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http: // www.ymj.ykt.ru

The articles are presented in the  
author's translation.

ISSN 1813 1905  
1(41) `2013



# YAKUT MEDICAL JOURNAL

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

*Quarterly*

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

*Registration number ПИ №19-0465*

*Subscription index: 78781  
Free price*

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

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

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M.I. TOMSKIY

**THE 10 - YEAR ANNIVERSARY OF THE FIRST PROFESSIONAL MEDICAL PERIODICAL PUBLICATION "YAKUT MEDICAL JOURNAL" OF REPUBLIC SAKHA (YAKUTIA)**

In March 2013 it will be the 10 years of printing of the first issue of "Yakut Medical Journal" founded by Yakut Research Center and the Government of the Sakha (Yakutia) Republic.

Publication of the magazine was one of the directions of organizational and methodological work of the Yakut Scientific Center, approved in its statutory activities. And it became the first professional medical publication in the Republic for workers of medical science, education, health care institutions of practical public health, epidemiological and pharmaceutical services and medical students.

From its establishment to the present time "Yakut Medical Journal" had two main objectives: to bring to the reader the successes and achievements of medical science in the Republic, the Russian Federation and foreign countries, to explore scientific problems and discuss solutions and to promote the formation of scientific and clinical vision of scientists, practicing physicians, actively promoting the principles of evidence-based medical practice.

Over the 10 years of its activity the magazine in over 30 columns represented to its numerous subscribers and users - the scientific and medical workers, teachers and students of medical schools not only in the republic, but also outside it the reliable information on prevention, diagnosis and treatment of various diseases, the organization of science, health and medical education, lectures and reviews on the issues of medical science and healthcare, publications on the anniversaries of famous individuals and institutions materials on the history of health and medicine, official documents of the Ministry of Health of the Republic Sakha (Yakutia), etc.

Active authors of publications in the journal are researchers, scientists and practitioners from Moscow, St. Petersburg, Ufa, Tomsk, Novosibirsk, Krasnoyarsk, Khabarovsk, Blagoveshchensk, Tartu, Baku, etc.

The members of the Editorial Board are well-known scientists and organizers of biomedical science of the Russian Federation and the Republic Sakha (Yakutia).

It should be noted that from the very beginning of the scientific and practical structure "Yakut Medical Journal" took biomedical direction. This circumstance determined the inclusion of the "YMJ" in the approved by the HAC RF "List of the leading peer-reviewed scientific journals and publications, in which publication of the main scientific results of dissertations for the degree of Ph.D in biology and medicine is recommended" in the edition of July 2007.

The editorial board of "YMJ" for 10 years, together with his co-founders (Ministry of Health of the Republic Sakha (Yakutia), the Medical Institute of the YSU named after M.K. Ammosov (now NEFU), SPC "Phthisiology", National Center for Disease Control and Prevention of AIDS, OAO GSMK "Sakhamedstrah", OAO "Argysmedstrakh" and FGUZ "Center of Hygiene and Epidemiology") and subject to the views of their authors and many users had held a lot of work to improve its activity.

"Yakut Medical Journal" from 2008 is included into (Russia Index of Scientific Citation) RISC. Since 2010, full-text English-language version of "YMJ" is placed on the site ymj.ykt.ru.

In 2010 "Yakut Medical Journal" was included into the international reference system for periodicals and serials «Ulrich's International Periodicals Directory».

In recent years, the requirements for professional print, which should be published in the



major scientific results of dissertations for the PhD and MD degrees, are being improved. There is a growing tendency to recognize as such, only the Russian newspapers and magazines, which are included into one of the international citation databases. Back in 2010 the chairman of HAC RF M.I. Kirpichnikov in an interview on the website "Science and Technology" announced that in 2013-2014 there would be no HAC list, instead of it public citation databases will take place.

In this regard, and the editorial board, and accordingly our authors have an important task to bring the material published in the magazine, in line with the requirements of international citation databases like Web of Science, Scopus, etc.

It is known that the value of a scientific paper today is determined by two parameters - its availability and citation, as well as the value of the journals in which these articles are published. It is primarily meant the journal to be included into the international bibliometric systems, and secondly, the undeniable relevance, scientific novelty and practical significance of the study and its results, accordance of methodology and research technique to international rules (requirements) of the biomedical research, and, of course, literarily verified English version of the publication.

However, the editorial board understands that in the process of obtaining the status of the magazine as the edition which is included into the international database citation, certainly, to some extent, the interests of authors and users – healthcare workers will be overshadowed, as well as publications in the allegedly "uninteresting" for English-speaking user categories.

However, we will continue the active work of the necessary practical health categories, as "Healthy lifestyle. Prophylaxis", "Topical subject", "Chief Specialist Tribune", "Advices. Consultations. Recommendations", "To help the practical doctor", "Case History", "Experience exchange", "History Pages", etc.

We are confident that through our joint active creative work - our writers and users, "Yakut Medical Journal" will be even more interesting and appealing. In front of us there is the wide road, where together we will not only keep our line, but to improve towards increasing the availability and citation of the journal.

Today, from a height of ten-year way of the magazine we remember with great respect the "Yakut medical journal" first editor, the first director of the Yakut Science Center RAMS and the Republic Sakha (Yakutia), Doctor of Medicine, Professor Alkiviad Isidorovich Ivanov, deputy editor, deputy director of YSC RAMS and the Government of the Republic Sakha (Yakutia) for Science, Doctor of Medicine, Professor Valery Arkhipovich Argunov, a permanent member of the Editorial Board, an active contributor, founder and thought leader in the field of health in the North, MD, professor Mikhail Afanasievich Tyrylgin. They made a great contribution to the formation and development of the "Yakut Medical Journal" as the first academic publication on medicine and health care in the Republic Sakha (Yakutia). Their names will be inscribed in golden letters in the history of the Science Center.

Dear members of the Editorial Board, the Editorial Council, "Yakut medical journal" numerous authors and users," I congratulate you on the 10th anniversary of the first issue of the medical professional periodical publication in the Republic Sakha (Yakutia), I wish further fruitful creative work, prosperity and happiness!

M.I. TOMSKIY – MD, professor, the Director of the Yakut Science Center of Complex Medical Problems SB RAMS, editor-in-chief of the "Yakut Medical Journal", Yakutsk, Republic Sakha (Yakutia), Russian Federation.



Ivanov P.M., Tomskiy M.I., Myreeva S.A., Makarova N.A., Aleksandrova E.N., Ivanova S.V.

### **Mortality of Republic Sakha (Yakutia) population from malignant neoplasms in the beginning of the third millennium and its socio-economic impact**

A retrospective analysis of the 12, 2 thousand deaths due to malignant neoplasms of Yakutia population for the period 2001-2010 is represented. The share of MN is 14, 8% (in Russia -13, 8%) of all deaths in the republic and in significance they are in the third place after cardiovascular pathology. In the dynamics mortality tends to decrease. Republic loses 20, 2 thousand person-years of life, including 8, 4 thousand - of working age.

**Keywords:** neoplasms, mortality, prognosis, effects.

#### **Introduction**

Increase of efficiency of the specialized oncological help is possible only in the presence of the scientific and reasonable program in which are considered the territorial, economic and climatic characteristic of the region. The organization of the oncological help in Yakutia, in the largest region the Russian Federation occupying more than 1\5 parts of its territory, certainly is connected with certain difficulties. According to City committee of statistics of the Republic of Sakha the last two decades (1991-2010) are characterized by existence for Yakutia of negative tendencies in dynamics of demographic situations. In connection with outflow of the population, mainly young, able-bodied age, the age structure of the population which was accompanied by increase in specific weight of senior citizens significantly changed.

**The purpose of the study.** To study the dynamics, population, the time pattern of mortality from cancer in the population of Yakutia and get their socio-economic damage.

**Materials and methods:** To the analysis data of official statistics for 2001-2011 are subjected. For this period in the republic 12,2 thousand cases of death from malignant new growths are registered. Statistical processing of a material is carried out with use of a package of the applied Statistics programs.

**Results and discussion.** Malignant new growths in the republic are one of the main reasons for death of the population. 14,8% fall to their share (in the Russian Federation-13,8%) from all cases of death in the republic, and on the importance take the third place after cardiovascular pathology and death from traumas and accidents. In 2010 in Yakutia the number of the dead from malignant new growths reached 1157 people that made 96,1% of level 2001, at average annual rate of decrease-0,40%. Among the dead of the man made 53,7%, and female-46,3 of %. The ratio of number of men and women corresponded - 1,2:1,0. In structure of mortality of the man's population of the Republic of Sakha from all causes of death, from malignant new growths fall to the share of the dead of 10,7 % (in the Russian Federation-14,7%). Today, 39,6 % fall to the share of tumors of gastrointestinal localization at the man's population, female population of-39,9%. Similar indicators across Russia made in 2010: 35,6%-at men and 36,7% - at women. The second place on frequency is taken by malignant new growths of respiratory organs (male-29,1% and female-13,4 %). The third place at men is taken by new growths of uric tracts (3,8%), at female bodies of genitals (11,6%). From 2001-2010 at men of loudspeaker of mortality as a whole it is characterized as tending to decrease, at women in age group of 0-29 years the essential gain, first of all at the expense of the raised indicators of mortality from malignant new growths of the central nervous system is observed, lymphatic and the haematogenic tissues and reproductive organs.

Thus, in the Republic of Sakha (Yakutia) malignant new growths are the third cause of death



on the importance after diseases of cardiovascular system and death from traumas and accidents which cause to society huge social and economic damage.

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A.G. Egorova, T.M. Klimova

### **Mortality of the working age population of Republic Sakha (Yakutia): trends and forecast**

The analysis of the dynamics, the nature of trends of mortality among working-age population of the Republic of Sakha (Yakutia) for the period 2000-2008 years was made and the prediction up to 2015 year was composed.

**Keywords:** mortality of working-age population, the trends, the prediction.

#### **Introduction**

The territory of the Republic of Sakha (Yakutia) refers to areas with adverse the climatic, geophysical and socio-economic conditions for a living population. The combined effects of these factors leads to a rapid depletion of adaptive reserves of the human body and development of environmentally induced disease, complicated by a current chronic disease, premature aging and at the rejuvenation mortality (V.I. Hasnulin and co-authors, 2005).

Study of regional characteristics of the formation of public health is a prerequisite for a rational organization of health system performance in a particular area (V.K. Ovcharov, 2000; J.P. Lisitsyn, 2001; O.P. Shchepin, and co-authors, 2004). According to some researchers, the mortalities are reliable and informative indicators of social, demographic and medical well-being of the population (L.V. Anokhin et al., 1999; M.S. Bedny, 1979, 1984; T.A. Korolkova 1999).

**Purpose.** To estimate tendencies in mortality of working-age population of the Republic of Sakha (Yakutia) for the period 2000-2008 years and make a forecast up to 2015 year.

#### **Subjects and methods**

To investigate the use of official statistics mortality of working age population of the Territorial Department of the Federal State Statistics Service of the Republic of Sakha (Yakutia) for the period 2000-2008. [1].

For analysis of mortality dynamics was calculated the indicators of the dynamic range. When drawing up the equation for calculating the prognostic index performed the alignment of time series by least squares [2, 3].

At T (average growth rate) from 0 to  $\pm 1\%$  of the estimated trends in the dynamics as a stable, at T of up to  $\pm 1,1\% \pm 5,0\%$  - moderately, at T more  $\pm 5,0\%$  - as expressed by [4].

#### **Results and discussion**

When studying the age structure of the population revealed that the period from 2000 to 2008 years indicated a slight (3,1%) increase in the proportion of working- age, while the share of persons under the working-age decreased to 4,9% (Table 1). The population growth over the study period increased from 4,0% to in 2000 year to 6,1% of the – 2008 year.

According to the WHO classification of the population is considered "old" if, before to those aged 65 and over up to 7% of the total population. In the country in 2008 year were 5,9% of residents of this age. The process demographic aging was more typical degree for women (in 2008 year proportion of men aged 65 years and older was 4,1% and 7,2% of women). This disparity is due to increased mortality of men.

In analyzing the dynamics of mortality of the Republic of Sakha (Yakutia) of working-age found that the total mortality for the period from 2000 to 2008 years decreased by 1,5% (Table. 2).

To assess the nature of the trends of mortality were calculated annual increase /decrease in mortality and the rate (Fig. 1, Table 3.). Calculated values show a decrease in mortality of the population of working-age, but the pace of decline has reached in 2006 year -7,7% in 2007 have decreased, while in 2008 year there is an increase of 4,4%. The average absolute increase and the average growth rate of mortality for the period 2000-2008 years presented in Table 4. With average absolute increase in total mortality of working age population of the republic in 2000-2008 years was – 1,34. According to our data, the trend in overall mortality during the analyzed period is regarded as stable. In separate groups of causes of death observed moderate opposite tendencies: increasing - from diseases of the circulatory system, digestive, infectious, endocrine and other diseases, the decline - due to external causes, neoplasms and diseases of the respiratory system.

The structure of the working-age mortality leading causes throughout of the under review the period were of cardiovascular disease, cancer, accidents, poisonings and injuries (Table 5). Their total contribution to the overall mortality rate in 2008 year was 80,5%.

The main contribution to deaths from the cardiovascular diseases has made coronary heart and cerebrovascular diseases (Table 6). Dynamics of mortality from diseases of the circulatory system during the analyzed period is characterized by a moderate upward trend, according to specific reasons (CHD and CVD) - a stable (Table 7).

Mortality rates of working-age population of the republic from external causes between 2000 to 2008 years are presented in Table 8. Throughout the analyzed period, the main causes of mortality from external causes were homicide, suicide and "other" reasons. The trend of mortality from all external causes is characterized by downward decrease with an average absolute increase in mortality was 34,26 per 100 thousand of population (Table 9). There is a pronounced tendency

reduce the Mortality from alcohol poisoning. Mortality of transport of reasons and murder has moderate downward trend, the rate of growth, respectively were -1,95% and 4,08%. The tendency to suicide is characterized as "stable."

With the use of least-squares method for aligning time series rates was calculated forecasting mortality for working-age population on 2009-2015 years. The equation of the linear trend is given by:  $\gamma_t = a_0 + a_1 t$

In this  $a_0 = \frac{\sum y}{n}$   $a_1 = \frac{\sum yt}{\sum t^2}$ . After calculating indicators (Table 10), the equation takes the following form:

$$\gamma_t = 7,478 + (-0,08667) * t \quad (1)$$

Standard deviation of the model was 0,33. The average error was 0,21%. Estimation of accuracy approximation model performed by calculating the coefficient of variation and Theil coefficient mismatch. The coefficient of variation was 4,4%, the coefficient of divergence of Theil — 0,02. In connection with this approximation is considered accurate.

The average absolute increase was as follows:

$$\Delta = \frac{y_n - y_1}{n - 1} = -0,03$$

$$\gamma_{2009} = 7,1 + (-0,03) * 1 = 7,07$$

$$\gamma_{2010} = 7,1 + (-0,03) * 2 = 7,04.$$

The average growth rate of:

$$k_p = \sqrt[n-1]{\frac{y_n}{y_1}} = 0,997$$

$$\gamma_{2009} = 7,1 * 0,997 = 7,07$$

$$\gamma_{2010} = 7,07 * 0,997 = 7,04$$

Prognostic indicators of mortality among the population of working-age from all causes in 2009-2015 years, calculated by the formula 1 are as follows:

$$\gamma_{2009} = 7,478 + (-0,08667) * 5 = 7,04$$

$$\gamma_{2010} = 7,478 + (-0,08667) * 6 = 6,96$$

$$\gamma_{2011} = 7,478 + (-0,08667) * 7 = 6,87$$

$$\gamma_{2012} = 7,478 + (-0,08667) * 8 = 6,78$$

$$\gamma_{2013} = 7,478 + (-0,08667) * 9 = 6,70$$

$$\gamma_{2014} = 7,478 + (-0,08667) * 10 = 6,61$$



$$\gamma_{2015} = 7,478 + (-0,08667) * 11 = 6,52$$

Thus, when save in the Republic of demographic and socio-economic status at the 2008 projected a moderate reduction in mortality of working age population to 2015 year to 6,5 per 1,000 of population.

### Conclusions

At the age structure of the Republic of Sakha (Yakutia) there is a trend of population aging, which is expressed in increasing the proportion of people over 65 years.

During the period 2000-2008 years riding in the causes of mortality in the structure of the population of working age were the external causes, diseases of the circulatory system and neoplasms.

The trend in total mortality of working-age population of the Republic of Sakha (Yakutia) generally regarded as stable. There is a moderate tendency to increase mortality from diseases of the circulatory system, digestive, infectious, endocrine and other diseases. Mortality from external causes, neoplasms and diseases of the respiratory system has a moderate downward trend. There is a strong tendency to reduce mortality from alcoholic poisoning. The tendency to suicide is characterized as "stable." In the period before 2015 year is expected to decrease the mortality rate of people of working age.

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Table 1. Age structure of population of the Republic of Sakha (Yakutia) for the period from 2000 to 2008 (%)

	Years
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Age	2000	2002	2003	2004	2005	2006	2007	2008
under working	28,18	26,52	26,37	25,56	24,88	24,20	23,62	23,32
Years	mortality	absolute	indicator of	indicator of	indicator of	indicator of	rate of	rate of
working-age	per 1000	increase	visibility	growth, %	growth, %	growth, %	increase/decrease	increase/decrease
pop.	62,03	63,51	63,67	64,40	64,87	65,25	65,38	65,17
non working-age	7,3	9,98	9,96	10,03	10,26	10,55	11,00	11,51
2000	7,9	0,6		108,2		108,2	8,2	
2001								
2002	7,8	-0,1		106,8		98,7	-1,3	
2003	7,7	-0,1		105,5		98,7	-1,3	
2004	7,7	0		105,5		100,0	0,0	
2005	7,8	0,1		106,8		101,3	1,3	
2006	7,2	-0,6		98,6		92,3	-7,7	
2007	6,8	-0,4		93,2		94,4	-5,6	
2008	7,1	0,3		97,3		104,4	4,4	

Table 2. The main causes of deaths of working-age population of the Republic of Sakha (Yakutia) for the period 2000 to 2008 (per 100 thousand population)

Causes	Years								
	2000	2001	2002	2003	2004	2005	2006	2007	2008
all	732,9	787,3	782,8	770,8	771,9	776,2	723,3	680,6	710,4
infectious diseases	18,6	18,6	20,0	21,0	15,5	17,6	15,4	13,2	21,6
neoplasms	77,5	69,1	79,0	76,9	80,5	78,4	71,3	77,5	69,5
endocrine	3,0	2,9	3,6	4,9	3,7	3,0	2,6	4,4	3,3
diseases of the circulatory system	193,2	240,9	230,8	233,4	239,9	265,1	235,9	222,7	238,1
diseases of the respiratory system	28,4	24,2	24,7	27,8	23,8	30,6	21,1	18,0	25,1
diseases of the digestive system	40,9	38,6	43,6	45,8	48,8	44,0	45,6	37,5	46,4
external causes	324,2	344,1	334,8	308,0	302,6	292,7	278,9	263,0	274,1
other diseases	47,1	48,9	46,3	53	57,1	44,8	52,5	44,3	32,3

Table 3. Indicators of the time series of mortality of working-age population

Table 4. Main characteristics of the mortality dynamics of working-age population in Republic of Sakha (Yakutia)

Causes	The average absolute increase	Rate of increase in average, T, %	Characteristic of trends
all	-1,34	-0,18	stable
infectious diseases	0,38	1,89	moderately
neoplasms	-1,00	-1,35	moderately
endocrine	0,04	1,20	moderately
diseases of the circulatory system	5,61	2,65	moderately
diseases of the respiratory system	-0,41	-1,53	moderately
diseases of the digestive system	0,69	1,59	moderately
external causes	-6,26	-2,08	moderately
other diseases	3,86	3,15	moderately

Table 5. The structure of the main causes of deaths of working-age population of the Republic of Sakha (Yakutia) for the period 2000-2008 (%)

Causes	Years								
	2000	2001	2002	2003	2004	2005	2006	2007	2008
all	2,54	2,36	2,55	2,72	2,01	2,27	2,13	1,94	3,04
infectious diseases	10,57	8,78	10,09	9,98	10,43	10,10	9,86	11,39	9,79
neoplasms	0,41	0,37	0,46	0,64	0,48	0,39	0,36	0,65	0,46
endocrine	26,36	30,60	29,48	30,28	31,08	34,15	32,61	32,72	33,54
diseases of the circulatory system	3,88	3,07	3,16	3,61	3,08	3,94	2,92	2,64	3,54
diseases of the respiratory system	5,58	4,90	5,57	5,94	6,32	5,67	6,30	5,51	6,54
diseases of the digestive system	44,24	43,71	42,77	39,96	39,20	37,71	38,56	38,64	38,61
external causes	6,43	6,21	5,91	6,88	7,40	5,77	7,26	6,51	4,49
other diseases	100	100	100	100	100	100	100	100	100

Table 6. Mortality of the working- age population in Republic of Sakha (Yakutia) from diseases of the circulatory system during the period from 2000 to 2008 (per 100 thousand population)

Causes	Years
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	2000	2001	2002	2003	2004	2005	2006	2007	2008
all diseases of the circulatory system	193,2	240,9	230,8	233,4	239,9	265,1	235,9	222,7	238,1
coronary heart disease	70,6	82,2	73,1	75,2	73,8	80,6	69,3	61,4	70,8
cerebrovascular disease	48,3	50,3	46,0	51,7	48,0	58,5	51,1	45,7	46,4

Table 7. Trends in mortality of working- age population Republic of Sakha (Yakutia) from diseases of the circulatory system during the period from 2000-2008 years

Causes	The average absolute increase	Rate of increase in average, T, %	Characteristic of trends
all diseases of the circulatory system	5,61	2,65	moderately
coronary heart disease	0,03	0,04	stable
cerebrovascular disease	-0,24	-0,50	stable



Table 8. The structure of the deaths of working-age population Republic of Sakha (Yakutia) from external causes between 2000 and 2008 (per 100 thousand population)

Causes	Years								
	2000	2001	2002	2003	2004	2005	2006	2007	2008
road accidents	24,0	35,2	30,9	29,1	27,8	28,7	31,5	19,3	20,5
murder	74,8	71,0	81,8	66,8	70,1	70,8	57,6	57,3	53,6
suicides	68,9	72,1	69,3	69,8	68,3	67,3	66,0	65,8	67,7
alcohol poisoning	13,8	17,1	15,2	19,9	14,7	14,8	10,6	5,4	7,4
other causes	142,7	148,7	137,6	122,4	180,9	111,1	165,7	147,8	124,9
all	324,2	344,1	334,8	308,0	302,6	292,7	278,9	263,0	274,1

Table 9. Trends in mortality in the Republic of Sakha (Yakutia) from external causes between 2000 and 2008 years

Causes	The average absolute increase	Rate of increase in average, T, %	Characteristic of trends
all	34,26	-2,08	moderately
road accidents	2,56	-1,95	moderately
murder	6,70	-4,08	moderately
suicides	8,46	-0,22	stable
alcohol poisoning	0,93	-7,49	expressed
other causes	15,61	-1,65	moderately

Table 10. Alignment of the time series of mortality of working-age population by the least squares

Causes	Mortality per 1000 pop. $\gamma_t$	$t$	$t^2$	$yt$	The theoretical level, $\gamma_t$
2000	7,3	-4	16	-29,2	7,73
2001	7,9	-3	9	-23,7	7,64
2002	7,8	-2	4	-15,6	7,54
2003	7,7	-1	1	-7,7	7,45
2004	7,7	0	0	0	7,35
2005	7,8	1	1	7,8	7,26
2006	7,2	2	4	14,4	7,16
2007	6,8	3	9	20,4	7,06
2008	7,1	4	16	28,4	6,97
$\Sigma$	67,3	0	60	-5,2	

Note: t - serial number of the chronological dates from the center.

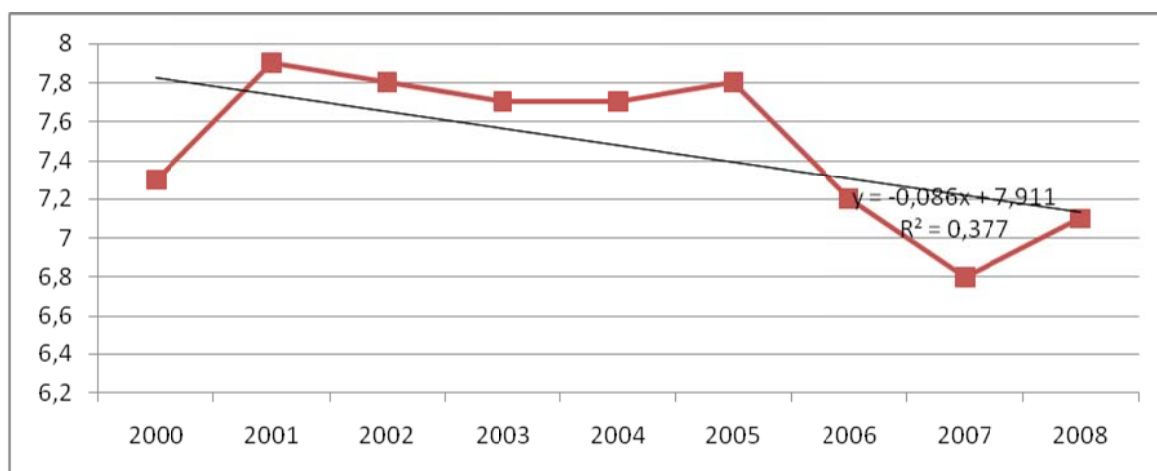


Fig. 1. The dynamics of the mortality of working -age population (per 1000 pop.) and the trend line for the period 2000-2008 years.

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## **Congenital anomalies and malformations of the urinary system as a background of chronic renal disease in children in the region of Mirny in Yakutia**

**T.I. Ryabichenko, Y.V. Kulakova, T.G. Kosyanova, G.A. Skosyreva, E.P. Timofeeva**

An inspection, examination and treatment of 2273 children of both sexes aged from 1 month to 17 years of Mirny in Yakutia region. Have been diagnosed the high level of pathology of the urinary system in children and adolescents. Found that children with congenital anomalies and malformations of the urinary system are at risk for the development of chronic pyelonephritis in the future, and so require special medical check-up and preventive measures.

**Keywords:** children, adolescents, organs of the urinary system, congenital abnormalities and malformations of the urinary tract, pyelonephritis.

**Introduction:** The pathology of the urinary system is a significant place among the diseases of childhood, maybe not so much the frequency as to severity and seriously of the forecast. One of the distinctive aspects of contemporary Pediatric Nephrology and Urology is the desire for early detection of various anomalies of the urinary system, in order to implement early prevention and early treatment. There are critical periods of fetal development, during which the action of adverse factors can form a variety of abnormalities of the kidneys and urinary tract infections that occur more frequently among the diseases of other organs and systems. The clinical significance of defects the urinary system is very variable: from minor anatomical changes that do not cause functional impairment, to severe malformations, leading to progressive renal failure and subsequent disability. In 30 – 40% of patients with abnormalities of the kidneys and urinary tract develop complications such as pyelonephritis, hypertension, secondary stone formation and shrinkage of the kidney [1,2,3].

According to many researchers, most patients with congenital disorders of the urinary system are no specific symptoms, which leads to late diagnosis in some cases it is delayed from 2 to 8 years [2,3,4,10].

This is evidenced by the prevalence of operated patients with malformations of the kidneys older children, which indicates the possibility of a long latency of the disease is not accompanied by severe clinical symptoms. For most children the disease is detected in the survey randomly [4,5]. At the present time attracts the attention of specialists connective tissue dysplasia. Given polyorgans and polysystem lesions in undifferentiated connective tissue dysplasia is difficult to find a medical

specialty in which the pathology would be of great practical importance. According to the literature in 13% of patients with the connective tissue dysplasia revealed abnormalities of the kidneys in the form of changes in the number, structure and location. The most common nephroptosis, atony pyelocaliceal system, a doubling of kidney and /or urinary tract. Connective tissue dysplasia is the basis for immune disorders, adherence to infection, including urinary tract [5,7].

Congenital malformations are the actual health problem because of their high prevalence [1,3]. Each year, according to WHO 7.9 million babies in the world accounted for 6% of children with congenital malformations. In Russia, the results of monitoring conducted in accordance with the Health Ministry Order № 268 of 10.09.1998 "On the monitoring of congenital malformations in children", the frequency of congenital malformations ranging from 0.27% in Dagestan to 2.47% in St. Petersburg. However, the prevalence of birth defects according to official statistics is low, because the epidemiological studies conducted in some regions of Russia, reveal higher levels from 2.75% in Yekaterinburg to 45.7% in North Ossetia [3,4]. According to official statistics, the prevalence of different congenital abnormalities in the Republic of Sakha (Yakutia) of 4.2/1,000 in the Mirny area – 1.9/1,000.

Malformations of the urinary tract are in fourth place in the structure of congenital malformations, and over the past decade, their prevalence has increased significantly. They occupy a leading position in the structure of causes of disability of children, leading to hardening of the renal parenchyma with the development of terminal chronic renal failure [5,7,8].

It should be noted a continuous increase in the prevalence of diseases of the urinary system as an adult and child population not only of the Mirny region, but also for the Republic of Sakha (Yakutia) in general. The frequency of chronic diseases of the urinary system in the region reaches 27.2%.

Activities aimed at improving the provision of medical and preventive care for children with congenital malformations of urinary system, should focus on early detection, prevention of risk of complications of this disease, to study the optimal form of follow-up [2,3,9,10].

**Objective:** to study particular pathology of the urinary system, the frequency of congenital anomalies and malformations, and their role in the formation of a chronic disease of the urinary system in children and adolescents in the region of Mirny in Yakutia.

**Materials and methods:** As part of a contract with "Alrosa" for the period from 1993 to 2011 years in nephrology and urology Children's wards of hospitals in Novosibirsk was examined and treated 2273 children Mirny in Yakutia region in age from 1 month to 17 years. Among the children surveyed the Mirny were – 72.2%, of the cities Lensk, s.s. Good luck, Ayhan, and other –

27.8%. The distribution of children's social status had no significant differences. All subjects lived in the Far North since birth. The examination program included the study of history, diagnosis, comorbidity, and anomalies of other organs and systems. Complex examination of children, along with the standard methods included a renal function tests and instrumental methods: ultrasound of the urinary system, excretory urography, cystoscopy, cystography, isotopic scintigraphy, and radiography, computed tomography, ECG, UCG, ultrasonography of the abdomen, on the testimony of a pelvic ultrasound. Based on the results of a survey of patients carried out verification of clinical diagnosis. According to the standard classification of ICD – X review of each child was exposed to primary diagnosis and comorbid conditions. For statistical processing of the material used the statistical software package Statistica 6. The survey was conducted with informed consent from children, their parents, with the permission of the Ethics Committee.

**Results and discussion:** on the basis of the data revealed that pathology of the urinary system, as the underlying disease was diagnosed in 500 (22.0%) of children treated in 2273. In addition, 236 children and adolescents (10.4%) was observed as a concomitant disease. Thus, the overall (primary and concomitant disease) pathology of the urinary tract occurred in 736 (32.4%) patients.

When analyzing the frequency of occurrence of diseases of the urinary system in children Mirny region revealed that during the period from 1993 to 1998 years it amounted to – 26.2%, from 1999 to 2004 – 24%, and from 2005 to 2011 years – 23.9%. The findings suggest that the frequency stability of hospital pathology urinary system. By gender differences were found. In the age group from 1 month to 3 years old was diagnosed in 19%, from 4 to 7 years – 33%, from 8 to 12 years – 36% from 13 to 17 years – 12% of cases. Analysis of the structure of urinary system disease in children and adolescents in 1994 – 2011 years showed that of 500 children with chronic kidney disease and urinary tract infections in 425 (85.0%) admitted there was a secondary chronic pyelonephritis, with 79.6% of patients developed against the backdrop of obstructive anomalies of the kidneys and vesicoureteral reflux (VUR) and 20 4% – on the background dysmetabolic nephropathy (DMNP). In 58 (11.6%) of children marked tubulointerstitial nephritis and various forms of chronic glomerulonephritis: glomerulonephritis with nephrotic component, hematuric and hereditary (in 24, 17, 15 and 2 children, respectively). Tubulointerstitial nephritis in all children proceeded against DMNP. Chronic renal failure was diagnosed in 6 (1.2%) boys – teens 13 – 15 years with bilateral ureterohydronephrosis.

The study of genealogical and obstetrical history has shown that parents and relatives have suffered from various diseases of the urinary system, and in 52% of cases – the mother. More than



half of those observed in combined pathology of the urinary system, and infectious-inflammatory diseases of the genitals. Pathological course of pregnancy as a threat of miscarriage, preeclampsia, low water levels, anemia occurred in 89%.

Comprehensive survey of children with diseases of the urinary system showed a high index of congenital malformations of various organs and systems, among which first place is occupied by urinary tract malformations (hydronephrosis, ureterohydronephrosis, a doubling of the urinary tract, VUR 2 – 4 degrees, hypoplasia, agenesis, double renal cystic disease). Hydronephrosis and ureterohydronephrosis often seen in boys. A doubling of the urinary tract and renal anomalies are more common in girls. In 49.6% of children showed a combination of malformations of the kidneys with abnormalities of the heart, 45% – with the anomalies of the gallbladder.

An examination of 425 children and adolescents suffering from chronic pyelonephritis, it was found that 209 patients (109 girls and 100 boys), chronic pyelonephritis proceeded against a background of undifferentiated connective tissue dysplasia – the main group. Group consisted of 216 patients (100 girls and 116 boys).

In the clinical status of children and adolescents of the main group there were: asthenic constitution (90%), underweight (79%), various types of violations of posture (100%), flat (90%), chest deformity (29%), joint hypermobility (89%), functional instability of the cervical spine (45%), hypotension (57%), muscular dystonia (63%), various types of arrhythmias (86%), mitral (12%) and tricuspid valve (6%), added the chord of the left ventricle (39%), their combination (9%), vegetative-vascular dystonia (76%), and various anomalies of the gallbladder (77%). Installed a high percentage of foci of chronic infection of nasopharynx (79%), pathology of the vision (myopia, hyperopia, astigmatism) in 19% of children under 9 years and 37% for teenagers, varicose veins of the lower limbs (5%), hypotonic constipation (39%), hemorrhoids (1%), periodontal (3%), multiple disemбриogenesis stigma (eye, dental, ear, skin).

For the children of the main group was characterized by: the diversity, intensity, combination, two-sidedness of various developmental abnormalities (99% and 14% respectively). In the main group of symptoms of pyelonephritis in the foreground of urinary symptoms. Every second child with connective tissue dysplasia pyelonephritis proceeded microsymptoms, latent, and detected by chance during outpatient examination. A decrease in renal function by tubular type. There was a high incidence of membranodestruction process, compared to the comparison group, as evidenced oksalaturia high (100% and 29% respectively), and crystalluria (79% and 15% respectively). Pyelonephritis in children with connective tissue dysplasia had a higher degree of inflammatory activity, which in combination with a longer period of acute (21 days in the

intervention group and 12 days in the comparison group) and frequently relapsing (89% and 27% respectively), can lead to the development of chronic renal failure in a shorter period of time.

The clinical picture of the disease control group of children were the predominant complaints of abdominal pain (77%), recurrent fevers (59%) and asthenovegetative manifestations (75%). Hypertension occurred in 18% of the comparison group of children, mainly with cystic dysplasia and congenital hydronephrosis. In 56% of children in both groups were observed functional disturbances of urodynamics (neurogenic bladder dysfunction).

The structure of secondary pathogens of chronic pyelonephritis significant differences have been received mostly recorded in both groups: *E.coli* (58,6%), *Proteus S.* and other *Enterobacter* (13,1%), *Pseudomonas* (13,2%), *Candida* (3.7%) etc. In 32% of children registered with the mixed infection – *E.coli* in combination with *Staphylococcus spp.* and *Enterococcus spp.*

To achieve the full clinical and laboratory remission in children and adolescents of the main group, as compared with controls were necessary for longer courses of antibiotics, uroseptic therapy, which may be explained by passage of urine during hypotension, urinary tract, the presence of membranodestruction process and lack of vitamin B 6.

Particular attention was paid to the study of reproductive function in adolescents of both groups. In 29% of girls – teen core group were diagnosed with various disorders of the reproductive system (sexual development lag, delayed emergence and prolonged menstruation, irregular menstruation as the dysmenorrhea and the hypomenstrual syndrome), 19% identified inflammatory diseases of upper and lower genital ways. According to a pelvic ultrasound revealed a variety of changes (hypoplasia of the uterus, multifollicular transformation of ovarian, retrodeviation uterus, saddle uterus, etc.). In 59% of adolescent boys with connective tissue dysplasia as diagnosed by a variety of disorders of the reproductive system (delayed sexual development, sexual development disharmonious, varicocele, a condition after surgery for varicocele, phimosis, inguinal hernia, hypoplasia of the right testicle, hypoplasia of the left testicle, hypoplasia of both testicles, gynecomastia).

