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## Characterization of vasoactive proteolytic systems in young children with chronic secondary pyelonephritis

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### INTRODUCTION

In the pathogenesis of many diseases, including in nephropathies of various origins, vasoactive proteolytic systems of blood plasma play an important role. A special place among them belongs to the kallikrein-kinin (KKS) and renin-angiotensin (RAS) systems. KKS components among the first react to the damage and participate in the development of an inflammatory response [1-10]. Angiotensin-converting enzyme (ACE) is the main enzyme of RAS, which is a key link between the RAS and KKS. ACE is well known as an enzyme that regulates blood pressure and takes part in a number of processes in the body [1-10].

An important role in the regulation of proteolytic systems play a specific protein-inhibitors, have the property to bind proteolytic enzymes. Of particular interest are  $\alpha_2$ -macroglobulin ( $\alpha_2$ -MG) and  $\alpha_1$ -proteinase inhibitor ( $\alpha_1$ -PI), which are the main natural inhibitors of serine proteases of blood plasma. They have a high affinity for kallikrein and inhibit its, also, they are indicators of acute phase of inflammation [2, 3, 5-7, 9, 10].

### PURPOSE OF THE STUDY

To study the activity of vasoactive proteolytic systems in infants with chronic secondary pyelonephritis.

### MATERIALS AND METHODS

We examined 49 infants with chronic secondary pyelonephritis (33 children were examined in acute of the disease and 16 children - in remission of the disease). Control group consisted of 40 healthy children of similar age.

A survey of children performed in nephrology branch at Children's Hospital №1 (Tomsk) according to medico-economic standards (MES) study of children with nephropathies. We investigated the status of kallikrein-kinin and renin-angiotensin systems: kallikrein (KK) and kallikreinogen (KKG) activities determined by the method T.S. Pashina (1974), angiotensin-converting enzyme activity – by the method P.P. Golikov (1998),  $\alpha_1$ -proteinase inhibitor and  $\alpha_2$ -macroglobulin activities – by the method of V.F. Nartikova (1979).

The diagnosis of pyelonephritis was verified based on medical history and survey data in accordance with the classification proposed by M.Ya. Studenikin (1982).

Analysis of statistical data performed using the program «Statistica 6,0 for Windows». To determine the significance of differences of qualitative characteristics used analysis of contingency tables with calculation of the  $\chi^2$  Pearson's exact criterion and Fisher's exact criterion. Differences between the groups being compared were considered significant at  $p < 0,05$ .

## RESULTS AND DISCUSSION

Investigation of kallikrein-kinin system in young children with chronic secondary pyelonephritis has shown that in acute disease KK activity significantly increased in 2,2 times ( $p_{1-3} < 0,001$ ) and KKG activity reduced at 24% ( $p_{1-3} < 0,001$ ) compared with controls (table 1). In remission of chronic secondary pyelonephritis KK activity reduced and KKG activity increased, at the same time these parameters were significantly different from the parameters of the control group ( $p_{2-4} = 0,013$  and  $p_{2-4} < 0,001$ , adequately).

The study of renin-angiotensin system state showed that in children with exacerbation of chronic secondary pyelonephritis ACE activity statistically increase in 1,3 and 1,2 times compared with the control group ( $p_{1-3} < 0,001$ ). In achieving remission of chronic pyelonephritis ACE activity is reduced by 1,1 times, but remains higher than the parameter of healthy children ( $p_{2-3} < 0,016$ ) (table 1).

Investigation of parameters of kallikrein-kinin system in chronic secondary pyelonephritis depending on the type of congenital renal disease showed that during exacerbation of the disease on a background of hydronephrosis and pyeloectasia KK activity significantly increased by 1,7 times ( $p_{1-5} < 0,001$ ,  $p_{3-5} < 0,001$ ), while the activity of KKG is reduced by 23 and 25% ( $p_{1-5} < 0,043$ ,  $p_{3-5} < 0,001$ ) compared with controls (table 2). No statistically significant differences in the activities of KK and KKG in remission of the disease, depending on the type of congenital renal disease, compared with the control group was not revealed.

Received data reflect the participation of KKS in the inflammatory process pyelonephritis, in which the KKG level is reduced by the contact activation system (CAS), the latter is the trigger mechanism, which promotes the transformation of KKG in KK. KK is a plasma inflammatory mediator that participates in the regulation of intercellular interactions and increases vascular permeability. In addition, the KK induces activation of kinins (bradykinin), which have a powerful vasodilating effect on renal blood vessels leading to polyuria, that can contribute to the mechanical elimination of the pathogen from the urinary tract [9, 10].

During the period of exacerbation of chronic secondary pyelonephritis on the hydronephrosis and pyeloectasia background activity of ACE significantly increased in 1,3 times that is equivalent to the control group ( $p_{1-5} < 0,001$ ,  $p_{3-5} < 0,001$ ) (table 2). In remission of chronic secondary pyelonephritis on the pyeloectasia background activity of ACE remains significantly

high ( $p_{4-5} = 0,003$ ), but on the background of hydronephrosis the activity of ACE does not differ from the control group.

The obtained data indicate that in chronic secondary pyelonephritis RAS is activated, it leads to an increase of intraglomerular pressure and transient disruption of renal glomerular filtration due to vasoconstrictor effect of ACE. Due to the activity of ACE breakdown of bradykinin catalyzed, that prevents its vasodilatory action through the activation of AT II.

Preservation of the high activity of KK and ACE during remission of chronic pyelonephritis can be regarded as an unfavorable indicator. Answer the question of how quickly and how completely indicators of KKS and RAS normalized is only possible when monitoring patients over time.

The study of activities of specific proteinase inhibitors in chronic secondary pyelonephritis showed that during exacerbation of disease  $\alpha_2$ -macroglobulin ( $\alpha_2$ -MG) activity was significantly reduced by 28% ( $p_{1-4} = 0,001$ ), while in remission  $\alpha_2$ -MG activity was increased and was not statistically different from the parameter of the control group (table 3).

During the period of exacerbation of chronic pyelonephritis with the hydronephrosis and pyeloectasia background  $\alpha_2$ -macroglobulin activity significantly reduced by 44 and 28% ( $p_{1-5} = 0,036$ ,  $p_{3-5} = 0,037$ ). In remission of the disease activity of  $\alpha_2$ -MG does not differ from the control group (table 4).

Activity of the  $\alpha_1$ -proteinase inhibitor ( $\alpha_1$ -PI) in chronic secondary pyelonephritis had no significant differences when compared with the control group, so the data not shown.

It is known that protein-inhibitors are markers of the acute phase of inflammation and their function is aimed at reducing excessive proteolysis in pathological states. So, decrease in activity  $\alpha_2$ -MG, which is the main regulator of the kallikrein activity, causes high levels of kallikrein in blood plasma, contributes to the manifestation of its pathogenic functions in pyelonephritis in children.

## CONCLUSION

Thus, in chronic secondary pyelonephritis in young children, regardless of the type of congenital anomalies of the kidney, there is activation of the KKS: KK activity increases, KKG and  $\alpha_2$ -MG levels reduce. This reflects an imbalance between vasoactive proteolytic enzymes and their inhibitors in response to inflammation in the kidney and is the adaptive-protective. Decrease in activity  $\alpha_2$ -MG, which is the main regulator of the kallikrein activity, causes high levels of kallikrein in blood plasma, contributes to the manifestation of its pathogenic functions in pyelonephritis.

Also, in chronic secondary pyelonephritis RAS is activated, particularly angiotensin-converting enzyme, which catalyses the breakdown of bradykinin and prevents its vasodilator action, provides vasoconstriction through activation of angiotensin II (ATII). By stimulating macrophage activation and phagocytosis, angiotensin II increases inflammation in the damaged tissue.

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**Table 1**

### The activity of kallikrein-kinin system's indicators in children with chronic secondary pyelonephritis

Indicator	Chronic secondary PN			Control group n=40 (3)
	Period of exacerbation n=33 (1)	Period of remission n=16 (2)		
KKG (IU / ml)	M±m	224,99±9,92	250,58±16,77	298,21±7,79
	Me	235,8	258	297,04
	Q3	173,16	204	274,19
	Q1	268,37	318	340,36
	p intergroup	0,44		
	p pairs	-		
	p norm	p <sub>1-3</sub> <0,001 p <sub>2-3</sub> =0,013		
KK (IU / ml)	M±m	126,20±7,33	97,84±5,44	75,69±4,34
	Me	127,52	93,6	66,375
	Q3	93,18	82,1	62,105
	Q1	147,05	116	78,16
	p intergroup	0,048		
	p pairs	p <sub>1-2</sub> =0,02		
	p norm	p <sub>1-3</sub> <0,001 p <sub>2-3</sub> <0,001		
ACE (mol / min • L)	M±m	60,20±2,16	53,13±3,04	47,04±1,51
	Me	61,68	54,2	46,17
	Q3	54,31	47,6	41,315
	Q1	69,9	59,2	51,18
	p intergroup	0,12		
	p pairs	-		
	p norm	p <sub>1-3</sub> <0,001 p <sub>2-3</sub> =0,016		

Note: PN - pyelonephritis,  $p_{1-3}$  - reliability of differences between children with chronic secondary PN during the exacerbation and healthy,  $p_{2-3}$  - reliability of differences between children with chronic secondary PN in remission and healthy.

Table 2

**Kallikreinogen (KKG) and kallikrein (KK) activities in infants with chronic secondary pyelonephritis depending on the type of congenital renal pathology**

Indicator	Chronic PN on the background of hydronephrosis		Chronic PN on the background of pyeloectasia		Control group n=40 (5)	
	Period of exacerbation n=7 (1)	Period of remission n=4 (2)	Period of exacerbation n=22 (3)	Period of remission n=12 (4)		
KKG (IU / ml)	M <sub>±m</sub>	229,58±28,41	260,06±35,77	221,90±11,82	247,42±19,79	298,21±7,79
	Me	235,8	227,77	217,625	224,175	297,04
	Q3	159,99	218,18	173,16	202,355	274,19
	Q1	292,665	301,95	266,36	319,175	340,36
	p intergroup	0,001				
	p pairs	$p_{1-5}=0,043$ $p_{3-5}<0,001$				
KK (IU / ml)	M <sub>±m</sub>	131,98±14,50	101,74±14,17	128,47±8,92	96,54±5,92	75,69±4,34
	Me	127,52	92,215	131,72	93,6	66,375
	Q3	122,145	81,67	95,34	79,1	62,105
	Q1	139,085	121,81	147,05	117,8	78,16
	p intergroup	0,001				
	p pairs	$p_{1-5}<0,001$ $p_{3-5}<0,001$				
ACE (mol / min • L)	M <sub>±m</sub>	60,13±5,95	47,34±10,26	60,54±2,38	55,06±2,4	47,04±1,5
	Me	61,68	47,925	59,98	54,155	46,17
	Q3	55,21	30,005	54,31	48,33	41,315
	Q1	67,825	64,68	69,38	58,22	51,18
	p intergroup	0,001				
	p pairs	$p_{1-5}<0,001$ , $p_{3-5}<0,001$ , $p_{4-5}=0,003$				

Note: PN - pyelonephritis,  $p_{1-5}$  - reliability of differences between children with chronic secondary PN on the background of hydronephrosis during the exacerbation and healthy,  $p_{3-5}$  -

reliability of differences between children with chronic secondary PN on the background of pyeloectasia during the exacerbation and healthy.

**Table 3**  
**Activity of  $\alpha_2$ -macroglobulin ( $\alpha_2$ -MG) in infants with chronic secondary pyelonephritis**

Indicator		Chronic secondary pyelonephritis		Control group n=40 (3)
		Period of exacerbation n=33 (1)	Period of remission n=16 (2)	
$\alpha_2$ -MG IU / ml	M $\pm$ m	2,36 $\pm$ 0,25	2,77 $\pm$ 0,30	3,28 $\pm$ 0,16
	Me	1,9	2,73	3,1
	Q3	1,4	2,26	2,48
	Q1	3,05	3,29	4,1
	p intergroup	0,29		
	p pairs	-		
	p norm	p <sub>1-3</sub> =0,001		

Note: p<sub>1-3</sub> - reliability of differences between children with chronic secondary pyelonephritis during the exacerbation and control group.

**Table 4**  
**Activity of specific proteinase inhibitors in infants with chronic secondary pyelonephritis depending on the type of congenital anomalies of the kidney**

Indicator		Chronic pyelonephritis on the background of hydronephrosis		Chronic pyelonephritis on the background of pyeloectasia		Control group n=40 (5)
		Period of exacerbation n= 7 (1)	Period of remission n=4 (2)	Period of exacerbation n=22 (3)	Period of remission n=12 (4)	
$\alpha_2$ -MG IU / ml	M $\pm$ m	1.84 $\pm$ 0,33	1,82 $\pm$ 0,53	2,34 $\pm$ 0,31	3,55 $\pm$ 0,35	3,28 $\pm$ 0,16
	Me	1,82	1,92	1,81	3,06	3,1
	Q3	1,27	0,91	1,4	2,46	2,48
	Q1	2,45	2,73	3,07	3,59	4,1
	p intergroup	0,002				
	p pairs	p <sub>1-5</sub> =0,036		p <sub>3-5</sub> =0,037		

Note: p<sub>1-5</sub> - reliability of differences between children with chronic secondary pyelonephritis on the background of hydronephrosis during the exacerbation and control group, p<sub>3-5</sub> - reliability of differences between children with chronic secondary pyelonephritis on the background of pyeloectasia during the exacerbation and control group.

**ABSTRACT**

Vasoactive proteolytic system involved in the regulation of various physiological systems and the development of many pathological states. In this work we investigated the activity of kallikrein, kallikreinogen, angiotensin-converting enzyme,  $\alpha_1$ -proteinase inhibitor,  $\alpha_2$ -macroglobulin in infants with chronic secondary pyelonephritis. In chronic secondary pyelonephritis, no matter what type of congenital renal disease, there is activation of vasoactive proteolytic systems that may have diagnostic and prognostic significance.

**Key words:** kallikrein, kallikreinogen, angiotensin-converting enzyme  $\alpha_2$ -macroglobulin, young children.

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**Constitutional features of sexual dimorphism and PHYSICAL DEVELOPMENT OF YOUNG MEN (YOUTHS) IN CENTRAL SIBERIA**

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Summary of Anthropometric survey of young men in Central Siberia has revealed uneven distribution of somatotype on sexual differentiation dominated mainly gynecomorphous somatotype and asthenia, with a gradual leveling age indicators. Found that, in adolescence the process of physical and sexual maturation is not completed.

**Key words:** physical constitution, sexual dimorphism, male, Siberia.

**Introduction**

It is well known that the formation of the same part of the Constitution shall take the external environment and heredity. Hereditarily is determined by the main features of the constitution - the longitudinal dimensions of the body and the dominant type of metabolism, the latter is inherited only if in

the same locality lived continuously 2-3 generations of people. The combination of these attributes determines the degree of similarity of many people with each other, allowing them to allocate 3-4 basic constitutional type [1].

Anthropological data follow the physical development of certain groups and in some cases to diagnose the disease [4]. Epochal dynamics of body size over the past 40 years in boys and girls have the same direction for some signs - increase in body length and leg length, girth reduction, and the sagittal diameter of the chest. For other signs observed some sex differences - a slight increase in body weight and shoulder width in boys, in the absence of the dynamics of these dimensions in girls, a reduction in the width of the pelvis in girls, in the absence of dynamics in boys [2].

Determination of the degree of somatic sexual differentiation by an index of D. Tanner (1968) found that youths in the development of modern, elevated gynecomorphous [7], is quite closely associated with physical inactivity [9], and the level of the index in boys and Tanner's level of physical activity in an equal dependent of each other [5]. Compared with studies last century has increased the number of young men with signs of asthenia and, especially, gynecomorphia in highly urbanized regions [8]. The purpose of the work - identification of features of sexual differentiation of males, depending on the physical constitution, weight and body density. Materials and methods A survey of 345 young people (from 17 to 21 years) according to the scheme of the age periods of human ontogenesis [10]. All the boys were Caucasians, living in the Krasnoyarsk region and the last 1-2 years have studied in universities of Krasnoyarsk. The measurements were performed on a voluntary basis in the first half of the day, in a light room standard set of anthropometric instruments and devices that have passed metric verification by well-known and accepted procedures [6,12]. In addition to absolute and relative indicators are calculated coefficients and indices: the index of sexual dimorphism (SDI) for J. Tanner, body mass index (BMI-Kettle2), the index of proportionality of body (a type of physical constitution) by L. Rees – H. J. Eisenk, the index of body density (Rohrer), the index of proportionality of the chest (Erisman), the indices of the chest, " wall, shoulder width (SRI) and pelvic-brachial index (TPU) to E.N. Khrisanfova [11] and others. The research results were introduced into the individual protocols and the electronic database. Statistical analysis was performed using a software package Statistics v.6.0 using the methods of parametric and nonparametric statistics. Results and discussion Results of gross studies have shown that sexual dimorphism index (SDI), which characterizes membership in one of the sexes and the degree of severity, all young men are gynecomorphous type ( $78,07 \pm 1,25$ ), and the index shows a moderate specific dysplasia of the floor and has a large interquartile variability (49,0-108,5). A more detailed description of youths on S.D.I. allowed to establish a moderate degree of severity of symptoms of dysplasia sex (gynecomorphizm) at 65.42% of the total number of examinees, mild dysplasia of the sexes (mesomorphism) at 29.50% and no signs of dysplasia of the sexes (andromorphizm) at 5, 08%. Body length in boys varies from 163.0 cm to 199.5 cm, with an average body length of  $180,24 \pm 0,54$  cm average body weight in this group of boys  $70,35 \pm 1,43$  kg, maximum weight - 115.0 kg, minimum - 48.2 kg.

Index Reece Eisenk, characterizing the proportionality of the constitution and physique, the youths belong to the asthenic type ( $109,83 \pm 1,0$ ), as evidenced by exaggerated pelvic-brachial index (TPU =  $79,46 \pm 1,07$ ) and undervalued (SRI) index than shoulder width ( $19,58 \pm 0,47$ ), for which they are dolihomorphous (asthenic) type. At the same time the indices related to the chest: (IUC) Chest ( $51,45 \pm 0,52$ ), «Wall (IS)  $-0,78 \pm 0,09$  and Erisman (IE)  $-2.58 \pm 4,16$ , can be attributed to the development of the boundary between the mesomorphic (normosthenic) and dolihomorphous. types.

Body mass index (Quetelet 2) indicate that the energy stability ( $21, 62 \pm 0,66$  kg / m<sup>2</sup>) and a sufficient density of the body, determined by the index Rohrer, ( $12,0 \pm 0,50$  kg / m<sup>3</sup>). However, BMI has for different individuals is very wide scope, from 16.29 kg / m<sup>2</sup> to 32.57 kg / m<sup>2</sup> at 50% quartile values within the normal range ( $19.6 -23.33$  kg / m<sup>2</sup>) (Table 1). Rohrer index figures are similar in orientation to the BMI, being within 50% quartile values from 10.91 to 12.77 lb / ft<sup>3</sup> and with a breadth of scope from

8.90 to 17.99 kg / m<sup>3</sup>. Clearly reveals the uneven distribution of somatotype on sexual differentiation and size parameters, the index Kettle 2 (Table 1).

The young men andromorphous somatotype showing the highest overall parameters of overweight, obesity and even chronic energy deficiency. Boys and mesomorphic somatotype gynecomorphous same height and weight, are also quite a few young men with excessive body weight and chronic energy deficiency (Khan).

Constitutional typing in selected groups of boys on gender L. Rees – H.J. Eisenk revealed a predominance of asthenic body type in gynecomorphous and mesomorphic somatotype and the lowest percentage of andromorphous. Normostenics have roughly equal gender distribution. At picnics severity of symptoms of the opposite sex occurs in the smallest number of boys. In general, the number of young men with signs of sexual dimorphism is reduced from asthenics to normostenics and picnics, and the expression of gender traits is growing at asthenics from andromorphous type to gynecomorphous type have normostenics remains at one level and have picnics down from andromorphous to gynecomorpham (Table 2).

Subsequent evaluation of the morpho-functional status of young men revealed that an integral feature content of tissues in the body (body density) indicates the presence of the organism boys all gender groups, the normal content of muscle and bone mass with their increase of gynecomorfii to meso- and andromorphia. In gynecomorphous and mesomorphic somatotype index Erisman - proportionally developed chest, the andromorphous - wide. But it's also seen a clear trend towards an increase in the width and circumference of chest (IUC) from gynecomorphous to andromorphous types (Table 3). The parameters characterizing the growth of body width (SRI, IC, TPU) and boys gynecomorphous mesomorphic types of gender-based anthropometric marked decrease in shoulder width, flattening of the chest and an increase in the width of the pelvis.

Determination of the degree of somatic sexual differentiation by an index of D. Tanner boys Barnaul [7] showed that in the juvenile period to andromorphous somatotype are 10,2% of the subjects, the mesomorphic - 13,1%, to gynecomorphous - 76,7%. In our study, the distribution of signs of sexual dimorphism remained the same, but the predominance of ginekomorphous somatotype below 11%, andromorphous below 2 times (5.08%), and mesomorphic higher in the more than 2 times (29.50%) of total surveyed, which may be associated with different numbers of youths, their different age requirement and varying degrees of physical activity, and, possibly, with different environmental conditions. Age-specific rankings for all major indicators revealed that the growth of young men 17-18 years of age in the years to almost no change, and body weight by 19 years of age decreased by 8,5 - 9% and 21 year of age up to 12,0%. Increase muscle and bone mass occurs most rapidly in the 17-18 years, as evidenced by high rates of Rohrer index and Kettle2, sequential decrease overweight with 30.0% in 17 years to 9,1% in 20 years and the incidence of obesity but increases with the chronic energy deficiency (Khan) of the total youth with 12.5% in 19 years to 23.0% in 1921 to life (Table 3).

In adolescence with a change in physical development varies and constitutional identity. Number asthenics with 80% decreased by 34.5% due to their transition to normosteniki (16,5%) and picnicking (by 18,0%). Accordingly, the physical constitution is a young progressive change in their somato-sexual constitution. In 17 years gynecomorphous somatotype was 70,0%, mesomorphic - 20,0% and andromorphous - 10,0%. By 1921 the number of youths ginekomorfnogo somatotype decreased by 18.5% due to their transition into the mesomorphic somatotype. Age-specific rates andromorphous somatotype had no statistically significant differences in value. Given that the androgen levels of blood plasma is positively correlated with the width of the shoulders relative to the width of the pelvis [2], parameters of physical development is closely correlated with indices of sexual dimorphism, and the latter with physical activity [5], the boys in Central Siberia during the period 17 - 21 years more largely preserved signs

ginekomorfnosti and, therefore, at a moderate physical activity does not terminate the processes of physical and sexual maturation.

Conclusion Thus, the results convince us that the boys from the age of adolescence is to improve the physical performance, reduced asthenia and gynecomorphism, the growth of bone and muscle mass and stability indices of density and body mass, but not completing the process of somato-sexual, and not just , maturing. Remains a high percentage of youths with chronic energy deficiency, obesity and overweight, which is known to depend on features of the autonomic nervous system [3].

Therefore, in adolescence need to be careful and binding on the state of knowledge of the physical health approach to the development of harmonious personality and physical training associated with athletic achievements. Perhaps it is time to think about the postponement of military conscription.

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Table 1

Anthropometrical showing depending on the sexual dimorphism in the youths.

J.Tanner, 1968)

№	showing	Gynecomophous	Mesomorphous	Andromorphous
		type (N=218)	type (N=107)	type (N=20)
		(M±m)	(M±m)	(M±m)
1	Body legnth, cm	180,0±0,58	180,12±0,46	184,13±0,47
2	Body mass, kg	69,12±1,39	71,41±1,29	80,03±2,00
3	Ketle 2 (ИМТ), kg/m <sup>2</sup>	21,28±0,63	22,04±0,63	23,53±0,97
	overweight, %	9,34%	17,24%	20,0%
	fatness, %	1,55%	-	13,33%
	Chronicle energy.shortness ., %	12,95%	6,89%	13,33%
	Standard (norm), %	76,16%	75,87%	53,34%

Table 2

Classification of the youths according to the sexual dimorphism and physical constitution.

Показатели	Gynecomophous (M±m)	Mesomophous (M±m)	Andromophous (M±m)
Physical Constitution (L.Rees – H.J. Eisenk), y.e.	110,66±0,96	108,81±1,00	105,05±1,33
asthenics	69,43%	66,67%	40,0%
normsthenics	26,94%	24,14%	26,67%
pyknics	3,63%	9,19%	33,33%

Table 3

Classification anthropometrical showing and indexes according to the sexual dimorphism in the youths.

№	Showing	Gynecomorphous (M±m)	Mesomorphous (M±m)	Andromorphous (M±m)
1	Bodythickness (Rorera's index), kg/m <sup>3</sup>	11,84±0,48	12,22±0,49	12,78±0,71
2	Chest index (CHI)	51,03±0,49	52,11±0,55	52,99±0,62
3	Erisman index (EI)	1,82±4,64	3,76±3,64	5,47±3,53
4	Index of the width of the shoulders (IWCH)	18,48±0,37	21,43±0,17	22,99±0,26
5	Stenia index (SI)	0,79±0,02	0,77±0,03	0,73±0,1
6	Hip shoulder showing (HSS)	83,83±0,94	71,93±0,39	66,87±0,71

**MODERN DIRECTIONS IN RESEARCH AETIOLOGIES AND  
PATHOGENESIS OF THE IDIOPATICHESKY SCOLIOSIS AT CHILDREN**

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**The resume:** the review of results of the spent researches and representations existing now about an aetiology and pathogenesis juvenile idiopatchesky a scoliosis (JIS) at children and teenagers Is given. Nejro-anatomic mutual relations and a role of system dysfunction in pathogenesis JIS are discussed. Modern theories of development, major factors of risk of development and progressing juvenile idiopatchesky a scoliosis at children, its basic components are reflected. Importance of continuation of researches JIS at molekulyarno-biochemical level, necessity of allocation of specific parametres - development markers idiopatchesky a scoliosis for perfection of approaches to diagnostics, forecasting of features of a current, preventive maintenance and treatment of the given disease at children is underlined.

**Keywords:** children, idiopatchesky, a scoliosis, aetiology, pathogenesis

**Introduction:** the Scoliosis - a cross-section curvature of a backbone, can arise at any age, and is in most cases presented juvenile idiopatchesky by a scoliosis which starts to develop at children at the age from 3 till 10 years. The Idiopatchesky scoliosis (IS) comes to light at 0,2-6 % of teenagers, mainly girls. Despite numerous researches idiopatchesky the scoliosis remains to one of the least understood diseases of the oporno-impellent device and it aetiology and pathogenesis till now remains to unknown persons [30]. Some hypotheses, aetiology and pathogenesis idiopatchesky a scoliosis, including genetic factors, biochemical, mechanical, neurologic, and also muscular and hormonal are historically considered. Till

now there is no accurate representation about an aetiology, the reasons of progressing or stabilisation of pathological process at JIS. Opinions of researchers on presence defined morphological genotype, existence of sexual distinctions and their influence on an estimation, results and approaches to treatment are ambiguous. It is established, that various factors can influence indirectly and not be a scoliosis immediate cause.

The main problem at children with IC is unpredictability of progressing of a curvature of a backbone. In understanding IS increasing growth rate and a parity of geometrical indicators of vertebrae - obvious risk factors of a progression of a curve. Asymmetric functioning of muscles is connected with the increased axial rotation which is in turn connected with increase in corner Kobbas and reduction kyphosis. The combination of these variables provides ability of penetration into an essence of physiology of three-dimensional biomechanical development of progressing of a curve at IS [12]. Asymmetric growth of a backbone is considered as one of possible etiologic factors in pathogenesis IS [7,51]. According to Goldberg CJ (2006) IS - result the asymmetric the growth limited not only a backbone [21,22]. Chu WC with co-authors (2008) considers, that the concept «asynchronous neuro-bone growth» in pathogenesis IS plays a considerable role [17].

In researches with use Jaderno-magnetic resonant tomography, concerning relations of growth of a spinal cord to a backbone at IS, the relative length of a spinal cord to vertebral to the channel was defined, authentic proofs of interest of a spinal cord are received by pathological changes at IS and the term «a double pathology» is offered. IS it is considered as disease with the general neuroanatomy a pathology: presence of a spinal cord of normal length, with simultaneously available short and rather incorrectly extended vertebral the channel. Probably, that precedes a curvature is excessively fast growth of a spine column rather intact a spinal cord that is shown by force of pressure between two ends, cranialis and caudalis. Thus, there is a presence of the increased intensity along a longitudinal axis of a spinal cord at IS [16,17].

