talykova et al. (2007) on the basis of studying of outcomes of 7254 pregnancies of the working women living in the northeast Russian Federation in Monchegorsk and Apatity has shown that on the average on one woman it was necessary 4,3 pregnancies. More than half of all pregnancies have been interrupted in the first trimester. 23 % of the women living in Apatity, had a spontaneous abortion, and in Monchegorsk - at 16 %, despite prevalence of the smoking women living in Monchegorsk (37 % against 24 %). The conducted research has allowed authors to draw a conclusion on influence on a female organism of degree of impurity of environment

The conclusion:

Having analyzed all situation on country regions, following positions of a new direction in obstetrics and gynecology — the general ecological reproductology (E.K.Ajlamazjan and others 1996—2000) are formulated.

43. The reproductive system of the woman is very sensitive to influence of adverse factors of the environment of any origin and any intensity, including subthreshold.
44. For formation of ecologically dependent pathology of reproductive system specific and nonspecific and common pathological reactions, and the last — in a greater degree.
45. Ecologically dependent infringements of reproductive system of the woman are shown by clinical, pathophysiological, hormonal, biochemical, immunological symptoms. All of them in most



cases have unidirectional, same character and have a strong likeness at influence of the most different anthropogenous factors.

46. Clinically arising frustration are shown by increase of frequency of infringements of menstrual cycle, nonspecific chronic diseases of genitals, hyperplastic processes, decrease of fertility, increase of a pathology of pregnancy and childbearing, deterioration of a condition of a fetus and the newborn, increase of neonatal mortality.
47. Expressiveness of adverse influence of the anthropogenous environment and stability to it of an organism are defined by a phenotype of the woman, age, profession and the work experience, life conditions, size of a dose and an exposition of damaging agents.
48. Ecologically dependent changes in reproductive sphere of the woman develop in three phases. The outcome of pregnancy and childbirth, destiny of a fetus and the newborn depend on what phase of adaptation of an organism to environment aggression there was when the pregnancy has come and on what phase the most part of term of development of a fetus proceeded.

Considering a normal functional condition of reproductive system as one of indicators of health of the woman, V.E.Radzinsky (2001) considers that it is necessary to warn "breakage" of this system as only healthy mother can give birth to the healthy child and only the healthy child can become subsequently healthy mother or the healthy father.

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Successful treatment of Fournier's gangrene

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In given article the general information on heavy disease to gangrene Fournier's is resulted. In it some epidemiological aspects of disease, etiology are opened, and also clinical cases of successful treatment of the given pathology are resulted. It is shown, that one of etiological factors of gangrene Fournier's is anaerobic the infection. Only the complex treatment including active surgical tactics and adequate volume of conservative actions help to reach good result of treatment.

Keywords: gangrene Fournier's, diagnostics, treatment.

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**The successful use of HBO in the child at long-term period after carbon monoxide poisoning
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Serdeshnova I.A., pediatrician of high grade, Deputy Chief Physician, Head Specialist on childhood (supernumerary), Koreneva E.V., pediatrician of high grade, Head of Somatic Department.

A clinical case of the successful treatment of the child at long-term period after carbon monoxide poisoning is presented in the article. The authors consider this case as demonstration of necessity of use of HBO.



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Treatment of idiopathic fibrosing alveolitis using corticosteroids alone

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A case of clinical practice of a patient with diagnosis "idiopathic fibrosing alveolitis" due to the rarity of the disease is presented. The patient is observed for 6 years. Favorable course of the disease.

Keywords: idiopathic fibrosing alveolitis, treatment.

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I.A. Ivanov

Was shaman insane?

I.A. Ivanov, psychiatrist of high grade, RPND, Yakutsk, member of the Russian Union of Journalists.

The role of the shaman in the past life of the Yakuts was diverse, but the main one is the treatment of diseases thought due to magical techniques. Sacrament shamanic nature, the secrets of their treatment have always attracted interest from scientists - researchers.



Egorov V.V.
"When a child is sick"

Egorov - anesthetist-resuscitator SBD "Children's City Clinical Hospital № 2", honored doctor of Sakha (Yakutia), a doctor of the highest category.

In 2011, the National Book Publisher "Bichik" started production of a series of popular books under the general title of "Family Doctor", which opened a guide for parents," When a child is sick, "written by doctors of the Children's Clinical Hospital № 2 in Yakutsk. The compilers are the chief doctor of the hospital Sophia Lavrentyevna Alexandrova, PhD, Excellent Health Worker of the Russian Federation, doctor of the highest category, and anesthetist-resuscitator of resuscitation and intensive care DGKB № 2 Valentin Egorov, Honored Doctor of the Sakha Republic (Yakutia), doctor of the highest category. Scientific consultants - Savvina Nadezhda Valer'evna, MD, Professor, Excellent Health Worker of the Russian Federation, doctor of the highest category, and Lyudmila Ilyasovna Verbitskaya, PhD, Honored Doctor of the Sakha Republic (Yakutia), doctor of the highest category.