All children carried out a comprehensive treatment with antibiotics, uroseptik, probiotics, vitamin therapy and symptomatic agents. During the period 1993 – 2011 years for congenital anomalies and malformations of the urinary tract, surgical treatment was 125 children (28.1%), and 6% for repeated surgery. All patients were discharged with improved and detailed advice on diet, a regime of drug therapy, herbal medicine, surveillance in the community pediatrician, nephrologist, urologist, and other specialists.

### **Conclusion:**





Analysis of hospital morbidity in children and adolescents Mirny in Yakutia region for the period 1993 – 2011 years showed that the pathology of the urinary system was observed in 21.9% of patients. Among the examined children were treated and dominated the age group from 4 to 12 years. The increase of birth defects and developmental abnormalities during the observation in 2.5 times. Chronic pyelonephritis in 41.8% of children and young people proceeded against a background of undifferentiated connective tissue dysplasia. Congenital anomalies of the urinary system is one of the underlying causes of chronic disease.

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M.I. Samsonova, M.V. Efimenko, A.S. Solovyeva, T.E. Burtseva, L.E. Nikolaeva

### Features of cellular immunity in adolescents of the Far East region

Native and non-native adolescents of the Sakha (Yakutia) Republic and Khabarovsk were surveyed. The features of the phenotypic characteristics of peripheral blood lymphocytes in the young indigenous of Yakutia were revealed. The revealed regional features of the immune status of Sakha (Yakutia) Republic adolescents are considered as adaptive, aimed at compensation of the effects of climatic, technological and emotional environmental factors.

**Keywords:** cellular immunity, adolescents, Far Eastern region.

#### Introduction

Is now generally accepted that the immune system is one of the earliest and most sensitive indicators of adverse effects on the environmental factors and may serve as a criterion of a significant risk of disease and dysfunction of the immune system may be responsible for up to 2% of child

mortality[5].

The immune system is an extremely complex system consisting of rapidly multicomponent and resting cells. Therefore, it is highly sensitive to the effects of various anthropogenic factors that determine the relevance of studying the immune response in children during the period of active growth and development [4]. Unfavorable climatic, ecological and geographical characteristics of the Far East region is largely determined not only by the formation of Regional Pathology and structure of infant morbidity, but also, primarily, is one of the reasons for changes in statutory rates. One of the conditions for the assessment of immunological resistance is the presence of regulatory indicators of immune status, characterized by regional specificity, due to climatic and geographical, social and living conditions and to a certain extent, the ethnic factor [1,2]. Therefore, when conducting immunological studies for the analysis of various physiological and pathological conditions in adolescents should take into account the level of immunological parameters of apparently healthy pediatric population [3].

Given the improvement of material-technical base, the regulatory framework, indicators are not absolutely unchanged immune status is necessary to investigate from the standpoint of modern immunological concepts to appropriate diagnostic and preventive measures, as well as the use of adequate and effective immune. Since the existing rules on the majority of indicators



developed in recent years of the last century, the relevance of determining the values of apparently healthy population is very timely. In connection with this study was to determine the features of cellular immunity in adolescents in the climatic and environmental conditions of the Far East.

### Materials and method

We examined adolescents Republic of Sakha (Yakutia), indigenous and migrant populations, a comparison group were practically healthy students of secondary schools in the city of Khabarovsk. The sample of 65 adolescents aged 10 to 14 years. The material for immunological studies served as the peripheral blood of healthy children who do not have the time of the survey and in the preceding month of acute exacerbations of chronic diseases and pathology. Identification of membrane markers of different clones of T-lymphoid populations was performed with a panel of monoclonal antibodies using imported ("Becton Dickinson") on the flow cytometer FACSCalibur firm "Becton Dickinson". Designation of clusters of differentiation (CD) is given in accordance with international classification adopted at the 4th International Meeting on differentiation antigens of human lymphocytes. The panel of monoclonal antibodies consisted of six markers to the following populations of lymphocytes:  $CD3^+/CD45^+$  (mature T-lymphocytes),  $CD19^+/CD45^+$  (mature B-lymphocytes),  $CD3^+/CD4^+/CD45^+$  (T-helper/inductors),  $CD3^+/CD8^+/CD45^+$  (T-suppressors/cytotoxic),  $CD3^+/CD25^+$  (marker of lymphocyte activation),  $CD(16+56)/CD45^+$  (natural killer cells),  $CD3^+/HLA-DR^+$  (activated T and B lymphocytes).

### Results and Discussion

The sensitivity of individual links the immune system to environmental factors varies. This leads to the formation of the body changes prenosological immune reactivity, which, on the one hand, are markers of unfavorable environmental conditions, and on the other - provide the basis for the subsequent development of disease, chronic or worsening of existing diseases. Conducting research on cellular immunity, we obtained the following data. In adolescents, the indigenous population of Yakutia was noted higher rates of the total number of lymphocytes in the peripheral blood compared with those in the comparison group ( $47,12 \pm 3,21$  and  $39,5 \pm 1,5\%$ , respectively), while the newcomers population of Yakutia is defined statistically significant decrease in lymphocytes (p < 0.01).

As a result, studies have identified the following features of phenotypic characteristics of peripheral blood lymphocytes. Reduce the percentage of  $CD3^+/CD45^+$ -lymphocytes in young indigenous occurred mainly at the expense of lymphocytes expressing CD4, whose number is significantly different from that of the index in adolescents Khabarovsk ( $41,0 \pm 1,13$  and  $29,82 \pm 1,55\%$ ,



respectively). In adolescents, the alien population there was a marked reduction of lymphocytes with CD3<sup>+</sup>-phenotype (1.8-fold) relative to the comparison group, and the decline was mostly on the phenotype, which characterizes the CD3<sup>+</sup>/CD4<sup>+</sup>/CD45<sup>+</sup>-subpopulation. Changing the number of regulatory lymphocytes, both helper-inductor properties and to suppressor-cytotoxic activity, could not affect the index of the ratio of these subpopulations. As a result, the immunoregulatory index was reduced in both groups of young native and alien population of the Republic of Sakha (Yakutia) with a high degree of confidence ( $p < 0.01$  and  $p < 0.001$ ).

The relative and absolute content of B-lymphocytes in young indigenous people were not significantly different from the same indicator in the comparison group, while the alien population was reduced by 1.6 times. The number of NK cells characterized by expression of CD(16+56)/CD45<sup>+</sup>, was reduced both in adolescents indigenous and alien population, and was  $4,20 \pm 0,73$  and  $4,32 \pm 1,01\%$  (in comparison group:  $14,5 \pm 1,02\%$ ). A similar situation was observed with respect to lymphocyte population with the phenotype CD3<sup>+</sup>/HLA-DR<sup>+</sup>: a young indigenous and migrant populations, and  $11,69 \pm 1,41$   $10,61 \pm 2,19\%$ , respectively, in the comparison group  $17,2 \pm 1,13\%$ .

### Conclusion

Thus, almost all teenagers Yakutia indicators of cellular link of immunity was significantly reduced compared with those characterizing the magnitude of cellular immunity teenagers Khabarovsk Krai. The regional characteristics identified the Republic of Sakha (Yakutia) are regarded as adaptive, designed to compensate for the adverse effects of climatic and geographical, technological and psycho-emotional factors of the environment. More pronounced features of cellular immunity in adolescents coming population of Yakutia indicate that inhibition of immune reactivity and reducing the reserve capacity of adaptation mechanisms in the unique regional conditions that may be pathogenetically important background for the formation of immune-mediated diseases.

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G. I. Sofronova, A.B. Palchik

### Features of the fetal alcohol syndrome manifestation in Republic Sakha (Yakutia)

58 children with fetal alcohol syndrome (FAS) from Republic Sakha (Yakutia) were detailed by means of 4-digit Diagnostic Code, routine and age-dependent developmental neurological assessment, brain ultrasonography, magnetic resonance imaging (MRI). In the various uluses of the RS (Y) the FAS rate varies from 0, 88 to 2, 10 per1000 live births, the fetal alcohol range disorders – from 0 up to 4, 86: 1000. Features of dysmorphic and structural cerebral abnormalities depending on ethnicity of the child are identified. Decrease of palpebral fissure length could be an early indicator of mental retardation

**Keywords:** fetal alcohol syndrome, ethnic features.

**The aim** of this investigation is to study ethnical features of fetal alcohol syndrome (FAS) in the Republic of Sakha (Yakutia, Russia).

**Methods.** Twenty-six Caucasian, 19 sakha and 13 native (even, evenks) babies in child hospitals and orphanages of 12 uluses (regions) and National Medical Center of Republic of Sakha (RS) with FAS aged from 40 postmenstrual weeks to 7 years were observed by means of 4-digit Diagnostic Code, routine and age-dependent developmental neurological assessment, brain ultrasonography, magnetic resonance imaging (MRI), Denver test and Zhurba Scale.

**Results.** Incidence of FAS varies from 0,06 to 0,9% in child population of different uluses, 0,3% in National Medical Center, and from 11.3 to 34.0% in orphanages.



Table 1.

The overall characteristics of observed children

Measures of variation	Caucasian			Sakha			Even/evenks		
	M	Me	Min-Max	M	Me	Min-Max	M	Me	Min-Max
Age, month	104.7	104.0	101-110	107.4	108.0	101-114	107.9	109.0	102-115
Gestational age.	35.8	37.0	27 – 40	37.2	38.0	28 – 41	35.9	36.0	30 – 40
Birth weight, g	2136	2060	900-3450	2140	2188	1120 – 2990	2099	2220	1350 - 2560
Birth height.	44.4	44.5	33.0-52.0	43.8	43.5	34.0 – 50.0	44.6	45.0	38.0 – 49.0
Weight at present	10518	9750	3600-19000	8125	7785	3000 - 18500	8527	8240	4200 - 14000
Height at present	84.8	85.0	52 – 108	70.1	71.0	56 – 112	75.5	69.0	56 - 108

Table 2.

Facial anomalies that are a key component of the diagnostic criteria for FAS

	Caucasian			Sakha			Even/evenks		
<i>Primary</i>	M	Me	Min- Max	M	Me	Min- Max	M	Me	Min- Max
Head circumference (centile)	4.4	3.0	3 – 10	6.4	3.0	3 – 25	3.5	3.0	3- 10
Palpebral fissures (mm)	18,8	19.0	15-22	15.6	16.0	14-25	16.7	16.5	12 – 20
Philtrum (score)	4.3	4.0	3 – 5	4.4	4.0	4 – 5	4.3	4.0	3 – 5
Upper lip (score)	4.2	4.0	3 – 5	4.0	4.0	3 -5	4.1	4.0	3 -5
<i>Additional</i>	Caucasian			Sakha			Even/evenk		
Low nasal bridge	16			17			11		
Low forehead	5			7			4		
Micrognathia	10			3			2		
Epicanthal folds	12			10			7		
Ptosis	9			5			4		
Short noses	6			9			5		
Minor ear anomalies	9			4			4		

Our investigation demonstrates that native babies with FAS were born pre-term more frequently than Sakha infants ( $\chi^2 = 4.54$ ;  $d = 0.033$ ). Sakha children with FAS have smaller birth weight and height than Caucasian ones ( $\chi^2 = 4.35 - 5.90$ ;  $d = 0.037 - 0.015$ ). Clinical assessment and neurovisualization show that Caucasian patients have ptosis and ventriculodilatation in significantly higher frequency than Sakha babies ( $\chi^2 = 5.11 - 5.97$ ;  $d = 0.024 - 0.015$ ); Sakha infants have muscle tone deviations, birth heart defects, visual nerve atrophy and subarachnoid space dilatation more often than other ones ( $\chi^2 = 11.55 - 4.10$ ;  $d = 0.0007 - 0.043$ ). Native children demonstrate better quality of social adaptation than Caucasian babies ( $\chi^2 = 10.26 - 4.10$ ;  $d = 0.0014$ ).

Spearman's correlation analysis achieved that quantity and frequency of the mothers drinking in

pregnancy correlate significantly with weight and height at present, smooth philtrum and micrognathia ( $r = 0.28 - 0.33$ ;  $p = 0.012 - 0.033$ ). The correlations are between age and social disadaptation ( $r = -0.41$ ;  $p = 0.007$ ).

Growth deficiency correlate with dysmorphology score (low nasal bridge, short noses, low forehead), malformation of locomotor system and congenital heart diseases ( $r = 0.28 - 0.34$ ;  $p = 0.01 - 0.37$ ).

The next high correlations are between decrease of palpebral fissure lengths and evidence of mental retardation ( $r = 0.64$ ;  $p = 0.001$ ).

There are the significant correlations between dysmorphology scores and defects in brain structure: between smooth philtrum and ventriculodilation; upper lip thinness and pachygyria; low forehead and subarachnoid space dilatation ( $r = 0.35 - 0.4$ ;  $p = 0.02 - 0.03$ ).

Magnetic resonance imaging studies have found the correlation between ventriculodilation with hearing disorders ( $r = 0.59$ ;  $p = 0.002$ ), anomalies of corpus callosum with hearing disorders and deformation of thorax ( $r = 0.39 - 0.46$ ;  $p = 0.002 - 0.05$ ).

We can do the following conclusions based on the previous research:

FAS and FASD among children in Republic of Sakha have specific difference in diagnostics depending from the institution and ethnical differences of places the research was made.

It's reliable that the diagnostics of FAS and FASD is much higher among native children.

There are the dysmorphical and structural cerebral disturbances depending from the nativity of child.

The multiple links revealed between anthropometrical, dysmorphical, structural cerebral parameters and the characteristics of clinical neurological status of disease. Particularly, the short palpebral fissures could be the early sign of mental retardation.

Our investigation shows the necessity of taking into account ethnical and regional features of FAS manifestation in epidemiological and clinical study.

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Morozova E.A., Morozov S.N., Donskaya A.A., Loskutova K.S.

**Effect of comorbidity on outcome in acute coronary syndrome patients with ST segment elevation**

In the article the comorbidity makes difficult to diagnose diseases, weights for the underlying condition, and requires additional treatment. From 835 patients with the acute coronary syndrome with the rise of ST segment comorbidity pathology was found in 98%. Thus on a background of current of the basic disease availability of aggravations on the first place-a chronic cholecystopancreatitis in 51 %, on the second place- erosions, ulcers top part gastrointestinal path in 44,1 %, on the third place-chronic colitis in 33,6%.

The results of the statistical analysis showed a significant increase of frequency of a lethal outcome in the group of patients with acute coronary syndrome with the rise of ST segment an exacerbation of chronic pyelonephritis for 5,7 % ( $\chi^2=5,51$ ; art. st. 1;  $p=0,019$ ) and with erosions , ulcers defeat of the top part gastrointestinal path for 4,7 % ( $\chi^2=4,1$ ; art. st. = 1;  $p=0,043$ ). In this connection, at delivery of the patient with acute coronary syndrome with the rise of ST segment in a hospital consultation of the physician for the selection of treatment comorbidity is required to a pathology.

**Keywords:** comorbidity, acute coronary syndromes with the rise of ST segment, gastrointestinal ulcers, chronic pyelonephritis, chronic colitis.

**Relevance of the topic:**

Under comorbidity understood the combination of two or more pathological syndromes or diseases of the patients, pathogenetically interrelated or overlapping in time [5,3]. Coronary heart disease in isolated form is quite rare. According Vertkin A.L., myocardial infarction (MI), clinically isolated is diagnosed in men in 17% of cases, and women - in 32% of cases [1,4]. All-in-all, in 78,6% of cases of MI comorbidity was identified, the most common of which are the carotid arteries (69%), diseases of the genitourinary system (78%), respiratory (73%), diseases of the gastrointestinal tract (70 %) [2]. In the clinical practice there is, often a combination of two or three of nosology, but in a few cases (2,7%) one patient can have the combination of 6-8 comorbidities simultaneously. The predictor of comorbidity, which can not be subjected to correction, is age. So in elderly and senile patients often reveal different comorbidity conditions are revealed[3]. Comorbidity

among people of age 80 and older found in more than 80% of cases [5]. In clinical practice, comorbidity is a significant problem in the treatment of acute coronary syndrome (ACS) connected with cumbersome diagnosis and worsening the underlying disease. In addition, comorbidity pathology requires additional treatment.

**Purpose:** To analyze the comorbidity status and its impact on outcome in patients with acute coronary syndrome with the rise of ST segment.

**Materials and Methods:** We analyzed 835 cases of ACS according to the call card emergency care, in-patient medical histories (IB), and autopsy reports in electronic and paper formats in Yakutsk, Blagoveshchensk, Komsomolsk-na-Amur, Yuzhno-Sakhalinsk and Petropavlovsk-Kamchatsky.

Deaths have been reported in 107 patients, including 64 men, an average age  $60,3 \pm 4,8$  years, and 43 women with an average age of  $67,1 \pm 5,5$  years. Clinico-morphological analysis was performed according to the rules of the clinical formulation and postmortem diagnoses according to ICD-10.

Electronic database is prepared in the program MS Excel 2007. Statistical analysis was performed using the software package IBM Statistics 19 version. To establish (the characteristics of the) learned population characteristics used bootstrap analysis with the calculation of percentile 95% confidence interval, based on 1000 random samples. Calculated interval estimates, expressed in percentage, were used to identify statistically significant differences in the frequency characteristics of the studied compared groups. To analyze the relationship of qualitative features used classic chi-square test of Pearson. Investigation of the effect on the frequency of comorbidity disease mortality was performed by calculating odds ratios with 95% confidence intervals.

The results and discussion leading to the admission of all patients in the Cardiac and cardiac branch was acute coronary syndrome with the rise of ST segment that at admission subjected to the differential diagnosis as unstable angina (UA) and myocardial infarction segment elevation ST (STEMI). In this case, the proportion of patients with UA was only 8%, and STEMI - 92%. In the analysis of the supporting vouchers health care, we found that in 43% indicates an additional diagnoses were indicated 23% did not agree with comorbidity in the final diagnosis. In 90% of comorbidity, as stated in the leaflet of health care, is not supported in the final diagnosis. It should be noted that the final diagnosis in 88% of patients established comorbidity. The discrepancies can be explained by the diagnosis that in the time of the ACS the contact between doctor and patient is usually of short duration and limits the possibility of a detailed examination of the patient medical history and the cause of which is the severity of the patient. Therefore, pre-hospital diagnosis and

interpretation of comorbidity are inappropriate. At the pre-hospital stage it is advisable to set the diagnosis of ACS and its severe complications, such as acute coronary syndrome with the rise of ST segment, acute heart failure. This language should not be considered in the event of any discrepancy exacerbations pain of chest, diagnosed in the hospital. When hospitalization cardiologist determines the tactics of the patient: meeting rentgenendovaskulyarnyh coronary interventions (routine or emergency) or conservative treatment. Based on this decision about a plan of the patient. The research we have found that counseling therapist held only 43% of patients at 3-5 days, and the remaining 57% of patients such consultation was undertaken. According to the results of the final diagnoses identified cases of acute concomitant diseases: chronic bronchitis - 23,2% (20,4-26,1%), pneumonia - 12.8% (10,7-15,1%), chronic cholecystopankreatitis - 51% (47,5-54,4%), erosions, ulcers defeat of the top part gastrointestinal path - 44.1% (40,6-47,5%), chronic colitis - 33,6% (30,4-36,9%), anemia - 21,6% (18,7-24,6%), chronic pyelonephritis - 34.0 (30,9-37,1%), artrozoartiriity - 29,2% (25,9-32,4%) . In the brackets the 95% confidence interval (CI) for the frequencies is pointed out.

Thus, among the number of comorbidity diseases lead chronic choletsistopankreatitis and erosive and ulcerative lesions of the gastrointestinal tract lead, which are observed in almost half of patients with acute coronary syndrome with the rise of ST segment. However, the pharmacological treatment of major groups, recommended for the treatment of this disease: proton pump blockers and H2-histamine blockers received only 12% of patients with this pathology. Chronic colitis with a tendency to constipation was diagnosed in one third of patients with drugs with laxative effects have been appointed only 2% of patients. About a quarter of patients were suffering from diseases of bacterial etiology. However, antibiotic therapy was given only to 19% of patients. A quarter of patients had anemia of varying severity, correction of iron supplements which held only 3% of cases. On the treatment of artrozoartriitis it is difficult to judge due to the fact that 80% of patients were treated with drugs from the group of non-steroidal anti-inflammatory drugs. The problem lies also in the fact that at present there are no clear criteria for determining the need for treatment of common comorbidity conditions (Figure 1.).

Fig.1. Exacerbations associated chronic diseases in patients acute coronary syndrome with the rise of ST segment (%)





The main cause of deaths in the study group had congestive heart failure, which was diagnosed in 72% of cases, while in 48% of cases it was accompanied by decompensated therapeutic pathology. According to the autopsy pathology comorbidity was found in 98% of 107 patients who died. The structure of comorbidity was a combination of two disease entities in 43%, three - at 30%, and four - in 20% of patients. Asthma therapeutic pathology in 37% of cases had been identified as the second competing disease. According to the results of our research in the structure of comorbidity the most common illnesses are gastrointestinal diseases (81%), respiratory (69%) and urinary system diseases (48%). According to the analysis of the frequency differences of clinical and post-mortem diagnosis was 7%. The main reasons were the under diagnosis and underreporting of clinical data in the additional 47%, the severity of the patient in 42%, short hospital stay in 11% of cases. One day mortality was ascertained in 40% of patients, 96% of which comorbidity severity was found.

Thus, in the area of the study a high frequency of comorbidity in patients is recorded, which increases the main disease and may effect the outcome.

Table 1.

The frequency of death in patients with acute coronary syndrome with the rise of ST segment with different comorbidity

pathology	lethality	The odds ratio		$\chi^2$ Pirson		p					
	with pathology	no pathology		significance	95% confidence interval						
		abs	%	abs	%		inferior	superior			
pneumonia		14	13,1	93	12,8	1,028	0,563	1,872	0,008	0,929	
chronic bronchitis		27	14,0	80	12,5	1,143	0,715	1,827	0,310	0,577	
chronic cholecystopancreatitis		63	14,8	44	10,7	1,448	0,959	2,185	3,127	0,077	
anemia		27	15,0	80	12,2	1,268	0,792	2,032	0,981	0,322	
chronic colitis		40	14,3	67	12,1	1,209	0,794	1,842	0,782	0,377	
chronic pyelonephritis		47	16,6	60	10,9	1,633	1,081	2,466	5,514	<b>0,019</b>	
erosions and ulcers upper gastrointestinal tract		57	15,4	50	10,7	1,520	1,012	2,284	4,102	<b>0,043</b>	
Arthrosoarthritis		35	14,4	72	12,2	1,215	0,787	1,887	0,775	0,379	

Where OR - the odds ratio, 95% CI - confidence interval; p - significance level

The influence of the most common comorbidity on the outcome of the disease (Table 1).

The study found that the presence of comorbidity chronic pyelonephritis death rate increases by 5,7%. In patients with concomitant erosive and ulcerative lesions of the upper gastrointestinal tract a similar increase is also observed in the incidence of death by 4,7%. The differences of frequency are statistically significant. The odds ratio analysis to evaluate the impact of disease on the outcome of the study showed that patients with chronic pyelonephritis in an average of 63% increase the probability of death. In addition, the presence of concomitant erosive and ulcerative lesions of the upper gastrointestinal tract as the probability of death increases in average of 52%. It should be noted that these probabilities are statistically significant. For other pathologies studied significant differences in the effect on the incidence of death was not found.

Thus, it was found that, first, erosive and ulcerative lesions of the gastrointestinal tract associated

with taking anti-inflammatory drugs, including aspirin, promote the formation of erosions and patients with ulcers, significantly increase mortality. So the immediate cause of death in ACS 2,8% of the cases was gastrointestinal bleeding from acute erosive and ulcerative lesions of the mucous membranes of the upper gastrointestinal tract. Second, an increase in mortality in patients with concomitant pyelonephritis causes more severe and difficult correctable hypertension.

The study revealed high prevalence rates of comorbidity in acute coronary syndrome patients with the rise of ST segment: every second revealed worsening gastrointestinal disease, one in three - pathology of the respiratory and urinary system diseases, which are associated with an increased risk of death.

### Conclusions:

1. About 90% of patients have cardiology therapeutic pathology comorbidity, with the most common gastrointestinal disease.
2. The lack of standards of cardiology patients with the presence of comorbidity disease positions is leading to its underestimation, inadequate drug therapy and the underlying disease burdens, and therefore, all patients admitted to the cardiac emergency in the first hour of the therapist must be inspected to determine the status and associated comorbidity with the risk of complications, and rational drug correction of comorbidity conditions.
3. In the case of hospital stay and revealing his acute comorbidity disease should be monitored daily by a therapist to correct treatment depending on the dynamics of the disease process.
4. To carry out these activities it is necessary to have regular units of the physician in a hospital of cardiology and cardiac surgery profiles.

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### **The influence of the season on the community-acquired pneumonia incidence in the military**

The medical histories of regular and contract service military men with community-acquired pneumonia treated in the pulmonary department of Branch № 1 FSI "321 OVKG," the Health Ministry in Novosibirsk in 2003-2005 were analyzed. Seasonal incidence of pneumonia in soldiers was found out: those in active service more often had pneumonia in winter and summer seasons of the year (January, May, June and July), the contract – more often in the winter and autumn (January, September and October).

**Keywords:** pneumonia, soldiers, seasonality.

**Introduction.** Community-acquired pneumonia – is one of the most common respiratory infections among military men. A.B. Belevitin and co-authors (2009) note the tendency of infection to rapid and heavy spread with the coverage of a considerable part of the staff for a short period of time that is the particularity of the modern epidemic process in case of community-acquired pneumonia in military groups (first of all among recruits). [1]

They distinguish year-round, seasonal and flare morbidity with community-acquired pneumonia in military men. Year-round morbidity appears in persons with low immune resistance inside military group or out of it in case of the contact with highly virulent strains of triggers. [1,6].

According to different authors, the analysis of the annual dynamics of the morbidity with pneumonias in conscripts showed that its growth began in October, mainly due to persons who had arrived in May. And in November with arriving of autumn reinforcements there is the excess of maximal year-round level. [3,4,5,7,8]. Herewith the most morbidity with community-acquired pneumonia is marked through 2-3 weeks after the arriving and reaches its maximum in 1-2 months depending on internal particularities of military group. [1,3,5].

Seasonal prevalence of the development of the disease has a great significance in community-acquired pneumonia that corresponds to the time constraints of the conscription in the Armed Forces of the Russian Federation, it means spring and summer conscription of recruits. [3,4,5,7,8]

There is a trigger moment of the activation of the epidemic process in military groups. It's the factor of "mixing" personal staff in the period of arriving of new recruits. It is this factor that according to findings of many authors "contributes to activation of the mechanism of transmission of pneumotropic triggers, the increasing of number of their carriers in the group, the increasing of virulence of pneumococci and other causative agents due to the passage among servicemen with low immune resistance". [1,6,8]



According to literature marked seasonal morbidity is noted in such groups where there is their significant renovation: educational, formed once again subdivisions and departments, military contingent in districts of states of emergency and armed conflicts. [1]

In many servicemen the development of community-acquired pneumonia is preceded with acute respiratory viral infection, the most morbidity is registered in the first 2 months after the conscription. [2,3,4,5]

So, the morbidity with community-acquired pneumonia among servicemen is an actual problem of the military public health.

**The purpose of research** is to study the rate of pneumonia in conscripts and servicemen on contract depending on the season.

#### **Materials and Methods:**

It was analyzed case histories of 1449 patients with community-acquired pneumonia being treated in the pulmonological department of the Branch № 1 of the FSE “321 DMCH” of MD of the Russian Federation in Novosibirsk in 2003-2005. There were 1425 male patients at the age from 16 to 86 and female patients (24) at the age from 24 to 90.

Pensioners composed 68 (4,6%) from 1449 examined patients, 25 (1,7%) – family members of servicemen. Due to that fact that during examination these two categories of patients were not servicemen and had less risk factors, they were not included in the research. Also it was excluded women on contract service – 8 (0,5%) and military men on admission who didn't have roentgenologic symptoms of pulmonary infiltration syndrome – 143 patients (9,8%).

So why 1205 (83,1%) of general amount of treated patients both conscripts and military men on contract were included in the research.

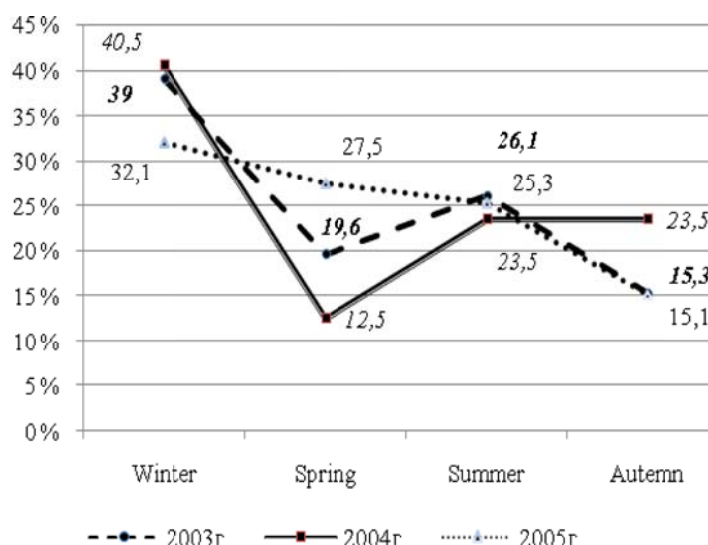
Due to the possible influence of the risk factors on the development of pneumonia connected with conditions of service considerably differentiated in conscripts, soldiers, cadets and officers all patients included in this research were divided into two groups.

In the main group there were conscripts – 2 years of service – 971 patients (80,6%), and in the comparative group there were military men of contract service (warrant officers and officers)- more then 2 years, and cadets – with 5 years of service – 234 patients (19,4%).

During the research we estimated the frequency of admission to the in-patient department both conscripts and servicemen on contract depending on the month and season of the year.

#### **Results of research.**

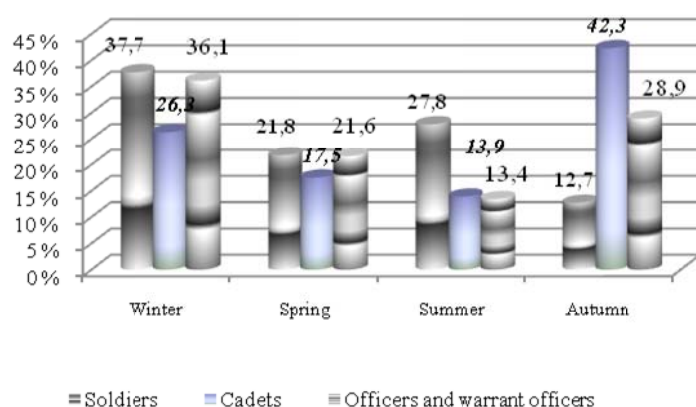
For all period of observation the rate of manifestation of community-acquired pneumonia in military men in winter season was 36,6%, spring season – 21,3% and autumn season – 17,3%.



Including: in 2003 in winter period – 39% cases, in summer – 25,3%, in spring – 19,6%; in 2004 in winter – 40,5% cases and with the similar frequency in summer and autumn – 23,5%, in 2005 in winter – 32,1% cases, in spring – 27,5% and in summer – 25,3% (pic. 1).

Picture 1. Rate of community-acquired pneumonia in examined patients according to seasons

It was studied the frequency of the development of pneumonias among examined military men in different periods of the year.

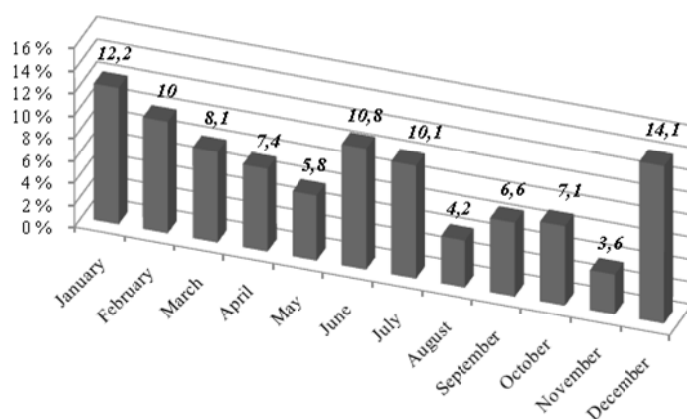


It was revealed some differences inside the comparative group in frequency of the development of the pneumonias. So cadets, officers and warrant officers were ill more often in autumn and spring, but among cadets the frequency of registration of community-acquired pneumonia in these periods was considerably higher.

Picture. 2. Rate of community-acquired pneumonia in servicemen according to the seasons.

Soldiers were ill more often in winter and summer periods. (pic. 2).

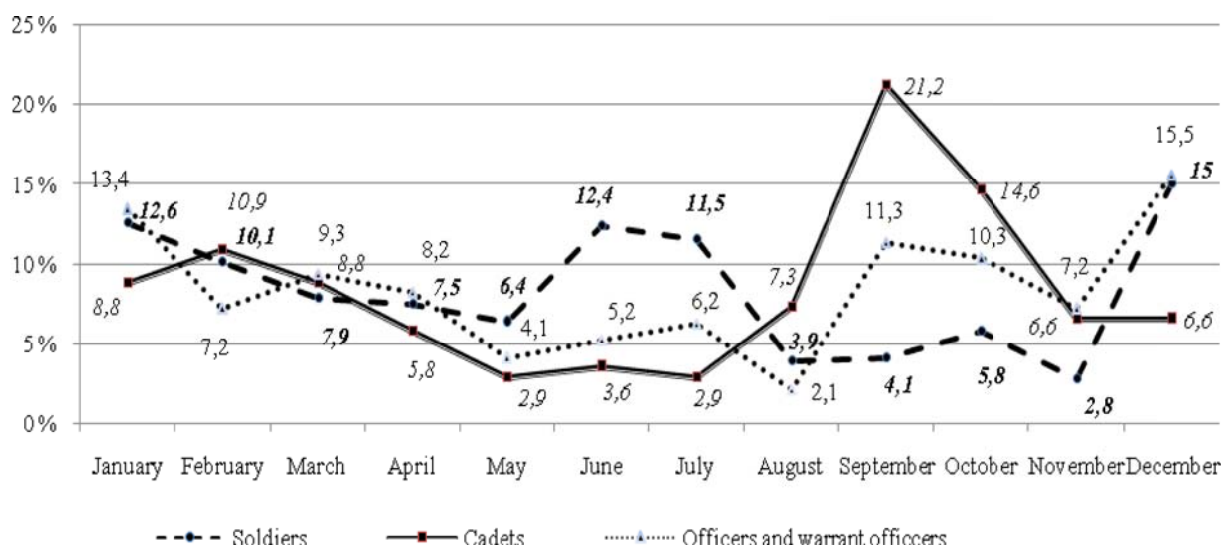
Taking into account the difference in compared groups according to the season of admission to the in-patient department it was analyzed months of the admission to the hospital. (pic. 3)



Picture 3. Morbidity with community-acquired pneumonia in examined patients according to months.

From the picture we can see that servicemen were admitted for treatment more often in winter months that composed 14,1% cases in December, 12,2% - in January and 10% - in February; less seldom they were ill in June and July – 10,8% and 10,1% respectively.

It was determined the differences according to months of the admission to the in-patient department among servicemen in the comparative groups. (pic. 4)



Picture 4. Morbidity with community-acquired pneumonia in servicemen by months

From the picture we can see that soldiers were ill with pneumonia more often in winter and summer months: in winter it was January – 12,6% cases, in February – 10,1%, in December – 15%; in summer – 12,4% in June, 11,5% - in July. Cadets, officers and warrant officers were ill more often in winter and autumn months: cadets were ill in winter – 8,8% - in January and 10,9% - in February; in autumn – 21,2% - in September and 14,6% - in October. Officers and warrant officers were ill in winter in January – 13,4% and 15,5% - in December, in autumn – 11,3% - in September





and 10,3% - in October.

**Conclusions:** 1. It was determined a seasonal morbidity with community-acquired pneumonia in military men.

2. Conscripts are ill more often in winter and summer seasons (January, December, June and July), but cadets, officers and warrant officers – in winter and autumn seasons (January, September and October).

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A.V. Nekipelova, G.B. Kalatushkina

### **Comparative analysis of immunogenetic determinants of HLA system A, B, C loci in the indigenous residents of the Khabarovsk territory, donors and psoriatic patients**

The paper gives the data of a study of HLA-antigens in 31 aborigines (the Ulch) of the Khabarovsk Territory, 1600 donors, 85 patients with psoriasis. In aborigines low frequency of HLA antigen A1 and tendency for increase of HLA B13 were found. Indices of HLA B-17 were the same as in the control group. In patients with psoriasis high frequency of antigens HLA A-1, HLA B-13, HLA B-17 and low frequency of antigens HLA A-28, B-7, Cw-3, Cw-4 was determined. This can point out the absence of genetic susceptibility for psoriasis in the Ulch.

**Keywords:** psoriasis, genetic susceptibility, HLA-antigens.

#### **Introduction**

According to modern concepts, psoriasis is an erythematous-squamous dermatosis of a multifactorial nature, having the genetic factors as the main reason in its development. It is characterized by hyperproliferation of epidermal cells and processes of keratinization, inflammatory reaction in the dermis, the changes in the various organs and systems. The prevalence of psoriasis in the population is about 0.1 to 3% [4]. Psoriasis occurs with equal frequency in men and women in different age periods.