Changes neuroanatomy and-or nervous dysfunction can be expressed only in serious cases. The concept of asynchronous growth of the kostno-brain channel is regarded as one of components in development JIS. One more making interrelation of this process is established between a brain and a skull at people with idiopathic scoliosis, as a result of research of some authors changes in a brain (intratentorial and supratentorial) and a skull have been found. Authors estimated position cerebellar tonsil, somatosensory potentials, clinical and neurologic examination was spent, the presence tendency tonsillar ectopia has been as a result revealed more often at chest and torakalno-lumbar curvatures. On the basis of what authors have come to conclusion, that lower position cerebellar tonsil can play the important role in aetiology and pathogenesis IS [17,45,46].

Relevance of concept of system dysfunction in pathogenesis JIS, and also influence of levels kalmodulin and a vascular pathology on development of asynchronous growth of the kostno-brain channel [17] is discussed. Morphological researches of an internal surface of a skull are carried out at JIS.

The first attempt to use a combination of medical knowledge, methods of the analysis of the image and scientific methods of visualisation with statistical techniques have undertaken Shi L, Heng PA et al. (2006 [45]). However, additional researches in the given direction are necessary. According to Masharawi YM (2008) development IS is connected with some moderately expressed forms of obverse asymmetry. Orthodontic deviations [4,29,33] influence also.

Detection of abnormal extra-back is left-right skeletal asymmetries of length of the top and bottom finitenesses, periapical parts of edges, a basin at children with IS has allowed to draw conclusions on skeletal bilateral asymmetry [9]. Results of the given researches confirm a hypothesis, that at children scoliotic curvatures are preceded by anomalies of skeletal proportions. These proportions are in three measurements: the left-right, tsefalo-kaudalnom and it is face-to-face-kaudalnom spine column measurements. The reasons of an origin of these anomalies are unknown, but probably they are the genetic and ecological factors operating in embryonal of a life, at early age they are not expressed phenotype, but shown after years after a birth [5].

Asymmetries of length of the top finitenesses are found out in patients with idiopatchesky a scoliosis, combined with a backbone curvature. It is informed on the top asymmetry of length of a hand at the chest scoliosis, substantially connected with apical vertebral rotation. The reasons of interrelation of asymmetry of length of hands with apical vertebral rotation are unknown, three factors are considered: neuromuscular mechanisms, relative bent neurocentral synchondrosis, excessively fast growth, including excessively fast growth of length of an edge, prospective anomaly of plates of growth. Now the further researches are carried out in a direction of revealing of ekstra-back skeletal asymmetry of length of the top finitenesses and periapical sites of edges at patients with chest IS [6,10,27].

Laterality (brain asymmetry) - doubtless, but not a major factor in scoliosis development, the preference of the left hand is revealed at a significant amount of boys with IS, but was present and at girls with IS [21]. Dysfunction is involved in aetiology IS not found out earlier neuromuscular. In norm the central nervous system it is necessary to adapt to quickly growing skeleton, and at IS there is a formation of asymmetry of a back owing to the various reasons. There are data, that progressing JIS is influenced by formation of the scheme "TSNS-BODY", namely a delay of maturing of the scheme "TSNS-BODY" during time pubertal growth. In particular, scoliosis progressing begins during fast growth of a back that speaks a delay of realisation of association of the scheme "TSNS-BODY". It can arise because of infringements of touch perception which weakenedly is perceived in a brain, and-or from a weak motility of the child.

In process of a curvature of a backbone at some patients can be involved peroxide oxidation lipids in nervous system [8]. Researches of an aetiology of a scoliosis at cellular level have shown infringements of homeostasis  $Ca^{2+}$ , changes in system  $Ca^{2+}$ -ATPase, including SERCA2b (sarco/endoplasmic reticulum -  $Ca^{2+}$ -ATPase) and PMCA (плазма мембранный -  $Ca^{2+}$ -ATPase) isoforms. System defect in

differentiation of the cages, involving caspase-3 is revealed. Authors are inclined to consider it as the new mechanism in aetiology and pathogenesis IS [11].

Longitudinal vertebral growth occurs from endochondrial bone vertebral growth plates. In research Wang S, Qiu Y. et al. (2007) plates of growth from the convex and bent parties of a backbone have been studied by a method of histology and immunohistochemistry to estimate growth activity, fast increase in a cage, apoptosis. It is established, that normal zona the architecture was observed on the convex party of a plate of growth, and unorganized architecture - on the concave party of a backbone. Proliferative potential indexes and indexes apoptosis chondrocyte in proliferative and a hypertrophic zone on the convex party were considerably above, than on the concave party. Essential distinction proliferative potential index between the convex and concave party on the top end of a vertebra is noted. Distinction in histologic variants and cellular activity between the convex and concave party, has specified, that at a bilateral plate of growth is various kinesia growth which can influence a progression of a curve of a backbone at patients with IS [52].

There are data about influence on development IS of position of the centre of weight of a body (Ostrowska B., 2006) [34]. Distinctions in force of bending and unbending muscles can make one of reasons IS [35]. There are messages, that the pathological morphology of a basin can be basic at idiopathic scoliosis at children [43]. Researches Karski T. (2006) the interrelation of deficiency of reduction of the right hip and IS is shown. There is a making part of a foot which can play a role in deficiency of reduction of the right hip at a scoliosis. It is revealed that at all children with IS was contracture the right hip, often connected with contracture rotations. Contracture the right hip, structural or functional, it is connected with «a syndrome contracture». Children with real contracture the right hip or its reduction make the first group of risk of development of a scoliosis on aetiology and pathogenesis a double S-shaped scoliosis. Originally change of rotation of a backbone, and the changes connected with gait takes place, begin in 3-4 years. At other patients having only restriction of reduction of the right hip, formation lumbar and pojasnichno-kresttsovogo or a pojasnichno-chest link sided S-scoliosis is noted. The third group has the minimum curves or has no them in general, but has pathological changes in a backbone. Such patients have problems with physical activity as at adult age it leads to considerable pains in a waist [27].

Asymmetry of movement of hips during gait causes asymmetry of loading and asymmetry of growth of both parties. Thus, the scoliosis is secondary indemnification for a pathology in a basin and a backbone. Such classification establishes the clear therapeutic approach to everyone etiologic to scoliosis group, considers possibility of carrying out of preventive maintenance. The understanding of biomechanical aetiology IS allows to prevent the reasons of these deformations [7,13,22]. It was spent biometry muscles at IS, research of anatomic data, volume of back muscles from both parties of a backbone. The muscle volume was big on the concave party, than on convex [12].

Attempt of performance of a method of mathematical modelling for a motor estimation of process of preservation of balance of a body has been made. The balance of a body, motor parameters of investigated children was estimated. The analysis of the received and settlement results has shown, that in scoliosis group there was a big loss of balance of a body, than at healthy children. Speed of preservation of balance at its deviation was more slowly and depended on a deviation corner. Thus, reaction of nervous system for an equilibration of changes at a scoliosis is obviously delayed and characterised by lower impulsiveness [3].

Grivas TB, Vasiliadis E. et al. (2006) the role of biomechanics of intervertebral disks in pathogenesis idiopathic scoliosis for the purpose of specification of a role deformation of an intervertebral disk in a progression scoliotic was studied by a curve. It has been shown, that deformation apicalis an intervertebral disk - the important factor influencing progressing of a scoliosis [23].

The role of genetic factors in development IS has been authentically registered: it is proved, that polymorphism of gene CHD7 is connected with predisposition to IS [20]. According to received Alden KJ (2006) results, the site on a chromosome 19p13 has essential value in an aetiology idiopathic scoliosis [1]. However messages on a certain way of genetic inheritance are not final. Current representations about the given pathology assert, that idiopathic scoliosis - multifactorial illness with genetic factors of predisposition [25,30]. With IS additional phenotypes which assume system dysregulation growth during a sexual maturity have a considerable quantity of patients. Having established the fact of communication of receptors alleles somatotropin with height of a body and the answer to development somatotropin, Qiu XS, Tang NL et al. (2007) have put forward a hypothesis, that a receptor somatotropin a - the contributing factor in occurrence IS [37].

Hormonal insulin-like growth factor plays a basic role in regulation of skeletal growth. Genetic research has revealed associations of a gene of the insulin-like factor of growth-I (IGF-I) with weight of a scoliosis and osteoporosis at IS. Importance IGF-I in skeletal growth does by its major factor which would play the leading part in interrelation of fast growth and a progression of a scoliosis [54]. The association of a receptor of vitamin D (VDR) and gene polymorphism is investigated at pathological growth of a bone at IS. Authors have come to conclusion, that polymorphism of site BsmI of a gene of a receptor of vitamin D can be connected with the wrong sample of growth and low bone weight at girls with IS [53].

The association between interleukin-6 and gene polymorphism MMP-3 is revealed at IS. On interrelation between a matrix metalloproteinases (MMPs) and a degeneration of an intervertebral disk have informed some researchers. One of the first researches, which authors have estimated possibility of that fact, that gene variants IL-6 and MMPs could be connected with a scoliosis and have assumed, that MMP-3 and IL-6 are the important markers for possible diagnostics of genetic predisposition to a scoliosis [2].

It is known, that IS is one of orthopedic pathologies at which clinical presence sexual dimorphism is most of all noted. Sexual dimorphism influences spine column growth, a morphotype, hormones and in a combination to environment, genetic factors it can lead to development of a phenotype of the patient with IS. The Same factors can play a role in a curve progression, despite surgical intervention and can help to explain, why curvatures of a spine column at some patients never change, and at others progress, despite spent correction. Essential distinctions in current IS take place, and it influences the diagnosis and results of treatment [44].

Kulis A, Zarzycki D, Jaśkiewicz J. (2006) levels estradiol at healthy and girls with IS at the age of 11-14 years were investigated. The received results specify in possible influence of changes of concentration estradiol during sexual development, and also on initiation and a progression of a lateral curvature of a backbone [28]. Some authors have revealed the raised level testosterone at girls with IS and have made the assumption, that the estimation of levels testosterone could be the important harbinger of progressing of a scoliosis, these researches will be continued [43].

Cross communication of an estrogen with melatonin - one of ways pathogenesis IS. IS represents the form of a scoliosis which progresses in puberty. This critical period coincides with many biological changes connected with an estrogen. Tang NL, Yeung HY, Lee KM et al. (2006) the effect on osteoblast was defined at IS in cross communication between an estrogen and melatonin at level of fibers. It is shown, that if to consider IS osteoblast, their functioning, an estrogen and melatonin become the important components in pathogenesis IS. Polymorphism of a site *aXbaI* a gene of a receptor of an estrogen, most likely, is connected with risk of development IS [29,50].

Presence of gene Aggrecan is considered as one of etiologic factors IS. Pathogenetic mechanism IS has been established on the basis of all-round morphological and biochemical researches of components of a back column at patients with IS. It is proved, that IS develops on the basis of synthesis change proteoglycane and formations vertebral growth plates. Found keratan - the fraction connected with sulphate, possibly, a marker of genetic changes in proteoglycane. Research has shown, that occurrence Aggrecan of a gene is considerably reduced in cultures chondroblast at patients with presence by the fraction keratan-connected with sulphate and keratan the sulphate increase is connected with increase lumnican [57].

Neuroendocrinal the theory as is based on deficiency melatonin in an organism of patients with IS. In researches Azeddine B, Letellier K, Wang da S, Moldovan F, Moreau A. (2007) development dysfunction melatonin in osteoblast, received from patients with IS which authentically differed at healthy patients is shown. Preliminary molecular classification of patients with IS, based on the cellular answer on melatonin and distinctions of interaction of fibers [3] is offered. A number of authors, investigating allocation uric 6-sulfatoxyl-melatonin and a glucose metabolism in epiphysis, have come to conclusion, that constant deficiency melatonin cannot be a scoliosis major factor. Changes of a metabolism of brain glucose also are peculiar for patients with a scoliosis [36,47].

The arrangement of receptors melatonin in paravertebral muscles asymmetrically also can be secondary change at a scoliosis. The hypothesis expresses, that unilateral backlog in growth initiates a scoliosis. In this direction comparison of concentration of receptors melatonin mRNA in bilateral paravertebral muscles was spent at IS [39]. The results received by authors have shown, that concentration of receptors melatonin in bilateral vertebral muscles at IS is asymmetric, but it can be and secondary change. These results confirm, that deficiency melatonin plays a part in scoliosis development, during too time experimental restoration of levels melatonin prevents development of a scoliosis [3]. And polymorphism of a receptor of a gene melatonin 1B (MTNR1B) associates with IS [32,38].

The role leptin is investigated at pathological growth at girls with IS, is revealed, that at girls with IS level leptin is authentically reduced. By authors it is shown, that level leptin is connected with weight of a body, an index of weight of a body and other parametres of growth. It is supposed, that leptin can play the important role at low weight of a body at girls with IS. Reduction of concentration of level leptin and its association with weight of a body and weight of a bone at girls with IS [40,58] is proved.

At children with IS is present osteosinging as in axial, and a peripheral skeleton. Results densitometria show, that at 86 % of patients with IS the constant of osteosinging during the period of maturing of a skeleton is registered. At IS the general takes place osteosinging and its association with wrong pubertal growth, a mineral exchange of a bone and calcium consumption. At IS the general low weight of a bone is registered. However, exact mechanisms and the reasons of loss of bone weight at IS are yet enough identified. Attempt of research of the relation between concentration in whey of the activator of a receptor nuclear ligand the factor kappaB (RANKL) and level serous osteoprotegerin (OPG) is undertaken. Results have shown instability and broken interaction RANKL and OPG which can be the important reason in pathogenesis reduction of mineral density of a bone at IS [14,15,48,49].

Some authors reveal lower degree of a mineralization in cortical a layer of bones at IS. The lowered density of a bone mineral was observed in trabeculae bones at considerable number of patients with IS. Both trabeculae, and cortical the mineral density in group with IS was much more low, than in control groups. Presumably, girls with IS could have changes in a bone mineralization during time prepubertal growth [55].

According to the literature, the broken metabolism of collagen of type 1 and 2 can be one of the reasons of development IS and, possibly, important factor in a scoliosis progression. At a scoliosis cartilages of vertebrae have signs of recourse and hypoplasia. The concave party of a vertebra is amazed more seriously, than convex. The increase collagen type 2 and TGF-beta1, bFGF in the concave parties apicale the parties at a scoliosis can be result of reconstruction of an extracellular matrix and reaction of indemnification which are caused by pathological biomechanical forces [24,41]. Low concentration calmodulin is found out in joints of a backbone of patients with IS [42]. Ecological factors too influence development IS. According to Grivas TB (2006) there is a proved association between prevalence IS at girls and geographical width: number of girls-teenagers with IS above in northern countries [23].

There are distinctions in concentration of selenium, copper, zinc in hair (and whey) at children with IS. Hair of the patients, suffering a scoliosis, have shown the increased maintenance of zinc and the reduced maintenance of selenium in comparison with control group. Relation Cu/Se in this group of patients was considerable above because of higher concentration of copper and lower maintenance of selenium in comparison with control group. Concentration of selenium in whey at children with a scoliosis has been considerably reduced. Various changes of the maintenance of microcells in biological samples are not casual. It can underlie formation of various forms trace elementosis in an organism at IS [18].

There are separate data about presence of deviations in blood supply of a thorax for girls - teenagers with a progressing scoliosis of chest department of a backbone. Possibly, dissymmetric current of blood promotes development of this kind of a scoliosis [26]. Cardiogramme deviations are quite often found out in children with IS. The tendency to a deviation of an axis of heart to the right is marked, changes QRS assume with the years a cardiological component in studying of a scoliosis at children and demands more profound kliniko-functional assessment of works of heart from children with IS [19].

Thus, continuation of researches IS are extremely important for perfection of approaches to diagnostics, forecasting of features of a current, preventive maintenance and treatment. Allocation of specific parametres - markers of development IS is necessary. Probably, research IS at molekularno-biochemical level will allow to leave on a new stage of preventive maintenance of the given pathology.

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## **THE HEALTH STATUS OF ADOLESCENTS WITH THE PUBERTAL PERIOD HYPOTHALAMIC SYNDROME**

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**SUMMARY:** 74 healthy adolescents and 142 patients with the pubertal period hypothalamic syndrome were examined. The indexes of protein, lipid and carbohydrate metabolic processes, hormone state, psychological peculiarities, quality of life, physical development peculiarities and reproductive function formation were investigated. Detected clinical and laboratory changes represent the early debut of the metabolic syndrome (MS) in the adolescents with hypothalamic syndrome (HS). The polymorphism of metabolic and endocrine disorders in the adolescents with HS reflects the high risk of early atherosclerosis and diabetes mellitus type 2 developments, progression of poly-endocrine pathology, resulting in reproductive disabilities.

**Key words:** adolescents, hypothalamic syndrome, health status, quality of life.

Pubertal period hypothalamic syndrome (HS) is the actual problem, depending variability of psychosomatic and neuroendocrine disturbances, influencing the quality of life, formation and prognosis of the adolescent's somatic and reproductive health. Actuality and social consideration of HS investigation were depended by the growth of such morbidity in children population, strong progression of the illness process, polymorphism of clinical manifestations and serious metabolic disorders [1, 2, 3, 4, 8, 9, 10]. For the last 5 years considerable growth of the HS patient's number was detected in Khabarovsk krai. The rate of this growth is much over than average for the whole Russia.

**The aim of investigation:** to examine the quality of life, health status, hormone status peculiarities in adolescents with HS in Khabarovsk krai.

### Materials and methods.

142 adolescents with HS (78 girls and 64 boys) were examined. Physical and sexual development estimation [7], major indexes of protein, lipid and carbohydrate metabolism was investigated. Control group consists of 74 healthy adolescents with appropriate gender and age. Hormone state was detected by immune fluorescence analyze (IFA): insulin, luteinizing hormone (LH), follicular stimulating hormone (FSH), prolactin, TTH, T3, T4, ST4, estradiol, testosterone, cortizole, DHEA-acetate and C-peptide. Ultrasonic examination of the internal organs, gonads, endocrine glandules; complex neurophysiological examination (M-ECHO, reoencephalography, brain MRI) were made. Aiming to investigate personal psychological features in the adolescents with HS, psychological testing were provide with usage of Aizenk, Spilberg, Shmishek, Lusher tests. The quality of life was estimated by mean of standard questioner – SF-36 Ped. For statistical analyze Statistika 6.0 program was used. All the investigations were made in volunteers and anonymous, this permitted to get highly reliable results.

### Results and discussion.

The prevalence of HS in girls was revealed (55%). The average age for the onset of the illness was  $13,8 \pm 0,05$  years. The majority of the patients were urban citizens. This fact submits the role of emotional and physical stress, high living rhythm and unfavorable ecological situation in the pathology formation. Unfavorable family anamnesis had 73,9% of respondents: arterial hypertension and ischemic heart diseases – 16,9%; obesity – 15,5%; thyroid disorders – 12,9%; in 7% of cases relatives had diabetes mellitus type 2. Among the perinatal risk factors for HS formation were revealed: mainly, pathological pregnancy (64,8%); chronic fetus hypoxia (61,9%); fetus – placenta insufficiency (41,5%); the danger of spontaneous abortion (31,7%); anemic state (37,3%). In 23,9% the delivery were provided by Caesarian section. All the patient were under the neurologist control from the 1-st days of life because of perinatal encephalopathy with the further realization into residual encephalopathy in 45,8% of cases. Among the HS development risk factors were revealed: chronic inflammatory diseases of the oro-rhino-pharyngeal zone, such as chronic tonsillitis, adenoiditis, inflammatory of the additional nasal cavities (54,2%).

The quality of life estimation in patients with HS revealed: common health status is satisfy; physical activity, reflecting the level of physical load limiting, was high – 82%. Actual physical health, including subjective self-estimation of the pain syndrome intensiveness, physical working capacity and physical load endurance in HS patients were marked as low – 40,8%, while in healthy persons these indexes were 64,5% ( $p < 0,005$ ). The adolescent's actual emotional functioning with such pathology in 1,75 times lower in comparison with healthy ones (36% and 63% correspondingly, ( $p < 0,001$ )). Every 3-rd respondent with HS suffers from constant psychological discomfort, has marked emotional instability, 33% of patients have decreased self-estimation, tendency for depression, moderate or severe anxiety level, disturbing normal functioning or any other every day activity (including increased time usage, decreased amount of work and it's depressed quality).

The considerable direct correlation of the neurophysiologic and psychological indexes with the anxiety and aggression, increasing under the pubertal hormone spurt, revealed ( $r=0,6$ ).

Neurophysiological examination (EEG) revealed pathological deviation in the bioelectrical brain activity in 23,2% of patients. These changes predominate in girls and are characterized by paroxysmal epileptic activity in forms of primary generalized absence. In 64,5% of cases diffuse changes, reflecting functional reserve decompensation and immature brain structures were revealed: the absence of zonal bioelectrical activity distribution, weak cortex activity distribution and marked thalamic – cortical desynchronizes.

Reo-encephalography showed angio-hypotonic brain hemodynamic type: depressed magisterial vessels tonus, difficulties in vein drainage (72%), evidence of hyper tension –hydrocephalus syndrome (33,8%). These facts explain the high frequency of the vegetative deregulation and cephalic pain syndrome (100%) and represent the main base for cognitive disorders in these patients (20,4%).

Cardiac interval metric analyze revealed the predominance of hyper sympatic reactivity (64,8%), decreased level of heart rhythm management centralization, determined by unevenness and retardation of regulative mechanisms maturation. Physical development of the adolescents with HS is characterized by the predominance of macro somatic markedly disharmonious development (71,8%) with body mass index over 25 (56,3%) and over 30 (35,2%); the obesity of 3-rd stage detected in 6,3% of cases.

As for secondary sexual signs (SSS) in girls is concern, the high common index of sexual formula was detected as a result of intensive mammas growth – Ma ( $12,21\pm 1,2$  years), pubarche ( $12,5\pm 1,7$  years). In the structure of SSS formation disorders, the syndrome of incorrect pubertal period is prevailing and was detected in 5,6%: early adrenarche ( $10,1\pm 0,9$  years), hirsute syndrome (22,5%). It can be explained by laboratory submitted correspondingly functional hyperprolactinemia and hyperandrogenemia. The age of menarche appearance was  $13,5\pm 0,07$  years, the regular cycle established in a period of 1 year in 32% of cases. At the age of 17 years only 57,6% of girls with HS have stable menstrual cycle. The rate of menstrual cycle disorders increases at the age of 15-17 years: algomenorrhea diagnosed in 41,8% of cases, secondary amenorrhea in 6,3%. At the age of 16-17 oligomenorrhea registered more often (21,8%) and opsomenorrhea (34,6%). Fibrosis mastopathy revealed in 6% of cases. Menstrual function disturbances correlates with the obesity severity ( $r=+0,5$ ), psychosomatic abnormalities ( $r=+0,78$ ). Ultrasonic examination showed increased uterine size ( $p<0,001$ ), ovaries ( $p<0,001$ ), endometrium thickness, in 23% of cases multifollicular ovaries revealed. The SSS formation in boys accompanied by high frequency of prolonged gynecomastia up to the Ma 2, 3 (18,7%), hypogonadism (14%) and ginoid type of subcutaneous fat distribution.

In the structure of concomitant somatic pathology among the examined adolescents, the disorders of gastro intestinal tract (GIT) were revealed more often in boys vs girls (84,3% and 70,5% correspondingly) not only because of high spread of functional disorders (reflux; esophagus, stomach and intestine dyskinesia), but also because of liver fat dystrophy ( $9,5\pm 1,7\%$  in girls and  $12,9\pm 1,17\%$  in boys),

increased rate of chronic “adult” pathology: chronic gastroduodenitis, erosive gastritis, stomach and duodenum ulcers). Symptomatic arterial hypertension registered in every 3-rd boys. Intracranial hypertension was diagnosed reliably more often in boys vs girls ( $38,0\pm 4,12\%$  and  $25\pm 3,2\%$  correspondingly,  $p<0,05$ ). High correlation of HS and endocrine pathology was established: diffuse thyroid gland hyperplasia revealed in  $26,9\%$  of girls and  $34,3\%$  of boys;  $26\%$  of patients had pancreas reactive changes. Moderate insulin resistance ( $4<HOMA-R<8$ ) revealed in detected in  $22,5\%$  of patients. Lipid-grama examination showed low and moderate hypercholesteremia in  $20,5\%$  of girls and in  $32,8\%$  of boys; B-lipoprotein level was increased up to  $62,0\pm 4,8$  U/L in  $20,5\%$  of girls and in  $40,6\%$  of boys; triglycerides level up to  $3,2\pm 0,2$  nmol/ml ( $p<0,05$ ) in  $33,3\%$  of girls and in  $39\%$  of boys; low density lipoproteins level up to  $12,8\%$  of girls and  $26,5\%$  of boys ( $p<0,001$ ).

In comparison with control group, the HS adolescents have reliably lower TTH level ( $1,41\pm 0,08$  and  $1,56\pm 0,08$  mkU/ml correspondingly) and considerable increased level of thyroxin active fraction – ST4 ( $14,3\pm 0,9$  and  $12,4\pm 0,2$  pmol/L correspondingly). Gender and age-dependent differences of the hypophysis-thyroid system functional activity were revealed. In girls, in comparison with control group, at the pre-pubertal period decreased level of TTH was established ( $1,16\pm 0,18$  and  $2,0\pm 0,3$  mIU/ml correspondingly,  $P<0,05$ ); at the pubertal period – decreased level of T3 ( $1,9\pm 0,09$  and  $1,6\pm 0,09$  mIU/ml correspondingly,  $p<0,05$ ). In the group of younger boys with HS no reliable differences in thyrotropic hormone content in comparison with control group was revealed; in the elder group, reliable decrease of blood T3 level ( $1,72\pm 0,1$  and  $2,0\pm 0,08$  nmol/L correspondingly,  $p<0,05$ ) and increased levels of T4 ( $102,2\pm 4,29$  and  $89,4\pm 2,7$  nmol/L correspondingly) and ST4 ( $13,9\pm 0,68$  and  $12,1\pm 0,41$  pmol/L correspondingly) were detected. These changes reflect the decreased processes of thyroxin deiodination under the situation of increased necessity in the active tryiodthronin. Relative sub clinical thyroid insufficiency was submitted by clinical status in the majority of teenagers with HS, which was characterized by increased rate of diffuse non toxic goiter of the 1-2 stages (WHO), structural thyroid gland changes – heterogeneity and decreased echogeneity, increased local blood flow.

The investigation of the pituitary gland gonad stimulating function revealed more early terms of the increased gonadotrophins secretion: high levels of the FSH and LH secretion in the young age group were established ( $p<0,005$ , Fig. 1). Blood serum prolactin (PRL) level, does not exceeding referent norms, was 1,8 times over than the similar index in both gender groups of healthy adolescents ( $p<0,001$ ). PRL high concentrations aggravate vegetative dysregulation; contribute high frequency of psychosomatic disorders and menstrual function abnormalities. These symptoms widely spread in HS patients. Revealed changes show the serious tension of the adoptive homeostatic mechanisms in HS. It might be note, that in the gender groups of the HS adolescents, opposite PRL secretion direction revealed: there is a tendency to increased content of PRL in girls of pre-pubertal and pubertal periods, while in boys the tendency to decrease in PRL level was marked.

Sexual hormones ( $E_2$ ) secretion in HS girls was reliably higher in comparison with healthy persons ( $105,7 \pm 13,0$  and  $68,2 \pm 7,6$  pg/ml correspondingly,  $p < 0,03$ ). In boys, the tendency for testosterone level decrease ( $13,9 \pm 2,0$  and  $15,5 \pm 1,5$  nmol/L correspondingly,  $p > 0,05$ ) and  $E_2$  level increase ( $50,6 \pm 6,4$  and  $41,6 \pm 5,0$  pg/ml correspondingly) was revealed. This fact is explained by increased fat tissue aromatization in HS patients and can be used as a predictor for reproductive disorders in young males. The investigation of adrenal secretion in boys did not revealed any changes. But in the HS girls high levels of cortizole, testosterone and DHEA-s in comparison with healthy persons were detected ( $p < 0,005$ , Fig.2).

Reliable peculiarities of the somatotropin secretion were not detected; active growth acceleration in HS patients is provided, mostly, by synergic growth-stimulating effects of the thyroid, adrenal and sexual hormones.

In conclusion, detected clinical and laboratory changes show the early start of metabolic syndrome in the HS adolescents. Complete form (four and over metabolic syndrome markers) was diagnosed in 7,7% of cases, non-complete form in 67,6%. Clinical-metabolic variant of the metabolic syndrome is characterized by abdominal obesity (81,7%), cardiovascular (95,8%) and psychopathological (11,9%) disorders; mixed clinical features were revealed in 91,5% of cases. Among the all clinical cases metabolic syndrome had a stable type in 31,6%; progressive type in 27,4%; relapse type in 15,4%; regressive type in 25,6%. The polymorphism of the metabolic and endocrine disorders in adolescents with HS shows a high risk of the atherosclerosis early development, diabetes mellitus type-2 development, progressive poly endocrine pathology appearance.