There are hypotheses about the role of bacterial and viral factors in the etiology of psoriasis and possible changes under the influence of the genetic apparatus. It is believed that psoriasis is a slow-moving lymphotropic retrovirus infection [3].

Immune disorders play an important role in the pathogenesis of psoriasis. Skin lesions are accompanied by the influx of activated T-lymphocytes. Increased synthesis of interleukin-1 (IL-1) by activated macrophages and keratinocytes induces T-cells to the production of IL-2, which in its turn is a potent stimulator of T-lymphocyte proliferation. Activation of T-helper cells is pathogenetically associated with proliferation of epidermal cells [6, 7, 8].

The cause of psoriasis is not evident, but a significant part is assigned to hereditary factors. Segregation analysis indicates a multifactorial inheritance with a share of the genetic component equal to 60–70%, environmental – 30–40%. There is evidence to link the various genetic markers, race, nationality and type of psoriasis. Hereditarily determined psoriasis is observed in most patients and is manifested in childhood and adolescence, with no family history of the disease, the risk of a child is 8%, the risk of both parents is 41%.

Clinical observations show that the indigenous people (Ulchi) rarely take medical advice of a dermatologist concerning psoriasis. Among patients with psoriasis in the Ulchi region only 0.03% are Ulchi. In this regard, we consider the data on the frequency of histocompatibility antigens HLA loci A, B and C in patients with psoriasis and frequency of histocompatibility antigens HLA loci A, B, C in indigenous peoples.

**The purpose of the study was to** investigate the HLA-antigens and analyze the data (residents of the Ulchi District, donors Khabarovsk and psoriasis residents of the Khabarovsk Territory), and to clarify, whether there was a predisposition to psoriasis in the indigenous

inhabitants of the Khabarovsk Territory.

### Materials and methods

In a comprehensive study of different groups of patients in the "HLA and disease" program in the Khabarovsk Territory a group of residents of the Ulchi District was surveyed (31 people were Ulchi). Immunogenetic indicators in indigenous people were compared with the same parameters in patients with psoriasis (85 "caucasoids").

Histocompatibility antigens were defined. The studies were conducted in the zonal center of immunological tissue typing "Hemotransfusion Station" (Head of Laboratory is G.B. Kalatushkina). Peripheral blood lymphocytes were investigated by means of the reaction of "complement - dependent cytotoxicity" using microtechnology of P. Terasaki [9]. - Control group of 1600 donors.

**To determine the association between histocompatibility antigens and disease criterion relative risk was calculated [1, 2]:**

$$RR = \frac{fn(1 - fk)}{fk(1 - fn)}$$

Formula 1. The calculation of the relative risk criterion association between histocompatibility antigens and disease

Blood group was determined using standard sera system AB0, Rh identity – using standard antirezus sera.

### Results

Table 1 shows that the frequency of histocompatibility antigens HLA loci A, B and C in patients with psoriasis in the Khabarovsk region is represented by the following genetic determinants: HLA A-1, HLA B-13 and HLA-17 ( $p < 0.001$ ) [5].

Carriage of certain HLA-antigens in humans is much too high for some diseases, indicating that predisposition to human affection with some form of the disease is genetically determined.

**Table 1**  
**Distribution of antigens HLA loci A, B, C in the indigenous population, donors and patients with psoriasis**

HLA antigens (loci A, B, C)		Donors in Khabarovsk (n = 1600) antigen frequency, %	Population of the Ulchi District of the Khabarovsk Territory (n = 31), antigen frequency, %	patients with psoriasis (n=85), antigen frequency, %	Relative risks (RR)
HLA-A					
A <sub>1</sub>		20.80±1.015	7.50±1.25**	37.50±5.25***	2.31
A <sub>2</sub>		47.25±1.248	50.0±8.8	56.50±5.37	1.44
A <sub>3</sub>		24.00±1.068	30.0±5.29	15.30±3.90	0.59
A23	A <sub>9</sub>	24.80±1.068	52.5±9.34*	18.8±4.24	0.75
A24			5.0±0.80*		
A25	A <sub>10</sub>	23.50±0.120	15.0±2.6	16.50±4.03	1.07



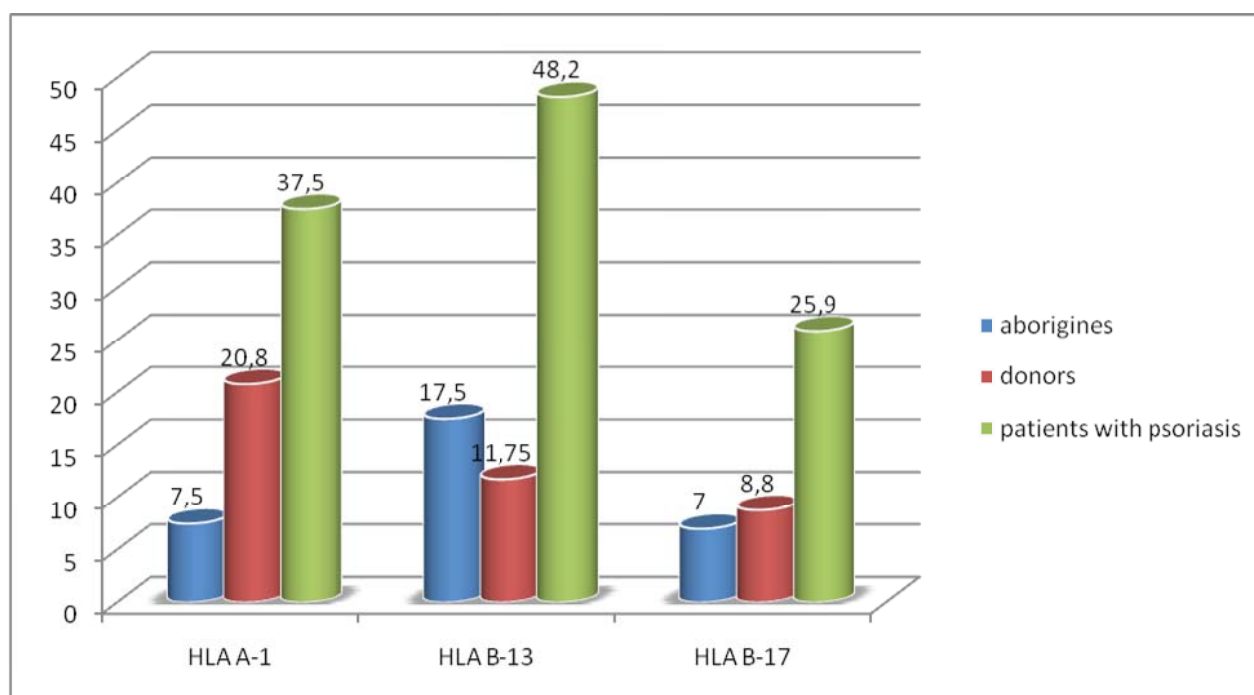
A26			15.0±2.6		
A <sub>11</sub>	14.50±0.880	10.0±1.7	14.10±3.77	1.00	
A <sub>19</sub>	15.80±0.910	7.5±1.25	10.60±3.34	0.66	
A <sub>28</sub>	5.40±0.570	10.0±1.7	1.18±1.17***	0.12	
A <sub>33</sub>		7.5±1.25			
HLA-B					
B <sub>5</sub>	12.50±0.830	10.5±1.79	16.50±4.03	1.42	
B <sub>7</sub>	21.50±1.030	17.5±3.05	8.24±2.98**	0.35	
B <sub>8</sub>	12.00±0.810	10.5±1.79	7.06±2.78	0.60	
B <sub>12</sub>	17.00±0.930	10.5±1.79	12.90±3.64	0.75	
B <sub>13</sub>	11.75±0.810	17.5±3.05	48.20±5.42***	7.00	
B <sub>14</sub>	5.00±0.650	-	4.71±2.30	1.04	
B <sub>15</sub>	9.00±0.720	20.0±3.5*	2.35±1.64	0.30	
B <sub>16</sub>	12.00±0.810		8.24±2.98	0.70	
B <sub>17</sub>	8.80±0.710	7.0±1.16	25.90±4.75***	3.65	
B <sub>18</sub>	10.70±0.770	7.0±1.16	7.06±2.78	0.68	
B <sub>21</sub>	3.40±0.450	2.5±0.35	4.71±2.30	1.57	
B <sub>22</sub>	4.40±0.510	2.5±0.35	-	-	
B <sub>27</sub>	9.80±0.740	12.5±2.15	10.60±3.34	1.12	
B <sub>35</sub>	23.20±0.110	15.0±2.6*	14.10±3.77	0.56	
B <sub>37</sub>					
B <sub>40</sub>	12.00±0.810		12.90±3.64	1.13	
B <sub>41</sub>			1.18±1.17	-	
HLA-C					
C <sub>W1</sub>	4.70±0.530	10.0±1.7*	5.88±2.55	1.38	
C <sub>W2</sub>	18.20±0.960	15.0±2.6	9.41±3.17	0.49	
C <sub>W3</sub>	23.40±1.060	35.0±5.83	10.60±3.34**	0.41	
C <sub>W4</sub>	12.70±8.320	7.50±1.25	2.35±1.64**	0.205	
C <sub>W5</sub>	0.86±0.230	-	-	-	
C <sub>W6</sub>	15.90±0.910	5.0±0.80**	18.80±4.24	1.26	
C <sub>W7</sub>	-	5.0±0.80	1.18±1.17	-	
***p<0.001; ** p<0.01					

Identification of a specific antigen by tissue typing in clinically healthy people indicates the likelihood of the disease. Genetic determinism of many pathological processes is implemented through concrete systems: structural features, levels of biochemical and enzymatic indicators.

The frequency of HLA-antigens depends on ethnicity and geographic area. Knowledge of the characteristics of distribution of HLA-antigens specific to different ethnic groups is necessary for studying the association to the HLA-antigens with diseases.

Histocompatibility antigens are defined in 31 native inhabitants of the Khabarovsk Territory. Immunogenetic indicators of the HLA loci A, B, and C are analyzed (Fig. 1). It was found that:

- antigen HLA A1 is  $7.5 \pm 1.25\%$  vs  $20.80 \pm 1.015\%$  of donors, and  $37.50 \pm 5.25\%$  \*\*\* in patients with psoriasis;
- HLA B13 antigen was  $17.5 \pm 3.05\%$  against  $11.75 \pm 0.81\%$  in donors Khabarovsk and  $48.20 \pm 5.42\%$  \*\*\* in patients with psoriasis.
- antigen HLA B17 is  $7.0 \pm 1.16\%$  against  $8.80 \pm 0.71\%$  in donors Khabarovsk and  $25.90 \pm 4.75\%$  \*\*\* in patients with psoriasis.



**Fig. 1. Immunogenetic determinants of HLA loci A, B, C in the indigenous inhabitants of the Ulchi District of the Khabarovsk Territory**

As seen in Figure 1: there is a decrease of antigen HLA A1 frequency:  $7.5 \pm 1.25\%$  ( $p < 0.01$ ); there was a trend to an increase in HLA B13:  $17.5 \pm 3.05\%$  ( $p > 0.05$ ); indicators HLA B17  $7.0 \pm 1,16\%$  ( $p > 0.05$ ) did not differ from the control group.

#### **Discussion of the results**

Genes encoding the major histocompatibility antigens are multifunctional. The clinical significance of leukocyte antigens is associated with susceptibility to certain diseases. In terms of histocompatibility antigens HLA loci A, B, and C in a group of residents Ulchi District a slight increase in the content of the antigen HLA B13 ( $p > 0.05$ ) was revealed in comparison with donors.

Some increase in the incidence of HLA B13 indicates that in this case the phenotypic characteristics have the most value. Therefore, under adverse conditions, trigger factors may contribute to the disease. This corresponds to the literature data, as the antigen HLA B17 is responsible for genetic predisposition, and the antigen HLA B13 - for environmental factors. As it was mentioned earlier, the proportion of environmental components in the multifactorial inheritance is about 30 - 40%, while the genetic component makes 60 - 70%.

The data show that the genetic determinants in the indigenous population of the Khabarovsk Territory have no predisposition to psoriasis. When analyzing the possible triggering environmental factors in the development of psoriasis in people of the Ulch district, one should pay the most attention to climate, stress, and nutrition as the most important factors for this population.

Adverse environmental factors in the first place should include climatic conditions. Climate of the Khabarovsk Territory is monsoon. It is created under the influence of the Asian continent and the Pacific Ocean. Climatic conditions of the individual parts of the territory vary considerably from north to south, and depending on the proximity of the sea, as well as the characteristics of the terrain. The variety of terrain distorts main flow directions, but the monsoon climate remains generally in all areas.

The second factor is stress. In modern life a man constantly is required to solve problems that naturally arise in the course of evolution. Therefore stress occurs in everyday life and we should give great importance to the adaptation.

Thirdly, attention should be drawn to the nutrition in the region. And if the first two factors (monsoon climate and stress) are the negative ones, the third is positive. Indigenous people in their way of life, especially in ethnic cuisine, found a cure. Eating fish (chum salmon) is useful. Biological resources of the Amur River (fish) contain omega-3 fatty acids, which have a protective effect in the treatment and prevention of psoriasis.

### Conclusions

1. Histocompatibility antigens were defined in the native inhabitants of the Khabarovsk Territory (31 people). The authors analyzed immunogenetic indicators of HLA. Decrease frequency of antigen HLA A1 ( $p < 0.01$ ), a tendency to increase HLA B13 ( $p > 0.05$ ) were revealed, while figures of HLA B17 ( $p > 0.05$ ) did not differ from the control group.

2. Indigenous genetic determinants have no predisposition to psoriasis in the Khabarovsk Territory. Some increase in the incidence of HLA B13 shows that not only genotypic features, but phenotypic ones play role.

3. Under adverse conditions, trigger factors may contribute to the disease. The most vulnerable are the patients with HLA B13 antigen, since the antigen is the most affected one by environmental factors.

4. It is very important for patients with psoriasis to have foods containing omega-3. This is pathogenetically justified and useful. Prevention of psoriasis is a balanced diet. Balanced nutrition allows patients to increase an interrelapsing period, to stay healthy longer.

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## HEPATOCELLULAR CARCINOMA AMONG PATIENTS WITH CHRONIC VIRAL HEPATITIS AND LIVER CIRRHOSIS OF ALCOHOLIC ETIOLOGY

The high incidence of parenteral viral hepatitis B, C and D markers is determined in patients with hepatocellular carcinoma (HCC). The data on higher rates of progression of HCC among patients with hepatitis B, C and D in comparison with patients with liver cancer in the absence of markers of hepatitis viruses are obtained. HCC with the greatest frequency occurred in HCV-infection with genotype 1b, HBV-infection - genotype D and HDV-infection - genotype I.

**Keywords:** viruses, hepatitis, hepatocellular carcinoma.

**Introduction.** The study of hepatocellular carcinoma (HCC) is rather complicated in comparison with the study of cancer at other sites, because this form of diagnosis is difficult, and the frequency of distribution is much lower than the stomach, lung and other organs. According to world literature, the frequency of HCC among men takes 5th place after lung cancer, stomach, prostate, and colorectal cancer and accounts for 13.1 per 100 thousand people. The incidence of liver cancer among women is in 8th place after breast cancer, cervical, colorectal, lung, stomach, ovary, uterus, and amounts to 3.5 per 100 thousand people [9]. Every year in the world is recorded more than 600,000 new cases of HCC. Mortality from this form of cancer takes the third place among all human malignancies [8, 13]. Hepatitis B and C are the most important etiological factors for the development of HCC [10, 14].

Thus, the detection rate of HBsAg among patients with HCC in Africa and Asia is 85-95%, in Japan, Italy and Spain - 50-75% in Western Europe and the United States - 10-25% [2].

The frequency of cirrhosis among patients who abuse alcohol is 10-20% and increases depending on the length of alcohol abuse. Therefore, there is particularly high risk of developing HCC in the older age group (over 60). Alcohol plays a cofactor role in carcinogenesis in patients with cirrhosis of the liver in the presence of viral infection and is a major and independent factor that induces the rapid progression of chronic hepatitis to cirrhosis and development of HCC [6,7].

Many studies have found that the similarity of clinical and biochemical symptoms of HCC with chronic progressive liver disease causes significant difficulties in the diagnosis of liver cancer at an early stage of the disease [3, 4].

**Objective:** based on a study of clinical and laboratory results, to identify features of HCC among patients with chronic viral hepatitis, taking into account the presence of markers of hepatitis viruses.

**Materials and methods.** To study and compare the clinical and laboratory characteristics of



HCC, depending on the presence or absence of hepatitis virus markers it were examined 178 newly diagnosed patients. Patients were divided into two groups. The first group included 53 patients with cancer of the liver without viral hepatitis. Among the men surveyed was 75.5%, women - 24.5%, between the ages of 54 to 76 years. The second major group consisted of 125 patients with liver cancer associated with viral hepatitis B, C and D at the age of 20 to 82 years, among them males accounted for 60.8%, women - 39.2%. Clinical, laboratory and instrumental, serological, molecular biological, histomorphological and statistical methods were used.

**Results.** HCC patients with a second group of hepatitis viruses most often diagnosed among people of working age (up to 39 and 40-49 years) at 7.2 and 19.2%. In the first group of 53 patients without hepatitis viruses, liver cancer is often encountered in older age groups from 50 and older. Liver focal lesions was identified among 18.9% of patients of the first group without hepatitis during the ultrasound examination while dispensary. It should be noted that these patients hadn't any complaints and the characteristic features of liver cancer. 66% of patients were sent to the Oncology Center for detecting their tumors in the liver during the medical examination at the worsening of chronic diseases of the gastrointestinal tract. 15.1% of patients in the dispensary on the compensated cirrhosis of the liver (for re-inspection within six months after the last visit) complaint about the reduction in amount of urine, abdominal increase, increase unwarranted weakness, weight loss, while maintaining appetite. However, these patients sought help in the later stages of the disease with an increase in signs of decompensated liver cirrhosis.

75.2% of patients with cancer of the liver associated with hepatitis viruses (second group), the reason for treatment in the health care setting have been signs of decompensated cirrhosis, in contrast to liver cancer patients without markers of hepatitis (first group). Among them 12.8% of patients in emergency indications were taken to hospital with bleeding from the varices of the esophagus and stomach. Liver cancer was diagnosed accidentally among 28,4% of patients, who came to the clinic, because of acute chronic diseases of the gastrointestinal tract.

Considering the fact that the majority of patients pass numerous medical procedures, blood serum of all patients were screened for markers of viral hepatitis by enzyme immunoassay to determine the most significant factor for HCC. In the sera of patients of the first group specific markers of hepatitis viruses did not reveal: HBsAg, anti-HBc IgM, anti-HBc IgG, HBeAg, anti-HDV, anti-HCV. In the first group, 54.7% of patients pointed to alcohol abuse. Probably this group of patients has primary liver cancer, which is developed in the outcome of liver cirrhosis of alcoholic etiology. Patients of the second group have HCC due to the outcome of chronic viral hepatitis, which was confirmed by the presence of hepatitis B virus markers and detection of viruses

B, C and D by enzyme immunoassay. In this case HBsAg found in 56.8% of patients. In 15.5% of patients HBsAg was not detected, the diagnosis of hepatitis B was confirmed on the basis of the presence in serum of other antibodies: anti-HBc IgM - 20,0 and anti-HBc IgG - 14,4%, anti-HBc total - 10,4%, HBeAg - 14,4 and anti-HBeAg - 9,6%. Among patients passed survey 17.6% of cases showed a-HDV IgM, in 11,2% - a-HDV IgG. From the total number of surveyed a-HCV IgM detected in 28.0% of patients, a-HCV IgG - in 4.8% of patients in the absence of other serological markers of viral hepatitis (Fig. 1).

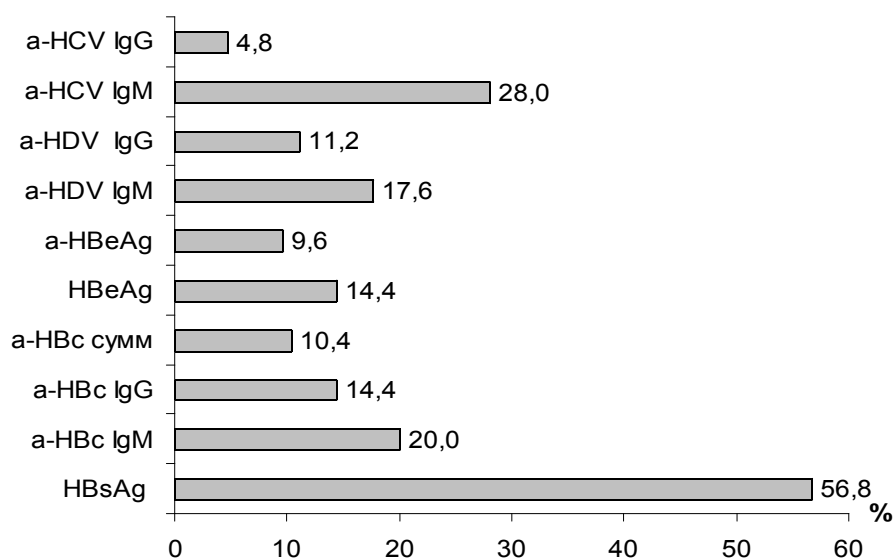


Fig.1. Serological markers of hepatitis B virus liver cancer patients (n = 125).

2.4% of patients aged 20 to 25 years of the second group firstly identified diagnosis of chronic viral hepatitis B during the medical survey. The mothers of these patients were hepatitis B virus carriers. This circumstance was regarded as the vertical infection with hepatitis B virus, which consistent in the literature [11, 12].

Comparing the frequency of manifestations of the main symptoms between the two groups, it was revealed significantly more severe course of HCC in cirrhotic patients in the outcome of chronic viral hepatitis. Most of the patients in Group 2 with markers of hepatitis viruses, asked for help with an increase in pain (83.2%), with signs of hepatic encephalopathy in 33.6% of cases with asthenic syndrome, manifested unwarranted weakness, fatigue in 88.8% cases. The phenomena of cancer intoxication in the form of reduced body weight and temperature subfebrile found in 68.8% of patients, signs of bleeding from the gastrointestinal tract in 28.0%. 5 (4.0%) patients had a strong, arching pain throughout the abdomen with the accession of bleeding from the gastrointestinal tract in the form of vomiting with coffee grounds and meleny.

The main reason for seeking medical attention were depletion of the autonomic nervous

system (60.4%) and pain (35.4%) syndrome among the first group of patients without markers of hepatitis viruses. Cancer toxicity was detected among 26.4% of patients. According to dynamic observation, 18.8% of patients had signs of liver failure.

Icterus as a sign of poor prognosis, and measure the vastness of liver damage was observed among patients of the second group in 44.8% of cases, the high frequency of hepatomegaly - in 60.8% of cases. Thus, among the first group of patients, icterus was detected in 13.2% of patients, increased liver in 32.1% of patients. The frequency of signs of decompensation of cirrhosis was significantly higher among patients of the second group than the first group (splenomegaly - 24.8 and edematous-ascitic syndrome - 35.2% against 16.9 and 9.4% respectively,  $p < 0.05$ ).

Comparative analysis of the main laboratory parameters between the groups showed a statistically significant difference on a number of indicators (Table 1). It was revealed a significant increase in aminotransferase activity, indicators of total bilirubin and alkaline phosphatase and thrombocytopenia and hypoalbuminemia among patients of the second group with markers of hepatitis viruses in comparison with patients from the first group without markers of hepatitis viruses.

The most important diagnostic feature of HCC is increasing of serum concentration of  $\alpha$ -fetoprotein - a protein produced in large quantities in the fetal liver of the fetus, followed by a rapid decline. After repeated determination of tumor marker, levels of  $\alpha$ -fetoprotein among patients of group 2 with markers of hepatitis viruses was significantly higher in comparison with a group without markers of hepatitis viruses.

Table 1.

The average values of laboratory parameters among patients with hepatocellular carcinoma

Indicators	The first group without markers of hepatitis viruses (n=53)	The second group with markers of hepatitis viruses (n=125)
	M±m	M±m
Erythrocytes $3.5 \cdot 10^{12}/l$	3,6±0,1	3,4±0,1
Hemoglobin 120-140 g/l	103,6±1,3	109,6±2,0
Platelets $180-320 \cdot 10^9/l$	150,0±3,5	112,7±4,6*
The erythrocyte sedimentation rate (ESR) 6-9 mm/h	43,3±0,7	44,0±1,1
Albumin 35-50 g/l	29,1±0,2	25,2±0,5*
Alanine Aminotransferase (ALT) 0-40 u/l	122,8±2,3	170,2±5,2*
Aspartate Aminotransferases (AST) 0-40 u/l	98,9±5,3	135,5±9,2*
Total bilirubin 8,5-20,5 $\mu\text{mol/l}$	31,4±3,8	112,2±10,5*
Alkaline phosphatase 0-270 $\text{ед/л}$	235,6±10,8	398,8±13,1*
Cholesterol 3,3-5,2 mmol/l	6,7±0,2	6,4±0,8
Glucose 3,5-5,5 mmol/l	4,3±0,1	3,8±0,1*
Prothrombin index (PTI) 80-110%	55,3±0,2	55,8±0,5
$\alpha$ -fetoprotein 10 ME/мл	292,4±31,2	321,6±30,5

\* Statistically significant difference in comparison with the first group,  $p < 0,05$ ;

To study the metabolic changes in the liver, observed under the influence of alcohol and hepatitis viruses, we determined the activity of alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (AIDG). The activity of dehydrogenases, and their ratio among patients with liver cancer varied depending on the etiology of the disease. Among 41.5% of patients without markers of hepatitis viruses, the ratio of ADH / AIDG was lower than among 59.6% of patients with viral hepatitis. It is noted that the increase in the ratio of ADH / AIDG leads to prolonged viral replication, and therefore more massive cytolysis virusinfitsirovannyh liver cells [1]. Found that the activity of these enzymes determines high risk of developing alcoholic liver disease in the indigenous population of Yakutia [5].

The presence of III degree of varices of the esophagus and ascites in the second group with markers of viral hepatitis showed great severity of portal hypertension in comparison with the first group with no markers of hepatitis B virus (14.4 vs. 5.7% and 35.2 vs. 9.4%). Complication of portal hypertension was bleeding from the EW, which led to the death 18.4% of patients from the second group. These ultrasound and computed tomography with contrast enhancement of liver tissue found malignant formation and the prevalence of liver cancer. 44.9% of patients with liver

biopsy confirmed the clinical diagnosis. Summary data of laboratory and instrumental studies have shown that 3rd and 4th stages of the disease by the TNM system were detected among patients from the second group, and the third stage of liver cancer among patients from the first group.

Two groups of patients with markers of hepatitis viruses since the detection of malignant tumors in the liver were observed during 3 months. The causes of early death were decompensated liver cirrhosis, variceal bleeding, tumor thrombosis of the portal vein and inferior vena cava and the rupture of the tumor sites. Terms observations of patients from the first group with no markers of hepatitis viruses were more persistent (year and 1.5 years).

According to the results of serological and molecular biological studies it was noted a high incidence of HCC among patients in the outcome of chronic hepatitis B and C (38.4 and 32.8% respectively). Low frequency of detection of liver cancer among patients with chronic hepatitis D (28,8%) showed a quickly progressing disease course, in which patients did not live up to the formation of cancer of the liver (Fig. 2).

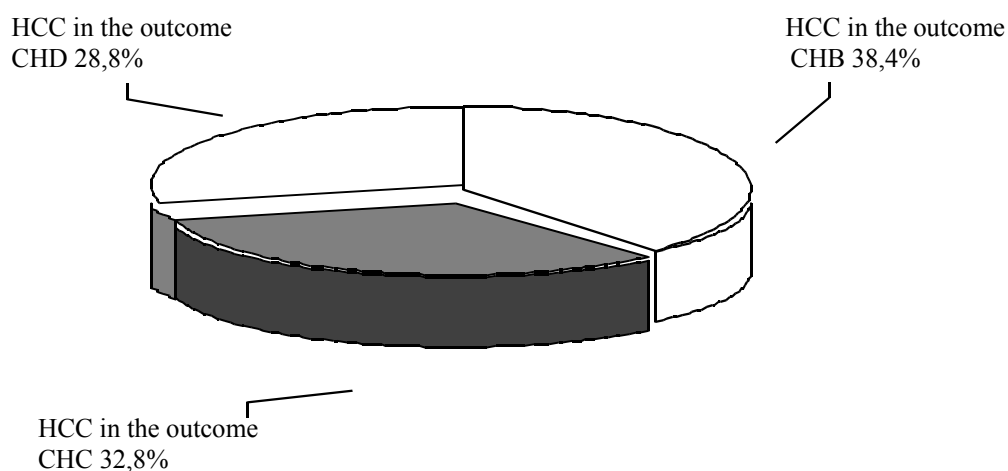


Fig. 2. Distribution of patients with hepatocellular carcinoma, taking into account markers of viral hepatitis (n=125).

Important to note that replication of hepatitis virus was observed in end-stage of cirrhosis, liver cancer. Most patients with HCC in the outcome of chronic hepatitis B and C indicated an active DNA replication of hepatitis B and hepatitis C RNA. RNA monoreplication of hepatitis D among patients with liver cancer in the outcome of hepatitis D showed high activity. In a third of the cases it was found mixedreplication of two viruses: hepatitis D RNA and DNA of hepatitis B. In the study of hepatitis virus genotypes among patients with HCC it was found a high frequency of formation of the cancer pathology with genotype 1b hepatitis C, genotype D viral hepatitis B and genotype I viral hepatitis D.



**Conclusion.** Thus, late detection of HCC caused by the absence of symptoms in the initial stages of the disease. The native inhabitants of the republic have a risk of developing liver cancer among alcoholic patients in relation to the low activity of the enzymes alcohol dehydrogenase and aldehyde dehydrogenase. The comparative analysis revealed a more severe progressive course of HCC in the presence of viral hepatitis in comparison with cancer patients without viral hepatitis. The vast majority of patients with HCC in the outcome of viral hepatitis were hospitalized in an advanced stage of disease, which determined the severity and course of disease. Obtained data may have prognostic significance in the outcome of viral hepatitis B, C and D with genotypes.

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## **Results of the study of hormones content in the blood and their evaluation depending on the duration of epilepsy**

The purpose of examination consisted in interrelation revealing between prescription of disease and the content of hormones in a blood of boys with epilepsy. Examination of hormones in bloods of children at duration of disease till 2 years, from 2 till 6 years and over 6 years was spent in age subgroups in which the content of hormones reliably differed irrespectively prescription of disease. Findings of investigation testify, that dependence of a level of hormones in a blood of boys with epilepsy from prescription of disease has the complex character and is or individual for some hormones, or the general for several hormones.



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## THE FACTORS OF DIFFERENCES IN THE LONG-TERM CATAMNESIS OF PARANOID SCHIZOPHRENIA PATIENTS (aged 50 and over)

S.N. Oskolkova, S.V. Lvova

The analysis of anamnestic, clinical-dynamic characteristics, demographical, social-adaptive peculiarities of paranoid schizophrenia patients with criminal and law-obedient behavior in later life on the basis of their long-term catamnesis examining is represented. System analysis (taking into account the dynamics of the leading syndrome, personal and situational characteristics) of remote catamnesis of the specified contingent was carried out. Several connections between trends in the course of the disease, personality, environment and behavior were revealed. In particular, the role of the tendency to weakening or to the stop of the progredience with stabilization of condition and reduction of psychopathological symptoms and the tendency to preserve the activity and progredience of schizophrenic process. The obtained results of the research may contribute to perfecting the prognostic criteria of the disease dynamics and prophylactic treatment of extremely dangerous offences.

**Keywords:** catamnesis, paranoid schizophrenia, elder age group, criminal and law-obedient behavior.

**Introduction.** The research of different aspects of psychopathology in elder ages is actual on account of several reasons: firstly, during the last 30 years, there has been an inclination to uncontrolled growth in a percentage of elderly and old-aged persons in the population of the developed countries, including Russia (1, 6, 8); secondly, there has been a tendency for the senescence of the population which is inevitably applied to the mentally sick, including schizophrenia patients. "Accumulation" of patients ill with schizophrenia of the age 50 and older has been happening for more than 20 years [5, 11, 13]. According to the data of WHO, during 15 years the number of patients ill with schizophrenia in the world increased by 30% and makes 45 million people (or 0,8-1%), the number of new cases per year is 4,5 million people. According to the data of A.A. Churkin, N.A. Tvorogova (2009), the incidence of schizophrenia in Russia in 2008 made 404,2 per 100 thousand of population. Clinical features of paranoid schizophrenia at remote stages were studied by many psychiatrists [5, 9, 13]. However, domestic clinical and epidemiological studies in gerontopsychiatry [3, 15], in addition to obvious rarity, were carried out

during a period of relative socio-economic stability. Epidemiological studies of M.E. Kuznets [9] showed an increase in frequency of committing socially dangerous acts by mental patients over 50 years.

According to research findings of B.V. Shostakovich [12], socio-economic changes in Russia over the recent 15 years have led to a marked increase in crime among mental patients, which further underlines the relevance of the work.

However, most clinical follow-up studies do not cover the entire life of patients ill with schizophrenia, they were performed on relatively small samples, and mainly reflected the patterns of clinical course of the disease in the mid-twentieth century, i.e. before the advent of a new generation of antipsychotics, which significantly increased therapeutic options and changed the quality of patients' life.

Pathomorphosis of mental illnesses [16] also determines the informativeness of a longterm catamnesis in the study of schizophrenia, including old age. Recently, the long-term catamnesis of patients with paranoid schizophrenia has almost never been studied. In a single study of J. Modestin et al. (2003) it was established that grave finite states are formed only in 1/3 of schizophrenic patients with a confirmed follow-up diagnosis; in 50% of cases observed the course of the disease was remitting and in 15% there was a practical recovery. Such conditions were defined by F.V. Kondratiev as "new health".

A preliminary review of the literature showed that the system analysis of data about the long-term catamnesis of patients with paranoid schizophrenia was not conducted. Therefore, it seems urgent to study predictors of favorable and unfavorable outcomes of the disease, the dynamics of productive and negative disturbances at a late stage of the disease, their effects on social functioning, as well as the public danger of schizophrenic patients of older age groups, which may contribute to the improvement of prognostic criteria and preventive medical and social activities.

Research aimed at the selection of the complex of factors contributing to the criminal activity of paranoid schizophrenia patients of the older age groups, as well as at the optimization possibilities of forensic psychiatric assessment are single [1, 2, 11]. At the same time, as it is known, psychogenic disorders (forensic investigatory situation) in elderly psychiatric patients, including those ill with schizophrenia, can significantly complicate the diagnostic and expert decision.

**The purpose of this study** is comparative system analysis of remote catamnesis (20-30 years) of paranoid schizophrenia patients of the older age groups who committed and did not commit socially dangerous acts (SDA) as the basis for improving the forensic psychiatric



assessment and prevention of wrongful conduct in a specified contingent.

**Material (object) of research.** 68 men of older age groups (50 years and older) with a diagnosis of «a continuously flowing paranoid schizophrenia». The average duration of catamnesis was 37, 7 years and more.

All the examined were divided into two groups: Group 1 - patients who committed socially dangerous acts (SDA) at the age of more than 50 years and who passed an in-patient forensic psychiatric examination in the State Research Center of Judiciary and Social Psychiatry named after V.P. Serbsky in the period from 2005 to 2011 (37 persons; 54,6%) and Group 2 - patients who did not commit crimes and who reside in psychoneurological nursing home (PNI) № 12 of the city of Moscow (31 persons; 45,4%). The age of patients in both groups at the time of the examination ranged from 50 to 73 years (the average age was 57, 6 years). In both groups the main clinical and social parameters for the period attributable to the onset of the disease, the ones during the first 10 years of schizophrenic process course and the ones to the period of follow-up study in 2005-2010 were compared. For standardization of the data received, a card- questionnaire was drawn up in which signs including passport data, clinical and dynamic characteristics, personality-adaptive characteristics and social-situational characteristics were recorded. In the analysis of the material the concept of system interrelation of the syndrome - the personality - the situation, developed F.V. Kondratiev in 1984-1996 years and enlarged in 2010 was used.

**Methods of research.** Clinico-psychopathological method, clinical catamnesis method, clinical-dynamic method, clinical and statistical method.