All these changes contribute reproductive health disorders.

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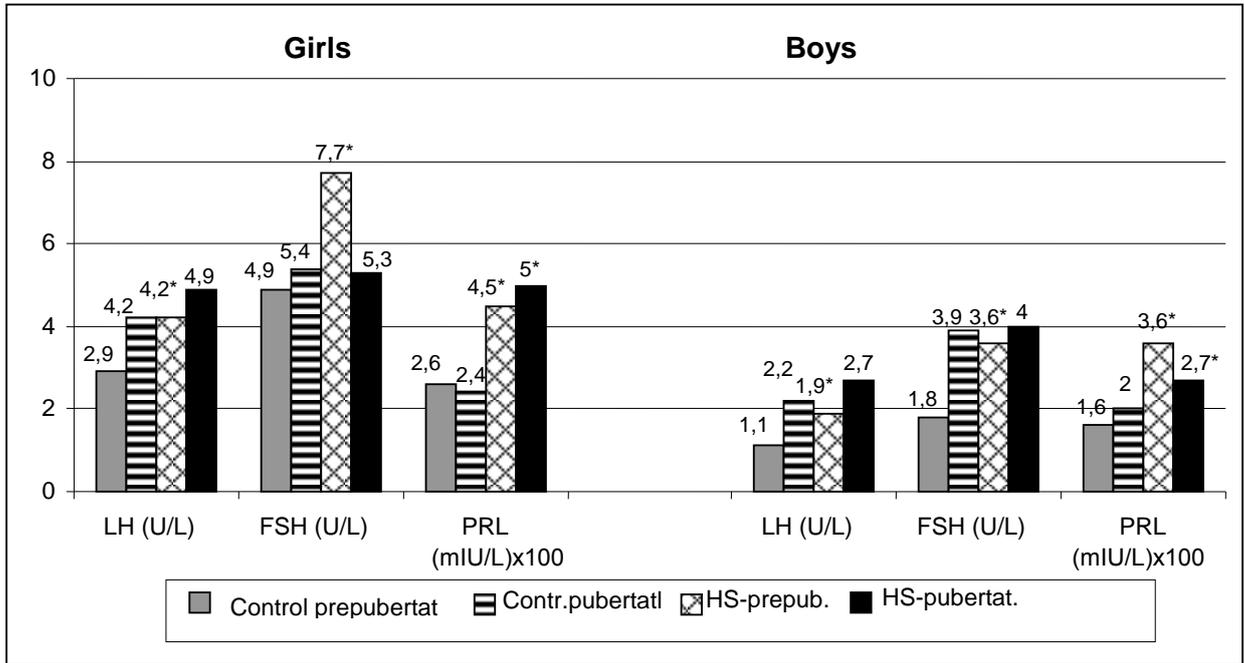


Fig.1 Gonadotropin and prolactin (PRL) levels in the HS adolescents in pre-pubertal and pubertal developmental periods

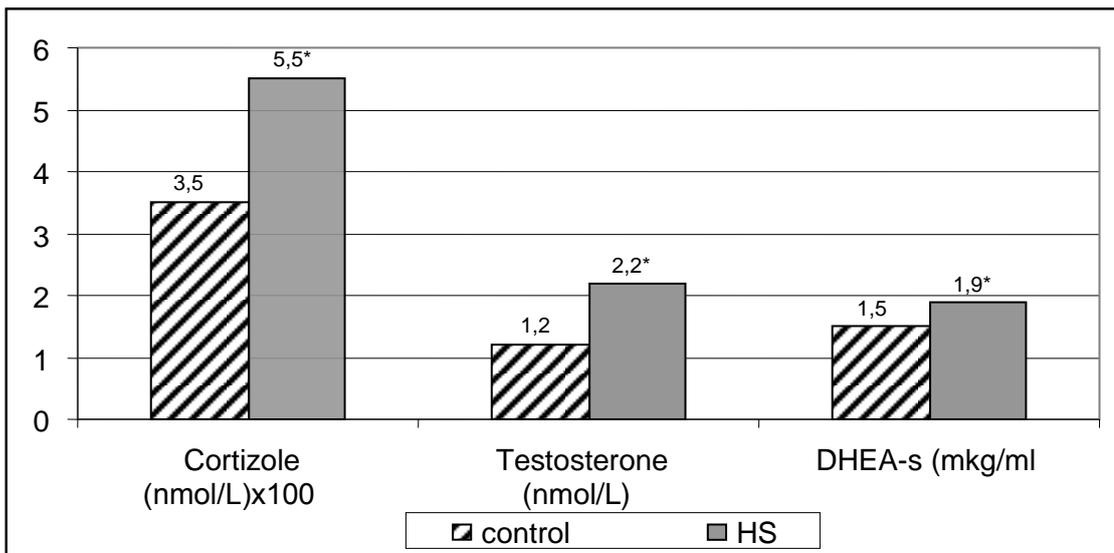


Fig.2 Glucocorticoids and androgens content in the adolescent girls blood serum

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**IMMUNOLOGICAL INDICES OF PATIENTS WITH CHRONIC GASTRITIS  
ASSOCIATED WITH HELICOBACTER PYLORI IN YAKUTIA**

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In research presents the immunological characteristics of patients with chronic gastritis. Survey participate 88 patients with chronic gastritis type B, indigenous (yakut), in age 30 to 50 years. In research the revealed dependence of the levels of immunoglobulins and cytokines on the degree of contamination *Helicobacter pylori* in the serum of patients with chronic gastritis.

**Keywords:** chronic gastritis, *Helicobacter pylori*, immunoglobulins, cytokines.

**Introduction**

In the Republic of Sakha (Yakutia), chronic gastritis (CG) is the most common disease in the structure of gastroenterological diseases [2,11]. According to the data of Goskomstat in Republic of Sakha (Yakutia) the diseases of the digestive system in the structure of general morbidity took third place (8.4%) in 2009. In 2008, the incidence reached 148.2 per 1,000 of population, while in Russia it is 112.7.

The frequency of atrophic gastritis, antral form among the native-born population of Yakutia (38.5 to 57.1% people) characterized by a latent course is much higher than that of non-native population (28.5%). In this case it's noted that the incidence of atrophic form of gastritis among nonresidents increases with the time of residence in the North [5].

Opening of *Helicobacter pylori* (HP) revolutionized the understanding of the pathogenesis of chronic gastritis. However, despite the great number of researches, some aspects of pathogenesis are controversial and debatable. HP has a pathogenic effect on patients with insufficient protection, especially of the immune mechanisms in the stomach lining. As the lining of the gastrointestinal tract refers to the local factors of the immune system protection, in the process of damage that occurs during the invasion of HP, its barrier properties are violated, and the passage of antigens through the mucosa increases. In addition, HP has a low immunogenicity, which leads to long-term interaction of microorganisms with the immune system of mucous and subsequent persistence of infection [6].

A high degree of HP infection among native-born population of Yakutia, which correlates with high rates of stomach cancer was educed by Sosin, S.S., Ivanov P.M. (2005), (20.7 per 100,000 population) [8].

In the Far North the state of nonspecific and specific anti-HP has a number of features. They are due to climatic, social and environmental conditions of habitat, the degree of adaptation of native-born people, their genetic and ethnic characteristics.

**The purpose** of this research was to evaluate immunoglobulins and cytokines in patients with chronic gastritis, depending on the degree of contamination of the HP.

#### **Material and methods:**

We examined 88 patients of native-born nationality (Yakut), suffering from *Helicobacter pylori* gastritis with chronic type B, 17 men and 71 women aged 30 to 50 years (average age was  $44,64 \pm 5,82$  years). The control group consisted of 20 healthy people without pathology of the gastrointestinal tract and the presence of HP (average age was  $43,85 \pm 3,84$ ).

Surveyed patients had never received *H. pylori* therapy. The diagnosis was verified clinically, endoscopically with histological examination of biopsy samples of the mucosa and on the basis of ELISA to CagA *Helicobacter pylori* antigen.

The investigation material was blood taken from patients' cubital vein on an empty stomach.

Immunological data were determined depending on the severity of *H. pylori* infection according to the morphological and immunological studies. Surveyed patients were divided into three groups.

Immunological data were determined depending on the intensity of *H. pylori* infection according to the morphological and immunological studies. Surveyed patients were divided into three groups.

The first group consisted of 26 patients suffering from chronic gastritis, in morphological biopsies [4], of which were found up to 20 microorganisms in the field of vision, and the antibodies titer ratio to the CagA HP antigen was 1:5, 1:10.

The second group included 18 patients with moderate severity of HP infection, varying from 20 to 50 microorganisms in the morphological biopsy, the antibodies titer ratio to CagA HP antigen was 1:20, 1:40. The third group consisted of 43 patients with severe degree, more than 50 microorganisms, with a positive titer of the antibodies' presence, the antibodies titer ratio to CagA HP antigen was 1:80.

The content of antibodies titer to CagA HP antigen in the serum was determined by ELISA test-system "HelikoBest - antibodies". C-reactive protein concentrations of immunoglobulins IgA, IgG, sIgA, the concentration of pro-inflammatory cytokine  $\alpha$ -tumor necrosis factor, IL-6 and anti-inflammatory cytokine IL-4 in blood serum were measured by ELISA using kits of reagents JSC "Vector-Best" (Novosibirsk, Russia) according to the instruction.

Statistical analysis was performed with using the software packages and Statistica for Windows (version 6.0). Significant differences between groups was assessed using t-test (t). Data in tables are presented as  $M \pm m$ , where M - medium, m - medium error. The probability of the null hypothesis was accepted at  $p < 0,05$ .

## Results and discussion

ELISA data are presented in the Table 1. The content of IgA in the blood serum in the first group was 1.5 times above normal ( $p \leq 0,05$ ), in the second group - 1.7 times above normal in the third - 1.8, compared with the control group (Table 1).

Increasing concentrations of IgA can be explained by intensified production mainly IgA-antibodies with the ability to prevent adhesion of microorganisms in the gastric mucosa, as the body protection against infection, particularly from HP, belongs to IgA.

Our results are consistent with published data. According to Lazebnik L.B. (2006) increased circulating of IgA in the blood serum of patients with chronic gastritis indirectly proves the severity of atrophic processes in the gastric mucosa [3].

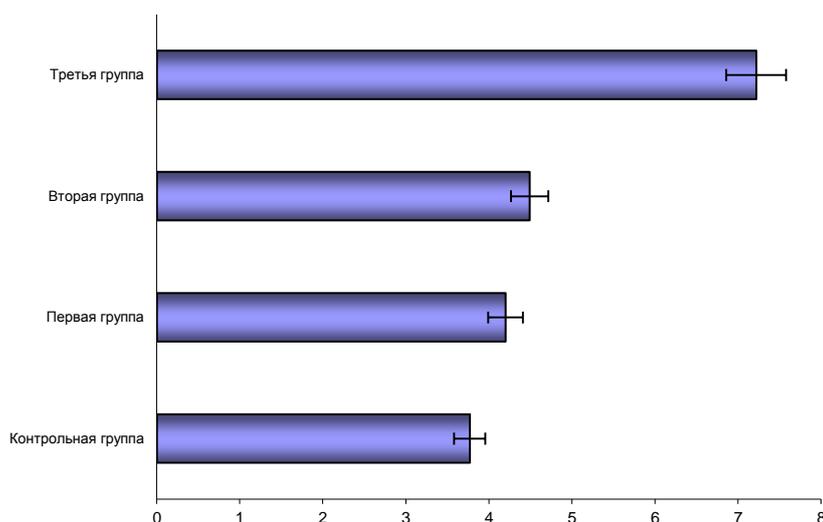
Our data showed that the concentration of IgG in the blood serum of the patients increased, depending on the degree of contamination of the HP. Thus, the content of IgG in the second group of patients was 1.5 times higher, in the third group - 1.2 times compared with the

control group ( $p \leq 0,05$ ). Perhaps the rise of IgG antibodies in the blood serum reflects not only the presence of HP colonization and the intensity of infiltration of the gastric mucosa by leukocytes, but also systemic immune responses to local damage in the gastroduodenal system. By the high level of IgG in the blood serum of patients, suffering from chronic gastritis we can estimate the intensity of inflammation in the gastric mucosa caused by the pathogenic effect of HP. Significant increase of IgG level in patients with moderate contamination indicates the activation of the immune system, while in the third group of patients with a high degree of contamination, the reserves of the immune system can be reduced. Thus, the morphological study of Loskutova K.S. (2006) shows that that native-born people with less degree of contamination have more severe changes of the gastric mucosa, compared with the nonresidents [7]. The increase of serum immunoglobulin was shown in the researches of such authors as: Petrova P.G. (1993), Fedorov A.I., Osakovsky V.L. (2008). According to these authors, enhanced synthesis of antibodies is one of the components of the organism alteration to the natural conditions of the Far North [10, 11].

We found a dependence of sIgA concentration on the degree of HP contamination. The level of sIgA in the first group was significantly lower (2.9 times) compared with the control group. In the second group sIgA level in the blood of patients was lower ( $p \leq 0,05$ ) 3.7 times below normal, in the third group 2.5 times ( $p \leq 0,05$ ) below normal, compared with the control group.

Effective protection of the gastric mucosa is determined by a balanced feedback of all levels of tissue immunity, however, the leading factor, according to all researchers, is sIgA. The failure of this component involves the colonization of mucous membranes by the microbes, increase the flow of allergens through the epithelial barrier and, consequently, increase of the load on the "second line" protection. Despite the numerous studies on the mechanisms of sIgA failure, there is no generally accepted concept that explains the reason for reducing the concentration of immunoglobulin in the lumen of the digestive tube. A.V. Kononov proved the possibility of a local shortage of sIgA in the gastric mucosa as a result of HP's ability to disrupt disulfide bonds [6].

The level of C-reactive protein (CRP) of the surveyed patients ranged from  $4,2 \pm 0,38$  to  $7,22 \pm 0,48$  pg / ml. The concentration increasing (CRP) in the blood serum of patients in the first and second group was insignificant, and in the third group the level of CRP was 1.9 times higher than in the control group ( $p \leq 0,05$ ). The concentration of CRP in the control group was  $3,77 \pm 0,6$  pg / ml (picture).



CRP level in the blood of patients suffering from chronic gastritis according to the degree of HP contamination.

The picture shows that the increasing of CRP concentration in the blood of patients depends on the degree of HP contamination. It is known that C-reactive protein (CRP) provides antimicrobial effect by binding with pathogens and activating the complement system in the classical way, and takes part in the regulation of immune cells, leading to the increased transendothelial migration of leukocytes. Statistically, the significant increase of CRP in the third group testifies that the patients have the activation of nonspecific immunity.

The cytokines regulate immunopoiesis and effect on all parts of the immune system, acting as the main mediators of the immune response. They contribute to immune responses directed at the elimination of the infectious agent, damaged structures and restoration of constant internal environment.

In 1996 for the first time, the group of Italian researchers found increased content of IL- $1\beta$  and IL-6 in the gastric mucosa with Hp-associated infection [15]. It was later established that cytokines play an important role in HP-induced inflammation. Taking into account the large area of HP extension in the stomach, as well as the recently identified possibility of bacteria's penetration into the cytoplasm of epithelial cells, the intercellular spaces and into the underlying lamina propria of the mucous, the systematic secretion of cytokines is not surprising in the HP-infection. It is unlimited with clearance and gastric surface epithelium.

An imbalance of pro-and anti-inflammatory cytokines, naturally circulating in the bloodstream plays an important role in the development of HP-associated pathology. In this regard, the content of anti-inflammatory cytokine IL-4 and pro-inflammatory cytokines IL-6 and  $\alpha$ -TNF in the blood serum of patients with chronic gastritis was evaluated.

In the blood of the first group patients the concentration of IL-4 was significantly lower 1.6 times compared with the control group, results of the second group were not significantly different; results in the third group showed significant decrease in the concentration of IL-4 1.9 times below normal (Table 2). Anti-inflammatory cytokines, particularly IL-4, are involved in limiting the inflammatory response by inhibiting the secretion of proinflammatory cytokines and regulating, thus, the severity of tissue damage. The most marked decrease of IL-4 levels was detected in patients with severe degree of contamination.

Production of proinflammatory cytokine IL-6 in the blood of the patients had a tendency to increase, depending on the degree of HP infection. In the first group patients' blood the levels of IL-6 was 1.3 times higher, in the second group IL-6 had a tendency to increase (1.1 times), and the third was higher at 1.2 compared with the control group. In studied group a significant increase of proinflammatory IL-6 was detected, compared with the control group, which reflects the activation of the inflammatory process occurring in the gastric mucosa of patients with *H. pylori* gastritis.

Analysis of the data showed that the level of  $\alpha$ -TNF in the blood of patients significantly increased in all groups of HP dissemination compared with the control group. The concentration of  $\alpha$ -TNF in the first group significantly increased 1.4 times above normal, in the second group it was higher 1.5 times ( $p \leq 0,05$ ), in the third there was an increase 1.3 times above normal ( $p < 0,001$ ) compared with the control group. Cytokines Th1-polarized immune response ( $\alpha$ -TNF) affect on the regulation of acid in the stomach, causing loss of cells and associated ulcerative defects or atrophy of glands, as well as cell proliferation, metaplasia, and epithelial dysplasia.

Thus, the experimental studies on mice with the transfer of T-lymphocytes demonstrate that the inflammatory response, with a dominant Th1-type results the stimulation of IFN-gamma G-cells. Gastrin activates the parietal cells, causing it to hyperfunction, which causes hyperacidity. As the depletion of the pool there is atrophy of the parietal cells of gastric mucosa [6]. Based on the data, increased  $\alpha$ -TNF can be characterized as a predictor of possible destructive changes in the gastric mucosa of patients with severe degree of HP contamination.

By the content of  $\alpha$ -tumor necrosis factor (Th-1) and IL-4 (Th-2) we can judge of the imbalance ratio of Th-1 and Th-2, particularly the activation of immune response of Th1. It is generally accepted that Th-2 reflects the persistence of chronic infection and colonization of HP, and Th-1 prevents the colonization of HP in gastric mucosa. According to some authors, the effectiveness of antibacterial response belongs to the Th-1 immune response, whereas humoral Th-2 pathway is not sufficient [1, 3, 15]. Others believe that the most appropriate immune response to HP would be a Th-2, which cause minimal damage to the gastric mucosa. Thus, Th-2

immune response explanation of the "African enigma": when an exceptionally high colonization of HP the natives rarely have a stomach ulcer and duodenal ulcer [13].

Our data indicate the dysfunction of the immune system of patients with chronic gastritis, depending on the degree of HP contamination. There is evidence of activation of immune response to Th1-type (anti-inflammatory cytokine reduction of IL-4 and increased pro-inflammatory  $\alpha$ -TNF), with increased synthesis of immunoglobulins IgA and IgG and lower secretory of sIgA.

### Conclusion

1. A significant reduction of secretory sIgA and increased serum IgA and IgG in the blood of patients with chronic gastritis associated with HP, compared with the control group is shown.

2. A significant increase in the concentrations of CRP inflammatory marker in patients with chronic gastritis with severe HP dissemination is found.

3. The increase of pro-inflammatory cytokines (IL-6,  $\alpha$ -TNF) against decrease of anti-IL-4 in the blood of the patients with chronic gastritis, depending on the degree of HP contamination is revealed.

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Table 1

Indicators of humoral immunity in the blood of patients suffering from chronic gastritis according to the degree of HP contamination.

Indicators	M±m (mg/l)			
	control group (n=20)	I group (n=26)	II group (n=18)	III group (n=43)
Ig A	1,8±0,76	2,66±0,26*	3,19±0,03*	3,24±0,25
Ig G	14,58±1,59	14,7±0,03*	21,97±0,03*	17,46±0,04*
sIg A	3,58±1,89	1,22±0,04*	0,97±0,04*	1,46±0,03*

Note: \* P ≤ 0,05 when compared with the control group

Table 2

Concentration of IL-4, IL-6 and α-TNF in the blood serum patients with chronic gastritis according to the degree of HP contamination

Показатели	M±m (pg/ml)			
	control group (n=20)	I group (n=26)	II group (n=18)	III group (n=43)
IL-4	0,22±0,01	0,14±0,01*	0,21±0,05	0,17±0,03*
IL-6	2,8±0,02	3,56±0,30*	3,08±0,18	3,31±0,26
α-TNF	2,5±0,06	3,56±0,12*	3,77±0,22*	3,34±0,15*

Note: \* P ≤ 0,05 when compared with the control group

УДК 616.12-008.9-008.313.2-08:615.272:612.017.

**THE INFLUENCE OF SIMVASTATINE ON THE IMMUNOLOGY  
PARAMETERS IN PATIENTS WITH METABOLIC SYNDROME IN COMBINATION  
WITH ATRIAL FIBRILLATION**

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*The aim* – estimate the influence of simvastatine (simvastole) on the parameters of matrix metalloproteinase-9 and its antagonist – tissue inhibitor of matrix metalloproteinase-1 in patients with metabolic syndrome in combination with paroxizmal atrial fibrillation. *Materials and methods.* The were investigated 60 men with metabolic syndrome in combination with paroxizmal atrial fibrillation. In all patients with immunoassay method investigated the serum level of matrix metalloproteinase-9 and tissue inhibitor of matrix metalloproteinase-1. *Results.* In men with metabolic syndrome in combination with paroxizmal atrial fibrillation there were significant decrease of matrix metalloproteinase-9 activity ( $P=0,043$ ) were estimated after the therapy with simvastol, and increase of the tissue inhibitor of matrix metalloproteinase-1 activity ( $P=0,018$ ) were estimated. *Conclusion.* The addition to usual therapy of simvastatine (simvastol) in patients with metabolic syndrome in combination with paroxizmal atrial fibrillation is useful with the pathogenetic position.

**KEY WORDS:** METABOLIC SYNDROME, MMP-9, TIMP-1, SIMVASTATINE

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**INFLUENCE OF LOCAL ANESTHETICS ON DYNAMICS OF IL-1 B  
AND IL-2 CONTENT IN PERSONS OF ELDERLY AND SENILE AGE  
IN THE CONDITIONS OF THE PROLONGED SPINAL ANESTHESIA**

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It is noticed in article that with ropivacain use on the operation beginning the highest level of proinflammatory IL-1 $\beta$  in a combination with the lowest IL-2 is marked, that has defined pronounced imbalance of interleukin production. For a moment of the most traumatic manipulations on the background of ropivacain application decrease in synthesis of proinflammatory IL-1 $\beta$  and strengthening of immunoregulatory IL-2 secretion were observed. Ropivacain provides immunopreserving influence.

**Keywords:** local anesthetics, interleukins, spinal anesthesia

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**Lipoprotein lipase - the important genetic factor of 2 type diabetes development in the native population of Yakutia**

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High association of gene LPL, Int8 SNP (rs320) with 2 type diabetes let us possible to make out proposition about mechanism and role of LPL in 2 type diabetes developing.

**Keywords:** lipoprotein lipase LPL, Int8 SNP (rs320), hypertension, macrophage.

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**ANALYSIS OF AEROBIC CAUSATIVE AGENTS OF GENERAL PERITONITIS  
IN PATIENTS OF MULTITYPE HOSPITAL**

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**SUMMARY: Objective:** The study of the structure and antibiotics resistance of aerobic causative agents of general peritonitis (GP) for the optimization of empirical antibacterial therapy.

**Materials and Methods:** The results of the microbiological study of peritoneal exudates of 147 patients with GP are presented. Results: All in all 160 (51,4%) strains of the family *Enterobacteriaceae*, 86 (27,7%) strains of non-enzyming gram-negative bacteria and 65 (20,9%) gram-positive causative agents were obtained. During staged debridement extra-hospital strains are replaced by nosocomial ones.

**Conclusion:** Initial antibacterial treatment of GP should be based on the local data on the range and

antibiotics resistance of intra-abdominal infection causative agents. Besides it is necessary to take into consideration the origin of peritonitis and the future technique of the abdominal cavity management.

**Key words:** general peritonitis, aerobic microflora, antibiotics resistance.

### Introduction

Despite the sufficient arsenal of antimicrobial preparations the choice of adequate antibacterial therapy of general peritonitis (GP) remains a problem of urgent surgery and intensive care [3, 4, 6, 9, 10]. Early and adequate empirical antibacterial treatment influences the incidence of complications in patients and their mortality [5]. As a rule, deferred adequate therapy already does not affect the clinical outcome. It is of special actuality in the intensive care of post-operative peritonitis and in staged abdominal cavity management [1]. Inadequate initial antibacterial therapy in this contingent of patients is mainly conditioned by insufficient information on the range of causative agents of GP in a given hospital and their antibiotics resistance [1, 2].

**Objective:** The study of the structure and antibiotics resistance of aerobic causative agents of GP for the optimization of empirical antibacterial therapy.

### Materials and Methods

147 patients with GP who were being treated in the department of purulent surgery and the intensive care department of MI of HS “City Clinical Hospital N6 named after N.S.Karpovich” in Krasnoyarsk were examined. Peritoneal exudates for microbiological study were obtained from all the patients with GP during the primary laparotomy and subsequent planned debridements.

Identification of the strains was carried out with the help of traditional methods. Determination of antibiotic susceptibility was done by the technique of dilution in Muller-Hinton’s broth in accordance with the recommendations and criteria of the National Committee on clinical laboratory standards (CLSI/NCCLS) [8].

For the interpretation of susceptibility to cefoperazon/sulbactam the criteria of cefoperazon were used. The results of determination of susceptibility of *P. aeruginosa* to polymixin B were interpreted according to the criteria SFM of 2003 [7].

For characterizing the microorganisms’ susceptibility to antibiotics the universally accepted categories - susceptible, moderately resistant and resistant – were used. For integral characteristics of drug resistance the term ‘non-susceptible strains’ combining moderately resistant and resistant microorganisms was applied.

Statistical processing of the data obtained was carried out with the methods of variation statistics on the PC using the applied programs «Statistics for Windows’ 6.1» (StatSoft, USA). The descriptive statistics is represented as percentage fractions and standard fraction error. For

comparison of rates of binary sign in the two unrelated groups the criterion  $\chi^2$  was used. On verification of the statistical hypotheses the differences at  $p < 0.05$  were considered significant.

### Results and Discussion

In 78.9% (116/147) patients GP developed as a complication of acute inflammatory diseases and traumas of the abdominal organs (extra-hospital peritonitis). In 21.1% (31/147) of cases GP was of nosocomial origin and complicated the course of the postoperative period after planned and urgent operations on the organs of the abdominal cavity (postoperative peritonitis). In 37.1% (43/116) of patients with extra-hospital GP and 77.4% (24/31) of patients with nosocomial GP staged debridements of the abdominal cavity were performed because of the intensity of the inflammatory process.

In patients with extra-hospital peritonitis etiologically important aerobic microorganisms were obtained in 145 cases (positive inoculations), from which 182 strains of aerobic causative agents were obtained. In 77.9% (113/145) of positive inoculations monocultures of microorganisms were found and in 22.1% (32/145) of cases – microbial associations. At the same time during the first operation and the first planned relaparotomy (PR) associations of microorganisms were seen in 7.1% and 13.8% of cases, respectively, on the third PR – in 88.9%, and on the fourth planned debridement – in all the patients.

In postoperative peritonitis 129 strains of aerobic microorganisms were obtained in 74 positive inoculations, out of which monocultures 35.1%, microbial associations – 64.9%. If the inflammatory process in the abdominal cavity was not stopped during 1-2 debridements, on the 3-4<sup>th</sup> debridements the infection was caused only by associations of microorganisms.

All in all 160 (51.4%) strains of the family *Enterobacteriaceae*, 86 (27.7%) strains of non-enzyming gram-negative bacteria (NGB) and 65 (20.9%) gram-positive causative agents were obtained.

Obtaining of *E. coli* was seen more often both in extra-hospital and nosocomial peritonitis – in 30.8% and 25.6% of cases, correspondingly. The results were similar for *Enterococcus* spp. – 15.4% и 14%, respectively. Statistically significant in nosocomial peritonitis were *P.aeruginosa* – in 17.8% of cases in comparison with extra-hospital peritonitis – 9.3% ( $p = 0.0276$ ), and also *Acinetobacter* spp. – 20.9% and 10.4% ( $p = 0.0102$ ), respectively. The rate of obtaining *S.aureus* in extra-hospital peritonitis was 7.1%, in comparison with 4.7% - in nosocomial peritonitis.