### **Research results**

In both groups the patients were brought up mostly in two-parent families. **In Group 1** hereditary load of different types of psychopathologies and alcoholism (55% of patients) was 118 observed more frequently, which affected the nature of intra-family atmosphere, life and upbringing of the patient. Upbringing in these families was carried out in the environment of constant psychological traumatic experience, which contributed to the formation of misconception of the norm of interpersonal communication, to easiness of aggression induction in conflict situations, to antisocial social circle. In about 80% of patients of the group a pathologic character of premorbid personality structure dominated by emotionally unstable, antisocial, and schizoid types was identified. **In Group 2**, the structure of premorbid personality of schizoid type dominated or accentuation of personality was lacking. Later under the influence of the painful process there happened intensification and distortion of existing characterological features, development of features that earlier were not inherent. In both groups the patients had predominantly secondary and

specialized secondary education (Group 1 - 86.6%: Group 2 - 60%). However, in Group 2, 30% of patients had undergraduate and higher education. More often the patients of Group 2 (70%) didn't serve in the Army ( $p<0.05$ ), they were either given an early discharge from military service (10%) in connection with psychopathology detection (50%), somatic pathology detection (25%), studying in institutions of higher education (25%). Patients in Group 1 were mainly engaged in unskilled labor (73.3%), many of them experienced decrease in labor adaptation. In most cases material problems (66,7%) and average material well-being were noted. **In Group 2**, patients whose main source of livelihood before entering the psychoneurological nursing home (PNH) was a disability pension, mainly of mental illness pension of the 2 group (70%), prevailed ( $p<0,05$ ). Most of the patients in Group 1 had no disability (64,3%), 26,8% of patients were given the second group of disability and 7.1% - the third group of disability. The average age of disability registration was the age of 33 years, but even after that many of the patients continued to make some money working as unskilled laborers or as casual workers. The average age of labour activity discontinuance was 39.4 years (in Group 1 – 42, 2 years). 80% of Group 2 patients were found to be legally incapable –  $p<0,05$  (the average age – 53,3 years). Family and living conditions of patients in both groups were relatively satisfactory. Most of the patients in Group 2 lived with relatives (60%). Only part of patients were married and lived with their families (**Group 1 - 26, 7%, Group 2 - 20%**). However, relations with relatives and spouses often had a hostile character, mutual understanding was lacking, and the family atmosphere was characterized by tension and conflict relations, violence, and alienation.

**In Group 1** patients were more often single (40%), persons without fixed place of residence made 20%. Most of those in Group 1 in their past had several convictions (40%), served their term or were held criminally liable. It is noteworthy that during forensic psychiatric examinations 42, 9% of patients were recognized as "sane" and an approximately equal number of patients were sent for compulsory medical treatment with the diagnosis of schizophrenia (45,5%). Patients of **Group 1** led more often an anti-social lifestyle, abused alcohol (66,7%), abused psychoactive substances (33,3%), they had a psychiatrist record due to dependency syndrome, they were treated in addiction clinics.

Duration of the endogenous process on the average in **Group 1** made 32,8 years, which is significantly smaller than in **Group 2** – 42,5 years ( $p<0, 05$ ). The onset of the disease in patients of Group 2 more often referred to puberty (70%), whereas in Group 1 it happened more frequently at the age of 19-25 (46, 7%). All patients of Group 2 were registered previously by a psychiatrist (the average age of putting on record was 21,8 years), but they attended a psychoneurological nursing

home mostly under compulsion of relatives, they received irregularly maintenance therapy with the formation of short, unstable remission. In Group 1 only 33, 3% of examined patients were observed by psychiatrists, 13% were on the books of a narcologist, of whom 28, 6% attended a psychoneurological nursing home. The main reason for registration in psychoneurological nursing home in both groups was acute psychotic state.

All patients of Group 2 were previously admitted to psychiatric hospitals, while in Group 1 only half of the patients (52,3%) were previously treated ( $p<0,05$ ). The average age at the moment of the first hospitalization in Group 1 was slightly higher – 28, 3 years. At this, the leading syndrome in 11 patients of Group 2 was hallucinatory-paranoid syndrome (40%), in Group 1 psychopathy-like syndrome, paranoid-hallucinatory syndrome and the syndrome of mental automatism (each made 20%) were detected with the same frequency. During the first 10 years the examined patients of **Group 2** were hospitalized each year in psychiatric hospitals (70%), while patients of **Group 1** – only 1-3 times ( $p<0,05$ ). The hallucinatory-paranoid syndrome with varying degrees of intensity (70%) prevailed in the clinical picture in most patients of Group 2 during this period. In Group 1 the same syndrome (40%), and the expanded Kandinsky - Clerambault syndrome were revealed (33,3%). Hallucinatory-paranoid syndrome in both groups was characterized by various delusions and auditory hallucinations, accompanied by emotional depletion, typical for schizophrenia thinking disorders, decrease in motivation to work.

The average age of patients in Group 1 at the time of wrong-doing was 56, 4 years. By the character of socially dangerous act crimes against persons (50%) (murders, infliction of bodily harm of varying severity) ( $p<0,05$ ), of which 80% was directed at persons of the nearest neighborhood and relatives, statistically dominated. Most often the offenses were committed by negative personal mechanisms and were situationally provoked (46, 4%), rarer by productive psychotic mechanisms with delusional motivation (21, 4%), with paraphrenic delusion – in 33,3% of cases. In 53, 3% of the patients signs of an active process, a psychotic stage of the disease were noted which determined specific criminality of the patients. However in 33, 3% of the examined patients we revealed reduction of productive symptomatology with delirium fragmentation, directed at specific individuals, the loss of affective saturation, disactualization, delusional ideas encapsulation, manifestations of schizophrenic defect highlighted in the clinical presentation. All the examined were recognized insane by the court in relation to their alleged acts and they were administered a compulsory treatment in a specialized mental hospital (60%) and in a general type mental hospital (20%); ( $p<0,05$ ).

The average age of **Group 2** patients at registration in the psychoneurological nursing home



(PNHI) was 51,8 years, more often the patients were placed into a nursing home because of unwillingness of relatives and friends to exercise proper care and supervision of patients, because of contentious relations between them (40%); 30% of patients, living alone, ran into difficulties in household use and needed help. 10% of patients were registered in the psychoneurological nursing home (PNH) by their own free will, “not to disturb close people”. The average length of stay in a PNI was 10.9 years. During the stay in the psychoneurological nursing home (PNI) in most patients older than 50 years exacerbations of schizophrenic process were not noted. Their mental state was characterized by the manifestation of mental automatism syndrome (40%), affective-delusional syndrome (20%), and asthenic-depressive syndrome (20%). In 60% of cases reduction of productive symptomatology with the absence of further complications was noted ( $p<0,05$ ), age-specific themes of psychopathological symptoms appeared (ideas of material and moral damage, jealousy, petty sabotage), which were aimed at individuals of immediate environment; fragmentary, lacking in affective saturation delusions of grandeur, of a particular value with hyperthymic background mood were revealed. In general delusions determined the patients' behavior to a lesser extent. The majority of the patients (60%) did not seek any activity ( $p<0.05$ ); in 20% of the examined patients the state of deep defect was noted. However in 30% of patients their behavior became more organized, they became more active, more sociable, part of the patients began to get involved in work processes within the psychoneurological nursing home (PNH), to participate in public events (in sports competitions, lessons with a teacher, psychologist, to attend cultural events).

The results obtained comparing the clinical and social characteristics of two groups of schizophrenic patients with long-term catamnesis largely coincide with those of other studies cited in justifying the actuality of the work [1, 4, 5, 9, 10, 13]. The behavior of elderly patients with the selected psychopathology, as decades ago, mainly depends on a complex of factors: clinical dynamics and phenomenological registration of the condition, on the response to therapy, its adequacy as well as microsocial situation. In a number of cases staying at psychoneurological nursing home (PNH) eliminates a number of conflicts that are meaningful to patients and ensures optimal monitoring and treatment. With continued research material processing using the Fisher test and Spearman's rank correlation is planned.

### Conclusions:

1. If a person is aged over 50, the schizophrenia does not always proceed negatively with the processes of malignant course, with rapid onset of hallucinatory-paranoid syndromes and paraphrenia, cases with relatively slow progredience of the process, with long-term neurosis-like or psychopathy-like stage with a relatively shallow positive and negative disorders are observed.





2. Paranoid schizophrenia in later life with a relatively favorable course is characterized by a rare hereditary load of ascent and in the generation of patients, by the prevalence in the premorbid of schizoid and hysterical character traits with hypersthenicity, monotonous activity, narrow-mindedness, but also with productive and even creative activity in one-way direction, as well as by relatively scarce productive symptomatology (more often in the form of reduced paranoid syndrome), with minor perceptual disturbances.

3. After the long treatment in cases of paranoid schizophrenia, if a person is aged 50 and over, subjective and objective improvement of the condition is possible, including subjective and objective improvement of life quality, decrease in actuality of productive symptoms, stabilization of present negative symptoms (schizophrenic defect).

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**P.I. Zakharov, V.S. Petrov, V.S. Popov, T.Y. Tomskaya**

## **ON THE QUESTION OF SURGICAL TREATMENT OF THE ACQUIRED HEART DISEASES**

Research of the surgical treatment results of patients with single (n-221) and multiple (n-269) valve heart defects has shown that risk factors of patients with single and multiple valve defects equally influence surgery outcome; and presence of two or more risk factors significantly increases the risk of hospital lethality.

**Keywords:** single and multiple valve defects, risk factors, acquired heart diseases, qualitative and quantitative indicators.

### **Introduction**

Operations on heart valves belong to the hi-tech treatment methods demanding high financial expenses, corresponding hardware, implanting materials (artificial limbs, endoprotheses, patches, etc.). It should be noted that the lethality at surgical correction of the acquired heart diseases (AHD) remains to be at a high rate and reaches today in single-valve correction – 5,0%, in multi-valve correction – 8,0% (according to the cardiovascular surgery commission of advisory board of Ministry of Health of the Russian Federation – 2011). Therefore, the relevance of studying the problem of surgical treatment of AHD becomes obvious.

**Research objective** – to study features of clinical progression and ratio of single- and multi-valve heart diseases in the north, as well as influence of risk factors on outcomes of surgical treatment of AHD.

### **Materials and methods**

This article shows the results of surgical treatment of 490 patients with AHD in the Cardiac Surgery Department of the State budget institution of Republic of Sakha (Yakutia) “Republic hospital № 1 – National Medical Centre” in the period of 2006 to 2011.

Etiological factors of valve diseases were congenital heart diseases – 18 (3,67%), infectious endocarditis (IE) – 98 (20,00%), rheumatism – 283 (57,76%), sclerodegenerative disease of valves – 51 (10,41%), congenital dysplasia of connecting tissue – 34 (6,94%), ischemic heart disease (IHD) - (1,22%).

Average age of the operated patients in various etiological groups was as follows: rheumatism – 56,2; infectious endocarditis – 41,2; sclerodegenerative disease of heart valves – 67,4; congenital dysplasia of connecting tissue – 37,3; congenital heart diseases – 39,7.

Distribution of patients by types of diseases is given in table 1.

All operated patients were divided into two groups: I – group of patients after single-valve correction (221 – 45,1%), II – group of patients after multi-valve correction (269 – 54,9%). The detailed characteristics of both groups are shown in table 2.

All operations were executed by standard technology via the median sternotomy in the conditions of artificial blood circulation and cardioplegia with the use of cold cardioplegic solution at a moderate or deep hypothermia.

## Results and discussion

The results of comparative analysis of quality indicators of the patients discharged from the hospital and the patients deceased in the hospital with one-valve correction point to the following factors of high risk: heart failure (HF) of the 3<sup>rd</sup> or 4<sup>th</sup> functional class (FC), repeated operation, pulmonary hypertension (PH) of the 3<sup>rd</sup> or 4<sup>th</sup> degree, hemorrhage in the postoperative period, pulmonary embolism (PE) in anamnesis, acute kidney injury (AKI) in the postoperative period (see tab. 3).

The analysis of quantitative indicators of the same group shows that high risk factors are initially low level of the ejection fraction (EF), increased level of creatinine, time of the artificial blood circulation (ABC) and time of aortic compression (see tab. 4). These data correspond with the results of many researchers [1,2,5].

The results of the main quality indicators analysis of the group of patients with multi-valve correction also correspond with the results of research of patients with single-valve correction, i.e. high risk factors remain the same: HF of the 3<sup>rd</sup> or 4<sup>th</sup> FC, repeated operation, PH of the 3<sup>rd</sup> or 4<sup>th</sup> degree, hemorrhages, PE in anamnesis, AKI (see tab. 5).

The research results of the main quantitative indicators of patients with multi-valve correction agree with the results after single-valve correction (see tab. 6). Thus, high risk factors in multi-valve correction are low level of EF, nephratony, duration of time of ABC and aortic compression. These results correspond with the data of the majority of researchers [1, 3, 4].



## Conclusions

Thus, our research and observation results show:

1. High percent of patients with multi-valve defects in the advanced stage of heart failure of the 3<sup>rd</sup> and 4<sup>th</sup> FC., which is a regional feature in connection with the extreme geo-climatic conditions and lack of the transportation infrastructure in the remote regions of the North.
2. Risk factors among patients with single- and multi-valve defects equally influence surgery outcomes.
3. Presence of two or more risk factors sharply increases the risk of hospital lethality.
4. In the conditions of the North it is necessary to diagnose heart diseases as early as possible.

This can be achieved by organizing mobile teams via air medical service.

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Table 1

## Distribution of the operated patients by types of defects

	Type of valve defect	Number of patients	Percent from general group
1	Isolated defect of mitral valve: a) with prevalence of stenosis b) with prevalence of insufficiency	137 81 56	27,96% 16,53% 11,43%
2	Isolated defect of aortic valve: a) with prevalence of a stenosis b) with prevalence of insufficiency	84 62 22	17,14% 12,65% 4,49%
3	Multi-valve defects: a) mitral-aortic defects b) mitral-tricuspid defects c) mitral-aortic-tricuspid defects	217 65 81 71	44,29% 13,27% 16,53% 14,49%
4	Combined defects of valves and coronary arteries: a) mitral defect and coronary pathology b) aortic defect and coronary pathology c) multi-valve defects and coronary pathology	52 7 12 33	10,61% 1,43% 2,45% 6,73%

Table 2

## Comparative analysis of patients in both groups

Indicator	Group I n = 221	Group II n - 269
Average age of patients	52,1 лет	55,4 лет
Men	103 (46,61%)	142 (51,79%)
Women	118 (53,39%)	127 (47,21%)
FC of HF (NYHA)		
FC 1	15 (6,79%)	4 (1,49%)
FC 2	54 (24,43%)	103 (38,29%)
FC 3	150 (67,88%)	141 (52,42%)
FC 4	2 (0,90%)	21 (7,80%)
Initial PH		
Degree 1 – 2	181 (81,90%)	194 (72,12%)
Degree 3 – 4	40 (18,10%)	75 (27,88%)
Atrial fibrillation	117 (52,94%)	204 (75,83%)
PE in anamnesis	4 (1,81%)	24 (8,92%)
Hypertensive disease	107 (48,42%)	137 (50,93%)
IHD	24 (10,86%)	28 (10,41%)
Left ventricular hypertrophy	98 (44,34%)	143 (53,16%)
IE in anamnesis	57 (25,79%)	47 (17,47%)

Table 3

Comparative qualitative indicators of discharged and deceased patients of group I

Indicators	Discharged patients (n – 216)	Deceased patients (n – 5)
Men	101 (46,76%)	2 (40%)
Women	115 (53,24%)	3 (60%)
Average age of patients	51,9	54,8
FC of HF (NYHA)		
FC 1-2	68 (31,48%)	1 (20%)
FC 3-4	148 (68,52%)	4 (80%)
Original operation	201 (93,06%)	2 (40%)
Repeated operation	15 (6,94%)	3 (60%)
Left ventricular hypertrophy	97 (44,91%)	1 (20%)
Degree of PH		
Degree 1-2	180 (83,33%)	1 (20%)
Degree 3-4	36 (16,67%)	4 (80%)
Thromboembolism in anamnesis	2 (0,93%)	2 (40%)
Hypertensive disease	105 (48,61%)	2 (40%)
IHD	22 (10,19%)	2 (40%)
IE in anamnesis	56 (25,93%)	1 (20%)
Coronary failure in postoperative period	5 (2,31%)	1 (20%)
Hemorrhage in postoperative period	7 (3,24%)	2 (40%)
AKI in postoperative period	2 (0,93%)	3 (60%)

Table 4

Comparative quantitative indicators of patient group after single-valve correction

Indicators	Discharged patients	Deceased in immediate postoperative period
EDD of LV (mm)	56,77	62,63
ESD of LV (mm)	39,13	49,93
Left atrium (mm)	53,27	61,21
EF of LV (%)	55,34	37,84
Creatinine (mg/ml)	88,15	116,40
Time of ABC (min.)	92,05	116,38
Time of aortic compression (min.)	58,38	82,58

Table 5

## Main qualitative indicators of patients with multi-valve correction

Indicators	Discharged patients (n – 256)	Deceased patients (n – 13)
Men	137 (53,52%)	5 (38,46%)
Women	119 (46,48%)	8 (61,54%)
Average age of patients	53,2	58,9
FC of circulatory failure		
FC 1-2	105 (41,02%)	2 (15,38%)
FC 3-4	151 (58,98%)	11 (84,62%)
Original operation	235 (91,80%)	8 (61,54%)
Repeated operation	21 (8,20%)	5 (38,46%)
Left ventricular hypertrophy	136 (53,13%)	7 (53,85%)
Initial PH degree		
Degree 1-2	190 (74,22%)	4 (30,77%)
Degree 3-4	66 (25,78%)	9 (69,23%)
Initial atrium fibrillation	191 (74,61%)	13 (100%)
Thrombembolia in anamnesis	18 (7,03%)	6 (46,15%)
Hypertensive disease	133 (51,95%)	4 (30,77%)
IHD	24 (9,38%)	4 (30,77%)
IE in anamnesis	45 (17,58%)	3 (23,08%)
Coronary failure in postoperative period	5 (1,95%)	3 (23,08%)
Hemorrhage in postoperative period	14 (5,47%)	8 (61,54%)
AKI in postoperative period	4 (1,56%)	8 (61,54%)

Table 6

## Main quantitative indicators of patients with multivalvate correction

Indicators	Discharged patients	Deceased in immediate postoperative period
EDD of LV (mm)	56,3	62,4
ESD of LV (mm)	38,2	45,3
Left atrium (mm)	57,3	64,5
EF of LV (%)	54,3	46,7
Creatinine (mg/ml)	84,5	112,8
Time of ABC (min.)	115,8	169,9
Time of aortic compression (min.)	82,5	97,8

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## Practical Experiment: The Use of Biological Glue Made of the Local Material for Wound Healing

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**Abstract:** The article shows the results of experimental studies of biological glue invented based on the sturgeon swimming bladder. The glue composition and its gluing ability in connecting strips of natural skin was studied using the IR-spectroscopy; the glue structure was studied using the methods optic and atomic force microscopy. We have the planimetric research results gained from the skin wound experimental model held on laboratory animals using the invented tissue adhesive. We found that covering the wound with a biological filter with medical fillers gives a good adhesion on the top of the wound. There is no irritating effect and it stimulates the dermatic wounds' healing process.

**Keywords:** biological glue, sturgeon swimming bladder, skin wound surface, experiment.

### Introduction

At present medical tissue glues of different nature are actively developed and introduced, making revolutionary changes in surgery [4,6]. Nevertheless the existing glue has its own advantages and defects. In particular, biological glues on fibrous base do not bear high power, syntetic glues are toxic from the point of histology, are weakly clamped with human tissues. The above mentioned defects of tissue glues limit the possibility of the using these composition in surgery. All stated is indicative of big urgency of the question of the development new optimum physiological active non-immune composition for increasing efficiency for surgical technology and conservative treatment, stimulates the conducting of joint studies among chemists, morphologists and surgeons.

Recently the treatment of skin wounds became actively developed and introduced the biodegrading materials on the base of biological polymer - collagen, gelatine, chitosan. The main advantage of these data material is high adsorbing ability, high adhesive in wound, absence of toxicity and irritating actions, favourable influence upon healing processes of the skin. The available literature has little studies on using biological composition on the base of fish collagen in wounds treatment. The works by V.I. Lukiyanenko shows that fish glue completely consists of collagen, related to human collagen [1,2,3,7].

So then we chose biological polymer from swimming bubbles of north sturgeon fish for making tissue glue. For a long time the people of sakha used sturgeon as food, boiled the glue from their air bladders, used them for glueing together timber, pasting skins of the deer to ski and other home necessities, as well as in ethnic medicine.

Purpose of the study: the working of biological tissue glue on the base of swimming bubbles of the north sturgeon fish and conducting of experimental treatment studies of skin wounds among animals.

In accordance with the target goal the following problems were defined:

To create the technology of making materials and compositions on the base of biopolymer (collagen of Siberian sturgeon swimming bladder).

To study a chemical composition as well as physical and chemical properties of biological composition material.

To model the dermal wound surface of experimental animals.

To research the influence of new-made tissue adhesive, based on biopolimer, on the repairing

process of the dermal wound surface of experimental animals.

### Materials and testing methods

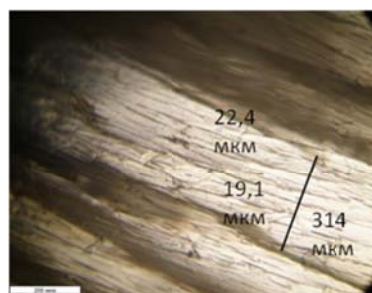
The experimental research included several stages: the first stage was to study a chemical composition as well as physical and chemical properties of biological composition material of Siberian sturgeon swimming bladder. The second stage was to create the technology of making materials and biological films on the base of the fish collagen. The third stage consisted of experiments on animals. The laboratory rats weighing 180-220 grams served as test animals. All of them were females since they have less coarse undercoat. All experiments were made under ether anesthesia according to "The rules of work with experimental animals". Before the experiment, during a week, all the animals were kept in a special room of the North-Eastern Federal University Medical Institute for the new conditions adaptation. They had a standard food ration with a free access to food and water. All the animals were weighed beforehand. They also underwent a close medical examination. The ill animals did not participate in the experiment.

The experimental model of the dermal wound was made after thorough shaving the upper dorsal part of the animal body. The boundary of the future wound was made with a marker in the interscapular region. Then the skin of the animal was cut with the lancet up to subcutaneous fat. Two kinds of biological films were made to study the repairing ability of the new-made biological glue on the base of the collagen of Siberian sturgeon swimming bladder: the first one did not have any medical components, while the second kind had medical additives of dymethylsulfoxide, calcium chloride, glycerin. The animals were divided into three groups. The first group was the control one, with experimental dermal wound surface without correction; the second group was a trial group, in which the wound surface was covered with a biological film without medical components; the third group was a trial group, in which the wound surface was covered with a biological film, containing medical components.

To estimate the repairing effectiveness, the thorough dynamic trial observations of the animals' general state, the local flow of the wounding process, the repairing path of the wound were held. The experimental model of the dermal wound was investigated on the third, seventh, tenth, seventeenth, twenty third days from the beginning of the experiment. The clinical judgement of the results was made on the base of dynamic visual and planimetric approaches. To calculate the daily speed of the wound surface reduction the formula, suggested by L.N.Popova in 1942, was used:  $V = (S - S_n) \times 100 / S \times t$ , where  $S$  is the value of the wound surface at the previous sizing,  $S_n$  is the value of the wound surface at the moment of the next control,  $t$  is the number of the first and the last measurement [5].

### The result of the research

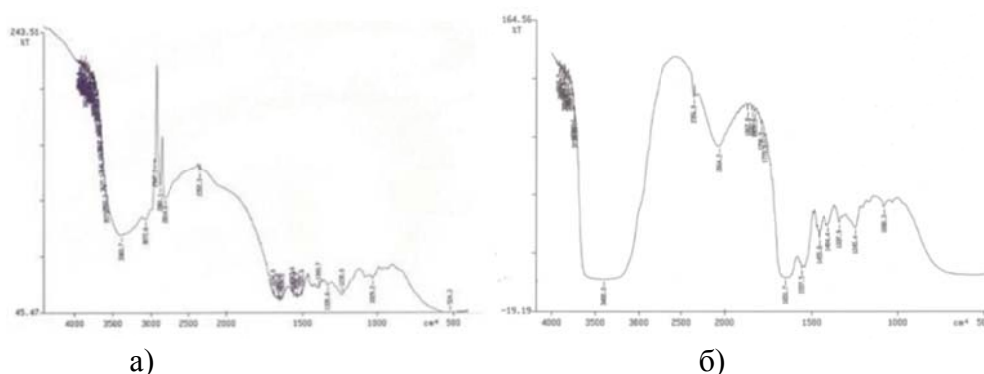
The fish swimming bladder almost completely consists of pure collagen. Collagen is a fibrous protein, the basis of the animals' connective tissue that makes it durable and elastic; it makes up about 1/3 of the total amount of all the proteins in an organism. It supports the extracellular frame of all the metazoan animals and it is a component of any animal tissue [4]. On the microscopic photos that we took on an optical microscope Olympus Bh-2, we can point out single collagen fibrilla, 19-23 microns in size, that are group in tracts in the form of fiber from 300 to 400 microns in size (Fig. 1).



**Figure 1.** The structure of a sturgeon swimming bladder, taken on an optical microscope (1-200 microns).

As the results of the atomic and absorption analysis show, in our research of the swimming bladder, the concentration level of heavy metals did not exceed the maximum allowable concentration, i.e., it can be used in contacting with the human body.

As for the chemical composition, the glue made of sturgeon swimming bladder is an aqueous solution of the protein collagen, the polymer molecule of which consists of over 20 amino acids. In the spectra of the swimming bladder and glue, taken from an IR-spectrometer Paragon-1000, there were a great number of relatively strong absorption bands that, as a rule, belong to the vibrations of the peptide group, the common structural element of the protein molecules. In the swimming bladder at the range of  $1660,1 \text{ cm}^{-1}$  there is a strong band that belongs to the CO group valence vibration and is called amide I; also at the range of  $1510\text{-}1570 \text{ cm}^{-1}$  the amide II band can be seen. The amide I and amide II bands show that there is  $\alpha$  – spiral. In comparing the spectra of the swimming bladder (native collagen) and glue made from it (denaturated collagen) there was seen a disappearance of the absorption bands amide I and amide II, i.e., there is a complete destruction of the  $\alpha$ -spiral, which happened due to denaturation of native collagen during thermal treatment (Fig.2).



**Fig. 2.** IR spectra of the sturgeon swimming bladder (a) and glue from it (b)

In order to evaluate the adhesion ability of the produced glue, there were model experiments carried out on the sample of natural skin, glued sheets by created glue and glue BF-6. The glue BF-6 is an alcohol solution based on polyvinyl butyral and bakelite varnish, which is one of the most famous types of medical glue in Russia, based on synthetic polymers. The force of delamination of the premature glued sheets was defined in accordance with the Unified State Standards №6768-75 “The method of defining the force of connecting between to sheets during delamination”

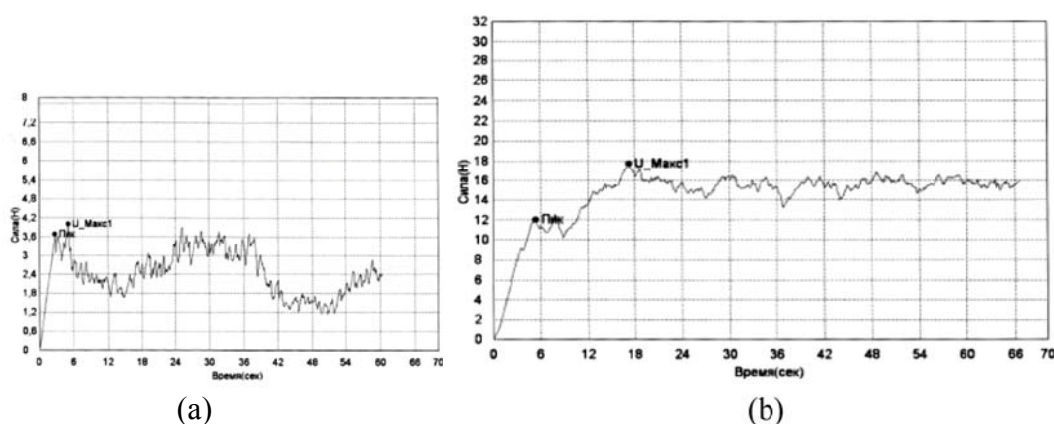
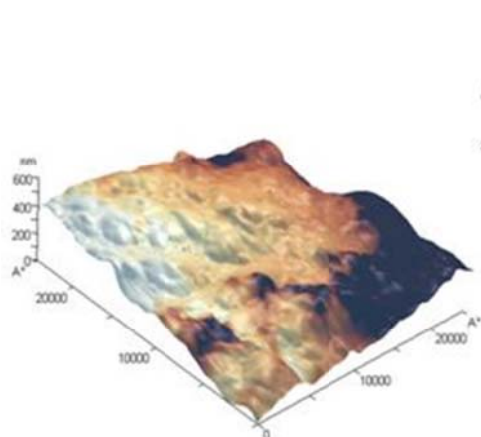


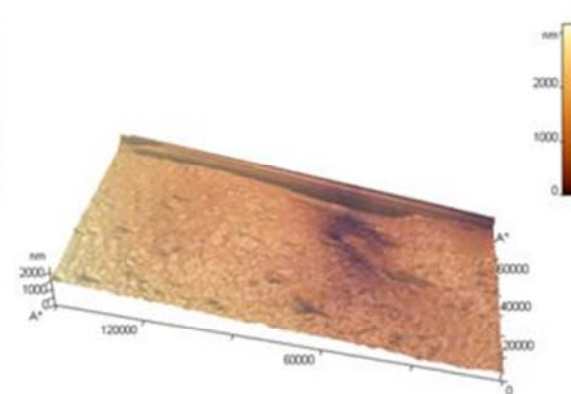
Fig. 3. The correspondence of the BF-6 glue specimens' connecting force ( $H$ ) to the time (a) and the swimming bladder glue (b).

The analysis of the force of delamination of the samples (table 1), glued together using medical glue BF-6 (Fig.3,a) and the glue made from swimming bladder (Fig.3,b) shows that the produced glue has a high gluing ability. When the samples of natural skin were glued together, the force of delamination of glue made from swimming bladder was 4.5 times higher, than the same rate for medical glue BF-6.

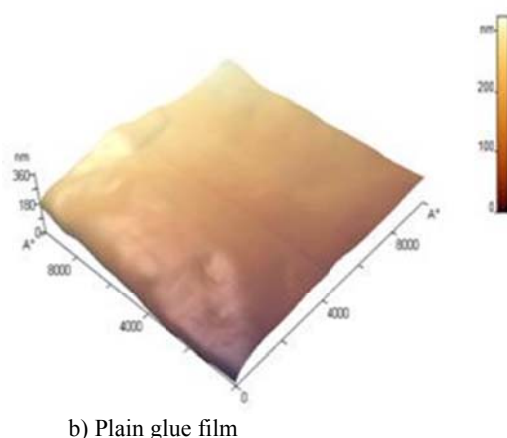
Studies of the collagen structures and its changes during the glue preparations using the method of atomic force microscopy show that there is a difference in the surface texture of the different component film samples in comparison with the initial swimming bladder (Fig.4). On the other hand, the surface of the swimming bladder is more embossed (Fig.4, a) and it corresponds to the fibrillar structure, which in turn, corresponds well with the optic microscope data. After a thermal treatment the structure of the films is amorphous, which corresponds to the collagen's transition into gelatins (Fig.4,b). The introduction of medical components does not influence the gelatin structure and the other qualities of the films practically, but the glue stickiness increases. (Fig.4,c).



a) swimming bladder



c) film made of glue, glycerol, dimethylsulfoxide and  $\text{CaCl}_2$



**Fig. 4.** Illustrations of the swimming bladder surface texture and different component film samples based on the initial swimming bladder in 3-D mode, that was made using AFM.

We held a through dynamic and visual research and observed the general state of the animals, the local wound appearing and healing process, in order to evaluate the effectiveness of the cure. On the third day of the experiment we observed that the first (or the control) animal group without the cure had a thin half-transparent red-colored layer, covering the wound and the skin adjoining the edges of the wound was swollen and congested. We also noticed a curved pink-colored interface 1 mm wide around the perimeter of the wound, which demonstrates the beginning of the boundary epithelialization process. The wound surface decreased by  $43 \text{ mm}^2$ , which gives an area  $98.27 \text{ mm}^2$ . In the same time period, the second animal group's wound is covered with the biological maroon filter with the medical components. The biological filter is hard and curved. The skin, adjoining the wound has no visible pathologies. There is a vivid pink interface, 1 mm wide around the perimeter of the wound. The wound surface decreased slightly (from  $141\text{-}109.5 \text{ mm}^2$  correspondingly) in comparison with the first day. The wound of the third group of animals is covered with biological filter with medical components. It is non-curved, maroon and there is a pink interface, 1 mm wide, which also shows the beginning of the regeneration phase process. The wound surface decreased by  $49.46 \text{ mm}^2$ , which makes up  $91.84 \text{ mm}^2$ .

On the seventh day of the experiment, the wound surface of the first (control) group was covered with a hard maroon wound crust. There is a pink interface around the perimeter of the wound, 2mm wide. There is small swelling and congestion remaining in the adjoining tissue. The area of the wound was  $43.55 \text{ mm}^2$ , which is  $54.72 \text{ mm}^2$  smaller, than on the third day. The wound of the second group of animals was closed by a thin curved maroon layer. There is a vivid pink-colored strip, 3 mm wide around the perimeter of the wound. The wound surface decreased from  $109.5 \text{ mm}^2$  to  $52.35 \text{ mm}^2$  in comparison with the third day. A flat thin maroon layer covered the wound of the third group of animals with a biological filter, modified by medical components. There is a pink interface 3-4 mm wide around the perimeter of the wound. The wound surface decreased from  $91.84 \text{ mm}^2$  to  $38.85 \text{ mm}^2$  in comparison with the third day.

On the tenth day of the experiment the base of the wound defect of the first group is under a thin hard curved maroon wound crust, which can be easily removed with a lancet. Underneath it, there is a wound surface, covered by a transparent red-colored layer. If the wound was slightly damaged, there was a strong punctuate bleeding. The adjoining tissue has no visible pathologies. The wound surface area decreased from  $43.55 \text{ mm}^2$  to  $17.89 \text{ mm}^2$  in comparison with the seventh day. The wound of the second group of animals with a biological filter without medical components is covered with a thin flat maroon layer; the layer is adherent with the wound surface. There is a small strip of scar tissue around the border of the wound. The are of the wound surface decreased insignificantly in comparison with the control and the third group and it is  $40.42 \text{ mm}^2$ . The wound



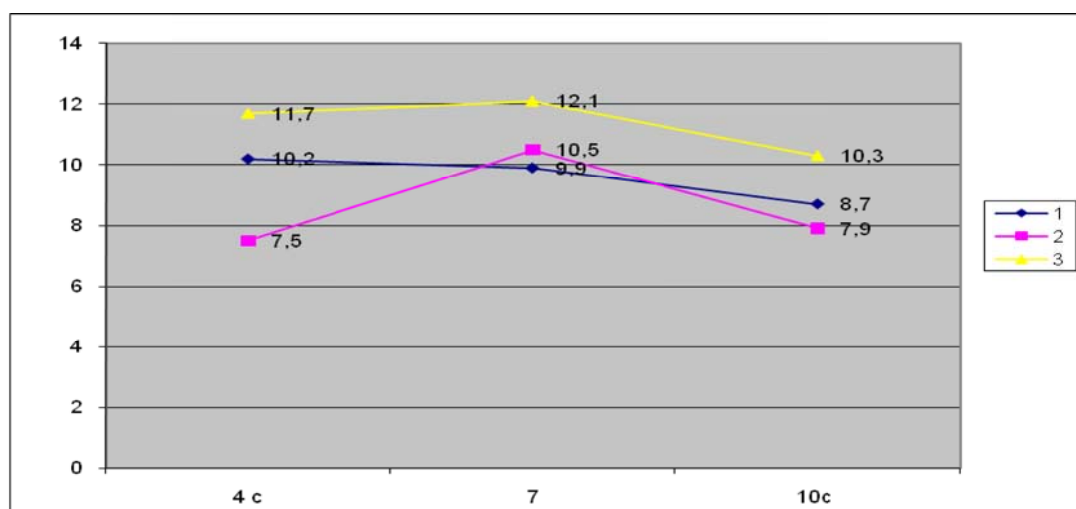
surface of the third group of animals with a biological filter modified by medical drugs, is covered with a thin flat maroon layer, which is adherent with the wound surface. There is a light-pink strip, 4 mm wide around the contour of the wound. The width of the wound corresponds visibly to the epithelium of the intact dermatic surface, which shows the beginning of border epithelialization. The area of the wound surface decreased to 10.59 mm<sup>2</sup>, which is 7.3% less, than the one of the control group and 29.8% less, than the second group.

Table 1. The area of the wound surface in the different time limits of the experiment (in mm<sup>2</sup>)

Group No	The wound area on Day 1	The wound area on Day 3	The wound area on Day 7	The wound area on Day 10
I	141.3	98.3(30.5%)	43.6(69.2%)	17.9(87.3%)
II	141.3	109.5(22.5%)	52.4(62.9%)	40.4(71.3%)
III	141.3	91.8(35%)	38.9( 72.5%)	10.6(92.5%)

The analysis of the daily speed of the dermatic wound healing among the groups of animals under study, showed that in the third group of animals with a biological filter, modified by medical fillers, the figures are bigger, than the in the control group without corrections and in the second group of animals with a biological filter without medical fillers. On the third day of the experiment, the wound healing speed in the third group was 11.7% per day, whereas the figures showed 10.2% per day for the control group and 7.5% per day for the second group. Provided that, we can see that the wounds of the animals of the second group heeled slower on the third day, than the ones of the control group. On the seventh day of the experiment the third group figures were also higher, that is 12.1%, whereas the control group had only a rate of 9.9% and 10.5% for the second group of animals. On the tenth day of the experiment, the daily wound healing speed was 8.7% for the control group. The third group with the biological filter, modified by medical components had the highest rates (10.3%) in comparison with the control group and the group of animals with biological filters without medical components.

Diagram 1. The dynamics of the experiment animals' daily wound healing





In conclusion, the visual observation and planimetric figures analysis of the experiment wound surface showed that covering the wound with a biological filter with medical fillers shows good adhesion. There is no irritating effect. The filter also stimulates the dermatic wounds healing processes and gives a basis for further experiments.

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Optimization of treatment of lumbar intervertebral disc hernias complicated with resistant compression- radicular syndrome using laser puncture sequester vaporization method

Osteochondrosis is one of the most frequent diseases of the musculoskeletal system. The conservative therapy has short period effect, because it doesn't remove the cause of the discogenic compression. The usage of laser puncture intervertebral discs reconstruction with simultaneous sequester vaporization method at the treatment of complicated forms of lumbo-sacral dorsopathies was investigated. It was revealed that the application of the method in most cases lead to the pain decrease, extension syndrome disappearance, radicular sensory disorders and motorical radicular prolapses disappearance. In 92, 9% of cases the total disappearance of orthopedic violations was noticed.

**Keywords:** laser disk reconstruction, sequester vaporization, lumbo-sacral dorsopathies.

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**Kudrina P. I.**

## **NEUROPSYCHOLOGICAL RESEARCH OF PATIENTS WITH CEREBROVASCULAR PATHOLOGY**

In article results of research of cognitive functions of the patients, with different variants of a cerebrovascular pathology (CVP) are reflected, depending on residing region. At comparison of research results of cognitive functions of CVP patients it was revealed that the patients more often had distresses connected with memory, attention and concentration disorders, herewith the patients of the Arctic zone who had the good ecological situation, had these disorders on rare occasions. In comparative-group ratio moderate prevalence of the specified distresses was marked in the inhabitants of Viljuisky region, which was known by the bad ecological situation.

**Keywords:** cerebrovascular pathology, region, memory, attention, elderly and senile age.

### **Introduction**

There are number of infringements of mental activity, besides focal neurologic distresses, in clinical displays of vascular insufficiency of brain blood circulation, both sharp, and chronic. These distresses are expressed in the form of implications of neurosis-like character against falling of mnestic-mental abilities; they can accrue to degree of the expressed psychiatric syndrome.

Each certain geographical region, each ethnic group of the population defines their own 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 [1]. Studying of a cerebrovascular pathology which representatives of elderly and senile age have, especially taking into account regional-ethnic factors, represents doubtless scientific and practical interest and has a special value for perfection of quality and efficiency of rendering of medical aid to older persons.

**Research objective** is to conduct neuropsychological research of cognitive functions of patients of elderly and senile age with a cerebrovascular pathology and who live in different regions of republic.

### **Material and research methods.**

197 patients with CVP have been surveyed, among them 79 patients with ischemic strokes (IS) in carotid pools, 118 patients with a chronic ischemia of brain (CIB), in other words discirculatory encephalopathy; DE of I stage (DE-I)-52, with DE of II stage (DE-II)-66 patients. During supervision all patients have been hospitalized in a neurology unit of the Geriatric

Center (GC). Criteria of statement of the diagnosis was clinically and instrumentally confirmed lesion of vessels of a brain at a corresponding clinical picture. Concerning the purpose patients have been subdivided into two groups: the basic, including 2 subgroups, and control. Criteria of division of a basic group into subgroups was the residing region. The basic group was made by 140 patients at the age of 60-85 years. In the I subgroup was 67 patients living in the Arctic zone, in the II - 73 patients living in Viljuisky area. The comparison group has been presented by 57 patients with a similar pathology aged in a range of 35-55 years.

In the Arctic zone small northern nationalities, Evens live. They are engaged in reindeer breeding, cattle breeding, fishing. Old traditions of a food, quieter, traditional way of life and ecologically good situation remained here. A basis of a food of the population make a venison, horse meat of the Yakut breed and meat of native Yakut cattle which contain polynonsaturated fatty acids of family omega-3, omega-6 and the reproduction vitamin, possessing cholesterol reducing effect [2].

In the Viljuisky zone the developed ecological equilibrium has been broken, there were irreversible changes in environment, health of the people living in region suffered. Vilyui has the negative influence on a river basin by the Viljuisky water basin and chemical pollutants which are accustomed at industrial processing of constituents of diamondiferous kimberlite breeds consisting of aluminosilicate, calcium-magnesian and ferriferous breeds, oxides of the titan, chrome, nickel, magnesium and others(3).

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 histories, extracts, and inquiries. Results of the first and all subsequent inspections as one of problems of our work was research of dynamics of clinical displays of a cerebrovascular pathology depending on region were thus considered and compared. For the purpose of definition and specification of a stage of DE, the anamnesis, complaints of patients, a condition of the neurologic status by 11 parameters have been analyzed. In a complex of medical actions all patients spent the standard medicament therapy which intensity depended on prescription of pathological process. Complex rehabilitation actions were carried out for the patients with II [3,4,5,8].

The statistical analysis was spent on IBM-compatible computer with the use of programs Microsoft Excel, Statistica, Biostat with material processing on groups by means of the methods of variation statistics, including calculation of mean values, errors of averages, standard deviations. Nonparametric methods, in particular a coefficient of correlation of Sperman, the Mann-Whitney

test, are used also. The table quick test of Strelkov was applied at the primary statistics. For each sample of indicators counted numerical characteristics of distribution. An estimation of the importance of distinctions between compared samples carried out with use of a parametrical t-student criterion at 95 % a confidential interval [6].

### **Results of research and discussion.**

For an estimation of cognitive functions A.R.Lurija scale was used. The given research was based on techniques on which A. R.Lurija's was based [7] including research of memory the classical principles, attention, emotions, ability of storing and reproduction of figures, words, concepts of dynamics lie.

Patients above 70 years had heavier infringements of cognitive functions that is coordinated with the data of the literature [9,10]. Changes of the majority of the higher mental functions are revealed with these patients. Patients had one more experimentally-psychological testing. During memory research the verbal material was reproduced by the patient directly after its presentation, and then after concerning a short pause (till 1-3 minutes) which has not been filled with any extraneous activity ("an empty" pause). As symbols words (simple nouns) and two-valued figures were used. We used series from 10 words not connected with each other by semantic concepts and the figures which are not developing in one number. Norm signs were, first, the same order of reproduction of symbols and, secondly, consecutive increase of number of reproduced elements after "an empty" pause (table 1).

It is revealed that process of storing and reproduction of symbols had norm signs only with younger people (comparison group), and patients of a basic group considerably more often had the emaciation of attention and narrowing, decrease mnestic functions, its volume, possibly, connected with local damage of a brain and progressing points accordingly. It means that in the clinic of DE stages are of great importance irrespective of living conditions.

### **Conclusions.**

By means of a technique of learning 10 words they revealed volatile memory infringements (quantity of the words reproduced after the first presentation), efficiency of storing (total of the words reproduced in repetition) and a long-term memory (quantity of the reproduced words after 1 hour after a presentation) with construction of "storing curves». Research was spent with the use of known techniques of A.R.Lurija.

In the process of progressing of disease DE-II efficiency of storing was broken that was expressed in reduction of quantity of the reproduced words and increase of faster exhaustion in the course of storing in all basic groups.

Neuropsychological inspection revealed infringement of cognitive functions in the form of dysmnias and attention mainly with patients of elderly and senile age. As a whole neuropsychological inspection did not reveal clearly authentic group distinctions in relation to region and ethnic characteristics.

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#### Data of primary research of memory

Table №1

Groups of supervision	Average quantity of the reproduced symbols			
	Words		Numbers	
	Immediately	After a pause	Immediately	After a pause
I basic group				
II (n=29)	3,5*0,16	3,0*0,14	3,90*0,18	3,10*0,14



DE-I (n=16)	4,10*0,29	3,10*0,23	4,30*0,31	3,30*0,24
DE-II (n=22)	3,60*0,2	3,0*0,17	3,80*0,22	3,0*0,17
II basic group				
II (n=28)	3,0*0,14	2,70*0,13	3,20*0,15	2,90*0,14
DE-I (n=21)	3,60*0,22	3,01*0,18	3,77*0,23	3,0*0,18
DE-II (n=24)	3,30*0,18	2,90*0,16	3,10*0,17	2,80*0,15
Comparison group				
II (n=22)	7,60*0,43	6,60*0,38	7,51*0,43	6,32*0,36
DE (n=15)	9,0*0,7	8,60*0,66	8,80*0,68	8,10*0,62
DE (n=20)	7,78*0,48	6,1*0,38	7,20*0,45	6,80*0,42

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## Hygienic Safety and Nutritional Value of the Yakut Horse Meat

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Heavy metal content in meat of Yakut young horse was under study.

It was revealed that concentrations of Zn, Cu, Fe and Mn in the investigated samples of meat didn't exceed maximum concentration limit (San 2.3.2.560-96.) and corresponded to hygienic requirements. In the investigated samples of meat pesticides were not noted. Estimations of amino acid and vitamin content of horse meat from Oymyakonsky region testify to rather high food value in the studied samples.

Thus background indicators of meat toxic elements depend on such conditions of animal husbandry as local, natural, climatic, fodder, ecological and territorial.

**Keywords:** heavy metals, toxic elements, horse meat, the Yakut horse.

### INTRODUCTION

Manufacture of ecologically safe production of animal husbandry is of great significance nowadays in connection with man's uninterrupted technogenic influence on ecosystems and growth of natural circulation of chemical elements. The latter has considerably increased the heavy metal absorption into the environment and human body through food chains.

Various aspects of ecotoxic receipt into biological objects of the environment and foodstuff of animal origin were studied (Bojarchenko E.K., 1983; Hecht. H., 1984; Kabata-Pendias A., Pendias Kh., 1989; Kraczkowski N., 1993; Talanov G. A, 1994; Nezavitin A.G., 1995; Sagitov E.S., 1995; Malyarov M. A, 1996; Tjutikov S.V., 1997; Smirnov P. N, Pavlova A.I., 1997; Tairova A.R., 1999; Nezavitin A.G., V.L.Petuhov, Vlasenko A.N., 2000; Fomichev J.P., 2000; Donnik I.M., 2000; Gabysheva Z.A., 2001; Kalsina O. I, 2001; Kolesnikov V. A, 2003; Kashin A.S., 2003; Pasternak A.A., 2003; Gerunova L.K., 2003; etc.). The works conducted by authors have shown that the content of heavy metals in animal husbandry production considerably exceeds maximum permissible concentration and depends on a degree of ecological intensity and infringement factors of natural complexes where this production is made [2].

Ecological purity and safety of animal originated foodstuff which prevail in diet of a man

living in the north are considered one of primary factors of health protection of the population. The Yakut horse meat has a specific structure and properties, and is of great interest for manufacturing special foodstuff. Today the population of the republic consumes basically the young Yakut horse meat aged 6 months. For the last five years the average meat consumption amounts for 48 kg per year, relative density of horse-flesh makes 70 %.

Improvement of people's living conditions includes also considerable improvement of food quality. The problem of nutrition is important, being one of the basic programs of rehabilitation of the population in regions of high technogenic and anthropogenic loading. In order to increase the product manufacture for rehabilitation appointment, to create new kinds of medical, dietary and baby food it is necessary to expand raw zones and process new kinds of raw meat products. Considerably the influence of foodstuff depends on its raw content and properties. The meat content has accurate specific and pedigree features. Besides, the meat content is influenced by dwelling conditions, structure and properties of consumed forages [1].

## **MATERIALS AND METHODS**

The research conducted by us comprised the basis of this work within the accredited Yakut republican vet-test laboratory in 2009-2010.

61 muscular tissue samples of the young Yakut horse aged 6-7 months from Srednekolymsky, Eveno-Bytantajsky, Njurbinsky, Mountain, Ust-Aldan and Ojmjakonsky regions of the Republic Sakha (Yakutia) were analyzed in this work.

Meat sampling was carried out according to NATIONAL STANDARDS 9959-91, 7269-79 "Meat. Sampling methods, organoleptic methods of flesh estimation", and also "Rules of veterinary survey of lethal animals and vet-sanitary examination of meat and meat products" (1998).

Horse-flesh and meat products should correspond to requirements of sanitary-and-hygienic norms for food raw products and foodstuff, adopted by the Ministry of Health of the Russian Federation (medical and biologic, 1999), and a level of heavy metal concentration should be controlled according to sanitary rules (maximum permissible concentration, 1986).

The heavy metal compound, amino acids, pesticides and vitamins in the young Yakut horse muscular tissue (NATIONAL STANDARDS 30178-96) were determined by the atom-absorption spectrum photometric method (AAS) on the analyzer "Spectrum-5". The samples prepared with optimal solution-concentrate for AAS was carried out in the autoclave "Ankon-AT" (MI 2221-92).

## **RESULTS AND DISCUSSION**

As a result of the quantitative analysis conducted we established that in foals' muscular tissue from Srednekolymsky region the maximum concentration limit indicators on cadmium exceeded on 0,25 mg/kg, Njurbinsky region being higher on 0,09 mg/kg. The lead and cadmium content in animal muscular tissue from Gorniy region was above MCL on 1,08 and 0,06 mg/kg accordingly.

The higher concentration of zinc was 33,78 mg/kg and ferrous was 37,66 mg/kg in the young Yakut horse of Ojmjakonsky region as compared with other investigated tests. The high content of copper in the meat from Ojmjakonsky region (1,47 mg/kg) was revealed as well.

Concentrations Zn, Cu, Fe and Mn in the investigated tests of meat didn't exceed maximum concentration limit (2.3.2.560-96.) and correspond to hygienic requirements. In the investigated samples of meat no pesticides were revealed.

Our researches confirm the findings of the sanitary-and-hygienic monitoring lab in the Center of hygiene and epidemiology in the Republic Sakha (Yakutia). In 1995-2001 more than 150 tests of local horse meat (horse-flesh) production were investigated. According to the results of the laboratory researches the content of heavy metals in horse-flesh and its production varies in following limits: copper of 0,57-3,54 mg/kg – 4,03 mg/kg, zinc of 15,42 – 18,33 mg/kg, lead of 0,05-0,09 mg/kg, cadmium less than 0,0025 mg/kg wasn't revealed, arsenic of 0,05 mg/kg was not revealed, mercury of 0,0005 mg/kg was not revealed. So the content of heavy metal salts in samples of local manufactured horse meat and meat products weren't revealed or do not reach (don't exceed) maximum concentration limit level according to SanPin of 3/2/1078-) 1 «Hygienic requirements of foodstuff safety and food value».

Estimations of amino acid (Table 2) and vitamin content (Table 3) in horse-flesh from Ojmjakonsky region testify to higher food value of the samples studied.

## THE CONCLUSION

According to the studied data on the concentration of heavy metals in the young Yakut horse muscular tissue we have come to conclusion that background indicators of toxic elements in meat are subject to the local natural-climatic, fodder and ecological conditions of the territory of animal husbandry.

The studies showed that the young horse meat from Eveno-Bytantajsky, Ust-Aldansky and Ojmjakonsky regions has been considered ecologically valuable. The Yakut foal's meat from Ojmjakonsky region appeared to have fuller value by its amino-acid and vitamin content.

The table 1. The content of toxic elements in the young Yakut horse meat in the territory of



Republic Sakha (Yakutia).

Regions	Content of toxic elements mg/kg					
	Lead	Cadmium	Zinc	Copper	Ferric oxide	GXCG (a,b,y-isomers)
Srednekolymsky and	0,342	0,309	10,49	1,36	11,55	0
Eveno-Bytantajsky	0,090	0,018	12,68	0,83	8,97	0
Njurbinsky	0,060	0,010	11,33	0,80	11,40	0
Gorniy	0,063	0,148	13,93	1,60	14,47	0
Ust-Aldansky	1,580	0,056	14,13	1,11	7,03	0
Ojmkonsky	0,310	0,020	33,78	1,47	37,66	0
Max. San Insp	0,50	0,05	70,0	5,0	50,0	-

Table 2. Таблица 2. Amino-acid content of the young Yakut horse meat of ojmkonsky population, % (n=10)

Arginin	Lizin	Tirozin	Fenilalanin	Lejtsin	Metionin
10,02	8,89	7,27	7,32	22,39	2,92
Valin	Prolin	Treonin	Serin	Alanin	Glitsin
5,61	6,79	5,1	4,36	7,25	5,96

Table 3. Vitamin content of the young Yakut horse meat of ojmkonsky population, % (n=10)

A, мг/кг	D, мкг/100г	B6, мг/кг	B12, мкг/кг	Biotin, мкг/100г	Niazin мг/100г
3,34	2,13	3,45	4,68	3,85	4,47
B3, мг/кг	B2, мг/кг	B1, мг/кг	Bc, мкг/100г	E, мг/кг	
4,52	1,43	3,68	5,35	4,34	



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MAIN TENDENCIES IN THE IMPROVEMENT OF MEDICAL CARE PROVIDED TO  
PATIENTS WITH CHLAMYDIOSIS OF UPPER RESPIRATORY TRACT

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**Abstract:** At present the problems related to Chlamydia infection are concentrated not only on urinogenital diseases. At the same time optimal organization of measures against extra-urinogenital Chlamydiosis, including that located in respiratory tract, had not been worked out yet and requires immediate solutions. Based on recent and new data on respiratory Chlamydiosis, the present article represents scientific rationale for urgency of working out the complex of measures and main tendencies for improving the organization of medical care for the patients with upper respiratory tract diseases, associated with Chlamydia infection.

**Keywords:** Chlamydia infection of upper respiratory tract, medical care for respiratory Chlamydiosis patients.

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## CHRONIC VIRAL HEPATITIS IN YAKUTIA

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**Summary:** Republic Sakha (Yakutia) is unfavorable territory for the chronic viral hepatitis and their adverse outcomes, and proved the role of blood-contact viral hepatitis in the development of primary liver cancer.

**Keywords:** viral hepatitis, genotype, cirrhosis, primary liver cancer.

### Introduction

Viral hepatitis (VH) with parenteral transmission mechanism is one of the most urgent and serious problems of modern medical science and practical public health around the world. This is due to the widespread distribution and high incidence of VS in different populations, and the infection of people of working age by various forms of parenteral hepatitis. The total number of patients with chronic hepatitis B (CHB) and HBsAg carrier is about 5 million, the number of patients with chronic hepatitis C (HCV) and hepatitis C virus carriers - at least 2 million people (3, 5, 8, 10, 13, 14, 18, 19). According to datas of S.J. Nadziyannis (1997), the world's hepatitis D affected more than 10 million people.

Yakutia is a region of high spreading of parenteral viral hepatitis B, and hepatitis C, hepatitis D (HD) (2, 4, 15, 17). The level of chronic viral hepatitis has no tendency to decrease, infection rate in 2011 amounted to 1502.5 per 100 thousand of population and according to the reference center for supervision of viral hepatitis it is highest in the Russian Federation.

This unfavorable epidemiological situation is connected, in particular, with climatic and geographical features of the Far North. Severity of parenteral viral hepatitis, further their chronicity associated with the presence of immunodeficiency states, the frequency of which increases significantly in adverse environmental conditions, in particular, and is characteristic of the Republic of Sakha (Yakutia) (2, 12).

**The purpose of this study** was to investigate the prevalence of virus hepatitis by the parenteral transmission, their clinical course, and outcomes to improve a set of preventive and



curative measures.

### **Materials and Methods**

We used materials of official statistics of Territorial administration of Russia's Customer Control Dept. of Republic of Sakha (Yakutia) and the data of the Yakutsk Republican Oncology Center (Chief doctor Karataev P.D). Analyzed the incidence of chronic hepatitis B, C and D, as well as their outcomes in the Republic of Sakha (Yakutia) in the period from 1996 to 2011. Official statistics are not taken into account data on the incidence of chronic hepatitis D, and liver cirrhosis, so the retrospective analysis of hospital morbidity in the period from 2000 to 2011 is carried out, according the data of the department of viral hepatitis SBE of RS (Yakutia) «Yakut Clinical Hospital»(Chief doctor, MD N.N. Vasiliev).

At diagnosis takes into account the epidemiological, clinical and biochemical data, specific serological markers of viral hepatitis and molecular biological methods.

### **Results and discussion**

Epidemic situation in Yakutia in chronic viral hepatitis B, C and D is still actual. The incidence of newly diagnosed forms of chronic viral hepatitis B and C in the Republic of Sakha (Yakutia) greatly exceeds that in the Russian Federation, and this trend can be seen for the entire 10-year period, with the greatest difference in 2003-2005. (Fig. 1). In 2011, the Republic of Sakha (Yakutia) reported of 839 cases of chronic hepatitis, the morbidity level was 88.4 per 100 thousand of population.

Fig. 1. The incidence of newly diagnosed chronic viral hepatitis in the Republic of Sakha (Yakutia) and in Russian Federation according to the official registration (at 100 thousand of population)

In the structure of chronic viral hepatitis proportion of chronic hepatitis B (CHB) and chronic hepatitis C (CHC) was 39.1% and 58.9% accordingly. According to official statistics in 2011 registered 328 cases of chronic hepatitis B, the rate of 34.5 per 100 thousand of population, also the first time revealed the 494 patients with chronic hepatitis C, the incidence rate is equal to 52.0 per 100 thousand of population. (Fig. 2.)

Fig. 2. The incidence of chronic viral hepatitis B and C in the RS (Y) according to the official registration (at 100 thousand of population).

During the analyzed period, the highest incidence of chronic hepatitis B in Yakutia was in the period from 2003-2006, with a subsequent decrease to 34.5 in 2011, but in comparison with the

level of morbidity in the Russian Federation the republican index higher in 2.6 times (RF – 13.04 to 100 thousand of population). There is increasing of CHC morbidity, from 15.4 in 2000 to 52.4 in 2011, while the republican data is also higher than the federal 28.3% (RF - 40.2 to 100 thousand of population).

Along with the manifest forms of hepatitis B, there remains latent pathogen circulation, which leads to the formation of the hard-diagnosed infections.

As shown in Fig. 3, starting from 2000, marked a significant reduction of carrier state, which may be explained by the formation in this group of the active form of chronic HBV-infection and / or more in-depth diagnosis of chronic viral hepatitis in the present stage. By 2011, the rate of HBsAg carrier state in the RS (Y) decreased by 8.3 times (32.8 per 100 thousand of population), compared to 2000 (272.6 to 100 thousand of population). However, despite the positive dynamics, in general, their level in the Republic of Sakha (Yakutia) is high: in 2011 identified 315 carriers of hepatitis B virus, which is higher than Russia's to 49.2%.

Fig.3. Number of new cases of HBsAg carriers in the RS (Y) in comparison with the Russian Federation (to 100 thousand of population)

Registration of antibodies carriers to hepatitis C virus (Fig. 4) shows a significant reduction of the carriage on the background of a stable increase in Russia. Indicator of antibodies carrier to hepatitis C virus in the Russian Federation in 2007 exceeded 1.7 times the Republic of Sakha (Yakutia) data, since 2009 the official registration HCV-carrier does not exist: all patients with the presence of HCV as a person registered with the CHC.

Fig. 4. Indicators of antibody carrier to hepatitis C virus in the Republic of Sakha (Yakutia) in comparison with the Russian Federation (to 100 thousand of population)

Analysis of hospital morbidity of liver cirrhosis SBE RS (Yakutia) "Yakutsk Clinical Hospital", showed increase in chronic hepatitis in cirrhotic stage of viral etiology. Of particular concern is the detection of early liver cirrhosis with decompensation and signs of portal hypertension (ascites, anasarca, splenomegaly, esophageal varices) in young adults 18-39 years, leading to extreme disability and death. In the structure of hospital morbidity, chronic viral hepatitis in cirrhosis stage among all chronic hepatitis B was 37.5%, while it is 53% of the cause of cirrhosis is HDV-infection, 40% of patients had chronic hepatitis C and in 7% of patients the liver cirrhosis is developed on the background of chronic mono hepatitis B.

The Republic of Sakha (Yakutia), together with Buryatia, Tyva and the Tyumen region, is one of Russia's regions with the highest rates of the incidence of primary liver cancer (PLC). When comparing the incidence of liver cancer in the population of the Republic of Sakha (Yakutia) and Russia from 2000 to 2010, revealed their excess to 4-5 times in the RS (Y), compared with those of the Russian Federation (Figure 5).

Fig.5. The PLC morbidity of Sakha (Yakutia) population in comparison with the Russian Federation in the period from 2000 to 2010 (to 100 thousand of population)

For a correlational analysis to determine the relationship between the incidence of primary liver cancer and blood-contact viral hepatitis B and C analyzed data carriers of viral hepatitis B and C and the incidence of ГЛК due to medico-geographical zones of the Republic of Sakha (Yakutia).

The results of correlation analysis revealed a significant relationship between the incidence of liver cancer and carriage of HBsAg ( $r = 0.64$ ), antibody to hepatitis C virus ( $r = 0.47$ ) among the population of RS(Y). A medical-geographical zones of Yakutia have identified a direct middle connection in the west ( $r = 0.65$ ), in the center ( $r = 0.58$ ) and weak in polar Yakutia ( $r = 0.36$ ,  $p < 0.05$ ), in which recorded a high infection rate by virus hepatitis B. The frequency of primary liver cancer incidence depends on the level of infection in the population of viral hepatitis B, C and D.

### Conclusion

The study of long-term morbidity of hepatitis B, C and D in the Republic of Sakha (Yakutia) has allowed to specify the frequency of different clinical forms of the disease (chronic hepatitis, virus carriage, cirrhosis and liver cancer). Despite the decreasing of the incidence of acute forms of viral hepatitis B and C, a high level of registration of chronic viral hepatitis B, C and D is persists in population, indicating the wide circulation of these pathogens in Yakutia.

The primary liver cancer morbidity in the Republic of Sakha (Yakutia) is 4-5 times higher than the data of Russia.

Considering the high prevalence of viral hepatitis, rapid chronization with the outcome of cirrhosis and liver cancer, leading to early disability and death of a young working population, greater economic losses for the treatment of patients, there is a need to improve medical care of patients with chronic viral liver disease.

It is widely implemented in practical public health of standard computer programs to create register "Chronic viral hepatitis in the Republic of Sakha (Yakutia)" to correct assessment of morbidity scope, molecular genetic diagnosis and non-invasive methods for the determination of



liver fibrosis, chronic hepatitis with modern antiviral drugs to the eradication of the pathogen, as measures to prevent the development of cirrhosis and primary liver cancer.

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## ABOUT THE PROBLEM OF COMBINED FORMS OF HIV INFECTION AND HEPATITIS B AND C

A.A. Jakovlev, N.I. Lapteva

In the article the literature data on the results of virological, immunological and clinical studies of combined forms of HIV and hepatitis B and C are given. The necessity of a systematic approach to the study of co-infections and research on the population level of the epidemic process is shown.

**Keywords:** combined infection, hepatitis B and C, HIV infection.

Combined infection (synonyms: mixed infection, associated infection, satellite infection) - an infection caused by two or more kinds of microorganisms. It may be viruses, protozoa, fungi, bacteria, mycoplasmas, spirochetes, rickettsiae, chlamydiae. According to V. Pokrovsky [9] of mixed infection should say when the infective process caused by the first one, then the activator in various stages of (or in conjunction with the launch of the first) can be associated with infectious process different etiology. According to some reports in the structure of mixed infections account for up to 50% with viral etiology – up to 30% of cases [1]. The main outcomes were possible interaction of two or more agents in the process of mixed infections: 1) independent reproduction; 2) exaltation-increased reproduction of one and all associates; 3) interference-suppressed reproduction of one or all associates; 4) complementation - specific dependence of reproduction of one associates from another. The latter is especially prevalent in associations of oncogenic viruses [2].

One of the features of the modern period is the increase in infections in the structure of the infectious pathology of combined forms of different etiology [11]. However, the reason for this is understudied. According to A. A. Selivanov [10] the occurrence of infections of mixed etiology should be considered from the environmental perspective of interspecies, not just as a coincidence arising associates. It is important to emphasize that the vital strategy of viruses is the quest for survival and replication, which is a modification of the human immune system, a high rate of mutations (appearance of quasispecies). Perhaps a combination of viruses in one organism contributes to these processes [12]. By of studies A.A. Yakovlev, E.S. Pozdeeva combined infections is a factor contributing to the self-regulation systems in the generated antroparasitic system of biocenosis.

In the characterization of combined infection is important to the order of: simultaneous (coinfection) or serial (superinfection). In mixed infections when the body develops multiple



pathogens, the relationship is complicated mechanism of various pathological processes that are extremely difficult to timely diagnosis, etiological decoding and selection of optimal therapies [2, 4].

Development problems of mixed infections, including elucidation of interactions in microbial associations, including bacterial and bacterial (intraspecific, interspecific, intergeneric etc.), bacterial and viral, viral and viral, bacterial and viral with the simplest and other pathogens, the study mechanisms of pathogenesis and immunity, the development of diagnostic, immunization, treatment, risk factors, and role in the development of the epidemic process have independent theoretical and practical significance [2, 14]. It is important to emphasize that the problem of mixed infections should be considered in line with the developed back in the 30's of the last century the theory of parasitocenosis E.N. Pavlovsky, according to which in infectology be aware that in the patient parasites are in a complex and varied relationship between themselves and the host organism [8].

Viral hepatitis and HIV infection as separate diseases have a worldwide distribution and considerable social importance. This is facilitated by a single haemocontact mechanism of transfer for them, which is being actively implemented parenteral, sexual and vertical ways, especially groups with a high risk of infection from these infections [16, 34, 40]. Viral hepatitis B (HBV) and C (HCV), HIV infection are among the ten leading causes of death from infectious diseases in the world. R. Weber et al. [49] note that in the era of antiretroviral therapy for HIV infection of liver disease are 14.5% of deaths of patients of combined infection. Actual fatality rates from liver disease in HIV-infected persons, apparently higher than registered [17].

Also the increased risk of transmission of HBV, HCV and HDV vertical and sexually in the presence of concomitant infection with human immunodeficiency virus. In particular, HCV transmission from mother to fetus is observed in the 15 - 36% of cases of coinfection with HIV and not more than 5 monoinfection% of HCV, which may be associated with increased sensitivity to hepatotropic viruses with immunosuppressive conditions [13].

If HBV in patients with HIV infection is the leading reason for the liver disease, HIV infection after virus hepatitis B causes a high risk of developing chronic hepatitis B [7]. Among the 15,728 people living with HIV in 498 (8.7%) had HbsAg and 3.6-fold increase in deaths compared with HbsAg-negative patients [30].

Since the HB and HC, as well as HIV infection, have a common mode of transmission, coinfection is quite often and is becoming a serious public health problem in all countries of the world [6, 30]. Last 10 years mixed infection (HIV and parenteral hepatitis) have become



widespread in our country, as a result of additional risk factors for social and behavioural character [7]. Also there is a hidden currents, as evidenced by the HB only DNA detection of HB, anti-HBc, in the absence of HbsAg. Approximately 9% of HIV-positive patients from industrialized countries are carriers of HbsAg [31, 46]. The prevalence HC rate among HIV-infected persons is 40% or more, varying in different risk group [20]. M. Sulkowski et al., [40] believe that GW is shown as an opportunistic infection in HIV-infected persons. In this connection, it should be noted that, among human pathogens microorganisms that hepatitis b virus is one of the most common worldwide. HIV and virus of hepatitis B have much in common, although cytotoxic T- lymphocytes in we are able to eliminate the virus from the body, assuming that most patients virus of hepatitis B remains in the body for a lifetime. Therefore, reactivation of infection can occur after many years of infection, such as immunocompromised patients with advanced HIV infection or chemotherapy, regardless of the spectrum of antibodies to hepatitis B, detected in the patient.

It should be emphasized that the possible interference as HB and HC on the course and outcome of HIV infection, and the last - for the development of parenteral hepatitis. In particular, for a mixed HBV/HIV - infection is characterized by rapid decline swarm of anti-HBs, and progression to cirrhosis of the liver [39, 41]. Hepatocellular carcinoma in this population begins to develop at a young age and is more aggressive [38]. Causes of progression of liver disease in HIV/HBV-associated infections remain unclear. Although the immune response of the host is an important trigger of liver disease in patients with HB, it cannot always explain the aggressive disease course. So in HIV-infected persons with evidence of chronic hepatitis B in reduction of CD4 + T-lymphocytes and CD4 : CD8 ratio violation. The decrease in the number of CD4 + T - lymphocytes especially expressed in patients with chronic active hepatitis. HIV infection reduces the clearance of HbsAg and HBeAg and stimulates DNA virus HBV in HIV-infected persons [50, 27].

Immunosuppression caused by HIV, it may reduce the levels of AlAt [32]. In patients with mixed form of HIV/HBV increased replication of HBV and have a low incidence of seroconversion to HBeAg [25]. It stresses the role of HIV - infection and virus-induced interference in the damage of the liver parenchyma [19].

Results of clinical studies on effect of HC for HIV infection more contradictory. On the one hand, according to some researchers, chronic HCV infection is the cause of death of coinfectd persons [17]. There is evidence that HIV infection is clinically 2-5 times faster progression to AIDS in the presence of the virus HS [23]. This effect is the high risk of developing cirrhosis of the liver, the more frequent prevalence of cirrhosis in these patients, rapid decompensated liver disease,

culminating in the death of patients [7, 26]. The presence of the virus in the blood, how HC and RNA of HIV increases risk of death from AIDS [35]. But is the value of viral load and its influence on the mortality of combined infection [24]. On the other hand, studies of a number of authors have shown that high levels of RNA virus HC of blood not only stimulates the progression of HIV infection, but also worsens the response to treatment active antiretroviral therapy and histological picture of liver [7, 15].

HIV infection substantially modifies the natural history of HCV infection, increasing levels viremia of HCV [23]. It affects all stages of infection the HC by reducing the frequency of spontaneous recovery from HCV infection [48, 36].

The degree of influence of the HC on the course and outcome of HIV infection depends on the path of infection by these viruses. In HIV-positive persons infected through blood transfusions and the introduction of drugs, the rate of liver cirrhosis in the first 15 years of follow-up was 15-25 % and in HIV-negative significantly less - 2.6 – 6.5% [42]. Many persons from among drug addicts and alcohol have combined HIV and HC. The progression process of HIV infection has taken place against a background of high content RNA of virus HC in blood serum [23] and reduced the number of CD 4 cells. An inverse correlation between the level of RNA virus HC and CD 4 cell count. At high levels of RNA observed reduced CD4, low - increased [47, 28]. In 87.3% of patients with HC in the presence of detection of HIV increased levels of activity AlAt and in 72.8% - fibrosis of the liver varying degrees. However, in patients with normal transaminases fibrosis is found only in 38.5%. Moreover, in patients with combined infection in 2.5 times more often marked the third genotype HC [7].

The influence of the HC on the progression of HIV infection is less certain. At the same time the risk of progression of HIV infection may be insufficient antiretroviral therapy. However, R.S. Nershow et al. [29] for long-term observation of a large group of HIV-infected women found no effect of HCV infection on the progression of the process. Moreover, there are reports that in HIV-coinfected patients have spontaneous GS climate Rens virus GS [44] and its frequency depends on the route of infection [45].

Thus, as the analysis of literary publications, the priority in the study of co-infections belong clinical, immunological and virological studies, where as epidemiological - very few [7, 5]. To some extent, this is due to the lack of official registration mix - forms of viral hepatitis with HIV infection. Moreover, in-depth study of the co-infections is just beginning. Undoubtedly, the importance of the study of cell-level interactions of the parasite and the host, as the only habitat of many pathogens is the host cell (from prokaryotes to man). «Here in my home they are



evolutionarily developed their parasitic forms of existence, including biological properties as items of pathogenicity, aggressiveness, invasiveness and others. It evolved and intraspecific fighting and synergies and satellitism and much more» [1]. At the same time, in accordance with a systematic approach to the study of epidemic process as complex multilevel system, the processes at the cellular, molecular levels, reflected in epidemic forms, that is at the population level [3,11,13]. Consequently, it is epidemiological studies can adequately integrate and interpret the data obtained from both clinical and virological surveillance.

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## TUBERCULOSIS EPIDEMIOLOGY TRENDS IN THE SAKHA REPUBLIC (YAKUTIA) FOR 2004-2011

M.K. Vinokurova, V.L. Aleksandrov, L.P. Yakovleva, N.M. Oshchepkova

### Summary

Tensed epidemiologic situation for tuberculosis has been determined in Sakha Republic (Yakutia) for the study period from 2004 to 2011, based on key indicators. We observed growth in incidence of TB cases presenting with destructions in lung tissue and bacillary-positive state, persisting trend towards increase in TB cases caused by MDR MTB, high proportion of deaths during the first year of outpatient follow-up for TB, and low coverage of the population with fluorographic mass examinations. The quality of anti-TB measures conducted by local health institutions varies between different socio-geographical zones of the republic. The study proved the need for better organized control of TB that would take into account differences in socio-geographic conditions, medical economics, technical resources, and staff availability in the regions of the republic, within the ongoing context of modernization of anti-TB service.