Both in extra-hospital and nosocomial peritonitis representatives of the family *Enterobacteriaceae* prevailed among the causative agents. But while in extra-hospital origin of peritonitis their share in the structure of causative agents was significantly higher than that of non-enzyming gram-negative microorganisms: 57.7% (105/182) and 19.8% (36/182), respectively ( $p < 0,001$ ), in nosocomial

peritonitis the share of the problem causative agents (*Acinetobacter* spp. and *P.aeruginosa*) increased and did not differ from the family of *Enterobacteriaceae* – 38.8% and 42.6%, respectively ( $p = 0.5263$ ).

It should be noted that in choosing the staged surgical treatment of extra-hospital general peritonitis the microbial landscape of peritoneal exudates changed with each subsequent planned debridement. If in bacteriological inoculations of peritoneal exudates on the first operation or the first planned debridement *E. coli* (39.6% and 30.3%, respectively), *Enterococcus* spp. (15.4% and 18.2%), *Proteus* spp. (8.8% and 6.1%) prevailed, then on the third-fourth debridements *Acinetobacter* spp. (20.7% and 33.3%, respectively), *P.aeruginosa* (20% and 22.2%), *K.pneumoniae* (15% and 11.1%) prevailed in the inoculations. On the primary operation the ratio of the family *Enterobacteriaceae* and NGB was 69.2% and 7.7%, accordingly, and on the second-fourth planned relaparotomy – 39.7% and 41.4%.

In nosocomial origin of general peritonitis in case of planned abdominal cavity management the similar dynamics of the microbial landscape of the peritoneal exudates was not noted.

All the obtained strains of the family *Enterobacteriaceae* preserved maximum susceptibility to carbapenems (imipenem, meropenem). Susceptibility of the strains obtained in nosocomial peritonitis was significantly lower than in extra-hospital peritonitis to the following antibacterial preparations: ampicillin – 50.9% and 86.7%, respectively ( $p < 0.05$ ), amoxicillin/clavulanat – 20% and 44.8% ( $p < 0.05$ ), cefepim – 67.3% and 87.6% ( $p < 0.05$ ), cefoperazon – 29.1% and 56.2% ( $p < 0.05$ ), cefotaxim – 27.3% and 71.4% ( $p < 0.05$ ), ciprofloxacin – 47.3% and 89.5% ( $p < 0.05$ ), gentamycin – 21.8% and 55.2% ( $p < 0.05$ ), piperacillin – 17% and 41.9% ( $p < 0.05$ ). Presence, in cases of extra-hospital peritonitis, of the strains *Enterobacteriaceae*, resistant to the majority of the used antibiotics is first and foremost explained by the fact that in performing staged debridements the extra-hospital strains are replaced by the nosocomial ones. Table 1 presents the dynamics of antibiotics susceptibility of the most frequently occurring in GP representative of the family *Enterobacteriaceae* – *E. coli*.

According to the data obtained, from the first operation up to the second-fourth debridements of the abdominal cavity susceptibility of *E. coli* had decreased to all groups of antibacterial preparations, except carbapenem. Thus, susceptibility decreased from 100% up to 80% to cefoperazon/sulbactam; up to 70% – to ampicillin, ceftazidim, cefepim and piperacillin/tazobactam; up to 50% – to ceftriaxon and ciprofloxacin; up to 40% – to cefotaxim and gentamycin. The number of insusceptible to amoxicillin/clavulanat and cefoperazon strains has significantly increased – from 13.9% and 11.1%, respectively, up to 70%.

NGB had maximum susceptibility only to polymixin. Good susceptibility of the strains obtained in both extra-hospital and nosocomial peritonitis was to imipenem – 91.7% and 92%, meropenem – 86.1% and 88% and cefoperazon/sulbactam – 72.2% and 74%, respectively. To all the rest antibiotics under investigation susceptibility was 50% and lower.

One should pay attention to low activity of NGB to the antibacterial preparations which are widely used for the treatment of severe infections, including intra-abdominal ones. Thus, susceptibility of the microorganisms obtained in extra-hospital and nosocomial peritonitis was 55.6% and 34% to ampicillin, 50% and 36% to cefepim, 44.4% and 34% to ceftazidim, 41.4% and 18% to ciprofloxacin, respectively.

Also low activity to these causative agents was noted in inhibitor-protected penicillins: piperacillin/tazobactam and ticarcillin/clavunat: 44.4% and 52.9% in extra-hospital, 38% and 56.5% in nosocomial general peritonitis, respectively.

Out of all antibiotics used for the treatment of severe abdominal infection ertapenem, imipenem, meropenem and sulperazon/sulbactam have a clinically significant activity against the strains of *Acinetobacter* spp. Polimixin B has the highest activity against the investigated strains *P.aeruginosa* but, unfortunately, this antibiotic is not available for usage in Russian in-patient departments. The preparations of choice for the treatment of extra-hospital general peritonitis caused by blue pus bacillus are imipenem, meropenem, piperacillin/tazobactam, cefepim, ceftazidim and ampicillin. As for nosocomial strains *P.aeruginosa*, only imipenem and meropenem are clinically significantly active.

Gram-positive microorganisms make 20.9% in the general structure of causative agents of general peritonitis. We obtained 19 strains *Staphylococcus aureus* – 6.1% (19/311) of all causative agents of general peritonitis. The frequency of obtaining *S. aureus* in extra-hospital and nosocomial peritonitis was 7.1% (13/182) and 4.7% (6/129), respectively. *Enterococcus* spp. was obtained significantly more often – 14.8% (46/311) ( $p < 0.001$ ). It was characteristic for both extra-hospital – 15.4% (28/182) and nosocomial general peritonitis – 14% (18/129).

All the obtained strains *Enterococcus* spp. preserved maximum susceptibility only to vancomycin. Out of 28 strains obtained in extra-hospital peritonitis 78.6% of strains preserved susceptibility to ampicillin, 67.9% - to ciprofloxacin and gentamycin, and 57.1% - to tetracyclin. The strains *Enterococcus* spp. obtained from peritoneal exudates in nosocomial peritonitis were susceptible to ampicillin in 66.7%, to ciprofloxacin in 22.2%, to gentamicin in 16.7%, to tetracycline in 27.8% (Fig. 4.8.).

Out of 13 identified in extra-hospital peritonitis strains *S.aureus*, 4 were MRSA. All strains MRSA in extra-hospital peritonitis were obtained from peritoneal exudates taken in planned debridements of the abdominal cavity. In nosocomial peritonitis the frequency of MRSA was 66.7% (4/6). All strains MRSA preserved susceptibility to vancomycin.

## Conclusions

1. In staged treatment of extra-hospital GP with each subsequent operation there is a shift of microbe landscape to microbe associations and replacement of extra-hospital strains by antibiotics-resistant nosocomial ones. In nosocomial (postoperative) GP no similar dynamics was noted.
2. The data received in our investigation show that *in vitro* carbapenems are the most active preparations in general peritonitis caused by nosocomial aerobic microflora.
3. While administrating empirical antibacterial therapy of GP one should take into consideration not only its origin (extra-hospital or nosocomial) but also the planned technique of the abdominal cavity management.
4. Antibiotics resistance of extra-hospital and nosocomial strains NG(-)B is a serious medical problem nowadays. In relation to NG(-)B only imipenem and meropenem have a clinically significant activity.
5. Microbiological investigation of intra-operative material in patients with general peritonitis is the basis for both adequate and timely individual antibacterial therapy and prognosis and planning of antibacterial therapy in the future.

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Table 1

**Dynamics of antibiotics susceptibility of strains *E. coli*,  
obtained in staged treatment of extra-hospital GP (%)**

Antibiotic	Primary operation (n=36)		1 PR (n=10)		2-4 PR (n=10)		All operations (n=56)	
	P	±m	P	±m	P	±m	P	±m
Amicacin	100,0	0	100,0	0	70,0	14,5	94,6	7,1
Amoxicillin/Clavulanat	86,1	5,8	50,0	15,8	30,0	14,5	69,6	14,5
Ampicillin	44,4	8,3	30,0	14,5	20,0	12,6	37,5	15,3
Gentamycin	100,0	0	70,0	14,5	40,0	15,5	83,9	11,6
Imipenem	100,0	0	100,0	0	100,0	0	100,0	0
Meropenem	100,0	0	100,0	0	100,0	0	100,0	0
Piperacillin	61,1	8,1	40,0	15,5	20,0	12,6	50,0	15,8
Piperacillin /Tazobactam	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Cefepim	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Cefoperazon	88,9	5,2	60,0	15,5	30,0	14,5	73,2	14,0
Cefoperazon /Sulbactam	100,0	0	80,0	12,6	80,0	12,6	92,9	8,1
Cefotaxim	100,0	0	80,0	12,6	40,0	15,5	85,7	11,1
Ceftazidim	100,0	0	90,0	9,5	70,0	14,5	92,9	8,1
Ceftriaxon	100,0	0	80,0	12,6	50,0	15,8	87,5	10,5
Ciprofloxacin	97,2	2,8	100,0	0	50,0	15,8	89,3	9,8

Note: n – number of strains *E. coli*.

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### INDIRECT LYMPHOTROPIC THERAPY FOR PNEUMONIA

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#### Introduction

The problem of pneumonia remains one of the most topical problems in modern medicine, both because of high morbidity, and because of the large number of wasps, complications of forms, despite the constant improvement of methods of diagnosis and treatment. Morbidity in the Russian Federation at present is from 5 to 20 cases per 1 thousand persons per year [9]. Remains a high incidence of pneumonia in the Russian Federation Armed Forces military personnel, military service by conscription (over 30 ‰), and the highest incidence rates recorded in the first half of the military services [7].

At the present time is clearly defined list of antibiotics that are all over the world consider it possible to use for empirical treatment of pneumonia. The choice of antibiotic from a specified list is determined by the range of actions, which include the major pathogens of pneumonia, as well as the peculiarities of pharmacokinetics / pharmacodynamics of drugs. In addition, the appointment of an antibiotic selection daily dose and multiplicity of introducing into account the severity of the pathologic process in lung tissue and data on the local sensitivity to antimicrobial agents of pneumonia in different categories of patients [7, 9].

The problem of managing patients with severe pneumonia and the presence of complications of the disease has prompted us to explore new ways of administration, which would significantly increase the concentration of antibiotic in the inflammatory foci and the self-mym increase its efficiency.

Number of studies proved that the effectiveness of antibiotics increases the directed their concentration increases in the lymphatic system [1, 2, 4, 5]. Traditional methods of administration do not allow sufficient in the lymph and of stable concentrations [8, 10]. Absorption of low molecular weight drugs, to which the eye is most of the antibiotics of subcutaneous fat and muscle tissue is carried out mainly in the circulatory system. Intramuscular

and intravenous routes of administration are accompanied by binding of antibiotics, blood proteins, rapid elimination from the body and enters the lymphatic system only a small part of them. In this situation, the creation of high concentrations of antibiotic in the blood in most cases is fraught with the development of undesirable side reactions [4].

One possibility for the delivery of medicines, including antibiotics, to the place of the pathologic process in lung tissue and a significant increase in the concentration of antibiotic in the area of inflammation is the use of lymphatics by indirect lymphotropic therapy (ILTT) in which percutaneous injection is performed in the anatomical region is richly endowed with superficial lymph collectors, the administration of drugs carried out in kletchatochnye space located close to the lesion with subsequent preferential resorption of the lymphatic system [3, 5, 6, 8].

The lymph vessels that drain this kletchatochnoe space, leech-proof falls into the lymphatic system, where a retrograde post-shock lymph Paet in the inflammatory focus and creates a higher concentration at the source of inflammation-than intramuscular or intravenous method of administration [3, 10 ]. In addition, the penetration of antibiotics into the lymphatic system, provides a direct impact on the antibiotic agents in the lymphatic bed [8]. With the introduction of lymphotropic drugs directly to turn out the action on the cell, interstitium and stored in the body much longer than the intravenous or intramuscular methods of administration that can reduce the doses of drugs [2, 3].

The method of indirect lymphotropic therapy provides a preliminary introduction of the drug-conductor. With this purpose the substance, which, by changing the conditions of permeability of lymphatic capillaries, can improve drug delivery in the link "interstitial-lymphatic capillaries. The most widely used enzyme preparations, drugs affecting coagulation and fibrinolysis (lidazy, terrilitin, trypsin, chymotrypsin). Enzymes, breaking down glycosaminoglycans, increased permeability of the connective tissue for water and dissolved substances and thereby facilitate the movement of drug in the intercellular spaces, which leads to increased penetration of antibiotics into the lymphatic system and the saturation of the lymph nodes [1, 10].

Preliminary subcutaneous lidazy promotes concentration of antibiotic introduced in the same area in the central lymph and exceeds the concentration of antibiotic administration without first applying lidazy [5].

Antibiotic from the lymph into the blood stream. Due to the fact that the rate of movement of lymph through the vessels is small, the antibiotic enters the blood from the lymphatic system periodically, in small portions, which creates a certain concentration of drug in the lymphatic system and more long-term supports in the blood [3, 4, 10]. The concentration of drugs in peripheral lymph, lymph nodes, organs and tissues in 4-15 times higher than the intramuscular

and intravenous injection [8]

The aim of the study. Comparative analysis of treatment and evaluation of the effectiveness of the method of indirect lymphotropic therapy (ILTT) in the treatment of patients with pneumonia.

**Materials and methods.** The observation of 90 patients with pneumonia - men aged 18 to 23 years ( $20 \pm 1,9$ ). Patients were hospitalized in the pulmonary department Military Hospital from 2007 to 2009.

The main group ( $n = 44$ ) consisted of patients with pneumonia, which antibiotics were administered according to the method ILTT, and the comparison group ( $n = 46$ ) consisted of patients who carried antibiotiotikoterapiya intramuscular way.

Localization of the pathological process in the lung tissues of the patient as follows: pneumonia in the middle lobe of right lung in 27 (30, 21%) patients, pneumonia in the upper lobe of left lung - 15 (16, 99%) patients, pneumonia in the lower lobe of right lung - 17 (18, 87%) patients, pneumonia in the lower lobe of left lung - 31 (33, 93%) patients.

Method lymphotropic administration was as follows: on the boundary of the mammary gland and the lateral surface of the chest in the defeat of the upper lobes and middle lobe of right lung, and at the subscapular and shoulder areas of the shoulder line in the defeat of the lower lobes on the affected side, subcutaneous injection after treatment with the operational field solution of alcohol with a needle for intramuscular injection at a depth of 1, 0 cm, first introduced 32 lidazy ED solution, then, without removing the needle, in 1 - 2 minutes - with an antibiotic solution (0, 5 g of ceftriaxone once-reference in 2 ml of 2% solution lidocaine). The procedure was performed 1 time per day.

The course of treatment was 5 injections. In all cases, ceftriaxone was used, since it was determined to high sensitivity of microorganisms. Antibiotics are used in monotherapy. In the comparison group of ceftriaxone administered intramuscularly for 1, 0 grams per day.

Patients in both groups had been appointed etiopathogenetic and symptomatic therapy in accordance with the standards of treatment of this disease. In addition to antibacterial drugs, patients received arterial mucolytics, fever and cold preparations, a complex of physical therapy and physiotherapy. All patients were in hospital until clinical and radiographic resolution of pneumonia.

Statistical processing of results of research carried out using a software package Excel 2007, and the program Statistica 6.0. For processing the experimental data obtained using the estimate of reliability between-group differences using the Student t-test for independent samples. Intergroup differences were considered significant at  $p < 0, 05$ .

**Results and discussion.** The results confirmed the effectiveness of injections of antibiotics method of indirect lymphotropic therapy. Patients who underwent ILTT, there was acceleration of the dynamics of clinical-ray and laboratory data. Thus, the study group significantly faster

stopped signs of infectious intoxication and other indicators of clinical course of pneumonia (cough, chest pain, fever, general weakness), 2 - 3 days earlier were stopped and objective signs of disease (the shortening of percussion tones over an area of destruction lung tissue, the weakening of the respiratory noise, wet finely wheezing) than in patients receiving antibacterial therapy intramuscular route of administration. .

As evidence of reduced toxicity, including an earlier decline of leukocytes and erythrocyte sedimentation rate, combined with a tendency to an earlier decrease in cough and sputum, then the latter can be regarded as favorable clinical symptoms. In the study group was complicated by pneumonia, acute respiratory failure of I degree, only 3 persons (5, 6%), whereas the comparison group in 5 patients (10, 4%) was found acute respiratory failure of I degree and in 2 patients (2, 6%), respiratory insufficiency of II degree. In the comparison group in 2 patients (2, 6%), pneumonia complicated by infectious-toxic shock and one patient - exudative pleurisy.

Suitable for a pathological process in patients of the group, coupled with the elk and less painful way to deliver an antibacterial drug in the organic mechanism, which also contributed to the rapid recovery of patients.

X-ray resolution of pneumonia patients from group occurred at 14, 2,  $\pm$  1, 1 day, length of hospital stay was 18,1  $\pm$  1,7 days., whereas the corresponding figures in the comparison group consisted of 17, 9  $\pm$  1, 4 and 22 , 8  $\pm$  1, 6 day respectively ( $p < 0, 05$ ).

**Conclusion.** Thus, the results gave reason to believe that the application of indirect lymphotropic therapy in pneumonia effectively due to more rapid suppression of pathogenic organisms in the lung tissue, and earlier onset of repair processes and tissue regeneration. In addition, long-term preservation of a high concentration of antibiotic in the lymphatic system has allowed to halve the daily dose of antibiotic. Made significant pharmacoeconomic impact by reducing the exchange rate in two doses injected antibiotic, shorten treatment time and hospital stay.

The proposed approach would not only improve treatment results and substantially reduce the cost of treatment, he and improve the quality of hospital stay due to the exclusion of painful intramuscular injections of antibiotics and reduce the length of hospital stay.

## SUMMARY

In order to study the treatment results and evaluate the effectiveness of the method of indirect lymphotropic therapy (ILTT) in the treatment of patients with pneumonia was a comparative analysis in groups of patients with pneumonia that antibiotics were administered according to the

method ILTT (n = 44) and patients that antibiotics therapy held the intramuscular route (n = 46).

Patients who underwent ILTT, there was acceleration of the dynamics of clinical and laboratory data significantly faster than stopped signs of intoxication and other indicators of clinical course of pneumonia in 2 - 3 days earlier were stopped and objective signs of disease than in patients receiving antibacterial therapy with the intramuscular route of administration. X-ray resolution of pneumonia in patients who underwent ILTT, occurred significantly faster, and length of hospital stay was significantly shorter than similar indicators of patients who received intramuscular antibiotics therapy way. Application ILTT allowed to halve coursework dose antibiotic.

Keywords: pneumonia, indirect lymphotropic therapy, soldiers

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**E. N. Tepikina**

## **DYNAMICS OF CYTOKINE PROFILE PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS.**

### **Abstract**

The results of immunological study of 58 patients with juvenile idiopathic arthritis. It was found in all forms of the disease observed substantial changes of cytokine status in serum and synovial fluid, the degree of severity depends on the variant and the activity of the inflammatory process. Study of cellular immunity was held to a differentiated approach to the choice of therapy, as well as the efficiency of the drugs varied depending on the variant of the disease. The greatest efficiency in the treatment of polyarticular and oligoarticular spreading form was observed in remicade, combination therapy with sandimmun-neoral and methotrexate is preferable to use at oligoarticular persistent form of juvenile idiopathic arthritis.

Key words: juvenile idiopathic arthritis, cytokines, interleukin-17, remicade, methotrexate.

### **Introduction**

Juvenile idiopathic arthritis (JIA) - one of the most common rheumatic diseases characterized by inflammation of the synovial membrane of joints, destruction of cartilage and bone tissues, the development of extraarticular manifestations of the spectrum, mostly making their debut in children younger than 16 years [3]. In the development of juvenile idiopathic arthritis a significant place given to the activation of T-cell immunity with the subsequent synthesis of inflammatory cytokines [2].

It is shown that Th-17 and produce cytokines involved in the pathogenesis of inflammatory, allergic and autoimmune diseases, as well as protect against extracellular microbes and parasites [4].

Studies conducted in cell cultures and animal experiments confirm the clinical involvement of interleukin-17 in the development of rheumatoid arthritis [11].

Study the mechanisms of development and differentiation of this cytokine in rheumatoid arthritis, revealed the involvement of interleukin-6 in the initiation of production of IL-17 as well as the effect of IL-17 on production of other cytokines [10].

Studying the role of interleukin-17 in juvenile idiopathic arthritis will deepen understanding of the pathogenesis, develop criteria for early diagnosis, effective treatment for the disease.

Currently, the treatment of juvenile idiopathic arthritis using a wide range of antirheumatic (sulfasalazine, gold preparations, methotrexate, sandimmun-neoral, etc.) with general immunosuppressive effect [1].

In addition, in recent years introduced drugs with selective action on the immune system. Infliximab (Remicade) has become one of the first widely used in rheumatological practice [5, 6]. He is a monoclonal antibody to tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ). Preliminary analysis of the efficiency of anticytokine therapy revealed that the majority of the surveyed patients had significant clinical improvement, reflected in a reduction of pain and swelling of affected joints, duration of morning stiffness, increased range of motion in joints, improve overall health [7, 8, 9].

However, the efficiency of medications used depends on correctly selected treatment regimens. Comprehensive study of immune cells is important for the selection of adequate therapy, since the beginning of the timeliness and adequacy of treatment will determine the length and quality of life.

**The purpose of the study** - to examine indicators of cytokines in children with juvenile idiopathic arthritis, to develop a differentiated approach to prescribing drugs for the treatment of disease.

### **Materials and methods**

In complex clinical - immunological study included 58 children aged 2 to 17 years, patients with different variants of juvenile idiopathic arthritis. The control group consisted of 30 apparently healthy children of the same age category. For inclusion in the study with informed consent from children over the age of 14 or parents of children under the age of 14 years.

Clinical studies were conducted on the basis of child kardiorheumatology and cardiac surgery departments of the Samara regional clinical cardiology clinic.

Immunological studies were performed at the Central Scientific Research Laboratory, Samara State Medical University.

Comprehensive clinical examination included a study of data from medical history, clinical indicators, laboratory and instrumental methods. Quantitative determination of lymphocytes and their subpopulations (CD3 +, CD4 +, CD8 +, CD19 +, CD3 + HLADR +) in serum was performed by the standard method of indirect immunofluorescence using monoclonal antibodies ICO-86 and ICO-31 to their surface antigens (NPK "drug", Russia).

Quantitative indicators of TNF- $\alpha$ , IL-2, IL-4, IL-6, IL-17 in serum of IL-6, IL-17, TNF- $\alpha$  in the synovial fluid of patients with JIA were measured by enzyme-linked immunosorbent assay (ZAO Vector-Best, Russia).

Clinical diagnosis was based on the classification of juvenile idiopathic arthritis EULAR (Durban, 1997, Edmonton, 2001), in accordance with which the children were divided into 3 variants of JIA:

1. oligoarthritis persistent - arthritis, affecting no more than 4 joints throughout the time of disease - 20 (34,4%);
2. oligoarthritis spreads - arthritis, which affects 4 or more joints after first 6 months of illness - 19 people (32,8%);
3. polyarthritis seronegative - arthritis, involving in the inflammatory process 5 or more joints during the first 6 months of disease, RF-negative - 19 people (32,8%).

The average age of patients was  $7,1 \pm 0,5$  years, mean disease duration -  $2,8 \pm 0,4$  years. All children with juvenile idiopathic arthritis were divided into groups depending on the obtained modifying therapy.

Formation of groups was such that in each group were presented to all age categories, the distribution of children was carried out on the floor, laboratory activity and the number of affected joints.

Combination therapy (Sandimmun-neoral + MTX) has been appointed 16 patients (27%), 10 (17%) were on treatment Remicade, 12 (21%) - sulfasalazine, 20 person (35%) were receiving methotrexate monotherapy.

Sulfasalazine treatment started with a dose of 5-10 mg / kg / day, gradually increasing to 30-40 mg / kg / day. Sandimmun-neoral administered at a dose of 1,5 - 3,5 mg / kg / day, methotrexate - 7,5-15 mg/m<sup>2</sup>/week intramuscularly 1 time per week, infliximab (Remicade) - 6 mg / kg, the first two infusions 2, 4 weeks, then every 8 weeks.

For statistical analysis we used the calculation of average values (M), standard deviations (m). The significance of differences of mean values between two samples was determined by Student's t-test. The critical level of statistical significance (p) was taken to be 0.05.

### **Results and discussion**

Indicators of the quantitative distribution of cytokines in different variants of JIA presented in Table 1.

Table 1

The most pronounced changes in cell populations of lymphocytes was accompanied by a version of polyarticular JIA. Changes in the composition of CD-markers for this option were clearly defined the character corresponding to the main pathogenetic mechanisms of disease: an increase in the total number of lymphocytes (CD3 +) and activated forms (CD3 + HLADR +), a significant increase in T-cell-helper (CD4 +), decrease in the activity of T-lymphocytes with cytotoxic activity (CD8 +), moderate increase of B-lymphocytes (CD19 +).

When oligoarthritis pervade most orientation changes of cellular immunity was of the same nature as that of a polyarticular form, only the degree of these changes were less pronounced.

With persistent arthritis also revealed changes in lymphocyte subpopulations, but most indicators are normal.

Analyzing the contents of cytokines in serum, observed a significant increase in proinflammatory IL-2, IL-6, increased levels of IL-17, TNF- $\alpha$ , decrease the concentration of anti-inflammatory IL-4 in all variants of juvenile idiopathic arthritis. More significant percentage of abnormalities observed in the polyarticular form of JIA, which is associated with the disease on the background of the maximum activity of the inflammatory process.

Definite interest to study the contents of individual cytokines (IL-6, IL-17, TNF- $\alpha$ ) in synovial fluid of affected joints (Table 2).

Table 2.

Indicators of cytokines in synovial fluid is much higher than those in the serum of patients with JIA. The highest content in blood serum and synovial fluid was observed in IL-6 ( $12,1 \pm 0,1$ ,  $369,9 \pm 0,3$  respectively). In addition, revealed high levels of IL-17 and TNF- $\alpha$ .

Thus, for children with juvenile idiopathic arthritis characterized by increased concentrations of proinflammatory cytokines in serum and in synovial fluid, which can be used for early diagnosis of the disease. In this case, the indicators differed significantly from the control group and depended on the variant of the disease and the degree of inflammatory activity. Reduction of interleukin-4 may indicate a decrease in anti-inflammatory activity in patients with JIA.

Clinical efficacy was assessed on the dynamics of the basic immunological parameters - the immunological system improvements, in which no or low efficacy - improved less than 25% from baseline, a satisfactory effect - improvement of 50% (IIU50), good effect - improvement of up to 75% (IIU 75), an excellent effect - improvement of more than 75% (IIU 100) (Table 3).

Table 3

In the analysis of the data revealed that the efficiency of basic drugs varies depending on the version of the JIA. In persistent oligoarthritis high immunological parameters were obtained with combination therapy sandimmun-neoral and methotrexate - IIU 100 - 36%. Remicade in the treatment of patients with oligoarticular pervasive and polyarticular JIA option at the most rapid immunological parameters - 55% and 51.3% respectively. Shows the efficiency of combination therapy Sandimmun-neoral and methotrexate compared with methotrexate monotherapy. In the application of sulfasalazine found the lowest rates for all forms of the disease.

Summarizing the findings can be stated that the optimal choice of the base of the drug should be made for a specific form of JIA. The results of the comparative immunological tests

have shown that early differential assignment of basic drugs is highly effective and contributes to the stabilization of the autoimmune process.

### Conclusion

1. In all forms of JIA marked change in cytokine and cellular status in the serum. The intensity of these changes depends on the variant and the degree of inflammatory activity.

2. The concentration of cytokines in synovial fluid is much higher than in the serum of patients with JIA.

3. Most effective for the treatment of polyarticular and oligoarticular pervasive form has Remicade in the treatment of persistent oligoarticular form option is preferable to use the combination therapy Sandimmun-neoral and methotrexate.

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Table 1. Ratio lymphocyte subpopulations and cytokines, depending on the version of the JIA.

Variant of the disease	Indicators of cytokine profile, pg / ml					Indicators of lymphocyte subpopulations, pg / ml				
	IL-2	IL-4	IL-6	IL-17	TNF- $\alpha$	CD3+	CD19+	CD3 HLA DR+	CD4+	CD8+
Control group	20 $\pm$ 0,3	6 $\pm$ 0,4*	2,5 $\pm$ 0,2	0,5 $\pm$ 0,1*	0,3 $\pm$ 0,4	1,7 $\pm$ 0,05	0,5 $\pm$ 0,1*	15 $\pm$ 0,5*	1,1 $\pm$ 0,1*	0,9 $\pm$ 0,4
Oligoarthritis persistent	18,3 $\pm$ 0,5*	3,7 $\pm$ 0,3*	4,54 $\pm$ 0,5	0,5 $\pm$ 0,3	0,4 $\pm$ 0,1	2,4 $\pm$ 0,3	0,5 $\pm$ 0,1	15 $\pm$ 0,09*	1,2 $\pm$ 0,05*	0,9 $\pm$ 0,2
Oligoarthritis spreads	19,2 $\pm$ 0,1	2,4 $\pm$ 0,1	7,2 $\pm$ 0,3	0,78 $\pm$ 0,1*	0,58 $\pm$ 0,05	3,2 $\pm$ 0,2	0,6 $\pm$ 0,2	16 $\pm$ 0,2*	1,5 $\pm$ 0,06	0,7 $\pm$ 0,6*
Polyarthritis seronegative	21,3 $\pm$ 0,05	0,9 $\pm$ 0,1	24,6 $\pm$ 0,1	0,99 $\pm$ 0,2	0,72 $\pm$ 0,04*	3,2 $\pm$ 0,4	0,81 $\pm$ 0,5*	16,8 $\pm$ 0,1	1,9 $\pm$ 0,1	0,3 $\pm$ 0,5

Note . \* - statistically significant differences from control at  $p < 0.05$

Table 2. Levels of IL-6, IL-17, TNF- $\alpha$  in serum and synovial fluid of patients with JIA.

Name of cytokines	Indicators of cytokines in serum, pg / ml	Indicators of cytokines in synovial fluid, pg / ml
IL-6	12,1 $\pm$ 0,1	369,9 $\pm$ 0,3
IL-17	2,27 $\pm$ 0,05	48,55 $\pm$ 0,1
TNF- $\alpha$	0,67 $\pm$ 0,3	8,45 $\pm$ 0,05

Note . \* - statistically significant differences from control at p <0.05

Table 3. Dynamics IIU criteria depending on the drug and the disease variant in children with juvenile idiopathic arthritis

Preparation	Variant of the disease								
	Oligoarthritis persistent			Oligoarthritis spreads			Polyarthritis seronegative		
	IIU 50, %	IIU 75, %	IIU 100, %	IIU 50, %	IIU 75, %	IIU 100, %	IIU 50, %	IIU 75, %	IIU 100, %
Sulfasalazine	31	42	27	48	29	23	57	32	11
Sandimmun- neoral + methotrexate	25	39	36	10	41	49	21,8	35,7	42,5
Methotrexate	27	40	33	39	36	25	45	28	27
Remicade	-	-	-	14	31	55	11	37,7	51,3

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**Kapustina T.A., Markina A.N., Lopatnikova E.V., Parilova O.V.**

### **FAMILY CHLAMYDIOSIS IN UPPER RESPIRATORY TRACT.**

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(headed by RAMS corresponding member Mr.V.T.Manchuk)

**Abstract:** The paper represents the results of studying 44 households with family members having upper respiratory tract diseases, associated with Chlamydia infection. Control group included 43 households with ENT family members, who didn't show Chlamydia. Diagnostics was provided by using the complex of laboratory methods (direct immune fluorescent and immune enzyme analysis, polymerase-chain reaction). The presence of one patient with respiratory chlamydiosis in a household results in infecting other family-members with Chlamydia.

**Key words:** Chlamydia infection in upper respiratory tract, household hotbed of respiratory chlamydiosis.

At present Chlamydia infection has the status of serious problem for international and national public health due to its high prevalence, variability in clinical signs, lesion location, high costs of diagnostics and treatment, liability to becoming chronic, influence on population reproduction of [2, 4, 5, 9, 11, 12, 13, 14, 15 and many others]. Complexity, heterogeneity and insufficient level of knowledge in Chlamydia infection pathogenesis dictate a necessity to aim the research at its different links, including such important pathogenic link as intra-family infecting. Previously the majority of research for ENT, associated with Chlamydia infection was based on the positions of a separate individual. The necessity to accept new approach in terms of intra-family infecting had escalated, taking into account such factors as type of transmission (droplet, contact), high susceptibility to pathogen.

Unfortunately the problem is being developed only concerning urinal genital chlamydiosis [7, 9, 10], despite every family member who has respiratory localization of Chlamydia infection can become the source of "family chlamydiosis" and the threat to infect all the rest of the family members. Household approach to preventive measures against extragenital diseases had been already supported by several scientists [2, 3].

Hereby, the target of the research was to study the frequency of respiratory chlamydiosis and characteristics of its signs in family members of ENT patients with verified Chlamydia infection.

### **Subject and Methods of Research.**

Subject of research are families of ENT patients, receiving treatment of acute and chronic pathology of upper respiratory tract in a hospital ENT-department. We tested 87 households by single-step method. There was a patient with identified Chlamydia infection in 44 out of them. These 44 composed main group with children patients in 24 of them and adult patients in 20. Control group numbering 43 households included family members who did not have confirmed Chlamydia. The number in cohort was determined according to V.I.Paniotto method (1982). Total number of subjects in the tested families was 245: 123 subjects in the main group (38 children, 85 adults) and 122 subjects in control (33 children, 89 adults). Family members from different groups matched each other in terms of age and gender.

Research laboratory methods included identification of two types of Chlamydia (Chlamydia trachomatis and Chlamydia pneumoniae). Two direct tests were used for revealing them (direct immune fluorescent analysis and polymerase chain reaction) and one indirect test (immune enzyme analysis). Polymerase chain reaction and immune enzyme analysis were carried out by test-systems "VectorChlamy-DNA-amli" and "ChlamyBest-strip" ("Vector-Best"). To provide immune fluorescent analysis we used test-system "ChlamySlode" ("Galart"-Liagnostikum).

The description of binaural signs is represented by relative frequency, expressed in percent and 95% of confidence interval (95% CI). Estimation of relevance in differences between indices was executed by Student's t-criterion and Fisher's exact criterion. Maximum reasonable possibility of  $\alpha$ -error (p) was accepted as statistical meaning level equal or lower than 0.05.

### **Research Results and Discussions.**

Research results showed high stage of Chlamydia infection contagiousness in hotbed of respiratory chlamydiosis. Among all family members, including ENT patients with identified Chlamydia – we found Chlamydia in 81 subjects (in 65.9%, 95% CI 57.3 - 73.9). The increase in the quantity of infected subjects was 30.1%. At the same time Chlamydia were identified in 73.7% (95% CI 58.7 - 87.7) children and in 62.4% (95% CI 52.0 - 72.7) adults. We didn't mark constituent difference in susceptibility to Chlamydia between children and adults (p=0.2). In 27.3% of households all the family members were infected. In 34.1% of households more than two thirds of the family members were infected. In 27.3% - from half to 60% of all family members. Only in 5 households (in 11.4%) less than one third of family members were infected.

In 28 households out of 44 (in 63.6%, 95% CI 49.0 - 77.1) with verified Chlamydia patients, there were other family members being infected. The increase of infected subjects in these families achieved 44.1%. Contamination of all family members was marked in 42.9%; more than two thirds of family members – in 46.4%; from 50% to 60% - in 10.7%. The absence of Chlamydia in members of 16 families of ENT patients with confirmed respiratory chlamydiosis can be supposedly explained by presence of persistent infection, hardly diagnosed by laboratory means or "recent" infecting of the subject who is the source of contamination.

We revealed 103 cases of different Chlamydia contamination in 81 family members (see Table.). Simultaneous presence of two Chlamydia types was marked in 17.9% of family members (in 15.8% children and in 18.8% adults). In children as compared to adults the frequency of Chlamydia pneumoniae infection was considerably higher than Chlamydia trachomatis verification (in 68.4% against 21.1%,  $p < 0.001$ ). We didn't find differences in the frequency of these types of Chlamydia in adults: the same indices were correspondingly 44.7% and 36.5% ( $p = 0.3$ ).

We revealed the following age peculiarities: Chlamydia pneumoniae was met in adults before the age of 30 considerably more frequent as compared to subjects of elder generations (in 64.3% against 35.1%). Mono infecting with Chlamydia trachomatis was found more often in ages older than 30 years (in 22.8% against 7.2%). We marked similar tendencies in children. The elder the child, the lower was the frequency of Chlamydia pneumoniae (in 93.8% in ages from 3 to 6 years against 50.0% in children older than 7 years old). Chlamydia trachomatis as mono infection was verified only in schoolchildren (in 9.1%). We didn't find gender dependency in susceptibility to upper respiratory tract Chlamydia infecting among family members.

We diagnosed ENT chronic pathology (including those of inflammatory genesis) in families with the hotbed of respiratory chlamydiosis 1.7 and 2.2 times more often ( $p < 0.001$ ), than in control: correspondingly in 73.2% (95% CI 65.0 – 80.6) against 42.6% (95% CI 34.0 – 51.5) and in 67.5% (95% CI 59.0 - 75.4) against 30.3% (95% CI 22.5 – 38.8). Besides, there were more subjects with combinatory pathology (in 22.8% against 6.6%,  $p < 0.001$ ) in families with chlamydiosis hotbed on the account of family members with two diseases of throat (in 12.2% against 2.5%,  $p = 0.002$ ) or simultaneous diseases of throat and nose (in 7.3% against 1.6%,  $p = 0.02$ ).

Regardless the presence or absence of respiratory chlamydiosis hotbed the more frequent localization of ENT chronic diseases was throat. In Chlamydia infected families this pathology was diagnosed more often (in 59.3% against 24.6%,  $p < 0.001$ ) on the account of higher frequency of tonsillitis (in 20.3% against 5.7%) and pharyngitis (in 35.0% against 10.7%). The share of throat diseases was 3 times higher than the share of nose diseases (74.6% against 24.6%). The same indices in families without chlamydiosis hotbed differed 1.6 times (55.0% against 35.0%).

Above-mentioned tendencies were typical for both children and adults in the families. In children from chlamydia hotbed families as compared to children from non-infected families the levels of total chronic ENT pathology, inflammatory chronic diseases, throat diseases were correspondingly 81.6%, 71.1%, 76.3% against 39.4% ( $p<0.001$ ), 15.2% ( $p<0.001$ ), 30.3% ( $p<0.001$ ). In adult family members the frequency of the mentioned pathology reached correspondingly 69.4%, 65.9%, 51.8% against 43.8% ( $p<0.001$ ), 36.0% ( $p<0.001$ ), 22.5% ( $p<0.001$ ). Among some forms of chronic nosology in adult members in infection hotbed families the following forms were more frequently revealed: pharyngitis (in 45.9% against 14.6%,  $p<0.001$ ). As for children, tonsillitis and pharyngitis were diagnosed only in families with the source of Chlamydia contamination (correspondingly 31.6% and 10.5% subjects).

Thus, patients with upper respiratory tract diseases associated with Chlamydia infection, are the sources of this infection and are the threat of infecting members of the family. That is why performing preventive measures against intra family respiratory chlamydia allows to improve health indices not only in a family, but in the society as a whole.

### Conclusions.

1. The contamination of family members with Chlamydia takes place in 63.6% families of ENT diseases patient with identified Chlamydia. Infection had been found in all family members in 42.9%, in more than two thirds of all family members – in 46.4%, from 50% to 60% - in 10.7%.

2. In family hotbeds of upper respiratory tract Chlamydia infection we diagnosed ENT chronic pathology 1.7 times more often as compared to families, where ENT patient is not infected with Chlamydia on the account of throat diseases such as tonsillitis and pharyngitis in other family members.

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Table. The prevalence of Chlamydia different types in family hotbeds of respiratory chlamydiosis.

Group	Mono infecting with Chlamydophila pneumoniae		Mono infecting with Chlamydia trachomatis		Chlamydia mixed infection		Totally infected by Chlamydia	
	n	%, 95% CI	n	%, 95% CI	n	%, 95% CI	n	%, 95% CI
Adults (n=85)	22	25.9 16.6-35.7	15	17.6 10.3-26.4	16	18.8 11.3-27.8	53	62.4 52.0-72.7
Children (n=38)	20	52.6 36.7-68.5 pch-a=0.01	2	5.3 0.5-14.5 pch-a=0.04	6	15.8 6.1-28.9 pch-a=0.7	28	73.7 59.7-87.7 pch-a=0.2
Total (n=123)	42	34.2 25.8-42.5	17	13.8 8.3-20.5	22	17.9 11.6-25,1	81	65.9 57.3-73.9

Note: p is statistical significancy for differences in groups of children and adults according to Student's and Fisher's criterion.

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## ANTIBIOTIC ACTIVE METABOLITE OF FUNGI OF THE GENUS *TRICHODERMA*

**Sharikov AM, Novitsky, IA, Mantchuk VT**

**Summary.** Were studied by the hole effect of metabolites of fungi *Trichoderma harzianum* on the number of gram-positve and gram-negative microorganisms: *Bacillus subtilis*, *Micrococcus luteus*, *Salmonella moskow*, *S. typhimurium*. Shown antibiotic activity of metabolites of the fungus *T. charzianum* against *M. luteus*, *S. moskow*. These metabolites are promising as producers of new antibiotic drugs.

**Key words:** bactericidal action, imperfect fungi, metabolites of fungi of the genus *Trichoderma*, the method of holes, gram-negative and gram-positve microorganisms.

### Introduction

It is known that the culture fluid of the lower fungi contain substances with antibiotic properties. Research in this area being quite active, constantly found new metabolites with useful properties. [1,2,4,8,9,11,12,13,14]. Fungi of the genus *Trichoderma* are well known as producers of exoenzymes and has long been widely used by man. Of them receive a cellulase, xylanase, lipase, lignindegidrogenazy, chitinase, pectinase, a number of specific oxidases used in medicine [3].

*Trichoderma* fungi are producers of metabolites having high antibiotic activity against fungi and bacteria. Research in this direction being very active, constantly find new metabolites with useful properties [3]. The initial task of our research was to study the biological activity of native fungal strains of *Trichoderma* species against a number of opportunistic microorganisms. Were studied following strains of fungi *Trichoderma*:

### Table 1

Found that the greatest spectrum of activity against the studied strains of opportunistic mikroorganizmov have metabolites produced by strain M 99/5 *Trichoderma charzianum*. Unfortunately, systematic studies on the biological activity of metabolites native fungal strains of *Trichoderma* species in Central Siberia against opportunistic microorganisms to date are not held in proper amount. Such studies would be particularly promising for the treatment of diseases caused by endemic to the area strains of bacteria [10].

The search mechanisms to lower fungi to successfully withstand the competition for resources with microorganisms, could help to find a very effective medication [5].

The aim of this work was to study the antibiotic activity of metabolites of the strain M 99/5 of the fungus *Trichoderma charzianum* on a number of opportunistic strains of microorganisms.

### Materials and methods

The object of the study were sterile metabolites derived from fungi of the species *T. charzianum* strain M 99/5. The influence of selected metabolites in strains of opportunistic microorganisms *Micrococcus luteus*, *Klebsiella pneumoniae*, *Salmonella moskow*, *S. typtimurium*, isolated from patients pankreanekrozom ill patients Clinical Hospital № 7 of the city of Krasnoyarsk.

Pre-cultivation of each strain was carried out on nutrient agar (RM-agar production of Federal State Unitary Enterprise State Scientific Center of Applied Microbiology and Biotechnology), followed by incubation in thermostat during the day at 37 ° C. Received isolated typical colonies of each species were collected for bacteriological loop and suspended in test tubes with sterile saline according to the standard turbidity. Sown dose suspensions of microorganisms were  $1.5 \times 10^8$  CFU/ml (0.5 turbidity standards McFarland). Sowing prepared suspensions was performed pressed with a cotton swab in three directions at the plate dried Mueller-Hinton agar, poured a thick layer in Petri dishes.

Determination of bactericidal activity of the investigated extracts was performed by the wells. Immediately after seeding, the standardized suspension of microorganisms in each inoculated petri dish with a sterile cork borer 1 cm in diameter were doing at the same distance six holes, then the automatic constant-volume pipette, Biohit volume of 100 ml in each well of a disposable sterile tip Axygen studied the culture fluid was added. Control study was saline.

After making the culture fluid petri dishes were incubated without turning in an incubator at 37 ° C for six days. All experiments were performed in triple replicates. Observations on the growth of test cultures started after days of incubation. Measuring the diameter of growth

inhibition of microorganisms held metal ruler with millimeter scale on the second, fourth and sixth day of incubation. Statistical analysis was performed using software package STATISTICA v.6.0. Calculated the mean and standard deviation, significant differences were determined by nonparametric Mann-Whitney test.

### Results and discussion

In the course of this work was established antibiotic activity of metabolites of the strain M 99 / 5 of the fungus *T. sharzianum* M 99 / 5 against *M. luteus* and *S. moskow*. The greatest value of the inhibition of growth ( $20,6 \pm 0,5$  mm,  $p < 0,05$ ) was found for strains of *M. luteus*. For strains of *K. pneumoniae*, *S. typhimurium* growth inhibition zone was not determined.

Table 2

The results suggest features of the mechanism of action of antibiotic substances isolated from the studied fungi. Presumably, it is associated with the effect on the cell wall of microorganisms. Action of metabolites of the fungus studied one species of Salmonella and the absence thereof, to another due, apparently, with differing levels of resistance to antibiotics of strains obtained earlier. The literature has been described to obtain from the culture liquid antibiotics trihopolinov A and B. These antibiotics are highly active against fungi, Gram-positive bacteria and mycobacteria [6,7].

Thus, against several strains of bacteria observed antimicrobial activity of metabolites of native strains of fungi of the genus *Trichoderma*. The obtained results allow us to justify the importance and prospects derived metabolites as raw material for new microbiological preparations.

### Conclusion

At the moment, described five groups protivogribnyh antibiotics; they include, in particular, 6-pentyl-a-pyrone, trihoviridin, dermadin, trichodermine, trihodermol, diatsetoksistsirpenol (T-2 toxin), gliotoksin, gliovirin and other antibiotic metabolites with unspecified structure. At this stage of investigation is not possible to specify whether this effect of some of the above antibiotics or a combination thereof. Obviously, the borrowing of methods used by lower fungi to increase their competitiveness in a changing environment are extremely promising. At the same time, increasingly there is a need to increase the already high doses of traditional antibiotics used in medicine. In addition, many of these drugs developed an almost universal resistance, and receiving economically promising way of allocating new antimicrobial agents from the substrate with a small amount of waste can be considered as one of the priorities in modern pharmacology.

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Table 1

Indigenous strains of fungi of the genus *Trichoderma*

Strains	
MK	<i>Trichoderma citrinoviridae</i>
TH4	<i>Trichoderma citrinoviridae</i>
0-97	<i>Trichoderma harzianum</i>
01-00	<i>Trichoderma asperellum</i>
МГ 6	<i>Trichoderma asperellum</i>
K 12	<i>Trichoderma asperellum</i>
M 99/5	<i>Trichoderma harzianum</i>
119/85	<i>Trichoderma sp.</i>
MO	<i>Trichoderma hamatum</i>
30	<i>Trichoderma asperellum</i>

Table 2

The value of the absence of zones of growth of microorganisms around the wells containing solutions the culture fluid of strain M 99 / 5 of the fungus *T. charzianum* ( $M \pm \sigma$ , mm)

	The duration of incubation of microorganisms, day.		
	2	4	6
<i>M. luteus</i>	19,8±0,4	20,0±0,7	20,6±0,5
<i>S. typhimurium</i>	–	–	–
<i>S. moskow</i>	18,4±1,1	18,6±1,1	18,8±1,3
<i>K. pneumoniae</i>	–	–	–

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**P.I. Kudrina, A.L. Ariev**

**The clinical and etiological characteristics of patients of elderly and senile age with discirculatory encephalopathy depending on residing region.**

The clinical and etiological characteristics of discirculatory encephalopathy (DE) depending on residing region has been studied. The analysis of risk factors has shown that the leading reasons of vascular defeat of a brain at all patients were the atherosclerosis and an arterial hypertension, thus at patients of I group at whom old traditions of a food and quieter, traditional way of life have remained, these risk factors were present less often. Clinical symptoms of discirculatory encephalopathy, as well as numerous subjective and clinical displays, have been most expressed at patients of the basic group, inhabitants of Viljujsky region, adverse in the ecological plan.

Keywords: discirculatory encephalopathy, region, risk factors, the clinical characteristic, elderly and senile age.

Introduction: the chronic asphyxia of brain (ChAB) on prevalence takes a leading place in structure of cerebrovascular diseases (1). Slowly progressing insufficiency of blood supply of the brain is meant by this term, leading to gradual infringement of its functioning (1,2). An atherosclerosis and arterial hypertension promote to blood circulation destabilizations as a whole, to gradual development of chronic cardiovascular insufficiency and, accordingly, development and progressing XHMK (3,4). Consider that the extremely difficult, and at times and an impracticable problem is an accurate definition of etiology of discirculatory encephalopathy at elderly (4,5). The reason of it is characteristic for persons of the senior age groups the combination of actually atherosclerotic changes with arterial hypertension, cardiac pathologies and other vascular pathological changes. At such variants of a pathology patients of elderly and senile age quickly enough, during 2 - 5 years pass all three stages of chronically developing insufficiency of brain blood circulation (6,7). Many researchers note a tendency to increase the share of discirculatory encephalopathy in structure of vascular diseases of nervous system that is connected with aging of the population.

Each certain geographical region, each ethnic group of the population define the features in epidemiology of this or that disease. There are separate researches about prevalence of vascular diseases of a brain in some regions of the Russian Federation (Baragin J.J., 1990). Studying cerebrovascular pathologies at representatives of elderly and senile age, especially taking into account some regional and ethnic factors, represents doubtless scientific and practical interest and has certain value for perfection of quality and efficiency of rendering of medical aid to older persons of this or that region of such big and multinational country, as the Russian Federation.

Research object - to study risk factors of development and progressing, and also to carry out the comparative analysis of a clinical picture discirculatory encephalopathy at persons of the elderly and senile age living in different regions of republic.

Material and research methods. 118 patients with discirculatory encephalopathy of 2<sup>nd</sup> stage have been surveyed. All patients during supervision have been hospitalized in neurologic branch of the Geriatric Center (GC). Criteria of statement of the diagnosis was clinically confirmed by defeat of vessels of a brain at a corresponding clinical picture. Proceeding from the purpose patients have been subdivided into two groups: the basic, including 2 subgroups, and control. Criteria of division of the basic group into subgroups was the residing region. The basic group was made by 83 patients at the age of 60 - 85 years: in the 1<sup>st</sup> subgroup there were 38 patients living in northern zone, in the 2<sup>nd</sup> - 45 patients living in Viljujsky area. The comparison group has been presented by 35 patients with a similar pathology aged in a range of 35-55 years.

Clinical research included careful and profound gathering of the anamnesis in the course of personal meeting with sick, their relatives, viewing of out-patient cards from polyclinic establishments in a residence, archival case records, extracts, and inquiries. Results of the first and all subsequent inspections were compared, as one of problems of our work was research of dynamics of clinical displays of cerebrovascular pathologies depending on region. For the purpose of definition and specification of stage of discirculatory encephalopathy the anamnesis, complaints of patients, a condition of the neurologic status on 11 parameter have been analyzed. The statistical analysis was carried out on IBM- the computer with use of programs Microsoft Excel, Statistica, Biostat with material processing on groups by means of the methods of variation statistics including calculation of average values, errors of average, standard deviations. Nonparametric methods, in particular factor of Spearman's correlation, Mann Whitney's test were also used. At the primary statistics the tabular express method of Strelkov was applied. For each sample of indicators counted numerical characteristics of distribution. An estimation of the importance of distinctions between compared samples was carried out with use of parametrical criterion of Steward at 95 % a confidential interval.

#### Results and discussions.

The analysis of risk factors (table 1) has shown that is the most frequent factors at chronic asphyxia of brain are atherosclerosis and arterial hypertension that can be coordinated with the literary data. Nevertheless, frequency of the named risk factors at patients of the 1<sup>st</sup> group was smaller, than in the 2<sup>nd</sup> group. Heart troubles, adiposity and the burdened heredity prevailed also at representatives of the Viljujsky zone. Seldom there was a considered pathology at patients of the 1<sup>st</sup> basic group - northerners (accordingly). Sick of a diabetes and smoking suffered almost equally. Alcoholism has been most extended among patients of the 1<sup>st</sup> basic group – northerners.

The comparative characteristic of occurrence of various complaints is presented in table 2. It should be mentioned that at discirculatory encephalopathy - II the most frequent complaint there were headaches and dizziness. Headaches had different localizations, frequency (from 1 - 2 times a month to daily), character (compressing, pressing, pulsing, holding apart), arose at various times a day, more often in second half of day. The most frequent reasons of headaches were fluctuations of arterial tension, changes of weather conditions, intellectual or physical overfatigue. Dizzinesses had more often not system character were caused basically by the same reasons, as headaches. An occurrence immediate cause, initiation of this symptom could be changes of a body position and a head. Essentially a percent of occurrence of various subjective displays of disease at patients of 2<sup>nd</sup> basic group. For example, headaches met in 77,7 % against 68,4 % at representatives of the 1<sup>st</sup> group, dizziness - in 87,5 % against 68,18 % in the 1<sup>st</sup> group;

dream infringements - in 70,85 % against 54,54 % - at patients of the 1<sup>st</sup> group; memory decrease - in 79,16 % against 72,72 % - in the 1<sup>st</sup> group.

By the end of treatments (table 2) subjective infringements regressed: the general condition improved, complaints to headaches, dizzinesses, noise in a head have decreased, the dream improved, emotional lability decreased. Improvement was more expressed at patients of the 1<sup>st</sup> group indicators of whom have appeared close to those in comparison group. The comparative estimation of frequency of objective neurologic symptoms of discirculatory encephalopathy-I and discirculatory encephalopathy-II on groups of observed patients is presented in table 4.

From it follows that at patients with discirculatory encephalopathy -II following neurologic symptoms were defined: ocularataxia often had bilateral character, weakness of convergence and accommodation, infringement from craniocerebral nerves (CCN), pathological reflexes (hand and foot), an extrapyramid syndrome, symptoms of oral automatism. It is necessary to note rather low indicators of changes of reflex sphere (39,5%) sensitivity (26,3%) and cerebellum activity (47,8%) at patients of the 1<sup>st</sup> group (northerners) in comparison with representatives of Viljujsky region. In the course of treatment recourse focal neurologic semiology has appeared insignificant at representatives of II group, but nevertheless it distinctly was present at patients of group of comparison and 1<sup>st</sup> the basic group in the form of performance normalization of coordinator tests, improvement of gait, expressiveness reduction disartria. Increase in muscular force (on 0,5 point) and volume of movements was observed the tendency to normalization of a muscular tone, including at patients with extrapyramid frustration was traced, frequency and amplitude of a tremor decreased, the tendency to decrease in expressiveness of other infringements was found out.

#### Conclusions:

1. Group distinctions on risk factors, a clinical picture at patients with discirculatory encephalopathy elderly and senile age in dynamics of disease depending on region are revealed.
2. The leading reasons of vascular defeat of a brain at all patients were the atherosclerosis and an arterial hypertension, thus at patients of the 1<sup>st</sup> group at whom old traditions of a food and quieter, traditional way of life have remained, these risk factors were present less often.
3. Clinical symptoms of discirculatory encephalopathy, as well as numerous subjective clinical displays, have been most expressed.