**Keywords:** tuberculosis, epidemiologic indicators, monitoring, multidrug-resistance, tuberculosis control measures.

**Introduction.** Tuberculosis (TB) in the Sakha Republic (Yakutia) and overall in the Russian Federation is still an important socio-medical problem [3,6]. Starting in 2004, anti-TB care for the population of Russia has been provided in accordance with the renewed legal framework [1,2]. Moreover, in some of the regions of Russian Federation, including Sakha Republic (Yakutia), measures have been fulfilled, funded by federal and regional target programs, by the National Priority Project On Health, and by a number of international projects, which greatly helped to improve the material resources of anti-TB institutions, strengthen the laboratory service, train TB doctors, lab personnel and primary care workers [4].

**The aim** of this study was to establish the main trends in the epidemiological situation for the period from 2004 to 2011.

**Material and methods.** Information was retrieved from the results of epidemiological monitoring for TB in Sakha Republic for 2004–2011. We statistically analyzed key epidemiological indicators for TB and the outcomes of anti-TB service activity in the capital city (Yakutsk) and the

34 regions of the republic, as classified to 5 socio-geographic zones (the city of Yakutsk, Arctic zone, Industrial zone, Rural zone, and Mixed type zone) [5]. Data from state statistical reports pertaining to the study period were used for analysis.

**Results and discussion.** Trends in TB incidence among the population (Report Form #8) of Sakha Republic during the period from 2004 to 2011 were generally similar to those of Russia, although levels of incidence were 1.4–1.8 times lower compared to incidence in Far Eastern Federal District for the study period. For the study period, there was a 9.2% decrease of TB incidence in the population of Sakha-Yakutia: from 91.1 to 83.4, per 100.000 population. In 2011 TB incidence level raised by 4.1% compared to the previous year, and exceeded the incidence level in Russia by 12.5% (Fig. 1).

Analysis of the trends in incidence between different socio-geographic zones of the republic (Report Form #33) shows that incidence had been declining from 2004 to 2011 in all zones except the Arctic zone. Decline was maximum in the Rural zone (1.5 times lower), and minimum in the Industrial zone (5.4% lower). But compared to the previous year, in 2011 TB incidence had grown in the Arctic, Industrial, and Mixed zones. In 2011, TB incidence among the population of the republic varied from 45.5/100.000 in the Industrial zone to 122.5/100.000 in the Arctic zone (Fig. 2).

New patients with TB disease were mostly patients with respiratory TB (RTB): 94.1% of cases in 2011. It is known, that detection rate for RTB cases presenting with destructed lung tissue is an important indicator, pointing primarily at untimely detection of the disease. The proportion of cases with destructed lung tissue among newly identified patients with RTB had increased during 2004–2011 from 37.2 to 40.4% that is 8.6% higher. The city of Yakutsk where the proportion increased by 19.6%, from 36.2 to 43.3%, was largely responsible for this increase, in Rural zone the proportion of the above cases remained the same as in 2004, 35.5%, while in other socio-geographic zones the proportions had somewhat decreased.

In 2011, compared to preceding year, this indicator had declined in all socio-geographic zones, ranging from 33.0% in the Arctic and Mixed zones to 47.8% in the Industrial zone.

Proportion of bacillary-positive cases among newly identified patients with RTB in 2011 was 26.1% higher than in 2004, increasing from 44.1 to 55.6%. This can be related to improved microbiological diagnosis on the one hand, and to untimely case detection on the other. Compared to previous year, in 2011 there was an increase in proportion of these cases in Yakutsk and Industrial zone, where the proportions were highest recorded: 64.3 and 54.7%, respectfully. Minimum level was observed in Mixed zone, 37.7%.

TB incidence level in children aged 0-14 is one of the reliable indicators for assessment of trends in epidemiological situation for TB. In 2011 rates of pediatric TB incidence in Republic Sakha were 1.7 times higher than in Russia and 6.3% higher than in Far Eastern Federal District. Through the period from 2004 to 2011 pediatric TB incidence reduced almost twice, from 56.7 to 28.7 per 100.000 of pediatric population (Fig. 3). This significant decrease was due to improved quality of diagnosis following the introduction of contemporary technologies (computed tomography, highly-specific tuberculin tests) and due to strengthening of organizational and instructional measures.

Because pediatric TB incidence had been notably declining in all socio-geographic zones throughout the study period, the 1.3-fold growth of incidence for the last reported year is an alarming fact. The situation is most unfavorable in Arctic zone, where the incidence had grown 2.8 times higher, reaching 108.9/100.000 of pediatric population. High incidence levels of pediatric TB were recorded in Rural and Mixed zones, and in Yakutsk (34.6, 32.3 and 30.1 per 100.000 of pediatric population). Minimum incidence level was recorded in Industrial zone: 6.0/100.000 of pediatric population.

Prevalence of TB is an important indicator that characterizes the way the detection of TB patients and the formation of ambulatory dispensary follow-up groups are organized, and reflects the effectiveness of anti-TB measures and the quality of the work of anti-TB dispensary. TB prevalence rate in the republic had decreased by a factor of 1.3 from 2004 to 2011. In 2011 the prevalence was 195.6/100.000, which is 14.0% higher than the all-Russian rate, but 1.5 times lower than the same rate in the Far Eastern Federal District (Fig. 4).

Analysis of the trends in TB prevalence for 2004-2011 shows that it had declined in all socio-geographic zones except the city of Yakutsk. Maximum decline was observed in Rural zone where it decreased by a factor 1.6, and minimum decline was seen in Industrial zone, where it was 12.8% lower. But compared to 2010, the decrease in TB prevalence was observed only in Rural zone, while in Yakutsk prevalence level was the same as in the former year, and increased in the rest of the socio-geographic zones. In 2011 the highest prevalence rates were seen in Yakutsk and in Arctic zone – 317.6 and 250.3 per 100.000, respectfully.

TB mortality rate is one of the most significant and informative indicators used in the assessment of the epidemiological situation. In Sakha-Yakutia the mortality in 2011 compared to 2004 had grown by 14.1%, nevertheless, it was 1.5-2.7 times lower than the all-Russian rate throughout the study period. In 2011 mortality caused by TB reached 8.9/100.000, which was 1.6 times lower than in Russia and 2.7 times lower than in Far Eastern Federal District (Fig. 5).

For the period from 2004 to 2011, mortality level increased in 3 socio-geographic zones: Arctic, Industrial and Mixed, and decreased in Yakutsk and in Rural zone. In 2011 mortality rates in Yakutsk and in Industrial zone exceeded the all-republic mortality level (11.9 and 9.1 per 100.000, respectfully), while the lowest mortality was seen in Rural zone (5.0/100.000). Compared to the former year, mortality had increased in all socio-geographic zones, most of all in Industrial zone (2.3 times higher) and least of all in Arctic zone (7.6% higher).

Among the deaths caused by active TB, the percentage of patients who died during the first year of ambulatory dispensary follow-up indicates a poor level of management of TB case detection by the primary healthcare institutions. In Sakha-Yakutia from 2004 to 2011, this proportion had reduced by 9.8% but still remains high and is assessed as 26.8%, which is 1.6 times higher than the same proportion in Far Eastern Federal District. The highest proportion was registered in 2011 in Mixed zone (44.4%). The high percentages were observed also in Yakutsk (26.5%), Arctic zone (25.0%) and Industrial zone (21.7%).

One more sign that signalizes the lack of organization in detection of TB patients is the insufficient coverage of the population aged above 15 years with fluorographic mass examinations: in 2011 only 62.0% were covered in the republic. The lowest coverage rates were observed in Industrial, Arctic, and Mixed zones (52.3, 56.3 and 57.1%, respectfully).

The characteristics of bacterial population circulating in the region, including data on drug sensitivity of the causative agent, are currently the most informative indicators that characterize the epidemiological risk presented by TB patients and are helpful in analyzing bacillary-positive case rates.

In Sakha Republic, number of TB patients with multidrug-resistance (MDR) tends to grow stably, still more complicating the general epidemiological situation and causing obstacles to organization of treatment. In 2004 primary MDR was documented in 9.6% of newly identified patients having bacillary-positive forms of RTB, but in 2011 the proportion of such cases increased by a factor of 2.4 (23.0%), 1.5 times higher than that in Russia and 1.4 times higher than in Far Eastern Federal District. The proportion of MDR cases among bacillary-positive patient populations had grown twice for 2004–2011, reaching 45.5%, 1.3 times higher than in Russia and 1.6 times higher than Far Eastern Federal District.

The main reasons for growth of MDR TB are mistakes in organizing the treatment of patients (incompliance with the standards, irregular chemotherapy, treatment default, problems with drug supply) on the one hand, and increased coverage of patients with drug sensitivity tests on the other hand. In 2011 the percentage of these tests performed in the republic was 89.4% which was

1.3 times more than in 2005 (66.2%).

For 2004-2011 the proportions of patients with MDR had increased in all socio-geographic zones of the republic. It should be noted that MDR detection rates among the patients with RTB widely varies, signaling that differences exist in availability of microbiological diagnostics, especially in Arctic, Industrial and Mixed zones of the republic, and that patients are incompletely covered with culture tests, and those culture-positive are insufficiently covered with drug sensitivity tests. In 2011 the highest level of primary MDR was registered in Yakutsk (24.2%) and in Rural zone (20.9%), and the lowest levels were recorded in Industrial (5.2%) and Arctic (5.8%) zones (Fig. 6). Proportions of MDR cases among bacillary-positive patient populations are likewise high in Yakutsk (42.6%) and in Rural zone (30.8%), while the lowest proportions are seen in Arctic (16.3%) and Industrial (21.7%) zones. This points at the need for improvements in bacteriologic diagnosis.

All of the above factors – insufficient coverage of the population of the republic with preventive fluorographic examinations, significant proportion of new cases who have destructions in lung tissue and are bacillary-positive, growth of drug-resistant TB – have negative consequences on treatment effectiveness. In Sakha-Yakutia, rates of treatment effectiveness in newly identified patients had decreased in 2011 compared to 2004: rates of sputum conversion decreased by 10.8%, from 82.3 to 73.4% (Far Eastern Federal District – 62.1%), rates of cavity closure decreased by 2.2%, from 73.9 to 72.3% (Far Eastern Federal District – 52.6 %).

In 2011 rates of sputum conversion between different socio-geographic zones of Sakha-Yakutia ranged from 61.6% in Industrial zone to 84.7% in Mixed zone; rates of cavity closure varied from 48% in Industrial zone to 89.2% in Rural zone.

Treatment effectiveness in TB patients is significantly influenced by the use of surgical treatment methods. In Sakha Republic the percentage of surgically treated patients among the patients with RTB had increased from 10.4% in 2004 to 14.6% in 2011, which exceeds the same percentage in Far Eastern Federal District by a factor of 2.3 (6.2%). The highest increase was observed in Arctic (3.4 times higher) and in Rural (1.6 times higher) zones, the lowest increase was observed in Industrial zone (9.8% higher). In 2011 maximum proportion of surgically treated patients among those with RTB was recorded in Rural zone (25.7%) and the minimum proportion in Industrial zone (10.2%).

In Sakha Republic, rates of sputum conversion in patient populations with RTB had increased from 43.6% in 2004 to 46.4% in 2011, which was 1.3 times higher than that in Far Eastern Federal District (36.1%). The same positive trend in sputum conversion rates was observed





in all socio-geographical zones except Yakutsk, where the rates remained the same as in 2004. In 2011 rates of sputum conversion in patient populations with RTB were maximum in Rural zone (64.8%), and minimum in Industrial zone (31.3%).

Rates of clinical cure in patients with RTB had decreased for 2004–2011 from 49.1 to 39.6% (by a factor of 1.2), although still 1.2 times lower than the same rates in Far Eastern Federal District (32.3%). High rates were recorded in 2004 both in the republic and in Russia – an explanation for this is that new definitions of dispensary follow-up groups for TB patients were adopted later (Order #109). During the next years the rate of clinical cure had been tending to decline in all the socio-geographic zones in the republic. But in 2010–2011 these rates were reported to have grown in Yakutsk, Arctic and Industrial zones (by factors of 1.2, 1.3 and 1.2, respectfully). In 2011 the rates of clinical cure in TB patients was ranging from 30.5% in Yakutsk to 56.5% in Rural zone.

### **Conclusions:**

Epidemiologic situation for TB in the Sakha Republic (Yakutia) remains intense, despite the overall trend towards decrease by key indicators for the period from 2004 to 2011; a growth in the overall population TB incidence, in pediatric TB incidence and in pediatric mortality caused by TB is observed for the last years.

Growing incidence of cases with TB of respiratory organs detected with destructions in lung tissue and bacillary-positive state, high proportion of deaths during the first year of ambulatory dispensary follow-up signalize a lack of organization in detecting TB patients at healthcare institutions of the republic.

There is a stable trend towards growing number of multidrug-resistant TB, which complicates even more the overall epidemiologic situation, causes significant difficulties to organization of treatment and patient rehabilitation, and leads to growth of infection reservoir that presents epidemiological risk.

Significant variance is observed in levels and trends of key epidemiological indicators and in treatment effectiveness indicators between the socio-geographic zones of the Sakha Republic, due to differences in quality of anti-TB measures conducted: organization of preventive work, case detection, bacteriological diagnosis, ambulatory dispensary follow-up for TB, controlled chemotherapy, and surgical patient treatment.

The above said calls for improvements in organizing TB control, paying attention to the specifics implied by socio-geographic, medical and economical differences, as well as differences in availability of material resources and staffing between the regions of the republic, within the ongoing context of modernization of anti-TB service.





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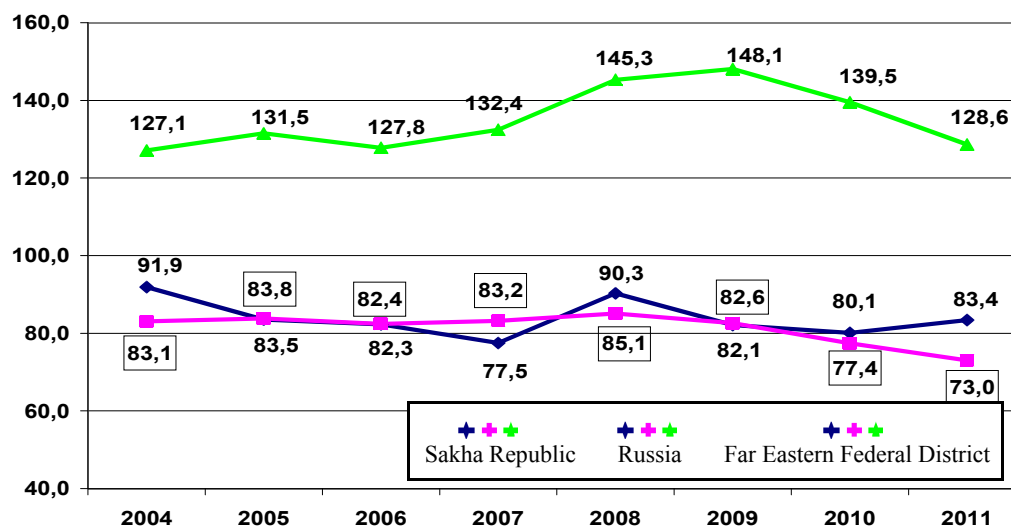
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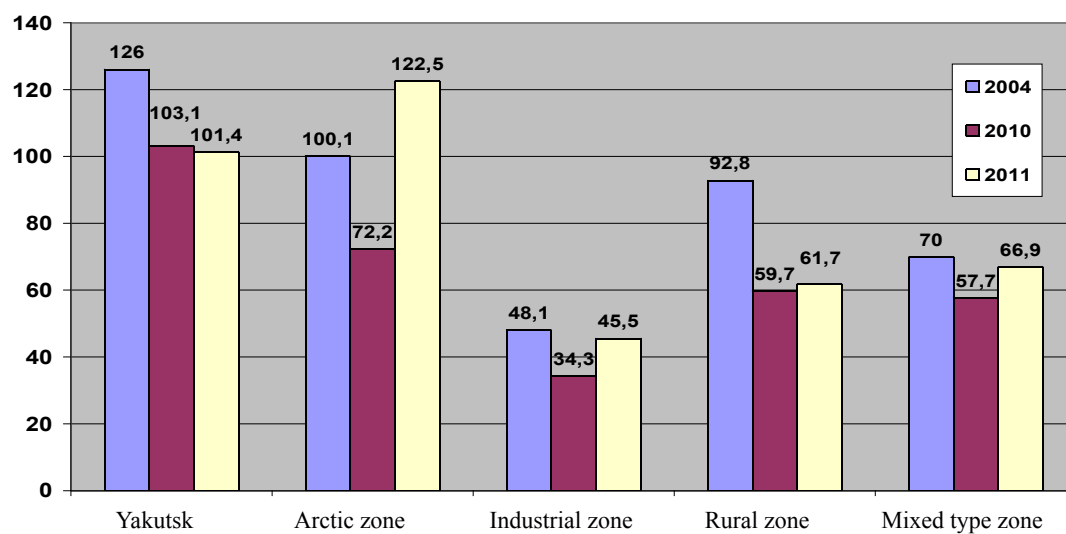
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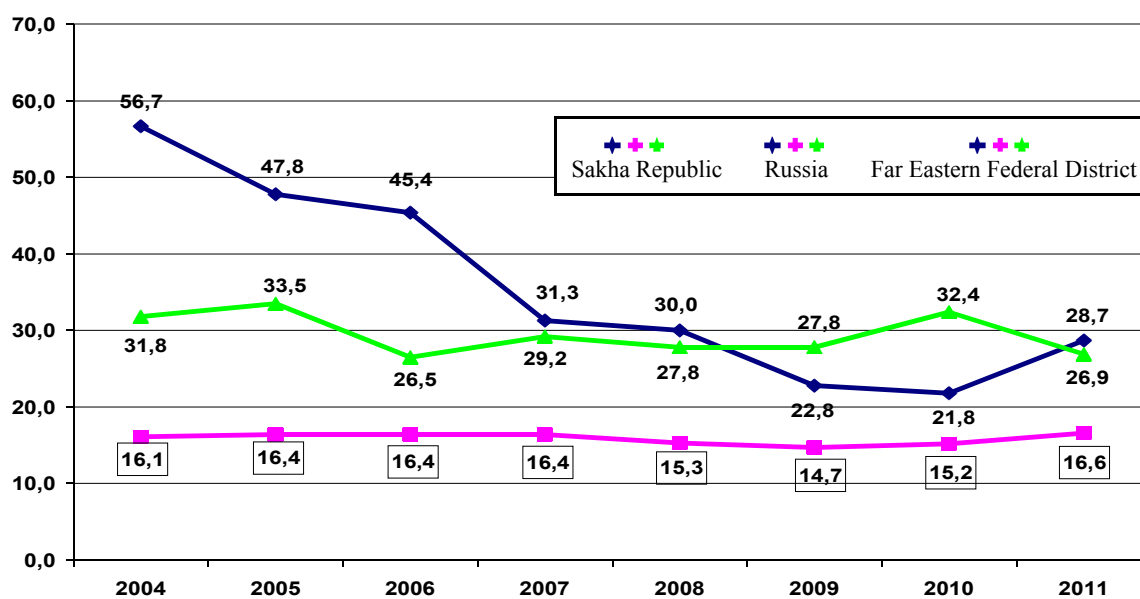
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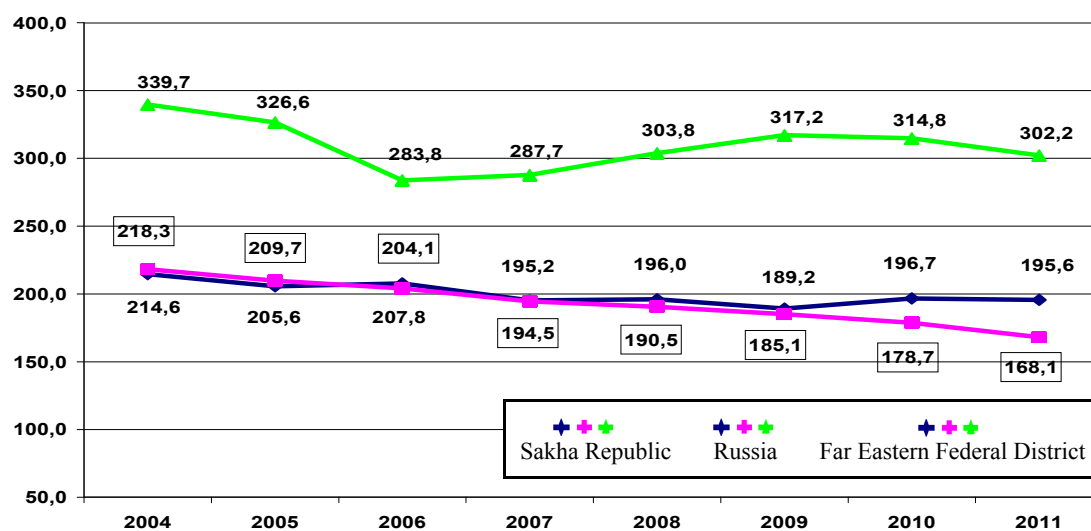
**Fig. 1.** Trends in population TB incidence (Form #8): Sakha Republic (Yakutia), Russian Federation, Far Eastern Federal District, 2004-2011 (per 100.000 population)



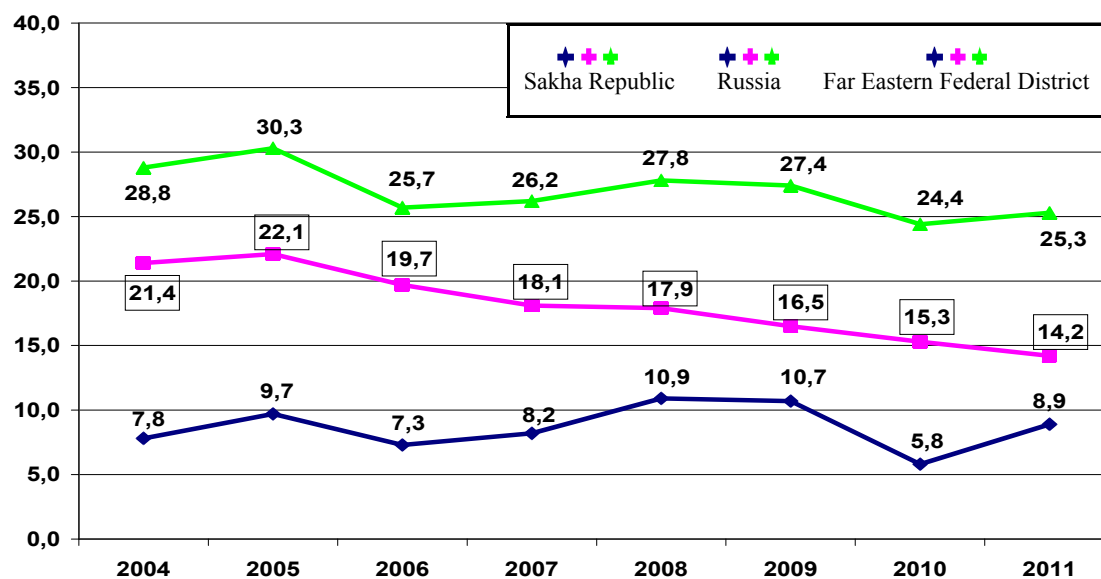
**Fig. 2.** Trends in population TB incidence: socio-geographic zones of Sakha Republic (Yakutia), 2004, 2010, 2011 (per 100.000 population)



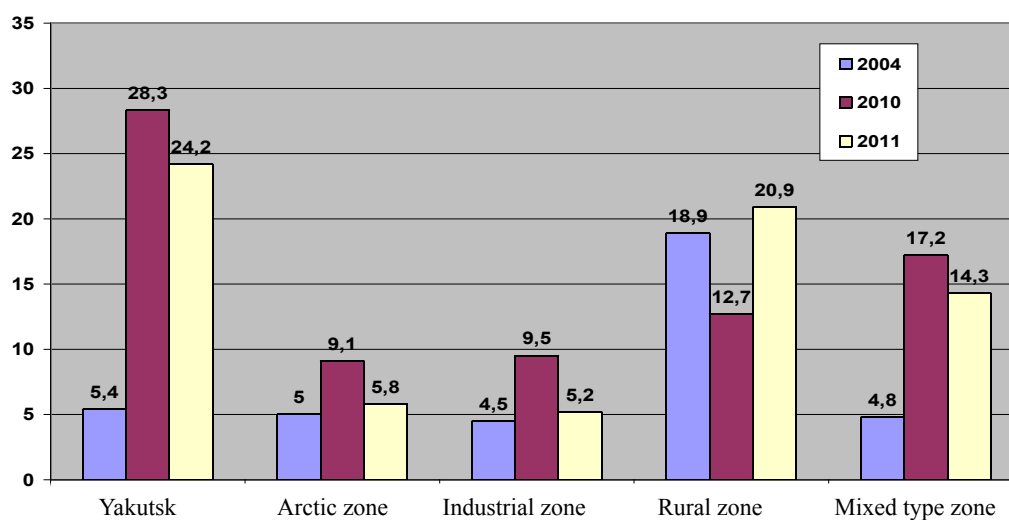
**Fig. 3.** Trends in pediatric TB incidence: Sakha Republic (Yakutia), Russian Federation, Far Eastern Federal District, 2004-2011 (per 100.000 population)



**Fig. 4.** Trends in TB prevalence: Sakha Republic (Yakutia), Russian Federation, Far Eastern Federal District, 2004-2011 (per 100.000 population)



**Fig 5.** Trends in mortality caused by TB: Sakha Republic (Yakutia), Russian Federation, Far Eastern Federal District, 2004-2011 (per 100.000 population)



**Fig. 6.** Proportions of MDR cases among newly identified patients with bacillary-positive forms of respiratory TB: socio-geographic zones of Sakha Republic (Yakutia), 2004, 2010, 2011 (%)

## PHTHISIOLOGISTS OF YAKUTIA: SCIENTIFIC AND PRACTICAL POTENTIAL

M.K. Vinokurova, E.S. Pavlova, Z.E. Lineva, S.S. Gavriliev

Phthisiologists working in the field of therapy for pulmonary tuberculosis and development of new treatment methods started their scientific and practical work in the 1950s. The first two stages of the work became history by now; the 2000s were the beginning of the third stage – the quest for contemporary methods to treat and overcome M.tuberculosis drug resistance. Thesis works and patents for inventions give eloquent illustration of the close interconnection between science and practice.

**Keywords:** tuberculosis, Yakutia, research work, methods of treatment for pulmonary tuberculosis, Russian Federation patents.

Yakutsk Branch of the Tuberculosis Institute, AMS USSR, was opened in 1950 and its Therapeutics Department opened in the same year.

Sanatorium/resort treatment, sanitation and dietary treatment were the ways to treat tuberculosis in the XIXth century throughout the world. The wide use of pneumothorax started at the turn of the XXth century. Starting in the mid 1930s, surgical methods began to be used for treatment of tuberculosis. Discovery of streptomycin, the first anti-tuberculosis drug, was the first big step in development of etiotropic therapy. Intensive use of para-aminosalicylic acid (PAS), tibon, and isonicotinic acid hydrazide (INH) for treatment of tuberculosis began in 1954, while the use of new highly effective agents such as rifampicin, ethambutol, pyrazinamid started in the 1970s. The spectrum of anti-tuberculosis drugs has widened (fluroquinolons) since the end of the XXth century. One can see how all these periods in the history of anti-tuberculosis therapy are reflected in the history of pulmonary tuberculosis therapy in Yakutia.

Scientific activity of Yakutsk phthisiologists can be divided to 2 historical periods for convenience.

**1st period (1950-1969):** therapy of pulmonary tuberculosis in Yakutia was conducted under the leadership of the doctors from central Russian cities and institutes, who were invited to Yakutia by E.N. Andreev, the first Director of the Yakutsk Branch of Tuberculosis Institute, AMS USSR. Scientific explorations of that time, carried out by the Therapeutics Department of the Yakutsk Branch of Tuberculosis Institute (later Yakutsk Research Institute for Tuberculosis of the RSFSR

Ministry of Health) sought to introduce new etiotropic medications, and to develop better treatment regimens. Doctors sent to work in Yakutia studied the situation with tuberculosis in the republic, defended their theses based on study findings, and eagerly shared their experience and knowledge with Yakutsk phthisiologists, many of whom later underwent postgraduate education in central Tuberculosis Institutes and successfully defended theses.

**2nd period (1970-2000):** the followers of the invited Russian doctors, who proceeded to degrees and acquired practical experience, began to educate young doctors in Yakutia. This time was the period of search for new methods to treat destructive tuberculosis and endobronchitis, including the cases complicated with drug resistance of the causative agent. Based on the results of these studies, a number of theses were again defended, and some treatment methods were patented.

**1st period.** In 1950 F.D. Zaveleva (Cand.Med.Sc.) became the Head of the Therapeutics Department. She was the first to propose combination chemotherapy regimen that included tibon and small doses of streptomycin; this regimen proved highly effective in patients with early forms of pulmonary tuberculosis (1951). Intermittent therapy method was also developed and adopted at this period (S.I. Torgovkina).

Treatment method for pulmonary tuberculosis based on the use of antibacterial agents in combination with tuberculin (in various dilutions) was developed and eventually adopted to the practice of Therapeutics Department under the guidance of S.L. Pekarskaya, Cand.Med.Sc. (1955-1965); she also wrote a thesis on epidemiology and treatment of disseminated pulmonary tuberculosis in YASSR. The use of this method increased treatment effectiveness up to 55-60%. On E.N. Andreev's initiative, therapists started to use some biostimulators in combination chemotherapy for pulmonary tuberculosis.

S.S. Gavriliev and E.A. Ivanov, who came to work in the field of phthisiology following their fresh graduation from the Medical Institute, acquired their first experience in anti-tuberculosis work under the supervision of the doctors from Moscow. In 1965 S.S. Gavriliev, the resident physician in the Therapeutics Department defended his Candidate thesis entitled "Experience with the use of pasomycin for pulmonary tuberculosis" during postgraduate training in the Central Research Institute for Tuberculosis, AMS USSR. In 1968 E.A. Ivanov defended his thesis on "Desensitizing therapy in patients with pulmonary tuberculosis". In the following years, both of them had headed at different time the Therapeutics Department of the Yakutsk Research Institute for Tuberculosis.

**2nd period.** This period was the productive prime of Yakutsk phthisiologists – the trainees of Russian phthisiologic school and their successors in Yakutsk Research Institute for Tuberculosis.

In 1969 S.S. Gavriliev (Cand.Med.Sc.) became the Head of Therapeutics Department. He



supervised the development and practical adoption (first in the practice of Therapeutics Department and then over the republic) of the methods: single administration of daily doses of medications (N.I. Strod); express intravenous administration of isoniazid (E.A. Ivanov); methods for rectal administration of anti-tuberculosis agents and methods for administration of various nosotropic agents (beginning in 1972). Methods that were aimed at improving the clinical effectiveness of treatment allowed achievement of conversion of bacillary positive state in 80% of cases, cavity closure in 70-75%, and abrupt reduction of side effects in new cases of destructive pulmonary tuberculosis.

One of the particularly interesting methods developed by S.S. Gavriliev is the method for rectal drip administration of tubazide and PAS used in combination therapy of pulmonary tuberculosis in the extreme northern environment (Rationalization proposal certificate (local novelty) granted to Yakutsk Research Institute for Tuberculosis of the RSFSR Ministry of Health, issued May 13, 1977) [1]. The method proposed was novel, promising, and best suited for use in patients with concurrent gastric or renal disease. After 13 years of reviewal by The Pharmacological Committee of the Ministry of Health of USSR (Protocol No.14, issued August 26, 1988), this treatment method was approved for use over the country, and isoniazid and PAS were approved for rectal administration.

As the scientific staff of the Therapeutics Department participated in all-union scientific research program "Side effects of anti-tuberculosis medications, detected in health institutions, in various geographic areas of the Soviet Union", study of side effects and intolerability of medications and development of prevention methods were under way. Serious attention was paid to developing alternative chemotherapy methods based on distinctive patterns of pathogenesis, extensiveness, localization and clinical form; such methods were needed for correction of therapy depending on the pattern of tubercular inflammation, and also for differential approach to treatment using antioxidants (Val' N.S., 1995).

Studies on nosotropic treatment methods for tuberculosis initiated by S.S. Gavriliev have been continued by the studies of Lineva Z.E., resulting in successful defense of her Candidate thesis "Etiologic treatment for destructive pulmonary tuberculosis in the environment of extreme north" (1985) on the use of ultrasound in combination with methyluracil and insulin for treatment of pulmonary tuberculosis. Use of the method led to 2-3-fold reduction in frequency of side effects and faster conversion of bacillary-positive state and faster cavity closure (up to 90.0% of cases). Use of semiconductor laser in combination with medications for correction of oxidative/antioxidative disorders became another highly effective method to treat pulmonary tuberculosis (Vinokurova M.K., 1996, 2005). Use of EHF therapy (extremely high frequency therapy) in combination with



antioxidants likewise showed high treatment effectiveness (Yakovleva L.P., 1999).

Z.E. Lineva's Doctor thesis "Gastric dysbacteriosis and methods of its corrections in patients with pulmonary tuberculosis" (1995) was devoted to the study of the pathogenesis of gastric dysbiosis during currently used chemotherapy for pulmonary tuberculosis and development of novel ways to correct this dysbiotic state.

S.S. Gavriliiev also guided the development of the following new treatment methods for destructive pulmonary tuberculosis: endobronchial administration of solubilized rifampicin [2]; deep phonophoresis of intercostally intramuscularly administered isoniazid [3]; inhalation of anti-tuberculosis agents diluted in silver water [4]; inhalation of kanamycin diluted in ammonia solution of silver nitrate, for pyogenic endobronchitis in patients, who have destructive pulmonary tuberculosis with polyresistant *M.tuberculosis* and non-specific flora [5]; intercostal administration of isoniazid in combination with laser exposure, for treatment of pulmonary tuberculosis patients with massive bacillary counts, and multiple destructions concurrent with endobronchitis (using deep photophoresis of intercostally administered 10% solution of isoniazid in combination with herbal therapy using 'breast tea') [6]. Alternative methods of medication administration allowed conversion of bacillary-positive state in up to 90% and cavity closure in up 76% of cases. Comprehensive analysis of treatment results in patients with complicated destructive pulmonary tuberculosis treated with alternative methods for medication administration was concluded by the Doctor thesis defended by S.S. Gavriliiev "Chemotherapy of destructive forms of pulmonary tuberculosis using various methods of medication administration".

**The year 2001** was the beginning of new phase in development of therapeutic departments. Disciples of S.S. Gavriliiev and Z.E. Lineva (Fig.) make the staff of the Phthisiatry Research Practice Center and the pulmonary tuberculosis departments; they are followers of the followers of doctors from Moscow, the second generation of Yakutsk phthisiologists.

In today's epidemiologic situation that grows more complicated from year to year, the search for novel effective combination chemotherapy methods goes on. Gavriliiev S.S. and Yakovleva L.P. proposed the rectal administration of ozone, potent antioxidant inhibiting free radicals, in patients with destructive pulmonary tuberculosis [7]. Gavriliiev S.S. and Pavlova E.S. continued the studies on region-specific features of pulmonary fibrosis and proposed another treatment method for destructive pulmonary tuberculosis, which is based on potentiating effect of ultrasound on lydase and hydrocortisone, allowing their deep penetration to an area of local pulmonary fibrosis projected onto the skin surface of the chest, and leading to increased penetrance and decondensation of the connective tissue, essential for full healing of cavities [8].

Considering the currently existing epidemiological situation for tuberculosis in Russia and in Yakutia, phthisiologists are working on new methods for treatment and surveillance of drug-resistant tuberculosis of the respiratory organs. The most attention is paid to the problem of overcoming the drug-resistance of *M.tuberculosis* and to adaptation of the WHO tuberculosis control program to extreme environment of Yakutia. Four different specialty therapeutic departments are currently functioning in the State Budgetary Institution of the Sakha Republic (Yakutia) Research Practice Center “Phthisiatry”. The doctors carry on the traditions laid by the founder phthisiologists, the pioneers of anti-tuberculosis service in Yakutia, and continue multidimensional research aimed at novel ways to improve chemotherapy effectiveness, based on region-specific patterns of adaptation processes during tubercular inflammation in the extreme north.



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## COMPARATIVE ANALYSIS OF MYCOBACTERIUM TUBERCULOSIS GENOTYPES IN THE REPUBLIC OF YAKUTIA AND IRKUTSK REGION

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In 2010, the Russian Federation had a tuberculosis (TB) prevalence of 136 per 100,000 population and the estimated proportion of cases of multidrug-resistant (MDR)-TB, defined as resistance to isoniazid and rifampin, among new cases (primary TB) was 18% [2]. Yet primary MDR-TB may be highly variable at the subnational level, with proportions varying from 5.4-28.3% in oblasts or republics with continuous surveillance data on drug-resistance as reported to the World Health Organization (WHO) [1].

In 2009 Irkutsk had a TB prevalence of 373 per 100,000 population, and is burdened by a significant HIV epidemic, timed initially with the dissolution of the Soviet Union and availability of injected heroin [3, 23]. Irkutsk carries one of the highest rates of HIV in the Russian Federation, with more than 21,000 people registered with HIV in the oblast and the majority reported from Irkutsk city [5]. In contrast, the Sakha Republic (Yakutia), is sparsely populated and 49% of the population are indigenous Yakuts [6]. TB prevalence was lower at 188 per 100,000 population and HIV is thought scarce [9].