**Risk factors (discirculatory encephalopathy).**

table №1

symptoms	I main n = 38		II main n = 45		III group comparison n = 35	
	n	%	n	%	n	%
Hipodynamia	4	10,5	8	17,7	5	14,3
Diabetes sugar	1	2,6	1	2,2	2	5,7
Affection heart ischemic	6	15,8	17	37,7	6	17,2
Obesity	1	2,6	3	6,6	3	8,6
Dislipidemia	12	31,6	19	42,2	7	20
Smoking	7	18,4	8	17,7	4	11,4
Alcohol	7	18,4	2	4,4	3	8,6
Heredity	1	2,6	5	11,1	2	5,7
Arterial hypertensin	21	55,3	36	80	16	45,7

## Subjective symptoms at discirculatory encephalopathy - II.

table

№2

cjmplaints	Before treatment						After treatment					
	I main n = 38		II main n = 45		III main n = 35		I main n = 38		II main n = 45		III main n = 35	
	n	%	n	%	n	%	n	%	n	%	n	%
Headaches	26	68,4	35	77,7	20	57,2	17	44,7	27	60	11	31,4
Tremor	3	7,9	5	11,1	2	5,7	2	5,2	4	8,8	1	2,8
dizzinsses	22	57,9	29	64,4	18	51,4	14	36,8	20	44,4	10	28,6
Hearing decrease	12	31,6	17	37,7	10	28,6	10	26,3	14	31,1	8	22,8
Stagger walking	13	34,2	25	55,5	3	8,6	5	13,2	19	42,2	1	2,8
Decrease memory	22	57,9	29	64,4	11	31,4	12	31,6	26	57,7	6	17,2
Stiffness	7	18,4	12	26,6	4	11,4	5	13,2	9	20	3	8,6
Speech disorder	3	7,9	6	13,3	-	-	1	2,6	4	8,8	-	-
Extremity weakness	18	47,4	28	62,2	10	28,6	10	26,3	19	42,2	4	11,4
Dysop(s)ia	12	31,6	19	42,2	6	17,2	9	23,7	16	35,5	3	8,6

**Objective symptoms at discirculatory encephalopathy - II.  
Before treatment.**

table № 3

symptoms	I main n=38		II main n=45		III main n=35	
	n	%	n	%	n	%
Extra pyramid syndrome	3	8,6	6	13,3	-	-
Oculomotor infringements	11	28,9	17	37,7	7	20
Symptoms of oral automatism	17	44,7	26	57,7	14	40
Anisoreflexion	15	39,4	40	88,8	18	51,4
Pathological reflex	7	18,4	10	22,2	7	20
Craniocereberal nerves	16	42,1	23	51,1	8	22,8
Changes of a muscular tone	8	21,1	13	28,8	6	17,2
Vestibular frustration	18	47,4	26	57,7	12	34,3
Sensitive frustration	10	26,3	13	28,8	6	17,2
Vegetative frustration	12	31,6	13	28,8	10	28,6

**Objective symptoms at discirculatory encephalopathy - II.  
After treatment.**

Table № 4

Symptoms	I main n=38		II main n=45		III main n=35	
	n	%	n	%	n	%
Extra pyramid syndrome	2	5,3	6	13,3	-	-
Oculomotor infringements	8	21,1	15	33,3	4	11,5
Symptoms of oral automatism	17	44,7	26	57,7	14	40
Anisoreflexion	12	31,5	35	77,8	15	42,8
Pathological reflex	7	18,4	10	22,2	7	20
Craniocereberal nerves	10	26,3	22	48,8	2	5,7
Changes of a muscular tone	5	11,1	9	20	1	2,8
Vestibular frustration	8	21,1	12	26,6	4	11,4
Sensitive frustration	5	13,2	9	20	3	8,5
Vegetative frustration	6	15,7	8	17,7	5	14,3

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**Effectiveness of superovulation induction in indigenous  
and non-native women with tubal-peritoneal infertility,  
living in the Far North**

**Semenova A.A., Bustritskaia T.S.**

**Summary:** There are submitted the results of superovulation stimulation in 30 native women of the North (the main group) and in 27 non-native women (the comparison group) with tubal-peritoneal infertility. In the main group the ovarian response to gonadotropin stimulation is diminished, the number of preovular follicles and oocytes are less than in the comparison group, the embryos development in vitro is slowed and the pregnancy rate in the program of In Vitro Fertilization (IVF) is almost 3 times lower. The use of superovulation stimulation protocols with GnRH-A in the main group increases the effectiveness of IVF by a factor of three.

**Key words:** infertility, ovulation stimulation, effectiveness of In Vitro Fertilization.

In the structure of infertility the tubal-peritoneal factor makes up 40-72% [4]. One of the main methods of treatment of tubal-peritoneal infertility is IVF [2]. Nowadays, indications for IVF, including infertility, not treatable by therapy, and higher efficiency of IVF as compared with other methods are determined. It should be noted, that the problem of increasing the effectiveness of IVF is still topical and requires more thorough studies [6]. Standard protocols of ovarian stimulation in IVF programs are well-developed, but the specialists' attention focuses on the possibilities of optimizing them according to the individual peculiarities of each concrete patient.

**The purpose of the study** was to explore the possibility of increasing the effectiveness of IVF programs in native women of Yakutia, living in conditions of the Far North.

**Materials and methods**

The study involved 57 women with tubal-peritoneal infertility who had indications for IVF. The main group consisted of 30 native women of the North and the comparison group - 27 non-indigineous women. Exclusion criteria were contraindications for superovulation induction and surgical interventions on the ovaries. Depending on the used schemes to stimulate ovulation

the following subgroups were identified: Subgroup 1 – of 15 women from the main group, whose ovulation was stimulated according to the scheme with the use of drugs, consisting of Gonadotropin Releasing Hormone-Agonist and Human Menopausal / Recombinant Gonadotropin (GnRH-A + HMG/rFSH) – Long protocol; Subgroup 2 – of 15 women from the main group whose ovulation was stimulated according to the scheme with the use of drugs of Human Menopausal/ Recombinant Gonadotropin and Gonadotropin-Releasing Hormone-Antagonists (GnRH-ant + HMG/rFSH) – Short protocol.

The following methods of investigation were used: clinical, hormonal and ultrasound. To determine the ovarian reserve on days 2-3 of menstrual cycle we studied the content of gonadotropins (LH, FSH) and total amount of Testosterone (Total Testosterone) in the blood serum using the test systems "Hema-medina" (Moscow). Ovarian volume and number of antral follicles were determined with the help of the ultrasonic apparatus "Acuson Aspen", using the sensor C9 - 5 MHz for transvaginal study in the two-dimensional gray scale scanning mode.

Stimulation of ovulation in IVF program and embryo transfer (ET) were conducted in 57 women. Dynamic hormonal and ultrasound screening, transvaginal puncture, in vitro fertilization and embryos transfer were performed by standard techniques. The duration of ovulation stimulation and doses of used preparations in the protocols of the examined groups were not significantly different.

The results of the study were processed by a standard software package "Statistica" for Windows 6.0 (Statsoft Inc., USA). To compare the data and evaluate the significance of the results' differences we used t – criterion of Student. Changes were considered statistically evident at the significance level of  $p < 0,05$ .

### **Results of the study**

The average age of women from the observed groups was  $33,4 \pm 4,2$  and  $32,9 \pm 4,4$  years old ( $p > 0,05$ ) respectively. The duration of infertility rated, on the average, from 2 to 14 years: in the main group -  $7,79 \pm 3,6$  years, in the comparison group -  $7,73 \pm 3,06$  ( $p > 0,05$ ). In 60% of women from the main group and in 59,2% patients of the comparison group the infertility was primary. The etiological factor in all cases was tubal-peritoneal.

When analysing the reproductive function it was revealed, that ectopic pregnancy ( $p < 0,05$ ) and its surgical treatment (tubectomy) was 3 times more often in women of the main group (33,3%) than in the comparison one. Chronic salpingo-oophoritis was marked in past history of all women in both groups.

Chronic endometritis was diagnosed in 33,3% of women of the main group and in 13,8% ( $p < 0,05$ ) of patients from the comparison group. The frequency of cervical diseases in the form of erosion, cervical dysplasia and chronic cervicitis was higher in the main group. Endometriosis, leiomyoma and polycystic ovary syndrome were more common in women from the comparison group.

The content of FSH, LH in the blood serum of women from the tested groups had no statistically significant differences. In the group of native women the amount of total Testosterone ( $1,3 \pm 0,8$  nmol/L) was lower as compared with the group of non-indigenous patients ( $2,8 \pm 1,0$ ;  $p < 0,01$ ), but for all women it was within the age rate.

In women from the main group the number of antral follicles in the right ovary was  $5,4 \pm 2,3$  and in the left ovary –  $4,9 \pm 2,6$ , while in women from the comparison group ( $p < 0,05$ ) their number amounted to  $6,7 \pm 2,7$  and  $6,3 \pm 2,6$  respectively. In women of the comparison group the volume of the right ovary was  $8,39 \pm 3,21$  cm<sup>3</sup>, of the left one-  $7,41 \pm 2,42$  cm<sup>3</sup>, that is larger than ovarian volume measured in the main group ( $p < 0,05$ ).

When analyzing the processes of follicle-, oocyte - and early embryogenesis (Table) it was found out, that the average number of growing ( $8,1 \pm 5,7$ ;  $p < 0,05$ ) and dominant follicles ( $6,7 \pm 5,1$ ;  $p < 0,05$ ) was larger in the comparison group. The number of fertilized oocytes did not differ significantly in both groups and amounted to  $3,7 \pm 3,1$  in the main group and  $4,5 \pm 4,2$  in the comparison group ( $p > 0,05$ ). The quality of oocytes had an effect on the number of embryos obtained, that was  $1,2 \pm 0,9$  in the main group and  $2,1 \pm 0,9$  ( $p < 0,05$ ) in the comparison one. The intensity of cleavage was assessed by the number of blastomeres of embryos on the day of embryo transfer. The analysis of the number of good quality embryos (of 8 blastomeres and blastocysts on the day of transfer) showed that their number was 2 times more ( $1,4 \pm 0,6$ ) among non-native women than in indigenous women ( $0,6 \pm 0,7$ ;  $p < 0,05$ ). The number of transferred embryos was on the average  $1,2 \pm 0,8$  and  $1,5 \pm 0,7$  ( $p > 0,05$ ) in the groups respectively. Embryos transfer was performed on the third and fifth days of cultivation. On day 5 embryos transfer was conducted in 34% of women from the main group, but only 39% of embryos in their developmental stage corresponded to the day of transfer. In the comparison group 42% of embryos transfer was made, but 64% of embryos were at the stage corresponding to the day of transfer. On the day of embryos transfer the endometrial thickness had no differences in both groups.

In the main group, pregnancy was achieved in 13.3% of cases and in the comparison group – in 37% ( $p < 0,05$ ).

Duration of superovulation induction in women with Long protocol was  $10.4 \pm 2,9$  days, that was 1,7 days longer than the one in the subgroup with Short protocol ( $p < 0,05$ ).

The average number of growing follicles was larger ( $6.23 \pm 3.05$ ) in the subgroup using the scheme of stimulation GnRH-a + rFSH/hMG, than using the scheme rFSH/hMG + GnRH-ant ( $4.35 \pm 1.93$ ,  $p < 0,05$ ). The number of fertilized oocytes was also larger in Subgroup 1 ( $5.62 \pm 4.23$ ), than in Subgroup 2 ( $3.06 \pm 1.85$ ,  $p < 0,05$ ). However, it had no effect on the quality of the fertilized oocytes, as the number of good quality embryos in the examined groups had no statistically significant differences. The average number of the transferred embryos did not differ in the both groups as well and amounted to  $1,5 \pm 0,9$  and  $1,2 \pm 0,7$  accordingly.

In the main group the pregnancy rate was 10.0% with the use of long scheme of stimulation of ovulation, 3,3% - with the short scheme and in the comparison group - 22,2% and 14,8% respectively. Among non-native women pregnancy was achieved in all age groups, among indigenous women – at early reproductive age group. In the main group pregnancy with twins occurred in one case and ended with operative delivery in time. In the comparison group two cases of twins, resulted in immediate operative delivery, were registered. Tubal pregnancy occurred in one woman in Subgroup 1.

## Discussion

In our study, all women had had inflammatory diseases of the genitals. Purulent process of the uterus, fallopian tubes and ovaries leads to marked functional and morphological disturbances, damage of the receptor system and tissues of these organs. The time for implementation of reproductive plans shortens as a result of early depletion of ovarian function [1].

The possibility of increasing the effectiveness of assisted reproductive technologies is widely discussed in literature [author]. However, reliable criteria, due to which one can predict the possibility of obtaining high-quality oocytes, have not been found yet. We were confronted with a task to study the possibility of increasing the effectiveness of IVF programs in women living in the Far North. Investigation of the parameters of ovarian reserve allowed us to highlight

the most significant ones: volume of ovaries and the number of antral follicles in each of them. The basal FSH level in our study turned out to be statistically insignificant.

The total amount of Testosterone in all women complied with relevant standards. In the group of non-native women the total amount of Testosterone was higher than the one in the group of native women ( $p < 0,05$ ). Recently, there have been data that the poor response is associated not only with the diminution of follicular reserve, but also with the weakening androgen-secreting ovarian function [8]. According to this concept, androgen deficiency inhibits the adequate development of follicles, that creates conditions for poor response by using inducers of ovulation [aut.].

The comparative analysis of follicle-, oocytes- and early embryogenesis revealed that the number of growing and dominant follicles was larger in the group of non-native women. The number of antral follicles being less than 7, indicates poor response to stimulation [3]

We found out the differences in the number of embryos of good quality - non-indigenous women had them in greater numbers than native women. In the induction of superovulation in IVF program achieving pregnancy is the end result.

In the group of indigenous women of the North the pregnancy rate was almost 3 times lower than in the group of non-native patients. The possibilities of increasing the effectiveness of infertility treatment by modifying the schemas of stimulation and, in particular, by the way of using GnRH-ant in Short protocol, are discussed in literature[7]. The analysis of protocols of superovulation stimulation revealed that the duration of stimulation turned out to be not long in the subgroups where GnRH-antagonist was used, that was in line with the other studies [5]. The average number of growing follicles and fertilized oocytes were larger with the use of Long protocol. In the subgroup of women, using the protocol with GnRH-a, pregnancy rate was higher by 3 times.

Comparing the results of treatment of 57 women, we have found that the effectiveness of treatment with IVF is determined primarily by the state of ovarian reserve, which has a negative effect on reproductive function.

## Conclusions

1. Indicators of ovarian reserve (ovarian volume and the number of antral follicles in each of them) are important in the reproductive potential of women and allow to predict the possibility of pregnancy during conducting IVF.

2. In native women of the North the ovarian response to gonadotropin stimulation is poor, the number of preovular follicles and oocytes are less than in non-indigenous women, the development of embryos in vitro is slow and the pregnancy rate in IVF programs is almost 3 times lower than the one in non-native women.

3. The use of protocols of superovulation stimulation with GnRH-a in native women of the North increases the efficiency of IVF by 3 times as compared with protocols using GnGR-ant.

Table

**Sonographic parameters of superovulation stimulation  
in IVF program**

Parameters	Main group (n=30)	Subgroup 1		Comparison group (n=27)
		(n = 15)	2-я (n = 15)	
The number of growing follicles	5,1±2,6*	6,2±3,0**	4,3±1,9	8,1±5,7
The number of dominant follicles	4,5±2,5*	5,3±3,2**	3,9±1,5	6,8±5,2
The number of fertilized oocytes	3,7±3,1	4,6±4,2	3,1±1,8	4,6±4,3
The number of embryos	1,3±0,9*	1,1±0,7	1,4±1,1	2,1±0,9
The number of "good" embryos	0,6±0,7*	0,4±0,7	0,7±0,7	1,4±0,7
The number of transferred embryos	1,2±0,8	1,2±0,9	1,2±0,7	1,5±0,7

\* -  $p < 0,05$  statistical significance of differences between the main group and the comparison group;

\* \* -  $p < 0,05$  - statistical significance of differences between the 1-st and 2-nd subgroups.

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**Slizovsky G.V., Maslikov V. M., Gjunter V. E.,**

**Titov M. V., Kuzhelivskij I.I.**

**Way of surgical correction of funneled deformation  
of thorax in children with use of nickelid  
titanium materials**

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**Summary**

Congenital chest distortions are the defects associated with changes in the chest shape. Funnel chest (FC) is the most common. [1, 3]. Besides cosmetic defect this malformation is accompanied by cardiovascular and bronchopulmonary functional disorders. According to Russian authors 0.06 - 2.3% of children have FC, 0.2 - 1.3% according to foreign authors [6, 10, 11].

Surgical treatment of congenital chest distortions in children is one of the most serious and urgent problems of childhood thoracic surgery. Currently, there are many methods of thoracoplasty in children with congenital deformities [5, 7, 9]. Improvement and widespread implementation of minimally invasive high-tech methods in surgical treatment of congenital chest distortions is a great stride in this direction [4, 8]. However, some vital questions associated with selection of the optimal method for treatment remain unresolved, i.e. methods of thoracoplasty and sternocostal complex fixation.

**Work objective.** To estimate the titanium nickelite use efficiency in the surgical treatment of funnel chest.

**Materials and Methods**

Research is based on the analysis of 78 FC thoracoplastic operations performed at orthopedic department of MLPMU Children's City Hospital No. 4.

72 male and 6 female patients aged 4-20 years were operated over the 1977 to 2009 period. Clinical material is divided into 3 study groups according to the method of surgical treatment.

The first group of 16 children aged 6-14 years was operated from 1977 to 1987 by the method of G.A. Bairov or N.I. Kondrashin [2, 7]. Marshev's splint was used for corrected chest fixation.

In the second group 20 patients underwent thoracoplasty (operated from 1986 to 1995). Round or flat wires were used for osteosynthesis, which were hypodermically implanted into the resected sections of ribs and sternum. Additionally we used a modified suspension splint with four movable supports. Traction threads were fixed by paired rings located on separate thread rods with a damper device. This provides even and graduated tension of traction threads throughout the mobilized sternocostal segment. The splint was easy and convenient to use, taking into account the patient's age.

The third group of 42 patients aged 4-20 years has been operated after 1996. Surgical treatment of this group can be divided into a few main stages.

Stage 1 - the deformed part was exposed by midline incision and mobilization of skin and muscle flaps as one unit.

Stage 2 - greater emphasis was made on mobilizing and correction of deformed ribs and sternum by their section or wedge resection.

Stage 3 - retrosternal commissures and ligaments were removed and parietal pleura layers were released after mobilization of the deformed part of the chest that provided visual control at the most difficult stage of the operation.

Stage 4 - transverse triangular wedge is harvested from the presternum (the upper edge of the funnel), which is subsequently used as an autograft, being fixed to the sternal split after its partial longitudinal section at the bottom of the funnel by Mylar thread.

Stage 5 - one, two or three titanium nickelide plates were used for rigid fixation of the eliminated chest distortion, depending on the appearance and depth of the funnel. They were placed on the front surface of the thorax in the transverse direction so that the curved ends leaned against unmodified parts of the ribs beyond the deformed region. Resected parts of ribs and sternum were fixed by interrupted sutures on the plates. Previously chilled titanium nickelide plates become blood-warm after implantation, thus creating additional corrective force due to thermodynamic properties and at the same time providing rigid correction of the deformation during 10-12 months till complete consolidation and alignment of the corrected segment. Retrosternal tube drainage was used for 3-5 days in the early postoperative period in most children, the wound was sutured by cosmetic stitch.

### **Results and Discussion**

Analysis of the immediate results of FC surgical treatment by various methods of thoracoplasty and stabilization in 3 study groups showed different clinical peculiarities, frequency and form of intra- and postoperative complications, immediate and remote results of treatment.

In the first group (20 patients) 12 children had pleura injury with manifestation of unilateral or bilateral pneumothorax, 8 patients had marginal or extensive tissue necrosis of mobilized skin flap in the area of deformation; in 4 cases there was soft tissue necrosis and osteomyelitis of rib in one case. The use of external Marshev's traction splint entailed bed rest for 2-3 months, then traction threads and the splint were removed. Length of hospital stay in the postoperative period ranged from 2 to 4 months. Loss of correction (recurrence of deformity) was observed during 1-2 years in majority of children from the first group - from mild to extremely severe.

In the second group (18 patients), pleural injury, pneumothorax and hemothorax was found in 8 children, soft tissue necrosis was observed in 7 cases, abscess - in 6 cases. Application of round and particularly flat wires reduced the frequency and intensity of the loss of correction. The splint was removed after 2 months, the wires were removed after 4-6 months. Good results were obtained in 6 patients, in 10 children - satisfactory, long-term follow-up showed recurrent deformation in 4 patients. Postoperative period in hospital is 2-3 months.

In the third study group (30 patients), clinical results were more successful. 6 children developed pneumothorax and hemothorax, abscess and tissue necrosis were not observed. After a 3-5-day stay in the ICU children were allowed to walk, and the sutures were taken out 10-12 days after the operation. The length of hospital stay in the post-operative period was reduced to 12-16 days. All children within a year after the operation every 1-2 months underwent test survey, and further examination was carried out 1-2 times a year. The plates were removed in 6-10-12 months outpatiently or with hospital admission for 1-3 days. In the follow-up period from 1 to 10 years 20 patients showed good cosmetic results after the chest correction, and 9 patients - satisfactory.

### **Resume**

Thus, the thermodynamic force of titanium nickelide plates provided not only postoperative stabilization of the corrected deformity, but an additional correction in the postoperative period. Application of shape memory titanium nickelide plates for FC correction in children and adolescents is the method of choice and gives good clinical results.

УДК 614.2+615.47 (571.56)

**Muksunov D.D., Savvina N.V.**

**Estimation of State and Efficiency of Using Medical Equipment in Medical Institutions of Sakha Republic (Yakutia)**

Estimation of state and efficiency of using medical equipment in medical institutions of Sakha Republic over the period from 2005 till 2009 years is presented. Changes of indices of medical equipments' state in dynamic was revealed: a rise of balance cost and deterioration of medical equipment; reduction of indices of replenishing and increasing medical equipments; doctor's fund index provided with medical equipment; a rise of index of using the medical equipment.

Keywords: medical equipment, deterioration, fund- provision index, growth factor, factor of use.

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**Introduction.** At present the material provision of medical-diagnostic process in medical institutions of the region is a necessary link of the Russian health care service management [5].

In modern conditions the problem of perfection of medical and technical policy becomes of great significance, as the development of local health care institutions is appreciably defined by a degree of technical equipment of medical and prophylactic institutions [1].

The problem of material provision in health care institutions can be solved not only by equipping and profitable acquiring of a new equipment, but also by its effective application [3].

Such indices as deterioration and fund-provision are noted to be of greatest value in the characteristic of using the basic funds. In combination to the factors reflecting degree of loading of the medical equipment, these indices of using the basic means give a full and objective picture of the state of medical equipment recourses, efficiency of its use on corresponding sites of the work [2, 4].

**Aim** of the research is the estimation of state and efficiency of using the medical equipment in health care institutions of Republic Sakha (Yakutia) from 2005 for 2009.

**Materials and methods.** The estimation of state of the medical equipment included the analysis of its balance cost; the analysis of deterioration degree of the medical equipment and intensity of its updating; the analysis of the doctor's fund-provision with the medical equipment, the analysis of efficiency of using the medical equipment. Indices of deterioration, fund-provision, factors of updating, timing off, indices of increase of the medical equipment, a ratio of the installed medical equipment are calculated by standard methods.

**Results and discussion.** According to the total cost of the basic means a part of cost of the medical equipment in municipal medical institutions of the republic remains at 20.9-18.6 %. Among the medical institutions of the republic a part of cost of the medical equipment is higher than in municipal ones and for the studied period it has increased from 31.1 % to 39.3 %. In 2009 52.3% of the total cost of the medical equipment of the republic is for municipal ME and the rest 47.7 % is a share of republican medical institutions (MI).

The rise of balance cost of the medical equipment for 2005-2009 has made 92.9 %, the residual cost of the medical equipment – 49.8 %, and index of deterioration – 132.8 % (Table 1)

Table 1

Balance, residual costs of the medical equipment and its deterioration for 2005-2009 (thousand roubles)

Index	2005	2006	2007	2008	2009	The rise in 2005-2009 гг., %
Balance cost	2 557 688.1	3 557 333.5	4 304 685.1	4 675 902.7	4 934 060.8	92.9
Residual cost	1 228 557.4	1 696 386.0	1 988 406.2	1 997 730.2	1 839 906.0	49.8
Deterioration	1 329 130.7	1 860 947.5	2 316 278.9	2 678 172.5	3 094 154.8	132.8

The deterioration of the medical equipment all over the republic was estimated at 62.7% in the late 2009 and increased up to 10,7% as compared with 2005. In municipal ME the level of deterioration increased up to 11.3%, in republican ME up to 10.2% (Table 2).

Table 2

A level of deterioration of the medical equipment in Sakha Republic (Yakutia) for 2005-2009 (in percents)

	2005	2006	2007	2008	2009
All over the republic	52,0	52,3	53,8	57,3	62,7
Municipal MI	53,0	50,7	54,1	59,0	64,3
Republican MI	50,8	54,1	53,4	55,4	61,0

For the studied period only 11 from 35 administrative territories had a level of deterioration of the medical equipment lower than 60 %: Allaihovskiy, Verhneviljujskiy, Verhnekolymskiy, Mountain, Zhiganskiy, Mirninskiy, Srednekolymskiy, Suntarskiy, Tattinskiy, Ust-Janskiy regions and Yakutsk city.

High levels of deterioration of the medical equipment are noted in 11 regions : Bulunskiy, Verkhoyansk, Lenskiy, Momskiy, Namskiy, Nerjungrinskiy, Nizhnekolymskiy, Njurbinskiy, Tomponskiy, Ust-Aldan, Churapchinskiy.

Of all state health care institutions a high percent of deterioration of the medical equipment (over 60 %) for 2005-2009 is estimated in SE «Republican hospital №2 - the Center of Emergency Medical Aid», SE «Bureau of Forensic Medical Examination of MH RS (Ya), SME RS ( «Republican hospital №3», SME «Yakutsk republican ophthalmologic hospital».

When analyzing the technical equipment of the medical institutions of Sakha Republic (Yakutia) it has been revealed that approximately 80 % of the maintained medical equipments has fulfilled their resources by 2004 in most central regional hospitals and town institutions of Yakutsk. The most part of medical devices and equipments have been operated for 15-20 years and more. The deterioration was estimated as follows: 77% of X-ray devices, 67% of ultrasonic equipment, 63% of endoscopic equipment, 83 % of labware .

By 2007 the medical diagnostic equipment had been provided by the priority national project within the decree of the Government of Sakha Republic (Yakutia) № 450 from October 1st, 2004 « Urgent measures on replacement of worn out medical equipment in the National Centre of Medicine, republican and regional medical institutions », in the field of the state purpose-oriented program “Health protection of the population of Sakha Republic” and federal programs, and this process caused the reduction of indices of the deterioration.

The table 3 demonstrates that from 2007 to 2009 the most expressed increase of deterioration was revealed among ultrasonic devices (19,6 %), labware (17,9 %), devices for functional diagnostics (15,8 %), endoscopic devices (14,4 %). Decrease in the level of deterioration were marked among LOR apparatus (15,3 %) and operational equipments (6,7 %).

Table 3

## Deterioration of groups of the medical equipment for 2007-2009 (%)

Groups of medical equipment	2007	2008	2009	Dynamics, 2007-2009 (%)
X-ray devices	40,6	45,6	50,1	+ 9,5
USD devices	49,3	59,6	68,9	+ 19,6
Endoscopic devices	54,5	59,6	68,9	+ 14,4
Labware	41,0	47,2	58,9	+ 17,9
Devices for functional diagnostics	48,9	55,5	64,7	+15,8
Devices for reanimation and anaesthesia	64,7	62,2	63,6	- 1,1
Operational equipment	58,5	51,1	51,8	- 6,7
Physiotherapy devices	64,5	70,3	73,2	+ 8,7
Disinfecting and sterilizing equipment	43,6	40,5	47,1	+ 3,5
Ophthalmological equipment	58,1	50,7	55,5	- 2,6
Otoloringologic equipment	67,2	62,7	51,9	- 15,3
Equipment of obstetric and gynecologic departments	50,7	54,5	57,2	+ 6,5
Stomatological equipment	57,4	58,7	59,3	+ 1,9

For the studied period the factor of updating of the medical equipment, characterizing a share of the new medical equipment in its general sum, has dynamically decreased in 74,1 % all over the republic. According to the table 4, the maximum indicators of the updating in municipal ME are noted from 2005 to 2007 (accordingly 0,16; 0,26; 0,16), in republican ME in 2005 (0,40) and in 2007 (0,17), as a whole on the republic from 2005 to 2007 (accordingly 0,27; 0,18; 0,16), these parameters connected with deliveries of the expensive medical equipment (x-ray and magnet-resonant tomographic devices, fluorography, USD devices, labware). In 2008 and 2009 the parameter of updating of the medical equipment was 0,09 and 0,07 accordingly on the average in the republic by the standard of its updating in 0,12 (Table 4).

Table 4

## Indices of updating factors of the medical equipment for 2005-2009

	2005	2006	2007	2008	2009	Decrease rate for 2005-2009, %
Municipal MI	0,16	0,26	0,16	0,06	0,06	- 62,5
Republican MI	0,40	0,08	0,17	0,12	0,08	- 80,0
All over the republic	0,27	0,18	0,16	0,09	0,07	- 74,1

The factors of discarding of the medical equipment, reflecting relative reduction of the cost at the expense of their discarding, in dynamics have decreased equally in 33,3 % as a whole in the republic, in municipal ME and republican ME (Tab. 5).

Table 5

## Indices of discarding factors of the medical equipment in 2005-2009

	2005	2006	2007	2008	2009	Decrease rate in 2005-2009 гг, %
Municipal MI	0,03	0,03	0,02	0,03	0,02	- 33,3
Republican MI	0,03	0,08	0,02	0,03	0,02	- 33,3
All over the republic	0,03	0,06	0,02	0,03	0,02	- 33,3

The growth factor of the medical equipment, characterizing a relative increase in the basic means at the expense of their updating, in dynamics has decreased in 85,3 % as a whole in the republic, 75,0 % in municipal, 90,5 % in the republican ME. The maximum ratio of the rise is noted in municipal ME since 2005 to 2007 (accordingly 0,16; 0,34; 0,17), in the republican ME in 2005 (0,63) and in 2007 (0,19), as a whole in the republic since 2005 to 2007 (accordingly 0,34; 0,19; 0,18) connected with deliveries of the expensive medical equipment (Table 6).

Table 6

## Indices of growth factor of the medical equipment in 2005-2009

	2005	2006	2007	2008	2009	Decrease rate 2005-2009, %
Municipal MI	0,16	0,34	0,17	0,03	0,04	- 75,0
Republican MI	0,63	0,03	0,19	0,09	0,06	- 90,5
All over the republic	0,34	0,19	0,18	0,06	0,05	- 85,3

The doctor's fund provision with the medical equipment is considered one of the indicators, characterizing efficiency of use of the basic means. The fund provision with the medical equipment per one doctor in 2009 has averaged at 845,6 thousand roubles in the republic, 625,1 thousand roubles in municipal ME, 1375,5 thousand roubles in the republican

ME. The fund provision with the medical equipment in republican ME is 2,2 times higher as compared with municipal ME and 1,6 times higher than the average territorial index. The indicator increase for the studied period has been 88,8 % in the republic, 89,2 % in the republican ME, 88,3 % in municipal ME. These parameters have been caused by the growth of balance cost for the medical equipment at the expense of increasing the volume of purchases of the medical equipment with relatively stable staff of doctors (Tab. 7).

Table 7

Indices of fund provision with medical equipment per one doctor in 2005-2009 (thousand roubles).

	2005	2006	2007	2008	2009	Growth rate, %
Municipal MI	331,9	473,3	569,7	603,6	625,2	88,3
Republican MI	727,0	984,6	1181,2	1305,6	1375,5	89,2
All over the republic	447,9	625,6	751,5	809,4	845,7	88,8

High indices of the fund provision per one doctor are marked in Gorniy, Olekminsky, Tattinsky, Verhnekolymsky, Mirninsky, Viljujsky, Ust-May, Eveno-Bytantajsky regions. Low indices are in Allaihovsky, Ojmjakonsky, Zhigansky, Abyjsky and Kobjajsky regions.

Among the republican ME high indicators of the fund provision with the medical equipment are revealed in 2009 in the SME RS (Y) «Blood Transfusion Station», SE «Republican hospital №1 - the National Centre of Medicine», SME RS (Y) «Republican Hospital №3», SE «Yakut Republican Oncological Clinic», SE NPC "Phthiology" of MH RS, SME «Yakutsk Republican Ophthalmologic Hospital».

The operating ratio of park of the established medical equipment, defined by the relation of amount of the actually working equipment to amount of the established equipment on the balance has been 0,94 all over the republic in 2005, 0,94 in 2006, 0,95 in 2007, 0,96 in 2008, 0,97 in 2009, these parameters showing the efficiency growth in use of the medical equipment and reduction of the equipment downtimes.

**The conclusion.** Thus, the basic characteristics of the estimation of state and efficiency of using the medical equipment in the health care system RS(Y) are as follows: the growth rate of balance cost of the medical equipment for 2005-2009 has amounted 92,9 %, the residual cost of the medical equipment has been 49,8 %, and deterioration has been 132,8 %; the deterioration of the medical equipment all over the republic at the end of 2009 has amounted 62,7 % and in comparison with 2005 it has increased up to 10,7 %; the updating factor of the medical equipment in dynamics all over the republic has decreased on 74,1 %; the discarding factor of

the medical equipment in dynamics has decreased on 33,3 %; the growth factor of the medical equipment has decreased on 85,3 %; the indicator increase of the fund provision has been estimated at 88,8 %; the operating ratio of park of the established medical equipment in dynamics all over the republic has increased from 0,94 to 0,97.

The balance cost growth of the medical equipment and doctor's fund provision with the medical equipment in dynamics is connected with the financing growth for acquiring and delivering the expensive medical equipment. But at the same time, the updating and growth factors of the medical equipment have decreased, and the deterioration of the medical equipment has been of a higher rate that is connected with the reduction of financial expenses for updating of the medical equipment in dynamics for years. The operating growth ratio of park of the established medical equipment testifies to the efficiency growth of using the medical equipment.

The analysis of state of the medical equipment and efficiency of its use as an active part of the basic funds, allows to make administrative decisions on rational use and reproduction, and also reveals the priority directions and expenses for reproduction of the medical equipment in health care institutions of Sakha Republic (Yakutia).

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**A.I. Rumyantseva\*, L.F. Timofeev\*\***

**Analysis of temporary disability payments in rural uluses (regions)  
of the Sakha Republic (Yakutia) in the period 2005-2009**

**Summary.** The article presents analysis of temporary disability payments effected in the republic's rural regions in the years 2005-2009. It includes figures on the average daily benefit amount, duration of payment in days, average duration of one temporary disability case.

**Key words:** morbidity with temporary disability, temporary disability, temporary disability benefits.

The demographic crisis in Russia, caused by low birth rate, high incidence rate and untimely death rate has become an issue of the national security. Overcoming this crisis is one of the priorities in social and economic development. The unstable social and economic situation remains, undermining viability of the able-bodied population, whose health is deteriorating faster than in children and elderly population, who used to be more vulnerable [1]. Unfortunately, the demographic crisis, spreading throughout the country, centers in the Russian villages. Negative trends in the population general morbidity also include morbidity with temporary disability (TD).

Economic losses from temporary disability are made up of healthcare budget expenses, social insurance and obligatory medical insurance, GDP losses, a family budget, etc. [2].

Our republic experiences the same processes as everywhere else in Russia. The present article analyzes payment of temporary disability (TD) benefits in the rural areas, including 13 uluses (regions): Amginsky, Verkhnevilyuisky, Vilyuisky, Gorny, Megino-Kangalassky, Namsky, Nyurbinsky, Olyokminsky, Suntarsky, Tattinsky, Ust-Aldansky, Khangalassky and Churapchinsky.

This group is chosen basing on medical and economic zoning conducted by L.F. Timofeev and V.G. Krivoshapkin (2006), who took into consideration social and economic, demographic, basic population health parameters. It is home to over 20 percent of the republic's able-bodied population. At the same time, in the recent years this group has shown more obvious trend for the working population decrease than the republic in whole (Table 1). The year 2009 saw the largest decrease in working population, compared with the year 2005, in Megino-Kangalassky (by 24.9%), Nyurbinsky (18.1%), Vilyuisky (15.8%) and Tattinsky (13.1%) regions.

The figures on primary and general morbidity in this group for the given period increase, but the morbidity structure figures are smaller than in the republic[3] (Fig. 1).

At the same time, comparing the year 2009 to 2005, general and primary morbidity increased in Amginsky region by 116.2% and 139% respectively; in Suntarsky region – by 42.1% and 48.7%; in Verkhnevilyuisky region – by 43.5% and 26.3% ; in Olyokminsky region – by 35.7% and 23.5%.

The analysis shows that the increase in morbidity led to increased number of days when temporary disability payments were effected (Table 2). Compared to 2005, the duration of payment

increased in Khangalssky (by 54.3%), Suntarsky (by 46.2%), Vilyuisky (by 40.7%) and Olyokminsky (by 40.1%) regions.

The analysis of the average TD duration shows that it increased from 10.8 days in 2005 to 14.7 days in 2009 (Table 3). However, starting from 2007, the rural areas demonstrate lower figures than in the republic in whole.

It is only natural that the above-mentioned figures on general morbidity and morbidity with TD cause increased TD payments, with the change percentage being larger in the rural areas than in the SR(Y) in whole (Table 4).

Compared to 2005, the largest change in the average daily benefit is seen the following regions: Tattinsky – increased by 70.4%; Ust-Aldnasky – by 67.5%; Verkhnevilyuisky – by 67.0%; Amginsky – by 63.5%.

**Resume.** 1. During the compared period, we witness the trend that number of working population in the rural areas decreased by 9.1%, which is by 2.4% more than in the republic in whole.

2. Given decreased number of working population in the rural areas, the duration of benefit payments increased by 30.4% in 2009 compared to the year 2005.

3. Since 2005, the average daily benefit in the rural areas increased by 47.0%. As for the percentage of change against 2005, the rural areas figures are higher than the republic's ones for the same period by 12.4%.

4. The average duration of a temporary disability case increased by 35.4% for the same period (with 41.7% in the republic in whole).

**Conclusion.** The recent years analysis shows that morbidity with TD in the rural areas do not decrease, like in the republic in whole. These data require detailed study of expertise in temporary disability (ETD), which is performed at the several levels: doctor – patient, consulting doctor – chair of medical commission, consulting doctor – expert doctor of a regional social insurance department, etc.

At the present moment, expertise in temporary disability in some rural areas leaves much to be desired: doctors lack qualification for conducting the expertise; clinics and hospitals management fails to control their activity. All these factors result in increased expenses for obligatory social insurance on TD benefit payments.

Given these circumstances, it would make sense to revive functioning of clinical expert commissions under healthcare authorities; to establish a board coordinating parties involved in the expertise, such as territorial social insurance and medical insurance bodies, medical and social expertise, Russian Health Inspection (Roszdravnadzor), branch trade unions, labor inspections.

The joint coordinated activity of these services should be aimed at improved medical aid rendered to the population, including health safeguarding and maintenance of the working population in rural areas, thus leading to decreased TD morbidity in the republic.

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Table 1. Average staffing number (people) in 2005-2009

		2005	2006	2007	2008	2009
1	Average staffing number:					
	- in rural areas					
	- in the SR(Y)	98,196	95,038	92,472	89,668	89,212
		449,595	446,753	441,691	428,272	419,508
2	Percentage of change against 2005:					
	- in rural areas	-	96.8	94.2	91.3	90.9
	- in the SR(Y)	-	99.4	98.2	95.3	93.3

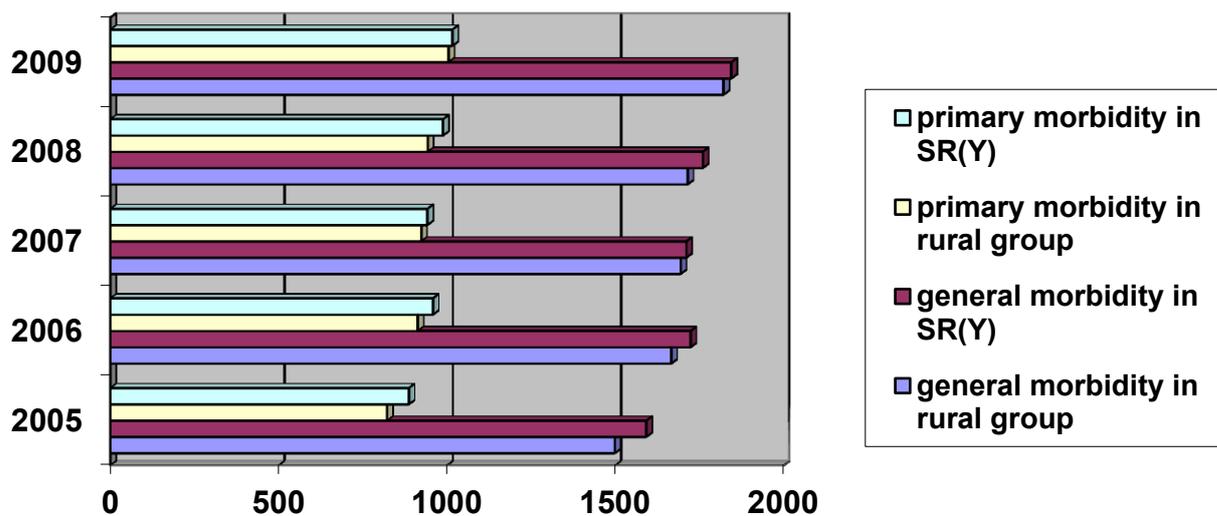


Figure 1. General and primary morbidity in rural area of the SR(Y) in 2005-2009  
(per 1,000 of population)

Table 2. Analysis of TD payments duration in rural areas of the SR(Y)  
in 2005-2009 (per 100 working people)

		2005	2006	2007	2008	2009
1	Number of days when TD payments were effected:					
	- in rural areas	657.0	703.9	854.7	867.1	856.5
	- in the SR(Y)	612.7	606.9	813.2	882.9	865.1
2	Percentage of change against 2005:					
	- in rural areas	-	107.1	130.1	132.0	130.4
	- in the SR(Y)	-	99.1	132.7	144.1	141.2

Table 3. Average duration of a TD case in rural areas of the SR(Y) (days, 2005-2009)

		2005	2006	2007	2008	2009
1	Average duration of a TD case (days):					
	- in rural areas	10.8	10.7	13.4	13.8	14.7
	- in the SR(Y)	10.4	10.3	14.0	14.5	14.8
2	Percentage of change against 2005:					
	- in rural areas	-	99.3	124.2	127.9	135.4
	- in the SR(Y)	-	98.9	133.8	139.2	141.7

Table 4. Analysis of TD benefit in rural areas on the SR(Y)

in 2005-2009

		2005	2006	2007	2008	2009
1	Expenses on TD benefit payments (RUR ths):					
	- in rural areas	174,607.6	202,174.0	222,570.5	258,082.3	303,904.9
	- in the SR(Y)	1,106,933.9	1,260,290.6	1,474,832.8	1,781,367.0	1,962,794.2
2	Average daily TD benefit (RUR):					
	- in rural areas	270.7	302.2	287.9	331.9	397.7
	- in the SR(Y)	401.8	464.8	410.6	471.1	540.8
3	Percentage of change in average daily amount against 2005:					
	- in rural areas	-	111.7	106.4	122.6	147.0
	- in the SR(Y)	-	115.7	102.2	117.2	134.6

**Svetlana Obutova<sup>1</sup>, Nadezhda Logvinenko<sup>2</sup>, Gorochova Z.P<sup>1</sup>**

**Evaluation of the influence of smoking on bronchial patency disorders of Gerontius Yakutsk**

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**Keywords:** spirometry, smoking, elderly age, the urban population, Yakutia.

**Introduction.** Timely and correct diagnosis of chronic bronchitis requires use of functional verification methods of diagnosis - study of respiratory function. Interpretation of clinical presentation and diagnosis depends largely on spirometric indices [1]. Spirometry is the simplest and safest for the patient study. Basic functional test for the detection of bronchial obstruction - a well-played in the dynamics of forced expiratory volume in first second (FEV1) [4]. .

At present, spirometry is used both for diagnosis of obstructive disease and for monitoring the performance of their severity. Decline in forced vital capacity (FVC) and forced expiratory volume in first second (FEV1) were independent predictors of morbidity and mortality in the elderly [3].

In elderly and old age is common fact of a long and rather intense smoking for life, which in combination with age morphological and functional changes in the bronchopulmonary system contributes to development and severe course of disease progression with complications that determine its outcome [2].

**The purpose and objectives:** to study the incidence and assess the impact of smoking on the severity of violations of FEV1 in Gerontius Yakutsk, depending on ethnicity.

**Materials and methods.** The object of the study was the population of Yakutsk in the 60 years of age or older. To evaluate the spirometry study used a sample population of persons aged 60 years or older on the basis of electoral lists Yakutsk method of random numbers using a computer program. The database pulmonologist were included 556 respondents. .

Before attending pulmonologist respondents consulted a doctor and manager in the absence of contraindications were sent to spirometry. Respondents with unstable hemodynamics, the presence of severe concomitant diseases, in order to eliminate unreliable data, spirometry was performed. Investigated the most important of the spirometric parameters - FEV1 in Gerontius Yakutsk, depending on ethnicity. Spirometry was performed in a manner consistent with published standards [1, 5]. Investigation of respiratory function was conducted by trained specialists, doctors in the study of functional status at the Republican Hospital № 3 (Yakutia) spirometry "Spirosift SP-5000 with peak flow meter (Japan), with regular calibration. Spirometer produce results on paper.

Total spirometric examination conducted in 180 respondents aged 60 to 89 years, which accounted for 32,3% of the total number participating in the survey, including 29,8% (77)

Indigenous and 34,6% (103) non-indigenous persons.

According to ethnicity has identified 2 groups of examinees: Indigenous people by smoking status of the respondents were divided into never-smokers, smokers present and former smokers.

**Results of the study.** Total violations FEV1 varying degrees of severity were found in 82,8% of respondents aged 60 and older. According to the severity of violations of FEV1 (GOLD, 2006) of the respondents were divided into 4 groups: no change (normal levels) -  $FEV1 \geq 80\%$ , moderate violations -  $FEV1 = 50-79\%$ ; severe disorders -  $FEV1 = 30-49\%$  and extremely severe violations -  $FEV1 \leq 30\%$ .

The analysis of the severity of violations of FEV1 in patients 60 years and over by ethnic origin (Fig. 1).

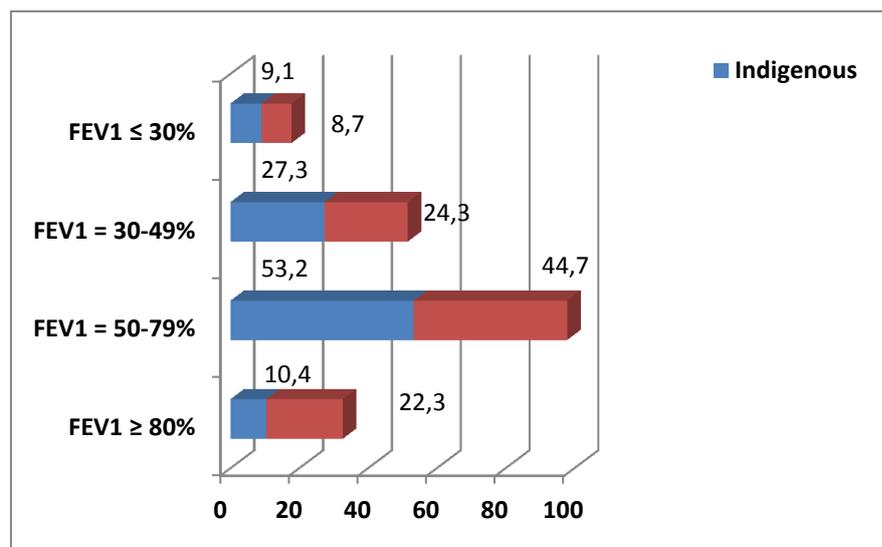


Fig. 1. Severity of violations of FEV1 in patients 60 years and over by ethnic origin.

From figure 1 that the normal indicators of FEV 1 ( $\geq 80\%$ ) is almost 2 times more likely (22,3%) were registered in non-indigenous representatives of the elderly (the root - 10,4%) ( $p = 0,037$ ;  $t = 2,099$ ). Moderate impairment ( $FEV1 = 50-79\%$ ) - were more common among indigenous Gerontius - 53,2% (44,7% for non-indigenous). Severe violations of bronchial obstruction ( $FEV1 = 30-49\%$ ) - almost equally often registered as the indigenous (27,3%), and among non-indigenous (24,3%). Extremely severe impairment ( $FEV 1 \leq 30\%$ ) of Indigenous respondents were 9,1%, while non-indigenous - 8,7%.

Of the 180 respondents, aged 60 years since the study of respiratory function 66.7% of respondents had never smoked, 17,2% - were former smokers and 16,1% - have continued to smoke at the time of the survey.

Bronchial obstruction of varying severity were recorded in 77,5% of respondents never smoked, 90,3% former smokers and 89,7% continued to smoke.

No significant differences between the studied ethnic groups in the frequency of violations of FEV1 as a function of smoking status is not revealed, although slightly more violations of FEV1 detected among the indigenous population. More severe violations of bronchial obstruction were observed among former and current smokers. In this case, significant differences were obtained in cases of severe bronchial obstruction, which is 3 times more prevalent in the group of former smokers among non-indigenous population.

**Conclusions.** In 82,8% of persons 60 and older registered with a high frequency of bronchial obstruction of varying severity. Normal indices FEV 1 ( $\geq 80\%$ ) almost 2-fold significantly more often (22,3%) were registered in non-indigenous residents of Yakutsk.

The changes revealed bronchial obstruction among former and current smokers argue that smoking is a major exogenous risk factors and in conjunction with the influence of meteorological factors (low temperature swings, humidity and barometric pressure during the day) reduces the functional reserves of the organism, which is manifested in a decrease with age, speed and volume characteristics of the respiratory system.

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**N.I. Lapteva, A.A. Jakovlev**

**THE INTEGRATION APPROACH A LOT OF STUDY OF THE DYNAMICS OF MORBIDITY BY INFECTIONS WITH HAEMOCONTACT MECHANISM OF TRANSFER (HIV, HEPATITIS B AND C) OF THE SAKHA REPUBLIC (YAKUTIA) AND EPIDEMIOLOGICAL ESTIMATION OF FACTORS ITS DETERMINING.**

Administration of the Rospotrebinspection of the Sakha Republic of (Yakutia), State Formations of Management of the Higher Vocational Training the Vladivostok State Medical University of the Ministry of Health and Social Development of the Russian Federation.

UDC 616.36-002+616-097-022:578.828.6 (571.56)

A conjugate retrospective analysis a lot of study of the dynamics in HIV, hepatitis B and C morbidity in the Republic of Sakha (Yakutia) having the general (haemocontact) mechanism of transfer in comparison with the determinants that are presumably able to affect its pattern. The leading significance of antiepidemic measures in health facilities and current trends in the prevalence of drug addiction in the population is shown. The difference in the mechanism of formation above infections disease in Yakutia as compared to other regions of Russia.

Key words: HIV, hepatitis B and C, epidemic process, risk factors.

**Introduction.**

The actual of a problem of infections with the haemocontact mechanism of transfer is caused by set of social, economic and epidemiological indicators [5,7,9,13]. In Far East Federal district one of the highest levels of prevalence parenteral virus hepatitis and HIV the Russian Federation [5,4,8].

Analysis of the literature has allowed us to conclude that the dynamics in different regions of the morbidity of infections with hemocontact mechanism of transfer along with the general features characteristic of the Russian Federation as a whole has especially [3,8,12]. Therefore in addition operating factors influence a regional conditions. However studies aimed for studying the epidemiological situation in Yakutia and the mechanisms of its formation in relation to such infections have not been conducted.

In epidemiology are traditionally considered isolated epidemic process (EP) of individual infections. As shown by our studies [10,11,12] an integrated approach to the study of the epidemiology of infections with the same mechanism of transfer allows a more objective assessment of the epidemiological situation and the conditions conducive to its formation. In this aspect of the epidemiology of HIV, hepatitis B (HB) and hepatitis C (HC) has not been studied.

The purpose of this study was to analyze many years dynamics of the disease incidence of infections hemocontact mechanism of transfer in the Sakha Republic (Yakutia) and the identification of factors influencing its development. The dynamics of morbidity is seen as a reflection of the factors that set and / or power of influence that change over time [1].

#### **Materials and methods.**

Materials for the retrospective epidemiological analysis was compiled using Federal State Statistical Observation by the Sakha Republic (Yakutia) - "Information about infectious and parasitic diseases (f.2) The registration of infectious patients (f.60), epidemiological survey map pockets HB and HC (p .357) for 1979 -2010.

Epidemiological evaluation given to the most important factors determining the development of EP infections hemocontact mechanism of transfer and recommended by the descriptive and evaluative studies [1,8]. To study the effect of vaccination on hepatitis B EP used "Information about preventive vaccination" (f.5). In order to assess the impact of epidemiological factors of drug abuse on the intensity of the EP used the data of the morbidity of the drug addiction in the Sakha Republic (Yakutia) of the annual collection of statistics SF "Yakut Republican Medical Information Analytical Center." The influence factor of disordered sexuality, in accordance with the recommendations of L.P. Zueva with the authors [2] evaluated the dynamics of syphilis morbidity.

For information about the morbidity of the HB and HC, HIV in Russia received the report of the Chief State Sanitary Doctor of Russia G.G Onishchenko (2010). We used statistical methods: tendency EP was evaluated using the alignment of the time series by least squares. Correlation studies were performed by the method of Spearman [1].

An epidemiological study used the techniques of formal logic: the methods of the similarities differences and changes accompanying residues [1].

### Results and discussion.

In result of study in spite of the common mechanism of transfer and consequently the factors influencing to the appearance and intensity of the EP the dynamics of HIV, HB and HC in the Sakha Republic (Yakutia) have different direction of type (pic.1) and particularly drew the attention of the morbidity of the acute hepatitis B (AHB). Its rise began in 1981 (Rate of increase = 8%) and peaked in 1988, 1989 and 1990. Then the disease incidence began to decline (Rate of reduction=-17,3% ) with a small splash in 1995 and 1996. And by 2010 reached a record low for the entire period of observation. It should be emphasized that from 1982 to 1995 the morbidity rate of the AHB in the Sakha Republic (Yakutia) were significantly higher than the average for Russia. Pronounced rise of the morbidity the acute hepatitis B in the Republic began much earlier than in Russia as a whole and therefore in most other parts of the country. [8,12]. By 2010 the morbidity rate of Yakutia with almost equal morbidity rate in the Russian Federation.

From 1994 in the Republic officially started to register acute hepatitis C (AHC). The disease incidence of infection throughout the period were lower than AHB and whole Russia. The dynamic of morbidity was not observed AHC such as AHB. Until 2000 the morbidity rate ranged at 5.2 prosantimil and then fell to 1-2-prosantimil and not different from AHB. The morbidity rate of OGB in the Republic was more lower than for Russia. In 1999 – 2000 the rise of the morbidity didn't mentione in Russia.

Until 1996 Yakutia was considered a free zone of HIV. Retrospective analysis of many years dynamics of HIV in the Republic to assign three periods. The first - from 1996 to 1999 was characterized by its elevation (Rate of increase = 71.4%) in 2000 (13.1% ooo). In the second period (2001-2005) assigned lowering of morbidity (Rate of reduction = 51%). But from 2006 again assigned the increase (Rate of increase = 20.3%). The appearance of the curve reflecting the dynamics of HIV in the Sakha Republic of (Yakutia) was close to Russia in 2000, not 2001, as in Russia. The morbidity rate in Yakutia the analysis were significantly lower than for Russia.

Pic. 1. The dynamic morbidity of the acute hepatitis B and C and HIV of the Sakha Republic (Yakutia) and whole Russian Federation (per 100 thousand population).

Epidemiological evaluation of factors that could potentially determine the specified EP infections in the Republic, showed sharp rise of the morbidity of hepatitis B since 1981 it was associated with medical manipulations. Form an opinion of the epidemiological history of patients for 1989 - 1991 years the most part of infections (60-70%) were occurred during the various parenteral manipulations blood transfusion and / or its components. It is not a clear which the reason for the sharp increase the risk population of Yakutia in the health facilities in 80s of last century. With the introduction of the practice of order MH of the USSR from 12.07.89 № 408 «About measures to reduce the disease incidence of viral hepatitis in the country» and in following tightening up of requirements in connection with the prevention

of HIV infection the effectiveness of lead anti-epidemic measures preferred the morbidity of AHB began to descend.

The leading factor contributing to the increase of morbidity of parenteral viral hepatitis and HIV infection in a different regions of the Russian Federation was growth of drug addiction [5, 8, 12]. In pic.2 explosive increase of morbidity of the drug addiction in Yakutia has not led to rise in the morbidity of any AHB or AHC, which began in early 90s of last century. Conducted a correlation analysis of morbidity between these infections and drug addiction showed no connection.

Pic 2. The dynamic morbidity of the acute hepatitis B and C, HIV and drug addiction of the Sakha Republic (Yakutia) (per 100 thousand population).

The analysis epidemiological history of patients revealed that from 1995 to 2003, most of parenteral viral hepatitis infections (47%) occurred in the health facilities in various medical manipulations [6]. Comparison of the morbidity rates of AHB in 80s and now suggests that the risk population of Yakutia in hospitals was failed. In last years, among patients predominates the sexual way (34%). The significant influence to level of the morbidity of parenteral viral hepatitis total population does not proved, because it reduces the activity factor of disordered sexual relations. This is evidenced by lowering trend from 1998 to 2006 and the stabilization of the population of Yakutia in the morbidity of the lues (pic.3) – the indicator of infection, reflecting the situation with the influence this factor in the region. the part of infected UGA and PSO with intravenous drug use accounts for no more than 15-20%.

Pic.3 The dynamic morbidity of the lues of the Sakha Republic (Yakutia) (per 100 thousand population).

Completely different mechanism of EP formed HIV in the Republic. In the first period (1996-1999) rise the morbidity of this infection occurred by a delivering incidents. A virus entered the local drug addicts and began to spread speed among them as a consequence of injecting way of infection, and sexual. This is indicated by the results of correlation analysis between the morbidity of HIV and drug addiction population of Yakutia (straight strong relationship  $r = 0,8$ ) and rise HIV, drug addiction and lues.