Molecular typing from surveillance studies have found the Beijing genotype, a pandemic lineage, in over half of *Mycobacterium tuberculosis* from the Russian Federation, with one of the highest prevalence in Irkutsk [4, 5, 24]. Comparative genotyping has not been performed from Yakutia. The Beijing genotype has previously been associated with the MDR phenotype and characteristic resistance mutations, as well as increased transmissibility [11]. Given the distinct sociocultural patterns between Irkutsk and Yakutia, we hypothesized that unique genotypic characteristics of primary MDR-TB would be found in each region. Thus the following study sought to characterize the molecular epidemiology among cases of primary TB from Irkutsk and Yakutia.

### METHODS

#### Study population

*M. tuberculosis* isolates were cultured during routine care of adults,  $\geq 18$  years of age, with primary TB from November 2008 to May 2010 at two regional referral centers, the Irkutsk Regional



TB-Prevention Dispensary in Irkutsk city, and the Research Practice Center for Phthisiatry in Yakutsk city (Yakutia). Primary TB was defined as a culture positive specimen in a subject without prior history of TB treatment.

### **Molecular typing**

The initial cultured specimen from each subject was used following mycobacterial growth on Lowenstein-Jensen agar slants. Isolation and species identification was performed per WHO recommendations at each site [21]. Drug susceptibility testing was carried out by the absolute concentration method on agar slants for rifampin (critical concentration 40 µg/ml), isoniazid (1 µg/ml and 10 µg/ml), ethambutol (2 µg/ml), streptomycin (10 µg/ml), ethionamide (30 µg/ml) and kanamycin (30 µg/ml). Flouroquinolone and pyrazinamide susceptibility testing was not routinely performed.

DNA extraction was performed on all isolates at the Institute of Epidemiology and Microbiology, SB RAMS, in Irkutsk city, using cetyltrimethylammonium bromide-NaCl according to prior protocol [18]. All DNA underwent typing by original 12-loci mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) analysis [19]. Region of difference (RD) deletions were used to define major strain lineages (e.g. RD105 and RD207 for Beijing) [10, 16]. Further lineage-definition was carried out using oligonucleotide primers for Ural strains as previously described [5]. The public database MIRUVNTRplus (<http://www.miru-vntrplus.org/MIRU/index.faces>) and online instruments [20] were used for phylogenetic tree construction by the unweighted pair group method using arithmetic averages. VNTR international type numbers were further confirmed with the online database SITVIT (Institute Pasteur de Guadeloupe; <http://www.pasteur-guadeloupe.fr:8081/SITVITDemo/outilsConsultation.jsp>) [6]. Comparison of genotype frequency between sites was by chi-square analysis with Yates correction or Fisher's exact test as appropriate.

### **Primary MDR-TB outcomes**

Those subjects identified as having primary MDR-TB were retrospectively traced for treatment outcome. Basic demographics and clinical characteristics were abstracted from registry databases including age at diagnosis, gender, means of referral (symptoms or screening fluorography), prior imprisonment and HIV status. Typically, patients were treated for TB as an inpatient for the intensive phase of chemotherapy ( $\geq 2$  months), then discharged to complete a continuation phase. Resources for directly observed therapy following discharge were not routinely available or programmatically enforced. Chemotherapeutic regimens for MDR-TB were variable but generally included a flouroquinolone and an injectable agent (kanamycin or capreomycin), at

times continued despite reported in vitro resistance. For selected patients, thoracic surgery for pulmonary TB was performed and data regarding this outcome was abstracted from the registry.

Subjects with documented culture conversion to negative and having completed the prescribed course of inpatient chemotherapy were categorized as intensive phase complete. Subjects having completed intensive phase and the prescribed continuation phase without symptom recurrence were categorized as treatment complete. Default occurred if a subject failed to complete the intensive phase of treatment. Death was attributed to TB, HIV and TB, or other cause as documented in the registry. Comparisons of pre-treatment characteristics and outcomes between sites were made by chi-square analysis, t-test for continuous variables or when appropriate, the Mann-Whitney U test for nonparametric data.

## RESULTS AND DISCUSSION

During the study period, 235 consecutive isolates from subjects with primary TB were available; 130 were from Yakutia and 105 from Irkutsk. Isoniazid monoresistance occurred in 16 (12%) from Yakutia and 19 (18%) from Irkutsk ( $p=0.27$ ). Multidrug resistance occurred in 36 (28%) from Yakutia and 25 (24%) from Irkutsk ( $p=0.55$ ). Of the subjects with primary MDR-TB, there were no significant differences in age, gender distribution or reason for referral between those in Irkutsk or Yakutia [Table 1]. Of critical difference, there were no HIV infected patients identified from Yakutia compared to 11 (44%) of subjects from Irkutsk ( $p<0.001$ ).

### Molecular typing

Strains of the Beijing family were the predominant cause of primary TB at both sites but significantly more common in Irkutsk,  $n=70$  (67%), than Yakutia,  $n=40$  (31%) ( $p<0.001$ ). Furthermore, a substantial amount of S 256 (11%), T 8 (7%) and Ural 171 (5%) were observed in Yakutia that were not found in Irkutsk [Table 2]. Importantly, the cluster of S 256 (MIRU profile 233325153325), previously unreported as an epidemic strain in the Russian Federation, was the most common among primary MDR-TB isolates from Yakutia and was fully 86% MDR [Table 2]. The S 256 strain was found to be resistant to streptomycin in all cases and kanamycin in 4 (29%), differing significantly from the other Yakutia isolates where kanamycin resistance was reported in only 9 (8%) ( $p=0.035$ ). In Irkutsk a previously described Beijing strain predominated among those with primary MDR-TB [9,10].

### Primary MDR-TB outcomes

All HIV infected patients died during the inpatient phase of therapy and accounted for 92% of all deaths from Irkutsk [Table 3]. Individual use of antiretroviral therapy was not known, but all



died within the intensive phase. Of those that died in Irkutsk, kanamycin resistance was found in 4 (33%) and was no more common than in those that survived, 4 (31%). All of those with HIV that died in Irkutsk had an isolate of Beijing family. In comparison, death was less common in Yakutia, occurring in only 4 (11%) of those with primary MDR-TB ( $p=0.002$ ), 3 of whom died of causes other than TB. Of the deaths in Yakutia, two occurred in subjects with the Beijing 17 strain (one of which was kanamycin resistant), one in a subject with a kanamycin susceptible S 256, and the other with a kanamycin susceptible strain of orphan lineage. Due to the proportion that died, significantly fewer subjects in Irkutsk completed intensive phase, but of those that completed, only 1 (13%) from Irkutsk went on to complete the full course of treatment, compared to 19 (71%) from Yakutia ( $p=0.01$ ). Overall surgery was well tolerated and performed in a similar proportion of subjects at both sites. All subjects receiving surgery were HIV negative. One death was reported in a subject from Yakutia unrelated to TB, while the remainder, 90%, completed the total treatment course. Four subjects from Irkutsk completed intensive phase, but 2 (33%) defaulted after surgery and were lost to follow-up.

We found that more than 25% of primary TB was MDR, among the highest proportion reported from the Russian Federation [1]. Importantly however, regionally specific genotypic patterns and resistance mutations were identified. Expectedly, primary MDR-TB was driven by strains of Beijing lineage in Irkutsk oblast [5, 13]. The dominance of Beijing strains has been described for over a decade in both civilian and prison populations from other oblasts, in greater association with drug-resistance secondary to common mutations at codon 531 of *rpoB* and 315 of *katG*, and in patients of younger age suggestive of more recent transmission [7, 12, 17]. Yet in the more geographically isolated population of Yakutia, a strain previously unidentified in the Russian Federation, S 256, had a MIRU profile recently described among Canadian Aboriginal populations [15]. In Yakutia, S 256 was highly drug-resistant and the most common genotype among cases of primary MDR-TB. Yet our findings are consistent with a recent report from Novosibirsk oblast that similarly included non-Beijing and S-family strains [17].

**Conclusion.** The phylogenetic patterns, certain drug-resistance mutations and treatment outcomes were regionally distinct. In Yakutia, a newly described genotype, S 256, appeared to drive the MDR-TB epidemic and may be more common among indigenous Yakuts. To contrast in Irkutsk, MDR-TB was found commonly in strains of Beijing lineage but was associated with higher mortality and HIV infection.



### Characteristics of patients with primary multidrug-resistant tuberculosis by region

Characteristic	Irkutsk N= 25	Yakutia N= 36	P value
Age, mean years ( $\pm$ SD)	34 (13)	32 (12)	P=0.76
Gender, male (% N)	17 (68)	23 (64)	P=0.79
HIV infected (% total reported)	11 (44)	0 <sup>a</sup>	P<0.001
Prior imprisonment (% N)	0 (0)	4 (11)	P=0.14
Symptomatic at referral (% total reported)	17 (68)	12 (50) <sup>a</sup>	P=0.25

Significance determined by t-test for age and chi-square or Fisher's exact for categorical variables, excluding those with missing values.

<sup>a</sup>In Yakutia HIV status was not recorded in 10 (28%) and referral symptoms in 12 (33%).

**Table 2**

### Genotype by region

MIRU-VNTR 12 <sup>a</sup>	Family/ VIT <sup>b</sup>	Irkutsk total =105, MDR = 25 N (% total) N (% MDR)	Yakutia total = 130, MDR = 36 N (% total) N (% MDR)	P value
223325153533	Beijing 16	32 (31) 7 (28)	12 (9) 1 (3)	P<0.001 P=0.006
223325173533	Beijing 17	13 (12) 6 (24)	10 (8) 7 (19)	P=0.27 P=0.76
233325153325	S 256	0	14 (11) 12 (33)	P<0.001 P=0.001
223125153324	T 8	0	9 (7) 0	P=0.005
227225113223	Ural 171	0	6 (5) 0	P=0.03
223325153433	Beijing 592	1 (1) 0	4 (3) 0	P=0.38

<sup>a</sup>MIRU-VNTR= mycobacterial interspersed repetitive unit-variable number tandem repeat (original 12 loci profile). Included genotypes found in 5 or more isolates only.

<sup>b</sup>VIT= VNTR international type. MDR = multidrug-resistant TB (conventional resistance to isoniazid and rifampin). Significance determined by chi-square analysis with Yates correction or Fisher's exact test when appropriate.

Table 3

## Multidrug-resistant tuberculosis treatment outcomes by region

Outcome	Irkutsk N= 24 <sup>a</sup>	Yakutia N = 36	P value
Death (% N)	12 (50)	4 (11)	P=0.002
HIV/TB related (% death)	11 (92)	0 (0)	
TB related (% death)	0	1 (25)	
Other cause (% death)	1 (8)	3 (75) <sup>b</sup>	
Intensive phase complete (% N)	8 (33)	27 (75)	P=0.003
Total treatment complete (% intensive phase) <sup>c</sup>	1 (13)	19 (71)	P=0.01
Surgery (% N) <sup>c</sup>	6 (25)	10 (28)	P=0.78
Intensive phase complete (% surgery)	4 (67) <sup>d</sup>	9 (90)	

<sup>a</sup>Excludes one patient from Irkutsk with unknown outcome.

<sup>b</sup>One patient died following surgery but unrelated to procedure.

<sup>c</sup>Excludes subjects that did not complete intensive phase due to death or default.

<sup>c</sup>All patients receiving surgery at both sites were HIV negative.

<sup>d</sup>Other 2 surgical patients from Irkutsk had defaulted.

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## EXPERIENCE WITH FIGHT AGAINST TUBERCULOSIS IN THE VERKNEVILYUYSKY REGION OF THE SAKHA REPUBLIC (YAKUTIA) UNDER CURRENT SOCIAL AND EPIDEMIOLOGICAL CONDITIONS

V.V. Eliseev

### Summary.

Analysis of 10-year tuberculosis control activities in the setting of one of rural agricultural regions in extreme north demonstrates that significant successes leading to considerable reduction in epidemiologic indicators for tuberculosis could be achieved by well-organized program regulating multifaceted interaction between municipal institutions, healthcare facilities, agencies and the leading all-republic specialized anti-tuberculosis institution. Improvements in epidemiologic situation are apparent from significantly decreased infection levels and tuberculosis incidence rates among children and adolescents.

**Keywords:** tuberculosis, epidemiology, incidence, morbidity, bacillary-positive cases, infection level, rural area, prevention, treatment for tuberculosis, organization of tuberculosis control

Verknevilyuysky region is a typical rural region of Sakha Republic (Yakutia), with aboriginal Yakut population of 21.400.

As of January 1, 2002, epidemiological situation for tuberculosis (TB) in the Verknevilyuysky region was estimated as highly difficult: key epidemiological rates of TB in the region by far exceeded the same rates for other regions in the republic and were higher than average all-republic rates by a factor of 2 to 2.5 (Table 1).

Table 1

Key epidemiological rates for tuberculosis in the Sakha Republic (Yakutia) and in the Verknevilyuysky region, as of January 1, 2002 (per 100,000 pop.)

Rate	Territory	
	Sakha Republic (Yakutia)	Verknevilyuysky region
Incidence	74.1	191.1
Morbidity	282.9	539.6
Bacillary-positive cases	94.6	214.6

Starting in 2002, the administration of Verknevilyuysky region has been taking emphasized measures for more intensified comprehensive efforts in the fight against TB, within the legal framework of Russian Federation and Sakha Republic (Yakutia) intended to protect the population from TB infection.

First of all, the main prerequisites for successful fight against TB were set up: good material and technical facilities, full-scale staffing and sufficient financing of TB control service.

Secondly, the Head of the Verknevilyuysky region, expressing his state political will, has organized the cooperative work between municipal bodies, health institutions, and the society. This provided a maximum fulfillment of the scope of anti-TB measures aimed at prevention, early



detection of TB, health examination of the population and hospitalization of TB patients.

Table 2

Population coverage with preventive measures for tuberculosis in 2004-2011

Rates	2004	2005	2006	2007	2008	2009	2010	2011
Total coverage with occupational health examination	80.4	74.3	81.1	73.3	75.4	73.6	71.4	65.7
Coverage with tuberculin skin testing	92.3	99.1	99.2	93.1	98.1	97.7	97.4	98.2
Number of newly identified patients	44	30	14	10	14	14	12	11
Proportion of patients detected by occupational health examination	81.8	73.3	78.6	80.6	50.0	50.0	50.0	36.4

Table 3

Preventive fluorographic examinations for tuberculosis in the rural population

Year	Number of rural settlements	Population	Fluorographic examinations performed (persons)	% of coverage	Patients with TB detected
2004	15	3028	2549	84.2	8
2006	17	6943	6070	87.4	4
2007	15	5812	4902	84.3	1
2008	12	4758	4192	88.1	2
2009	15	4615	4092	88.7	0
2010	6	2298	2031	86.0	0

Beginning in 2004, new “MEDYUG” portable digital fluorographs are used for fluorographic examinations.

Table 2 shows total coverage of the eligible population with occupational health examinations. Table 3 demonstrates achievement of maximum high population coverage rate with fluorographic

examinations in rural healthcare areas, owing to active cooperation between the administration of *naslegs* and local medical workers. A high TB detection rate by occupational health examinations is seen during the first two years, in the region on the whole and in rural healthcare areas. Starting in 2006 (the third year since comprehensive measures have been under way), the absolute number of new cases in rural healthcare areas has fallen abruptly, and those detected are minor forms of TB, which is an evidence for the effectiveness of preventive examinations.

Maximum attention was paid to effectiveness of clinical treatment and rehabilitation of the population cohorts with TB disease, as they were the source of TB infection.

As an infectious disease, TB has common regular patterns with other infectious diseases. General rules of successful action against infections are localization and eradication of the infection source. In the case of TB infection, “infection source localization” means hospitalization of patient cohorts to TB in-patient clinics, and “infection source eradication” means curing the patients of TB.

As a result of the strengthened comprehensive work with the above named regional administrative and healthcare institutions, coverage with hospitalizations was achieved in 100% of the active TB patient cohort, i.e. the source of TB infection was localized.

In this way, during the regional-level phase (phase I) of the comprehensive fight against TB, which consisted in setting up key prerequisites to and enabling cooperative work so that patients with active TB were completely covered with hospitalizations, we set up a serious foundation for successful realization of step II – a specialized phase of anti-TB work, aimed at radical improvement of the quality of work.

Phase II is a specialized part of anti-TB work and presents a huge scope of diagnostic, treatment, outpatient dispensary follow-up and consultation measures – greater part of this, and more complex part, is conducted in cooperation with the leading TB institution of the republic, the State Budgetary Institution of Sakha Republic (Yakutia) “Research-Practice Center ‘Phthisiatry’” (Table 4).

It should be stressed that it is the cooperative specialized work that plays the crucial role in radically improving the quality of special care for TB patients from regions.

‘Phthisiatry’ Research-Practice Center is the base for a years-long, successfully functioning centralized system for controlling basic anti-TB activities: diagnosis, supervision of treatment effectiveness and treatment course correction, appointment for surgical treatment, supervision of the effectiveness of dispensary system for regular population health examinations. Under this centralized control system, any patient from any region of Sakha Republic has the opportunity to be completely cured of TB.

Intensive use of this centralized control system resulted in a huge amount of work that had been conducted cooperatively from 2002 to 2011 (Table 4): 1964 patients received specialist’s consultation, 221 were treated in the clinical department of the ‘Phthisiatry’ Research-Practice Center, 119 underwent surgeries for TB, 123 were excluded from smear-positive follow-up groups, and 308 patients were cured of TB.

Such system of cooperative work provided a highly effective treatment and follow-up: the rates are presented in Table 5, showing that average rates of clinical cure for 2002-2010 were 44% in Verknevilyuysky region, 37.7% in Sakha Republic, and 29% in Russian Federation.

Intensive comprehensive efforts against TB resulted in radical reduction of key epidemiologic rates for TB achieved in the Verknevilyuysky region for the period from 2002 to 2011 (Table 6).

Absolute rates (Table 7) likewise indicate stabilization of TB infection in the Verknevilyuysky region. Yet stabilization in incidence among newly identified patients is seen starting in 2005, while rates among patients with active TB started to stabilize later, in 2008.

Table 7

Stabilization of TB infection in the Verknevilyuysky region (abs. n.)

Rates	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Total number of newly identified cases	30	33	44	30	14	10	14	14	12	11
Of them, children and adolescents	13	8	11	6	2	4	1	3	1	1
Population cohort with active TB	131	114	95	90	72	56	41	37	37	35
Of them, children and adolescents	25	20	17	10	10	4	2	2	2	3
Bacillary-positive population cohort	67	41	30	32	22	22	19	17	24	18

In prospect, the fact that there is visible prognosis of healing children and adolescents of TB infection is an encouraging factor.

From 2002 to 2011 reduction had been achieved in:

- absolute numbers of children and adolescents with active forms of TB, down from 23 (2002) to 3 (2011), i.e. 7.7 times lower;
- TB infection in children, down from 12.0 to 6.8%, i.e. 1.7 times lower;
- TB infection in adolescents, down from 12.9 to 7.2%, i.e. 1.8 times lower;
- numbers of children at increased risk of TB disease, down from 402 to 124, i.e. 3.2 times lower;
- numbers of adolescents at increased risk of TB disease, down from 132 to 35, i.e. 3.8 times lower.

The proof for the above stated prognosis is the real reduction of TB infection source, i.e. numbers of bacillary-positive patients, from 67 to 18 (by a factor of 3.7) during the study period.

Thus, experience with fight against TB in the Verkhnevilyuysky region for the period from 2002 to 2011 conducted in cooperation with municipal bodies, health institutions and agencies, and the “Phthisiatry” Research-Practice Center, the leading republican specialized TB institution, demonstrated that TB is a controllable infection and that there is a real possibility to radically reduce key epidemiological rates for TB, and next, to heal the population of TB infection in any region of the Sakha Republic.

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Table 4

**Amounts of consultations, diagnostic procedures, clinical care, and dispensary patient follow-**

**up work, conducted in cooperation with the leading republican antituberculosis institution  
from 2002 to 2011**

	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Total
Number of patients who received specialist's consultation in the "Phthisiatry" Research-Practice Center	331	290	343	282	212	211	163	139	118	100	106	1964
Coverage of the patient cohort with consultations (%)	57.5	84.7	84.7	95.5	95.0	94.4	98.1	97.5	97.8	97.3	100.0	94.4
Coverage of the patient cohort with clinical treatment at the "Phthisiatry" Research-Practice Center (%)	5.3	22.9	30.7	29.5	27.7	27.7	23.2	39.0	26.7	67.6	47.2	221
Clinical treatment of children and adolescents at the "Phthisiatry" Research-Practice Center	34	25	29	20	26	28	22	12	15	10	9	186
Patients who underwent surgeries in the Pulmonary Surgical Department of the "Phthisiatry" Research-Practice Center	4	19	12	19	13	19	9	8	7	5	8	119
Patients excluded from smear-positive follow-up groups	12	18	9	21	15	23	10	6	7	6	8	123
Clinically cured patients	27	35	48	47	48	35	30	11	19	18	17	308

Table 5

**Effectiveness of clinical care and dispensary follow-up based on the rates of clinical cure in Verkhnevilyuysky region, Sakha Republic (Yakutia), and Russian Federation**

Territory	2002	2003	2004	2005	2006	2007	2008	2009	2010	Average rate
Verkhnevilyuysky region	28.5	41.2	49.4	53.3	48.6	53.6	25.5	45.9	49.0	44
Sakha Republic (Yakutia)	34.4	34.2	49.1	38.3	32.9	37.3	36.1	39.9	33.9	37.3
Russian Federation	19.3	21.4	39.4	28.7	30.1	31.0	31.9	-	-	29.0

Table 6

**Changes in key epidemiological rates for tuberculosis per 100,000 population**

Rates, Territory		2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Incidence	Sakha-Yakutia	86.9	75.5	84.9	75.6	72.9	65.7	69.1	67.1	68.2	
	Verkhnevilyuysky	137.0	152.8	207.1	141.5	65.9	47.0	62.9	64.3	55.8	51.2
Morbidity	Sakha-Yakutia	256.7	252.7	214.6	205.6	207.8	195.3	194.9	187.5	192.3	
	Verkhnevilyuysky	525.4	440.1	424.5	339.7	263.1	192.7	211.0	170.0	171.9	158.4
Bacillary-positive cases	Sakha-Yakutia	88.6	89.6	89.8	91.6	95.4	88.8	96.8	97.1	95.4	-
	Verkhnevilyuysky	199.0	189.9	146.2	151.0	103.4	103.4	89.4	78.1	106.9	83.6

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## EFFECT OF THORACOPLASTY ON CARDIORESPIRATORY AND IMMUNE SYSTEMS OF TUBERCULOSIS PATIENTS

A.F. Kravchenko

Study findings on the effect of thoracoplasty (one of the chief surgical treatments for pulmonary tuberculosis) on respiratory function, central hemodynamics, and immune status are presented. High compensatory capacities of the respiratory system and increased humoral immunity were detected, canceling the need for remedial therapy. Treatment with nitrates and ganglionic blockers was proposed for remedy of hemodynamic abnormalities.

**Keywords:** tuberculosis, thoracic surgery, thoracoplasty, cardiorespiratory system, immune system, remedial therapy

**Background.** Surgical treatment of consumption – pulmonary form of tuberculosis – was first attempted by Austrian surgeon Sauerbruch F. in 1888 [18], when he removed small rib portions close to the spine, at the diseased side. The effect of the surgery topped all expectations; the patient recovered. From that time on, thoracoplasty has become a chief method for surgical treatment of tuberculosis, being successfully used until now. Many variations of the original surgical procedures have evolved [5,10]. Fairly detailed descriptions have been made for post-resection conditions as a problem in surgically operated lung [1,2,6]. At the same time, thoracoplasty produces a certain biophysical effect of collapsed lung, unlike resection [9], and thus has various effects also on cardiorespiratory system and on indicators of systemic immunity. [11,12,16].

### Material and methods

197 patients having pulmonary tuberculosis were the clinical material for the study; of them, 84 (42.6%) with fibrocavitary TB, 84 (42.6%) with cavitary TB, and 29 (14.8%) with disseminated TB. All patients underwent standard upper posterior thoracoplasty by Bogush L.K. [3].

Home-produced “Metatest-2-02” equipment was used to study respiratory function. We determined respiratory frequency (Rf), minute ventilation (MV), maximum voluntary ventilation (MVV), vital capacity (VC). Flow-volume loop rates, peak expiratory flow rate (PEFR), PEFR at 25%, 50% and 75% of VC, forced expiratory volume in 1 second (FEV1) were assessed using “Spirosift” equipment from Fukuda Denshi (Japan).

Forced expiration rates were compared to reference predicted normal values by Klement

R.F. [8], interpretation of the respiratory function test findings with determination of the type and severity of the impairment of pulmonary ventilatory capacity were done based on recommendations by Nefedov B.V. [15].

Central hemodynamic rates were assessed using MLC-1200 computer densitometer from “Nihon Kohden” (Japan). Additionally, M.I. Tishchenko’s method of integral rheography [17] was employed for dynamic observation in follow-up period. Systolic pulmonary artery pressure (sPAP) was assessed using electrocardiography via V.P. Melnik’s modification [13] of S.A. Dushanin’s indirect method [7].

Cell-mediated and humoral immunity were assessed by standard methods [12].

All examinations were performed before the surgery and on days 9–12 and 30 postoperatively. Besides that, central hemodynamics was assessed either for 2–3 days, or hourly if medications were administered to correct central hemodynamic abnormalities.

Statistical data processing was done by Microsoft Excel tools for statistical analysis, employing standard methods for variable assessment. Assessment of statistically significant (reliable) differences in mean values between the study groups was done by Student’s test and chi-square test for 95% ( $p=0.05$ ) probability of unmistakable prediction, and based on the presence of correlations by linear correlation analysis ( $r$ ).

**Results.** For dynamic assessment of the effect of thoracoplasty on the function of respiratory organs, tests were performed in 116 patients, who had the following forms of pulmonary tuberculosis: 83 (71.5%) with fibrocavitary TB, 4 (3.4%) with disseminated TB, 29 (25.1%) with cavitary TB. Decreased MVV ( $77.7\pm4.09\%$ ), along with the heightened MV ( $190.6\%\pm10.6\%$ ) were the most noticeable baseline patient characteristics, which indicated the presence of 1-2 degrees of respiratory distress. Importantly, the increase in MV levels developed not only due to increased tidal volume (TV) ( $9\pm4.5\%$ ), but due to increase in frequency as well. After thoracoplasty, respiratory function indicators reduced abruptly, down to 40% of the baseline levels, due to the injury of the respiratory organs (intercostal muscles, deep and superficial thoracic muscles, rib removal). On the other hand, while MV increased by 8.6%, TV was decreasing to 7.1%, which was evidence that compensatory mechanisms are producing a smoothing effect on respiratory distress. Study of the expiratory fraction (PEFR at 75% of VC) in early postoperative period showed decrease to  $17.6\pm6.09$ ; this finding signaled about the obstructive component in larger bronchi. But nearer to the day 30, respiratory function indicators were observed to restore: VC restored by 9.7%, MVV restored by 35.4%, MV decreased by 40.1% together with the increase in TV to baseline indicators, patency of the large bronchi improved (PEFR at 75% of VC) to  $26.6\pm5.6\%$ .

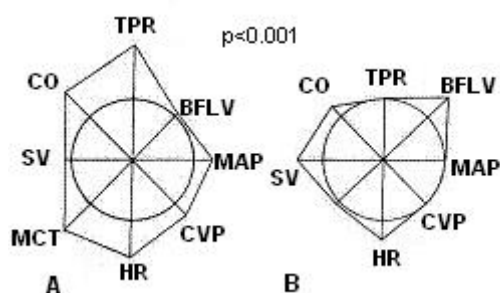


To determine the effect of thoracoplasty on central hemodynamics, examinations at various stages of thoracoplasty were done in 82 patients, of them 55 with fibrocavitary (67.2%), 7 with disseminated (8.5%), and 20 with cavitary (24.3%) pulmonary tuberculosis.

By E.A. Vagner's classification [4], blood flow types at baseline were as follows: 58 (70.7%) patients had eukinetic circulation, 16 (19.5%) had hypokinetic circulation, 8 (9.7%) had hyperkinetic circulation. Pre-operatively, no meaningful differences were found in central hemodynamic indicators of patients with different clinical forms of tuberculosis, possibly because of similar extents of the specific tuberculosis process.

In early postoperative period, thoracoplasty caused sharp changes in hemodynamic indicators. Cardiac index (CI) heightened from  $1.80 \pm 0.04$  to  $2.40 \pm 0.10$  L/min/m<sup>2</sup> ( $p < 0.05$ ). Systolic pulmonary artery pressure increased from  $42.01 \pm 1.22$  to  $44.53 \pm 3.24$  mmHg ( $p > 0.05$ ). Left-side thoracoplasty was associated with more marked hemodynamic disorders, then right-side surgery. Pulse, stroke volume (SV), CI and sPAP ( $P < 0.05$ ) remained significantly high at all stages of treatment; this should be regarded as typical effect of thoracoplasty on cardiovascular system.

Analysis of postoperative hemodynamic indicators suggested unequal rearrangements in systemic and pulmonary circulation of the patients after thoracoplasty. We supplemented the anesthetic care with antispasmodics: 0.01% solution of nitroglycerin (NG) in drop infusions. Such care was sufficient to provide adequate anesthesia and to stabilize hemocirculation. The use of pentamin (0.01-1.2 mg/kg body weight) provided total sympathetic blockade, manifesting as improved flow of blood to the heart, due to neutralized post-exercise vascular resistance.



**Fig. 1 Correction of central hemodynamics: A - before; B - after**

For correction of hemodynamic abnormalities, nitrate (nitroglycerin) and ganglionic blocker (pentamin) classes of drugs were administered in threshold doses under monitoring. Use of nitroglycerin was associated with marked systemic vasodilation, manifesting as the reduction of systolic and diastolic AP to 14% from baseline ( $p < 0.05$ ). Total peripheral resistance (TPR) decreased concurrently with the increase in levels of cardiac output (CO) (from  $4.87 \pm 0.23$  to  $5.54 \pm 0.23$  L/min/m<sup>2</sup>;  $p < 0.05$ ) and SV (from  $58.3 \pm 4.2$  to  $75.6 \pm 3.4$  mL/min/m<sup>2</sup>;  $p < 0.05$ ), decrease in levels of central venous pressure (CVP) (from  $6.9 \pm 0.4$  to  $3.9 \pm 0.3$  mmHg;  $p < 0.05$ ) and venous tone;



the latter contributed to improvement of blood flow to the heart. However, the decrease in pulmonary arterial vascular tone was not reliable. Use of pentamin produces the desired clear effect of decreased pressure in pulmonary circuit. This effect was confirmed by shortening of mean circulation time (MCT) (from  $20.1 \pm 0.12$  to  $13.9 \pm 0.43$  sec;  $p < 0.05$ ), which was an adequate reflection of the reduced pulmonary hypertension (Fig.1).

Considerable traumaticity of thoracoplasty can be smoothened by means of similar vasoparetic agents that improve the adequacy of the anesthesia care. These agents provide sufficient antistress defense and restrict the pulmonary arterial barrier. This facilitates adaptation of respiratory and cardiovascular systems to altered postoperative functional state; this adaptation is directed primarily at optimization of ventilation-perfusion ratios.

Immune status indicators at different stages of thoracoplasty were studied in 32 patients, of them: 14 (43.8%) with fibrocavitary tuberculosis, 9 with cavitary TB and 9 with disseminated TB (28.1%) respectfully.

Patients' baseline immunological assessments were compared to relative assessments in normal individuals. Pre-operative status of T-cell-mediated immunity in surgical patients was on fairly high level, as measured by total counts of T-lymphocytes, although levels of regulatory cells showed the predominance of T-suppressors. Analysis of immune indicators in patients with different clinical forms of TB showed that T-cell immunity reduced most profoundly in disseminated TB ( $45.9 \pm 3.65$ ,  $p < 0.05$ ), while in cavitary disease T-lymhocyte counts approximated those in control group ( $52.3 \pm 5.84$ ,  $p < 0.05$ ). T-helper subpopulation counts reduced more in patients with fibrocavitary or disseminated TB, and less so in patients with cavitary TB. The latter contributed to predomination of T-suppressors and hence to reduction of immunoregulatory index.

Intensification of humoral immunity was noted in all cases, due to increased relative and absolute numbers of B-cells. In turn, predomination of B-cell immunity correlated with the increase in levels of serum class A and G immunoglobulins.

Study of immune response at postoperative days 9-12 showed changes in T-cell immunity: reduction in T-helper content from  $27.15 \pm 1.53$  to  $23.54 \pm 0.9\%$  ( $p < 0.05$ ), increase in T-suppressors from  $22.0 \pm 1.66$  to  $26.33 \pm 2.57\%$  ( $p < 0.05$ ). B-lymphocyte counts were observed to decrease from  $28.25 \pm 1.58$  to  $13.01 \pm 2.08\%$  ( $p < 0.05$ ).

In stage 3 of the study (postoperative day 30), total populations of T-lymphocytes rose to baseline levels; the same trend was observed in T-helpers. These positive changes in immunoregulatory cells were observed in all patients irrespective of the clinical form of tuberculosis, although more markedly in patients with cavitary TB ( $p < 0.05$ ) and less manifested in

disseminated pulmonary TB ( $p < 0.05$ ).

Positive changes were observed in B-cell indicators as well, with more pronounced manifestations in fibrocavitary TB ( $p < 0.05$ ) and a bit less so in cavitary TB, compared to disseminated TB. Immunoglobulins showed a trend to normalization in IgA and IgG levels, reflecting the reduction of inflammatory activity in the lungs (Table 1).

Table 1

**Systemic immune indicators at various stages of thoracoplasty**

No	Immune response indicators	Baseline levels (M $\pm$ m)	Postoperative period (M $\pm$ m)	
	Test timings		Days 9–12	Day 30
1.	T lymphocytes ( $\times 10^9$ )	$0.935 \pm 0.06$	$0.737 \pm 0.04$	$1.07 \pm 0.08$
2.	T lymphocytes (%)	$50.09 \pm 1.88$	$49.56 \pm 2.19$	$51.05 \pm 1.98$
3.	T helpers (%)	$27.15 \pm 1.53$	$23.54 \pm 0.9$	$25.35 \pm 1.31$
4.	T suppressors (%)	$22.0 \pm 1.66$	$26.33 \pm 2.57$	$23.58 \pm 2.03$
5.	Leucocytes ( $\times 10^9$ )	$6.22 \pm 0.12$	$19.62 \pm 1.78$	$31.45 \pm 1.04$
6.	Lymphocytes (%)	$28.25 \pm 1.58$	$13.01 \pm 2.08$	$26.94 \pm 1.6$
7.	B lymphocytes ( $\times 10^9$ )	$0.533 \pm 0.02$	$0.405 \pm 0.03$	$0.570 \pm 0.02$
8.	B lymphocytes (%)	$27.13 \pm 1.21$	$22.93 \pm 1.06$	$21.5 \pm 0.07$
9.	Ig A (%)	$2.35 \pm 0.11$	$2.34 \pm 0.09$	$2.15 \pm 0.07$
10.	Ig M (%)	$0.95 \pm 0.33$	$1.07 \pm 0.06$	$0.92 \pm 0.04$
11.	Ig G (%)	$14.3 \pm 0.46$	$12.37 \pm 0.7$	$13.38 \pm 0.37$

To conclude, changes in immune indicators in postoperative period gave evidence for various degrees of the damaging effect that disease persistence and adaptation of the body to new postoperative state have on immune system. In patients with cavitary TB changes in immune indicators testified for better and quicker restoration of immune system, than in patients with disseminated or fibrocavitary forms of TB.

**Conclusions:**

1. Although spirometric indicators were acutely reducing after thoracoplasty, significantly improved breathing activity and partially restored respiratory function were found on postoperative day 30, demonstrating high compensatory capacities of the respiratory system. This can be



attributed to the fact that thoracoplasty is less traumatic for the lung and preserves lung parenchyma, which is of greater clinical and prognostic significance, than the surgical damage to respiratory organs.

2. In short term following thoracoplasty, systemic and pulmonary hemodynamic indicators are found to be inhibited ( $p < 0.05$ ), and this is a condition requiring corrective therapy. Use of nitrate and ganglionic blocker classes of drugs substantially improves the central hemodynamics and ventilation/perfusion ratio ( $p < 0.001$ ).

3. Changes in immune status indicators following thoracoplasty had a compensatory nature caused by natural rearrangement of immune system, and did not require active immune corrective therapy.

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## THORACIC SURGERY OF YAKUTIA: VIEW THROUGH THE PRISM OF PHTHISIATRY

A.F. Kravchenko

Thoracic surgery as a specialty had been developed in Russia since the postwar years, but was officially established as a specialty in 1996. Absolute majority of thoracic surgical operations in the USSR were performed in anti-tuberculosis institutions. In Yakutia, thoracic surgery developed in three stages: start-up, assimilation of new techniques, development and introduction of in-house original methods of surgery.

**Keywords:** Yakutia, thoracic surgery, phthisiology, pneumonectomy, thoracoplasty, collapse therapies, airtight stump closure, anesthesia.