A tendency to reduce the morbidity of hepatitis B associated with vaccinal prevention [8]. In Yakutia it was started in 1996. The first time it has covered health care workers and newborn of mothers-carriers of HbsAg and students under 13 years. And the last vaccination was carried out in order to prevent the risk of disease in a group of 15-19-year-old who along with 20-29-year-olds are carry in the main contribution to the disease incidence HB and HC. Since 1998 began to inculcate students from high and secondary educational institutions children's homes and other groups. However a vaccinal prevention

HB in Yakutia was started from the time when the disease incidence of this infection was lowered. As the experience of other countries vaccination of only high-risk groups can not achieve lowering the disease incident of the population [8]. In accordance with the order of the Ministry of Health and Social Development of the Russian Federation № 229 of 2001 in the Yakutia started to vaccinate all newborns and children 13 years old. As of 31.12.2010 vaccinated 84.6% the total population of the Republic the modern period affects level the morbidity of population in Yakutia HB and prevents the risk of possible infection in the future. Moreover studies show as a result of the integration competitive interrelation between viruses HB and HC it is possible that vaccination may also influence the development of EP HC [10,12].

### CONCLUSIONS:

1. A lot of years of the dynamics of morbidity infection with hemocontact mechanism of transfer in the Sakha Republic of (Yakutia) in 1979-2010 years appears the activity of a number of social and biological factors among which the priority of the organization and have the actual effectiveness of control activities in health facilities as well as the preading of the drug addition.

2. Rise of morbidity ABC (1981-1990.) and HIV (1996-1999) caused by different factors. The growth of drug addition in the Republic did not affect the dynamics of morbidity of parenteral viral hepatitis. This mechanism of morbidity of these infections the population of Yakutia is different from other Russian regions.

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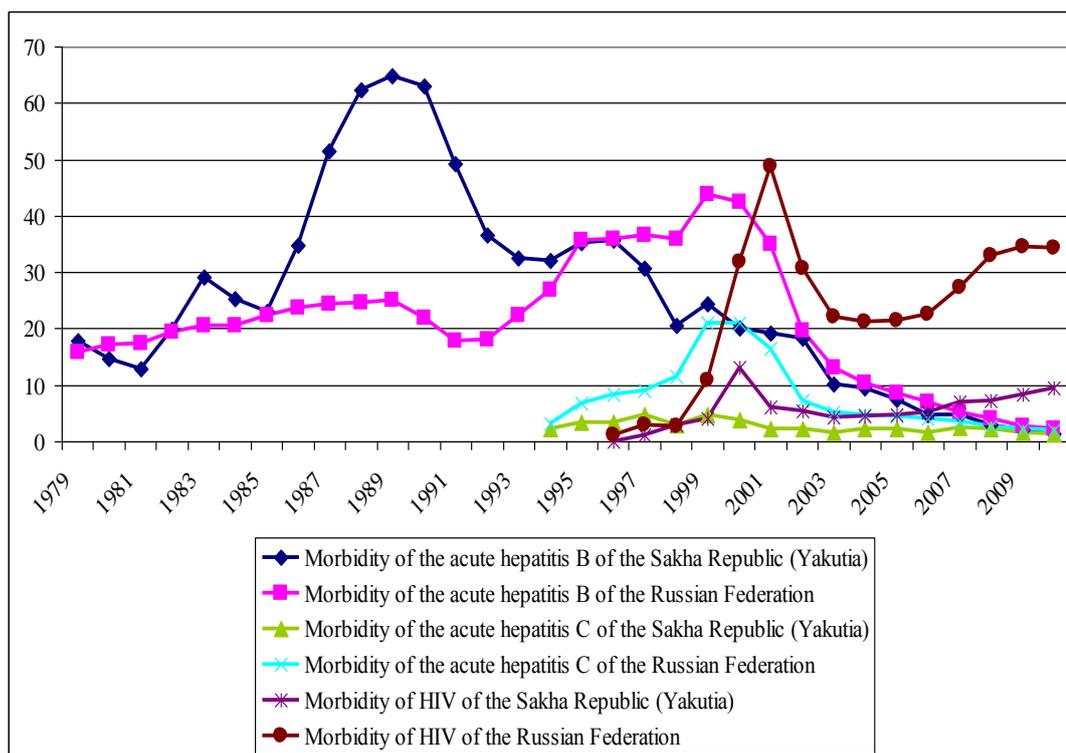
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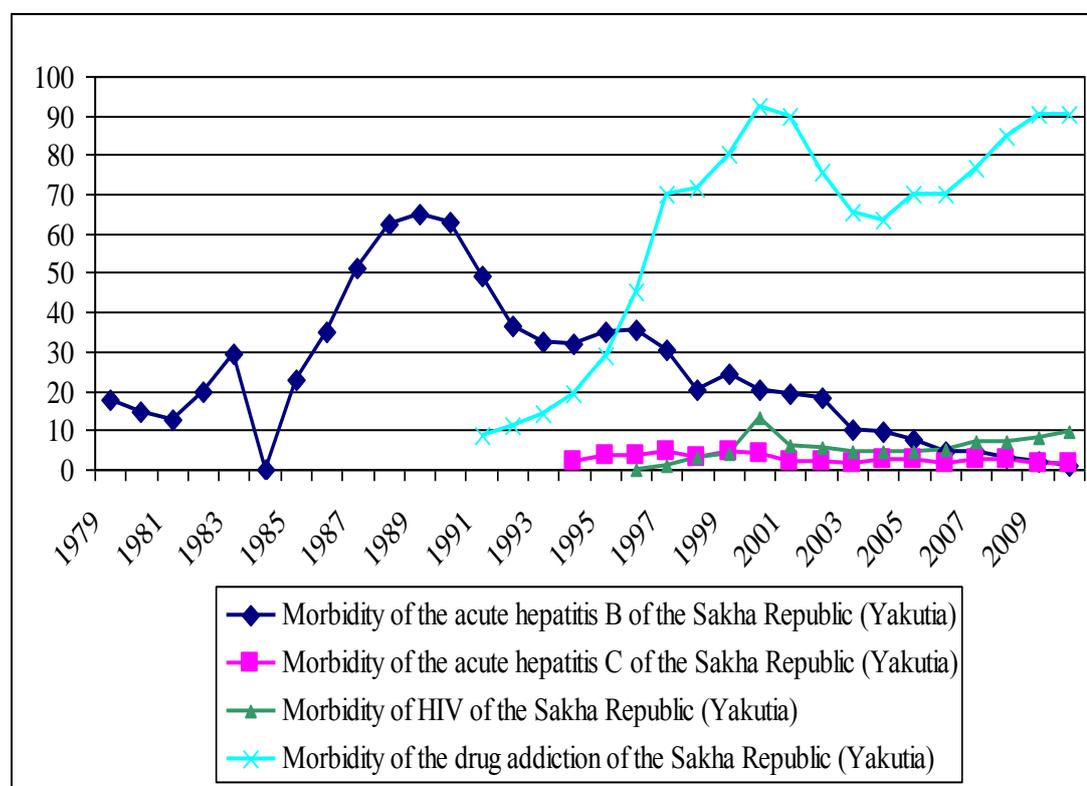
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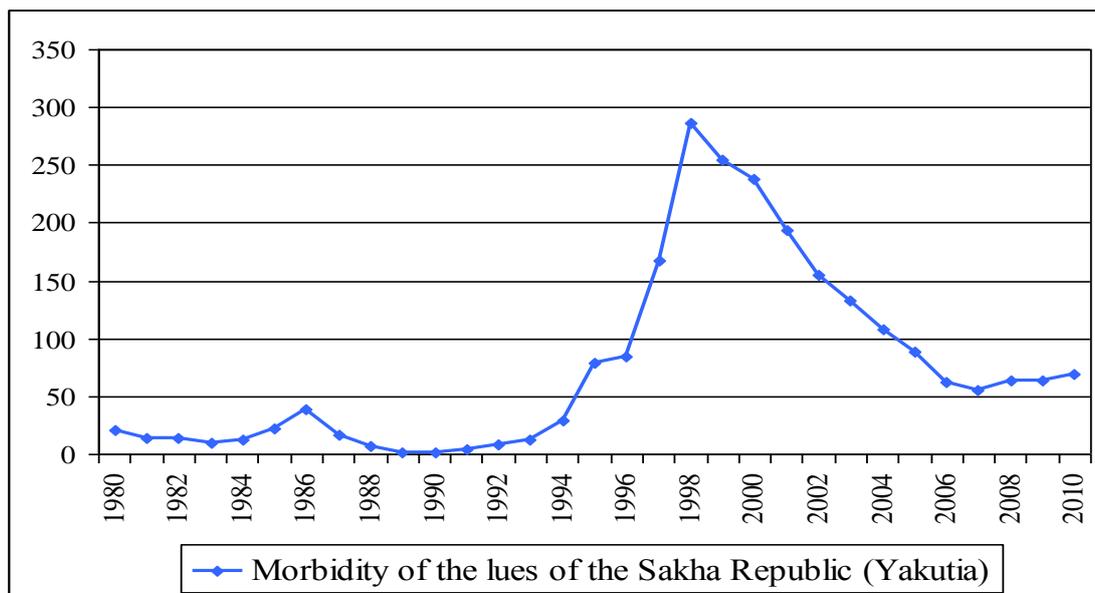
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Pic. 1. The dynamic morbidity of the acute hepatitis B and C and HIV of the Sakha Republic (Yakutia) and whole Russian Federation (per 100 thousand population).



Pic 2. The dynamic morbidity of the acute hepatitis B and C, HIV and drug addiction of the Sakha Republic (Yakutia) (per 100 thousand population).



Pic.3 The dynamic morbidity of the lues of the Sakha Republic (Yakutia) (per 100 thousand population).

**Plehanov A.N.**

### **Anthrax- especially dangerous infection in clinical practice**

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In article tactics of rendering medical aid to the anthrax patient is submitted. The brief characteristic of organizational actions is given at treatment of 7 patients with this especially dangerous infection. On a clinical example anthrax rare complication as a gastric bleeding is shown. Endoscopic picture of plural ulcer defects in a stomach differs that on periphery of ulcer inflammatory infiltration shaft is absent, and ulcer surfaces are covered with necrotic scab. Tactics of anthrax patient treatment complicated with a bleeding is shown.

**Keywords:** anthrax, clinical cases, diagnostics, treatment.

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## **NN Shats, MM Shats**

### **SOME FEATURES OF REGIONAL PUBLIC HEALTH IN THE NORTH**

(Medico-ecological aspects and ways to improve)

#### Introduction

In recent decades, the development of the Northern Territories, which occupies a large part of Yakutia, has led to serious harm done to the environment as a republic and state of health of its population. Previously been shown many health and environmental problems that inevitably arise in areas of intensive development, and on his condition close to intact.

#### Current status and basic problems

At the same time, the special natural, economic and social conditions of Yakutia, allow us to consider it as potentially one of the main centers of economic development. The main natural factors that have a material adverse effect on the body of inhabitants of republic first note the extreme climate of [1-5]. For this reason, some of the common climatic

factors contributing to the living conditions of the northern territories and their health status include:

a) extremely low winter temperatures, dropping down to the extreme values, truncated to three months in spring and autumn transition periods with sharp fluctuations in air temperatures and strong winds.

Average monthly air temperatures in January, the coldest month, dropped to  $-40^{\circ}\text{C}$  and minimum - up to  $-60^{\circ}\text{C}$ . This requires the use of special clothing and footwear (Fig.1), with total weight for children about a half to two kilograms, and for adults - 4-5 kg, and compliance with safety rules when you stay outdoors, even when morally be in the "milk" the fog is not easy. Low temperatures and strong winds in spring and autumn-winter periods, which reduce the time fresh air to a minimum, deprived children, including students, an important recreational and hygiene factors.

For the population of Yakutia is characterized by significant features of the causes and course of most diseases. This primarily refers to diseases of the respiratory system arising in extremely cold climates. Thus, in winter increases the frequency of respiratory illnesses such as laryngitis, tracheitis, bronchitis, especially in young and middle age. This is because the cold air when inhaling through the nose does not have time to warm up in the nasopharynx, and goes to the upper airway cold.factors - the cold air, heavy clothing, covered with a scarf lower face - provoke exclusion from the act of breathing the lower parts of the lungs, which causes insufficient oxygenation of brain tissue and internal organs. Designated provoking climatic factors in winter periods contribute the majority of the population of the republic weakened immune system. Therefore, the seasonal growth of SARS and influenza has, in spite of extensive prevention activities in communities, towards a quantitative increase.

As a preventive measure for this group of diseases and to strengthen the immune system, but the use of immunomodulators, and vaccination against influenza in preschool institutions should pay serious attention to breathing exercises. Particular attention has never stipulated a similar thematic articles, the authors draw on the consequences of driving on poorly maintained roads of the city. For Yakutsk, like many northern cities of Russia are characterized by extremely complex permafrost-soil conditions, when the basis of many roads lie fragile to external shocks with very high permafrost. In addition, the entire road system, year-round naked and available to extremes, with an amplitude of up to  $70^{\circ}$ , air temperature, is experiencing serious vertical and horizontal tensile strain. As a result, the surface pavement, and underlying his horizons and rock materials are in very poor condition, and this applies both to the city proper (Fig. 2-4) and to the backbone of the republican road network

(Fig.5).

When driving on such roads in the automotive and, especially, bus transport and is a traumatic impact of sharp fluctuations of the body on the spine with its structures, and articular cartilage of the lower extremities. Daily ride on the coating consisting of pits and potholes (Fig. 4), traumatic intervertebral discs and ligaments, resulting in cracks appearing rather quickly violated the elasticity and integrity of the anatomical structures. Thus, the preconditions for the occurrence of intervertebral disc hernia are created for this reason at an early age. Therefore, diseases of the spine in our time tend to rejuvenation and progress in this direction. Naturally, the constant juxtaposition of provoking factors, which are mentioned above, aggravated radicular for osteoarthritis, muscular and vascular syndromes, which leads to impaired spine even in young people. Number of non-specific arthritis, triggered by a cooling factor and lead to arthritis, arthritic joints deformations, also tend to rejuvenation. As the prevention of osteochondrosis and osteoarthritis, in addition to carrying out physiotherapy, orthopedic aids and the use of medicines requires review of the relationship of departmental services to the quality of road surfaces. In 2011, major repairs of the road network of the city, and hence improving its status, highlighted the huge funds and their judicious use is essential to improve public health.

Growth of diseases of the genitourinary system in adolescents is associated with characteristic continued most of the year cold period omissions in the clothing and carefree attitude of youth towards their health. Therefore, in the junior growing number of cases of pelvic and urinary tract such as pyelonephritis, glomerulonephritis, cystitis, adnexitis (inflammation of the appendages). As a result, suffered in his youth adnexitis, comes secondary infertility among women of childbearing age. In terms of prevention of the listed diseases requires systematic education, both by doctors and by educators, sociologists and family. The second negative factor affecting the health of the population, is b) the absence or short-term intake of sunlight with a low degree of insolation in the long cold period lasting from September to March (polar night), as well as the long days and bright "white" nights during the summer. Polar night, when for a few months the sun never appears above the horizon, and the polar day, when it is somewhat shorter period does not go, seriously affect the natural physiological processes in the body like sleep and wakefulness.

Significant reduction in the quality of natural light in winter background with an extension of time under artificial light cause diseases of the view that due to the increased voltage of the visual apparatus, in both children and adults. Number of early visual defects in school increases for the whole school period. In high school, 70% of students have myopia of moderate and severe with the initial degenerative changes in the retina.

Orthopedic disease of the child population of the northern territories is directly related to a deficit of vitamin D3. A disease of the whole organism, as rickets, is widely known in areas with short sunny period, gives visible to the eye changes in lesions of bone and muscle systems of the child during the period of accelerated growth.

Vitamin D3 is essential for the absorption of mineral salts of calcium, magnesium, zinc, phosphorus from the intestine into the bloodstream and their uptake in the bone tissue. Without vitamin D3 mineral salts rapidly eliminated from the body, not assimilating into bone tissue, resulting in the loss of bone mass. As a result, the vertebrae and the bones of the lower limbs are deformed under the load. The children appear rachitic varus deformity of the lower limbs, there rachitic kyphosis of the spine in the form of a hump (gibus), especially noticeable in the sitting position, slowing the process of physical and psycho-emotional development. Since wearing warm clothing and heavy winter is a necessity since childhood, the vertebral structures (ligaments, joint capsules and discs) have an additional chronic stress. In the back muscles, shoulder girdle and limbs develop congestion with areas of muscle tension, which in no small measure contributes to the development of osteochondrosis in early adolescence with the typical symptoms of the disease [5].

In adults, osteoporosis, fraught with pathological fractures of vertebral bodies and pelvic bones in a vulnerable area of the hip joint. Therefore, in the northern areas is widely used prevention of rickets in infants. And the adults after the fortieth recommend regularly used drugs with the vitamin-mineral complexes.

The growth of mental illness associated with chronic stressful situation, when in the winter due to lack of sun naturally display depressed mood with pronounced vulnerability of the psyche and nervous system. Specialists are watching teenagers progressive increase in depressive states, which are badly special treatment and have a protracted nature. Forensic doctors ascertain the growth of suicide among children older than 10 years. The role of family, social workers, psychologists and psychotherapists in the prevention of such depression and suicide among young people is hard to overestimate. However, in the North, with widely scattered settlements, specialized psychological help is difficult.

#### Conclusion

Thus, the natural conditions, as well as specifics of life in some northern regions differ significantly, which should be considered for a correct assessment. The special attention needs to be turned on that vital terms, and together with them and the state of health of population of north regions Russian FEDERATION must become priority definitions in the system of estimation of quality of life of citizens of all age-related groups.

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**THE PROBLEMS OF ADAPTATION AND PATHOLOGY FORMATION  
IN THE EXTREME NORTH POPULATION.**

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**ABSTRACT**

The review includes modern scientific data on organism adaptation response under the Extreme North Ecology and level of their potential in native and alien population. There have been summarized the results of the research in pathophysical processes in organism and factors, which determine their nascency under extreme conditions of the North. There are scientific opinions on associations of pathophysical disturbances with the formation and specifics of the prevalence of different forms of somatic pathology in adults and children in natives and aliens of the northern regions.

Key words: ecology, adaptation, organism, the North, health, pathology.

To great extend the risk of health deprivation depends from ecological conditions of life [11]. Human ecology is the theory, which describes in common the conformities of interactions between environment and society [14]. It was proved that extreme ecological conditions of life lead to higher risks of pathology formation. By this reason the most unfavorable climatic geographical area for human is the Extreme North. This territory is located northwards the Polar Circle and in accordance with Geneva conference recommendations corresponds to the term “high latitudes”. This term comprises some regions, located to the south from Polar Circle because of their climatic, zoological, botanic characteristics and permafrost. Extreme North corresponds to 64.0 % of Russia territory [2]. In terms of biology and medicine humans are affected by integral influence of extreme climatic factors in the Extreme North: long severe winter, sharp disturbances in photoperiodicity, “light hunger”, light excessiveness, magnetic perturbation, geochemical specificity of elements in soils, poorness of flora and fauna [1].

Any biological system can adapt under the influence of environment factors. In this process the system is keeping its species composition and individual characteristics, but changing its functional

activities to achieve adaptive result. The aim of adaptation reaction of any living system in changing conditions of life is supporting stable internal environment [5]. The mechanisms of individual adaptation are genetic by nature. They are based on inherited norm of response and realized via changes in biosynthesis and cellular metabolism controlled by genome [33]. In terms of evolution the development of adaptive restructuring mechanisms is performed on population level [41].

Aimed at estimating human health in the Extreme North, we examined population as three groups: native nationalities, native aliens and aliens. Adaptation is one of the fundamentals and in its primary manifestation it is greatly important for alien population of the North. Ecological adaptation and ecological pathology reflect the peculiarities of native population. Now they faced a necessity to get adapted to urbanization [26]. Northern populations carry relic values and unique features which they possessed in the process of evolution selection. Inherited adaptation abilities allow modern generation of natives to stand the complex of extreme ecological conditions, typical only for their regions [37].

We formulated the concept of adaptive types in terms of ecological variability of morphofunctional characteristics in human population. Adaptive type is the norm of biological response in all the population species to the complex of bioclimatic conditions of the region, which provides the balance between response and conditions, being reflected in morphofunctional status of population [6, 16].

Nutrition plays considerable role in the formation of adaptive-inherited abilities in native people of the North. It was being formed within long period of time under the influence of regional ecological and social economic peculiarities and was characterized by the prevailing of fat and albumen of animal origin with low content of carbohydrates [37]. As it is confirmed in the works of home [43, 44] and foreign [45, 47] authors, native people of circumpolar districts of the world show more positive indices of somatic health if having traditional nutrition, but their life duration is shorter [46].

Life under the conditions of high latitudes is affected by increased energy consumption [42]. Energy processes are determined by air temperature in the environment. Body mass, exteriority and proportions as well as the indices of main and lipoid metabolism prove this. In this connection there is a need to work out differentiated approach to defining the “norm” for value, adequately providing adaptation to regional conditions [4]. High level of energy consumption in the North is accompanied by higher consumption of oxygen. Restructuring of oxygen-transporting system more often leads to the formation of “circumpolar hypoxic syndrome” [21].

Considerable influence upon human organism belongs to psycho emotional overpressure in the Extreme North. Changes in photoperiodicity cause deviations in conduct and neurohumoral response. Under the changes of geophysical and weather factors the subjects with exhausted adaptive reserves show expressed psycho physiological declinations to negative emotions, different clinical signs of vegetative malfunction. This testifies on disynchrony formation. There is homeostasis destabilization in different

functional systems, accompanied by increased stress. In the sphere of vegetative functions parasympathetic influence tonus prevails [34, 35].

Numerous research show that the increase of free-radical oxygen compound is one of the relevant factors, forming the basis of unfavorable tendencies in population health formation in the North, being co-product of advanced energy metabolism [10, 24, 25, 34]. Mismatch between antioxidant protection and the level of oxidation process is commonly regarded as the head of pathology formation process. Antioxidants regulate lipid peroxide oxidation, which regulates the level of bioenergetic and plastic processes in cells and tissues, the proportion of cata- and anabolism processes [10, 24, 25]. Stability of antioxidant protection is affected by nutrition, seasonality and ecology, ageing, diseases, toxic substances, genetic (ethnic) peculiarities [24, 36]. Proportion of lipid metabolism indices and antioxidant system informs on the type of adaptive response to stress factor [20, 28]. We marked higher reserve abilities in the system of endogenous antioxidant regulation of peroxide lipid oxidation, including in the natives of the North including small children [10]. Important role in supporting the processes of antioxidant protection in the natives belongs to traditional northern nutrition. The formation of oxidation stress is not obligatory state for aliens. Organisms with high adaptive mechanisms response by means of augmenting free-radical compounds and the level of endogenous antioxidants. The growth of the last ones anticipates the intensification of lipid peroxide oxidation processes [36].

Chronic stress in people of northern regions is accompanied by initial formation of dystrophy and atrophy in parenchymal organs with the formation of diffuse reactive stroma sclerosis as well as expressed decrease of biosynthesis processes in cells. By the authors opinion plastic insufficiency is developing under the lowering or stopping of albumen synthesis in cells caused by exogenic and endogenic damaging factors and under decompensation process. As a rule these pathology processes in an organism are formed in accordance with functional load discrepancy to plastic provision of functions [34,35].

Complex influence of Northern ecology upon human changes adaptive opportunities of an organism and calls generalized reflection response to cold. It interrupts reactivity, corticovisceral relationships. In both adults and children it results in the formation of regional and ethnic specifics in prevalence and clinical course of viscera diseases: bile-excreting, cardio-vascular, bronchopulmonary systems [7, 18, 19, 39, 15].

Besides, in terms of epidemiology and clinical features, there are great differences between Mongoloid group populations [23, 38]. Molecular genetic studies showed genetic heterogeneity in natives of Northern Asia. This finding can explain the peculiarities of predisposition to some forms of somatic pathology in different populations [13].

The most acute reaction to negative environmental factors was marked in functionally immature organisms of children. There is scientific data on permanent replacement or switchover of development

genetic programs during the whole period of childhood. Physiology and genetics research classify this as discretion of ontogeny, which leads to the existence of critical time periods in the development, when a child is especially vulnerable to the influence of disturbing factors of environment. This determines the peculiarities of age pathology to large extent [12, 16, 17, 27].

Researches, devoted to health formation and protection in children, show that a child senses the influence of extreme conditions of the North even on embryo -fetal stage. Pregnancy and delivery in females, especially in those who are new in the North, are often complicated [22]. In such cases physical development in newborns and then in children is getting slower [29].

Better expressed deviation in metabolic processes was revealed in children of the North, which explains high risk of pathology in them. Prospective predisposition to the formation of pathology was marked in neonate period [32]. The author implements results of the research in Evenkia and Taymir children of native and alien populations with the tendency to growing number of children with lower coefficient of membrane stability.

We obtained the data on distinctiveness of cytochemical indices of lymphocyte metabolism in children in northern regions. Children, living in the Extreme North show the lowering of average activity in lymphocyte succinate dehydrogenase and the increase of subpopulation of these cells with low activity, which testifies on chronic tissue hypoxia [31]. There were considerable differences between Europoids and Mongoloids. At the same time representatives of the natives showed most optimal ontogenetic curves of cell multiplicity level and lymphocyte enzyme activity, the authors consider that these peculiarities are caused by adaptation of northern ethnoses to unfavorable ecological conditions of the region, having been programmed genetically [40].

Singularity of metabolic processes in children, living under extreme ecological conditions of the Extreme North is the leading pathophysiological factor, which determines the high risk of the formation of pathology states in an organism. We marked higher prevalence of secondary immune-deficit states in children, which were registered in 45-65% pupils of the first grade (aged 7). This circumstance predisposed to higher prevalence of bacteria/ virus diseases in children, mostly in bronchopulmonary system [32].

Generally we marked as typical the unfavorable course of wide range of the diseases in Europoid children of the North, such as vegetative vascular dystonia (its course was characterized by expressed disturbances in vegetative homeostasis) [3], chronic ENT-pathology [8], gastrointestinal tract [9]. At the same time natives, including children, showed lower course of pathology processes as compared to the Europoids.

So, the living under extreme conditions of the Extreme North is excessive threat of pathology formation in organism. The threat of health deprivation in northern region is caused not only by extreme factors of the region but characteristics of biological subject as well and its ability to adaptation in order

to support adequate functional level of physiological systems of organism in the life support process. Native inhabitants possess great capabilities in adaptation to ecological conditions of the Extreme North with traditional adaptive mechanisms on genome level. Children possess the least adaptation reserves to the influence of extreme northern conditions because of physiological morpho-functional peculiarities of their organism.

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**Fomina N.A., Dolgikh V.V., Kulesh D.V., Jaroslavtseva J.N.**

**Experience of conducting the register of arterial hypertension  
in the children's population in the conditions  
SB RAMS, Science Centre of Family Health Problems and Human Reproduction**

Creating and maintenance of functioning of system of the register of patients with essential arterial hypertension (EAH) from children's and teenage age becomes rather actual. EAG register in children and teenagers of Irkutsk allows defining gender and age structure of children with EAH, disease tendencies, indicators of frequency of occurrence of the given disease, the indicators characterizing hereditary predisposition. The register gives the chance to establish in what medical institution the given patients are observed, where and when they undergo inspection and treatment, to estimate a regularity and the characteristic of medicinal therapy, and also to establish the list of children with EAH, reached 18 years, who should be included in system of AH monitoring at their transfer to adult network.

**Keywords:** arterial hypertension, the register, the children's population, monitoring.

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**Grebennikova V. V., Petrova M. M., Bobrova O.P.**

**Pharmacoepidemiological aspects of antihypertensive therapy  
in persons of elderly and senile age**

The medical records of the hypertensive patients treated at the Krasnoyarsk regional hospital for war veterans have been analyzed in order to study the pharmacoepidemiology of elderly and old patients' hypertensive disease and its conformity with the latest recommendations. It has been found out that the treatment of hypertensive patients in the Krasnoyarsk regional hospital for war veterans meets the present-day recommendations. The study shows that basic classes of antihypertensive agents prescribed by the physicians of the Krasnoyarsk regional hospital for war veterans are the angiotensin - converting enzyme inhibitors (55,44% of the cases), diuretics (17,99%), calcium antagonists (9,11%). The proportion of combined antihypertensive agents prescribed to patients with HD is 100%.

**Keywords:** hypertensive disease, pharmacoepidemiology, elderly and senile age, antihypertensive therapy.

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