Medical specialty of “thoracic surgery” was officially established as specialty in 1996, although its development had been ongoing in Russia since the postwar years, owing to such seasoned scientists with world-wide reputation as B.V. Petrovskiy, I.S. Kolesnikov, M.I. Perel'man, F.G. Uglov. “Chest Surgery” was the branch of general surgery at that time. N.M. Amosov, an internationally renowned cardiothoracic surgeon and the Head of the Kiev Cardiovascular Surgery Clinic was awarded the USSR State Prize for developing the surgical procedure of pneumonectomy in patients with tuberculosis (TB). M.I. Perel'man's monograph on pulmonary resections was published in 1963 and from that time on, thoracic surgery started to develop quickly.

A.A. Priymak observes that until “perestroika”, 85% of all thoracic surgical operations in the USSR were performed in anti-tuberculosis institutions. Consequently, by improving and developing new approaches to pulmonary surgical procedures, TB surgeons made a huge contribution to advancements in thoracic surgery.

In view of the above, it looks interesting that the pace of progress in thoracic surgery in Yakutia can be conveniently divided to 3 phases:

I<sup>st</sup> : establishment and formation (until 1970s);

II<sup>nd</sup>: adoption of new techniques (until 2000s);

III<sup>d</sup> : development and adoption of original surgical methods (since 2000s).

In 1952 during the formative period, Jacobaeus operation and phrenicotomy with nerve alcoholization were first performed by D.A. Guriev and G.M. Koksharskiy, who undoubtedly were the founders of chest (thoracic) surgery in Yakutia. In 1953 the first upper posterior thoracoplasty



for TB was performed (D.A. Guriev) under local narcosis; this surgical operation was actively practiced in the USSR at that time. Year later G.M. Koksharskiy performed extrapleural pneumolysis in combination with oleothorax, which in the following years became the “hallmark” of the established Yakutsk Branch of Tuberculosis Institute of the USSR Academy of Medical Science, now renamed to Central Research Institute for Tuberculosis RAMS (fig.1).

At that time in the era of mask anesthesia, D.A. Guriev was performing thoracoplasty in Pulmonary Surgical Department of the Yakutsk City Anti-TB Dispensary. With the adoption of intubation anesthesia technique, Guriev performed in consecutive order lobectomy (1957), pneumonectomy (1960), one-stage pulmonary lobe resection with thoracoplasty (1961), and finally wedge resection of the lung.

Today all these surgical procedures are among the basic repertoire of thoracic surgery in clinical and general practice, both for TB and cancer. Bearing in mind the period and conditions, when these surgical techniques had been mastered and then practiced, D.A. Guriev, Honoured Doctor of YASSR and RSFSR, Cavalier of the two Orders of Lenin, Order of the October Revolution, Order of the Badge of Honour, Deputy of the two Congresses of the Supreme Soviet of YASSR, can easily be named the patriarch of Yakut thoracic surgery.

One of the newer technology-intensive surgical techniques introduced to Yakutia were the surgical operations by A.I. Borovinskiy (performed in Yakutia by Stepanov K.N., Afanasiev N.Kh.), i.e. staged extrapleural pneumolysis with extrapleural thoracoplasty, cavernotomy (cavernostomy) followed by cavernoplasty (1982). At this time, Linev N.I. received his authorship certificate for accelerated epithelialization of the “open cavity” that allowed substantial reduction of treatment duration. A.G. Malitskiy’s method on formation of a “small” lung was introduced in 1987. Precision pulmonary (tuberculoma) resection (A.A. Kornilov, N.Kh. Afanasiev), electroanesthesia in combination with pharmacological agents (S.M. Kolesov, S.K. Kononov), and administration of anti-TB agents to internal thoracic vein (I.I. Vinokurov) were introduced in 1988.

In 1989 I.I. Vinokurov performed one-stage surgery on two lungs via L.K. Bogush’s transsternal approach; in 1994 two surgical teams at once performed one-stage surgery on two lungs by anterolateral approach (I.I. Vinokurov, Yu.S. Ivanov). Intrapericardial ligation of pulmonary artery was performed in 1998-1999; retrograde pleuropneumonectomy was performed some time later. One-stage surgery on two lungs accessed via unilateral intercostal mediastinal approach through anterior mediastinum was performed in 2001 (A.F. Kravchenko).

Overall, these surgical interventions allowed the surgeons significantly enhance their skills,





and determined the performance level of Pulmonary Surgical Department.

The 2000s have marked a new leap in the advancements in thoracic surgery. Starting in 2001-2003, new methods of collapse surgery have been developed and practically adopted, which later were protected by patents for inventions: extrapleural method for pulling down the lung apex and then securing it with the hammock-like mesh; two-stage “cascade” thoracoplasty preceded by preliminary pleurodesis; extrapleural plombage of the lung apex using latex balloon (A.F. Kravchenko et al.). The following devices were developed to perform the above surgical interventions: net weaving device; plombage latex balloon; distributing switchboard for analgesics. The devices were later patented by Russian Federation utility model patents (A.F. Kravchenko, N.S. Byutyaeva, A.I. Obutova, E.N. O-Zhi-Kho) [1, 4, 7, 8] (fig.2).

In 2010 the method of costoclavicular thoracoplasty was developed and patented by the team of authors (I.I. Vinokurov, A.F. Kravchenko, Yu.S. Ivanov et al.). The difference of this method is that, unlike in standard thoracoplasty, certain clavicle length (derived by calculation) is removed also, to achieve maximum collapse of the hemithorax [6].

Patented new method of analgesia intended for use in thoracoplastic surgery is somewhat unconventional technique among all the above newly developed collapse surgical interventions (A.F. Kravchenko) [3]. The method is an equivalent of S.S. Yudin’s technique (1960) for paravertebral anesthesia; the difference is that catheters for postoperative administration of analgesic agents are placed as near to the spine as possible, along the beds of removed ribs (fig.3).

Increased number of surgical interventions performed, including organ-removal operations, and hence increased frequency of postoperative complications have lead us to search for ways to resolve such complications as bronchial fistulas, or the failure of main bronchial stump. In view of this, we have adopted the technique for reamputation of the primary bronchus (I.I. Vinokurov, A.F. Kravchenko). Starting in 2005, the procedure of mainstem bronchus occlusion via transsternal and transpericardial approaches has been mastered and adopted for practice, with no outside guidance (Fig.4). Our other methods that have been likewise developed and patented are: reinforcement of the mainstem bronchial stump with malpighian layer; airtight closure of the mainstem bronchial stump by stump reduplication using the proper membranous part of the bronchus (I.I. Vinokurov, A.F. Kravchenko, Yu.S. Ivanov) [2, 5] (fig. 5).

Nearest targets for further development of thoracic surgery are:

To certify thoracic surgeons in specialties of general surgery, oncology, and endoscopic surgery.

To master the surgical skills to perform mainstem bronchus occlusion (resection) via retropericardial approach in patients reoperated for bronchial fistula.



To expand the use of video-assisted endoscopic thoracic interventions for tuberculosis and other thoracic diseases.

To determine the applicability and prerequisites for the anastomosis of trachea to the main bronchus of contralateral lung after the removal of the lung with its main bronchus and the carina due to extensive cancer of the respiratory organs.

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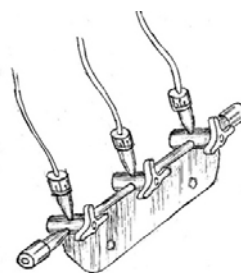
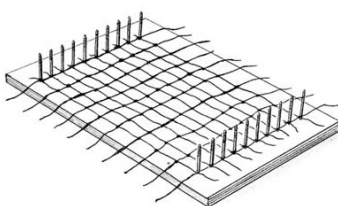
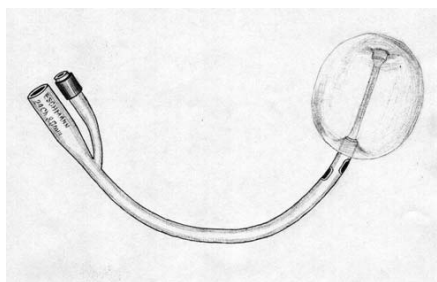
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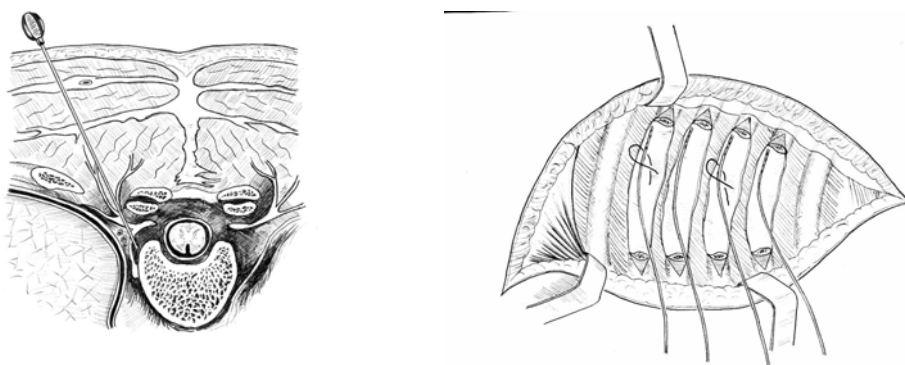
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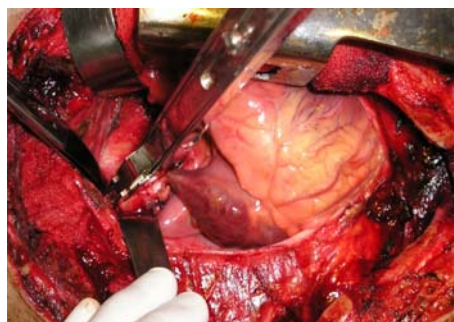
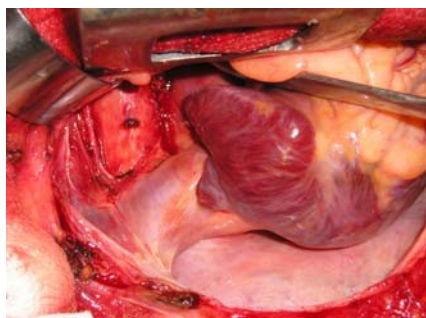
**Fig.1 Guriev D.A. Koksharskiy G.M.**



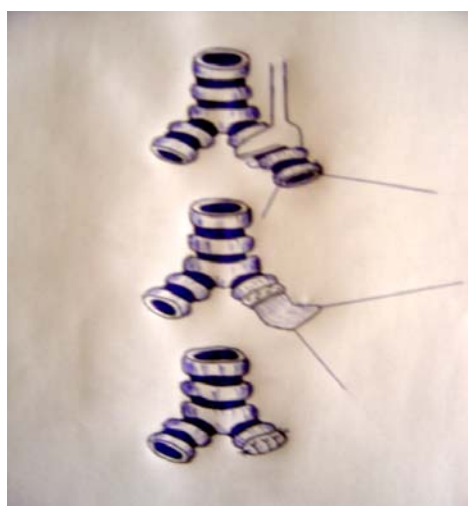
**Fig.2. Devices for use in collapse surgery (Device for compressing the lung by means of latex balloon; Net weaving device; Distributing switchboard for postoperative analgesia)**



**Fig. 3. Paravertebral anesthesia methods (Yudin's paravertebral anesthesia;  
Conduction post-thoracoplasty analgesia)**



**Fig. 4. Transpericardial approach; Right mainstem bronchus occlusion**



**Fig. 5. Airtight closure of bronchial stump using proper membranous part of the bronchus**

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**E.F. Luginova**

**RESULTS OF SURVEILLANCE FOR BCG COMPLICATIONS IN SAKHA  
REPUBLIC (YAKUTIA)**

**Summary**

Results of monitoring for complications to BCG vaccine in children in Sakha Republic (Yakutia) are presented. Incidence and nature of complications to vaccines against tuberculosis infection and the clinical structure of complications were analyzed; causes of complications were determined. For the last years, we observed growing incidence of complications to vaccines against tuberculosis. The study established that complications develop most often to BCG vaccine, and rarer to BCG-M vaccine. Lymphadenitis was the prevailing diagnosis in the clinical structure of complications. Severe forms of complications were registered more frequently in children under 3 years of age. Complications in children immunized at pediatric polyclinics or rural first aid posts were mostly due to wrong administration technique. Main causes for complication development were: perinatal pathology, underestimation of counterindications, infectious or virus diseases in postvaccinal period, faults in vaccine administration technique.

**Keywords:** BCG vaccine, tuberculosis, pediatric population

**Introduction.** BCG vaccine was created in 1921 by French microbiologist Albert Calmette and veterinarian Camille Guérin for human immunization against tuberculosis. In USSR, BCG vaccine was introduced in 1925. Later, results from experimental and clinical studies were systematized, showing the effectiveness of vaccination: mortality from tuberculosis in vaccinated groups of children exposed to bacillary-positive persons was significantly lower than among non-vaccinated children. In our country, starting in 1928, BCG vaccination had been recommended for newborns from the infectious disease foci, and starting in the 1950s vaccination was made mandatory all over the country [1].

Today according to national immunization schedule, vaccination to prevent tuberculosis in children is done on days 3-7 after birth; revaccination is done in 7 and 14 year old children. In Sakha Republic 93-95% of newborns in maternity hospitals are covered with BCG vaccination annually; coverage at age 1 is 98-98.4%. The first revaccination covers 82-85% of predicted



population; the second revaccination covers 60-78% of children.

In 2010, 994 children in Sakha Republic did not receive BCG, which is 6.9% of newborns (880 in 2009; 718 in 2008). Among vaccination counterindications in newborns, the first reason was premature birth (19.2%), and the second and third reasons were perinatal encephalopathy (14.4%) and intrauterine infection (9.3%), respectfully.

The problem of complications after BCG vaccination and revaccination has grown important for the last years. In view of this, in 2003 a new patient follow-up group was established and added to existing groups of patients followed-up in anti-tuberculosis dispensaries: group V for children with complications after vaccines against tuberculosis (Order #109, issued March 21, 2003). This enabled precise monitoring of the incidence of complications to vaccines against tuberculosis and improved registration and follow-up of this patient population.

According to the Order #109 (issued March 21, 2003) complications developing after BCG vaccination are divided to 4 classes:

Class 1 complications: localized lesion (subcutaneous infiltrate, cold abscess, ulcer), regional lymphadenitis;

Class 2 complications: persisting or disseminated BCG infection without lethal outcome (lupus, osteitis);

Class 3 complications: disseminated BCG infection, generalized pathology with lethal outcome, observed in cases with congenital immune deficiency.

Class 4 complications: post BCG syndrome (erythema nodosum, granuloma annulare, skin rash).

By official statistical reports, postvaccinal complications are found in nearly 300 newborns annually in Russian Federation. M.V. Shilova notes that in Russian Federation in 2010 the most severe complications (dispensary follow-up group VA) were registered in 154 children (132 in 2009; 105 in 2008), which made 0.7/100.000 pediatric population (0.6 in 2009; 0.5 in 2008). Complications of medium severity (dispensary follow-up group VB) were diagnosed in 353 children (552 in 2009; 447 in 2008), which was 1.6/100.000 children. The most minor complications (dispensary follow-up group VV) were found in 82 children (76 in 2009; 105 in 2008) or 0.4/100.000 pediatric population. Hence it is seen that complications after tuberculosis vaccines have been aggravating in terms of clinical structure and incidence [2].

In 2008 the regions of the Russian Federations with the incidence of tuberculosis lower than 70.0/100.000 population switched to vaccination of newborns with BCG-M vaccine, in compliance with the Order of the Russian Federation Ministry of Health and Social Development #673 (issued

October 30, 2007) “On national immunization schedule based on epidemic indicators”. Because of persisting high incidence of tuberculosis on the territory of Sakha Republic, newborns had been vaccinated with BCG vaccine until 2009. Use of BCG-M vaccine has started only in July 1, 2009, following the Order of the Ministry of Health of Sakha Republic (Yakutia) #01-8/4-387 (issued April 15, 2009).

**Aim:** to assess the results of the monitoring for incidence of complications after BCG vaccines in children in Sakha Republic, and to identify the characteristics and major causes of complications.

**Material and methods.** We analyzed medical documentation on children who developed complications after BCG vaccination for the period from 2003 to 2011. Total of 63 children with various complications had been followed-up in Republican anti-tuberculosis dispensary, of them 12 (19%) in Group VA, 35 (55.5%) in Group VB, 16 (25.4%) in Group VV. Incidence of complications started to sharply increase in 2005; the largest number of cases with complications to BCG vaccines over the republic was registered in 2009 (19 cases).

Children under 1 year of age made 26.9% of the total number of follow-up patients, with boys predominating (58.7%). In 58 (92.1%) of 63 cases children were vaccinated with BCG, while only 5 (7.9%) were vaccinated with BCG-M. Majority of cases developed complications after vaccination (89%), and more rarely after revaccinations (11%).

By clinical structure of complications, lymphadenitis developed most often and was observed in 39 children (61.9%). Tuberculosis of bones was diagnosed in 10 (15.8%), cold abscess in 6 (9.5%), cutaneous tuberculosis in 3 (4.8%), keloid in 2 (3.2%), ulcer in 1 (1.6%), generalized BCG infection in 2 (3.2%) children with primary immune deficiency.

The most severe complications (dispensary follow-up group VA) with bone and joint involvement and generalized BCG infection were registered only in children under 3 years, including 4 children under 1 year of age.

In all detected cases of complications to BCG vaccine children were prescribed specific therapy either inpatiently in tuberculosis hospital, or outpatiently. The length and treatment regimen depended on nature of complications. Dispensary follow-up was managed with regard to clinical form and class of complication.

**Results and discussion.** Complications to tuberculosis vaccines were registered most often in children in Yakutsk (42.8%), Mirninsky region (12.7%), Neryungrinsky region (11.1%), and rarer in other regions of the republic.

Analysis of the incidence by health institutions showed that 76.2% of children were



vaccinated in maternity departments, 20.6% in polyclinics, and 3.2% in (rural first aid posts).

There were 15 (23.8%) cases with unfound causes of complications and 48 (76.2%) cases with established causes. Among the established causes of complications, the most frequently identified causes were wrong administration technique (39.7%), program errors (20.6%), and wrong patient appointment for vaccination (15.9%).

Analysis of internal investigation reports showed that the structure of clinical forms of postvaccinal complications directly depended on where the children were vaccinated. Thus BCG-lymphadenitis developed mostly in children vaccinated in maternity hospitals (76.2%), cold abscess – in children vaccinated in polyclinics (75%), keloids and ulcers – in children vaccinated in polyclinics (100%), BCG-osteitis – in children immunized in maternity departments (75%).

Complications to BCG vaccines in children who were immunized in maternity hospitals were distinctly more severe and had more vivid clinical manifestations. 3 of 10 cases of BCG-osteitis developed as result of gross violation of the instructions for use of BCG vaccine, as evident from the fact that blood samples for phenylketonuria test were collected on the day of vaccine administration. High incidence of BCG-lymphadenitis in children who were vaccinated in maternity hospitals or rural first aid posts signaled, as a rule, about wrong appointment of children for vaccination. The nature of complications in children vaccinated in polyclinics showed that they were largely due to technical faults during administration of vaccines.

It should be emphasized that in 16 (25.4%) cases out of 63 complications to BCG were detected with delays. This group (dispensary follow-up group VV) included patients with lymphadenitis in reverse development phase (calcification). BCG-lymphadenitis in reverse development phase was detected by radiological chest examination. This type of complications was difficult to diagnose at early phases because of the scarcity of symptoms during the progression of lymphadenitis, and because no pain syndrome or skin changes were seen at early phases of the disease.

Localized complications (ulcer, cold abscess, keloid) were detected on visit to a doctor. Children were referred to anti-tuberculosis dispensaries from medical districts covered by pediatricians. Patients with cutaneous tuberculosis (3 cases) visited dermatologist first. Average time to referral from primary network to phthisiologist was 1.5 to 2 months.

Cases of BCG-osteitis were the most difficult to correctly diagnose. After thorough history taking visible contraindications to BCG vaccination were absent in 88.8% of children with BCG-osteitis; the fact of trauma in postvaccinal period was ascertained in 37.5% of patients; superimposition of acute virus or other infections was established in 25%; vaccination against DPT

was present in 37.5%. These children were not exposed to persons with tuberculosis disease. Precipitating factors (trauma, intercurrent diseases etc.) were present. Various localizations of bone lesions were observed in patients, with a picture of reactive arthritis in earlier stages of the disease, followed later by osteomyelitis. Moreover, circumscribed involvement of bone tissue was observed, with the absence of lung or intrathoracic lymph node involvement. There was notable disparity between rather extensive bone destruction and the “mild” disease progression with scarce clinical manifestations and with periods of remission and exacerbation in BCG-osteitis, unlike in non-specific diseases of osseous-articular system. Clinical picture was characterized most often by heightened temperature, gait abnormality, swelling, and absence of marked intoxication syndrome.

It should be pointed out that in Sakha Republic awareness among primary network specialists (pediatricians and pediatric surgeons) has considerably raised for the last years, in what regards the management of patients with this disease. As a result, patients with osseous-articular diseases referred for operation to surgical department of Pediatric Center of the Republican Hospital No.1 (National Center for Medicine) undergo histological and bacteriological examinations, and have consultation with the phthisiologist.

Etiologic confirmation is important in verifying osseous-articular tuberculosis and BCG-osteitis. Reasons for the necessity of etiologic confirmation in children are: differences in organization of antiepidemic activities, chemotherapy regimens and substantive actions, which are taken into account during the diagnosis of either tuberculosis disease, or complication to BCG vaccination.

In 9 of 10 cases of BCG-osteitis vaccine strains of tubercle bacilli (*M.bovis*-BCG) were present in surgical material. Histological confirmation of the diagnosis was established in 10 patients with BCG-osteitis. Importantly, 2 species of staphylococci (*S.aureus* and *S.epidermidis*) were cultured in operative material from 3 (30%) patients. Sensitivity to tuberculin in children was moderate, judging by the results of Mantoux test with 2 TU; mean papule size was  $11.3 \pm 1.3$  mm. Diaskintest used in our republic since 2009, was negative in 3 patients; this test was not used in other patients.

All patients with BCG-osteitis received consultation in the Federal State Budgetary Institution “Saint-Petersburg Research Institute for Phthisiopulmonology”. All 10 patients underwent surgical treatment, of them 8 patients were treated by high-tech surgery.

**Conclusion.** Results of monitoring for complications to tuberculosis vaccines in Sakha Republic showed growing number of complications to BCG vaccine. Complications were registered most often in children under 1 year, vaccinated with BCG, or much rarer with BCG-M vaccine. The



most severe complications with marked clinical manifestations developed in children who were vaccinated in maternity hospitals, signaling failure to determine indications and contraindications to vaccination. In children who were vaccinated in pediatric polyclinics or rural first aid posts complications develop more often due to faults in administration technique. Perinatal pathology, underestimation of contraindications, infectious and viral diseases in postvaccinal period contribute to development of complications to BCG vaccine. All of the above said requires strengthening of measures to control the quality of BCG vaccination and revaccination.

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## INCIDENCE OF TUBERCULOSIS IN THE STAFF OF HEALTHCARE ORGANIZATIONS AND RESPONSIBILITY OF REGISTERED NURSING STAFF IN CONDUCTING ANTIEPIDEMIC MEASURES

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**Summary.** We comparatively analyzed the incidence of tuberculosis in the staff of various specialty healthcare organizations, through the case of the Sakha Republic (Yakutia), and monitored clinical *M.tuberculosis* strains for susceptibility/resistance to disinfectants. Incidence of tuberculosis among the staff of anti-tuberculosis institutions was 3 to 4 times higher ( $p<0.05$ ), than in the staff of other healthcare organizations; among them, tuberculosis occurred mostly in registered nursing staff and in nurse assistant staff.

Disinfectants types that played main role in the control of nosocomial transmission of *M.tuberculosis* were chlorine compounds, and quaternary ammonium compounds (QAC) in combination with aldehydes.

**Keywords:** tuberculosis, *Mycobacterium tuberculosis*, incidence, antiepidemic measures, medical staff, disinfectants

**Background.** Overall epidemiologic situation with tuberculosis (TB) in Russia, and in Sakha Republic (Yakutia), is still stressful, despite recent stabilization in some indicators of TB prevalence and despite organization of anti-TB activities for population protection [1,5]. Incidence of nosocomial TB keeps growing, and has increased twice over the last 10 years [4]. Intrahospital non-specific antiepidemic measures start to play increasingly important role in today's unfavorable epidemiologic situation with TB; these measures consist essentially in decontaminating various inanimate objects by means of disinfecting agents [2,3], and in preventing nosocomial transmission of *M.tuberculosis* (MTB) [9].

To prevent possible emergence of strains with resistance to disinfectants, hospital strains must be monitored for resistance to disinfectants currently in-use in the hospital, and disinfectants must be rotated subsequently, i.e. disinfectant of one chemical type must be systematically replaced by disinfectant of another chemical type, when necessary [7]. Sanitation measures aimed at

prevention of nosocomial infection, including TB, are largely defined by antiepidemic schedule [10], while registered nursing staff plays the key role in effective conduct of this schedule [6,8].

**Aim.** To comparatively analyze the incidence of TB in the staff of healthcare organizations of diverse specialties, through the case of Sakha Republic (Yakutia); to conduct monitoring for susceptibility/resistance to disinfectants in clinical MTB strains.

**Materials and methods.** The study was held from 2007 to 2011; the subjects and materials included:

Patients (staff) with occupation in healthcare organizations, newly diagnosed with TB, of them, 57 working in healthcare organizations and 23 working in anti-TB institutions. Patient groups were randomized according to job positions held by medical staff in various healthcare organizations.

Disinfectants used in anti-TB institutions, grouped by chemical composition of their main active substances.

Tuberculocidal properties of disinfectants were tested using the techniques [11,12] based on procedures adopted from the widely known method accepted in disinfectant testing practice, i.e. submerging coarse calico test-objects contaminated with the test-microbes into a disinfectant.

The following test strains were used to assess the effectiveness of disinfectants: 1. Clinical strain *M.tuberculosis* No.255, resistant to streptomycin at 10 mcg/mL MIC, to isoniazid at 1 mcg/mL MIC, to rifampicin at 40 mcg/mL, and to capreomycin at 30 mcg/mL; 2. Drug-susceptible clinical strain of *M.tuberculosis* № 258.

More than 500 control samples were collected and tested to study the effectiveness of 9 disinfectants used in anti-TB institutions: 1. "Chloramine B" (0.5% concentration); 2. "Sulphochlorantine D" (1.0%); 3. "Chlormisept-R" (0.2%); 4. "Slavin" (1.2%); 5. "Brilliant" (2.0%); 6. "Aqua-chlor" (0.1%); 7. "Mirodez-univer" (1.0%); 8. "Ecobriz" (2.0%); 9. "Alphadez" (1.0%).

The study findings were summarized using statistical methods: calculation of the median, with minimum and maximum values; calculation of mean square deviation; Student's test (t); Pearson's/Fisher's  $\chi^2$  tests with correction factors (Yates, McNemar) to check the reliability of differences (p), with at least 9% confidence interval.

**Results and discussion.** TB incidence rate in medical personnel (Table 1) was lower (median 56.84; min 53.1; max 56.9), than in civil population of Yakutia (median 68.8; min 65.7; max 73.9), ( $p>0.05$ ). Low min/max amplitude indicated that incidence level in medical staff tended to be more stable. Comparison of the incidence (per 100 000 employees) rates between healthcare



organizations and anti-TB institutions showed statistically meaningful difference: incidence among the staff of anti-TB service was 3.5-4 times higher, than in the staff of other healthcare organizations: 12 (46.7) and 3 (163.3) cases, respectfully ( $\chi^2=24.22$ ;  $p<0.001$ ).

The highest TB incidence was revealed among the staff of the “Phthisiatry” Research-Practice Center: 513.7/100 000 pop., 7.5 times higher than the incidence among civil population of Yakutia ( $\chi^2\text{-Pearson}=332.0$ ;  $p<0.001$ ) (Fig.1).

Among the rest of healthcare organizations, high TB incidence was documented in the staff of the Center for Emergency Care (Republican Hospital No.2): 459.4/100 000 pop., 6 times higher than the incidence (68.2/100 000 pop.) among civil population of Yakutia. ( $\chi^2\text{-Pearson}=282.7$ ;  $p<0.001$ ).

Patients are hospitalized to the Center for Emergency Care (Republican Hospital No.2) by emergency ambulance – unexamined patients seeking emergency care. Such high incidence may be predetermined by the absence of infection control system, low effectiveness of antiepidemic measures or disinfectants.

We analyzed TB case detection methods in 80 patients, of them, 23 employees of anti-TB institutions and 57 employees of other healthcare organizations (Table 2). In personnel of healthcare organizations, TB disease cases were detected more often on visit to a doctor due to feeling unwell, while in the staff of anti-TB institutions, TB cases were detected via occupational health examinations, and this difference was highly significant ( $\chi^2\text{-Pearson}=9.03$ , with Yates correction  $\chi^2\text{-Yates}=7.61$ ;  $p\leq 0.027$ ). Analysis of the time to case detection showed that TB cases detected in other healthcare organizations were significantly more often bacillary-positive ( $\chi^2\text{-McNemar}=6.88$ ;  $p<0.05$ ) or had destructions in lung tissue at the time of detection ( $\chi^2\text{-Fisher}=0.58$ ;  $p>0.05$ ). Hence TB disease in the staff of healthcare organizations was detected in the late stage, when bacterial expectoration and lung destruction were already present; this is confirmed also by generalized indicator of delayed detection ( $\chi^2\text{-McNemar}=9.85$ ;  $p<0.01$ ).

Study of the incidence of TB among healthcare workers in relation to different job positions (Table 3) showed more frequent incidence among registered nursing staff (36; 45.0%), followed by nursing assistants (32; 40.0%), with rarer incidence among doctor staff (12; 15.0%) ( $\chi^2\text{-Pearson}=27.64$ ;  $p<0.001$ ). This may be explained by direct exposure to patients with TB and spending much time near the patients, some of whom are bacillary-positive, as well as by low level of hospital infection control and low effectiveness of antiepidemic measures.

Decontamination of indoor spaces and inanimate objects is an important component of antiepidemic measures against TB infection in healthcare organizations. We analyzed the activity of

several disinfectants with different chemical compositions, to determine the effectiveness of disinfectants recommended for use against MTB strains (Table 4). All disinfectants tested are widely used in healthcare practice, and none of them (used in recommended regimes) demonstrated 100% tuberculocidal effect on test strains of MTB, both multidrug-resistant (MDR), and drug-susceptible. Overall, of 9 disinfectants recommended for accepted practice, 5 (55.5%) disinfectants were effective against drug-susceptible MTB, and 2 (22.2%) were effective against MDR MTB. Tuberculocidal effect on clinical MTB strains was demonstrated by the following types of disinfectants: chlorine compounds, quaternary ammonium compounds (QAC)+aldehydes.

The study showed that, because nursing and nurse assistant staff is most vulnerable to TB infection, new approaches are needed to improve the performance of these groups of anti-TB service personnel. The key measures to achieve this should include: ensuring safe working environment; staff education on principles and methods of infection control; creating the quality management system for nursing care that would help to shape the body of knowledge and skills to remain up-to-date with contemporary requirements. To conduct effective antiepidemic measures, essential emphasis must be made on monitoring for microbial susceptibility/resistance to disinfectants used in the hospital.

### **Conclusions:**

1. Incidence of TB among the staff of anti-TB institutions was 3.5-4 times higher than in the staff of other healthcare organizations. Among the staff of anti-TB institutions, TB occurred mostly in registered nursing staff and in nurse assistant staff ( $p < 0.001$ ).
2. In the staff of anti-TB institutions, preventive health examination was the chief TB detection method in 74% of cases; in the staff of other health organizations, 63% cases were detected on visit to a doctor due to feeling unwell ( $p < 0.05$ ).
3. The personnel of emergency care was 6 times more ( $p < 0.001$ ) predisposed to TB infection, than civil population of Sakha Republic (Yakutia).
4. Among disinfectants, chlorine compounds and QAC+aldehydes had tuberculocidal effect on clinical strains of MTB isolated in the territory of Sakha Republic (Yakutia).

### **Proposals:**

1. Medical staff must be continuously educated on issues relating to high risk of nosocomial transmission of TB infection.
2. Personnel of emergency healthcare organizations must undergo mass fluorographic examination twice a year, with the purpose of early detection of TB.
3. Uniform procedure of disinfection processes (routine and final disinfection in TB infection

reservoir) for TB prevention must be developed, taking into account also data from hospital MTB strain monitoring for resistance to disinfectants in-use.



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**Table 1**

**Incidence of tuberculosis in the staff of healthcare organizations, Sakha Republic (Yakutia), per 100.000 pop.**

Year	Total		Of them:			
	Absolute number	Rate per 100 000 pop.	Healthcare organizations		Anti-TB institutions	
			Absolute number	Rate per 100 000 pop.	Absolute number	Rate per 100 000 pop.
2007	16	56.2	8	30.1	8	415.3
2008	18	63.5	14	53.0	4	205.9
2009	15	53.1	10	37.9	5	259.8
2010	16	56.9	13	49.5	3	160.5
2011	15	55.5	12	46.7*	3	163.3**
Total	80		57		23	

Note: \*/\*\* - p<0.001

**Table 2**

**Tuberculosis detection methods in the staff of healthcare organizations (absolute number, %)**

Year	Total		Detection method				MTB (+)		CV (+)	
	Anti-TB institutions	Other healthcare organizations	Occupational examination		On visit		ATBI	OHO	ATBI	OHO
			ATBI	OHO	ATBI	OHO				
2007	8	8	7(87.5)	3(37.5)	1(12.5)	5(62.5)	4(50)	3(37.5)	2(25)	4(50)
2008	4	14	2(50)	6(43)	2(50)	8(57)	1(25)	9(64)	1(25)	7(60)
2009	5	10	4(80)	4(40)	1(20)	6(60)	4(80)	6(60)	2(40)	1(10)
2010	3	13	2(67)	5(38.5)	1(33)	8(63)	1(33)	7(53)	1(33)	7(37)
2011	3	12	2(67)	3(25)	1(33)	9(75)	1(33)	5(42)	1(33)	2(17)
Total	23	57	17(74)*	21(37)*	6(26)*	36(63)*	11(48)	30(53)	7(30)	21(36)

Note: \*/\*- p<0.01

**Table 3**

**Occurrence of tuberculosis in the staff of healthcare organizations in relation to job positions (absolute number, %).**

Year	Total	Job positions					
		Doctors		Registered nursing staff		Nursing assistants	
		abs.n	%	abs.n	%	abs.n	%
2007	16	4	25	7	43.75	5	31.25
2008	18	1	5.5	14	77.8	3	16.7
2009	15	3	20	4	26.7	8	53.3
2010	16	3	18.75	6	37.5	7	43.75
2011	15	1	6.7	5	33.3	9	60
Total	80	12*	15.0	36**	45.0	32**	40.0

Note: \*/\*\* - p<0.001

## Incidence

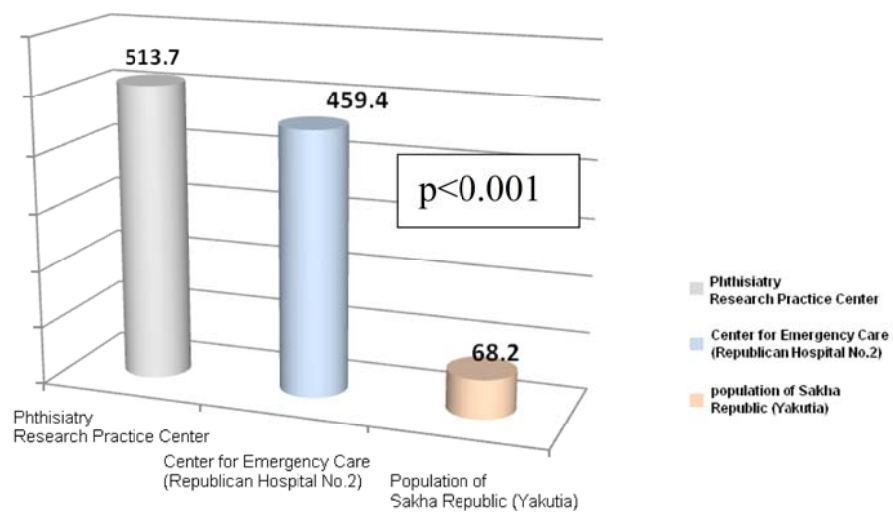


Fig.1.1

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Table 4

**Control of the effectiveness of disinfectants against clinical strains of *M.tuberculosis* circulating in the territory of Sakha Republic (Yakutia)**

Disinfectants	Disinfectant type and class		Clinical strains of <i>M.tuberculosis</i>	
	Disinfectants grouped by active substances	Toxicity class	<i>M.tuberculosis</i> strain No.258, susceptible	<i>M.tuberculosis</i> strain No.255, MDR
“Slavin”**	guanidine+aldehyde	3	Growth	Growth
“Sulphochlorantine D”****	Chlorine-based	3	No growth	No growth
“Chlormisept-R”****	Chlorine-based	3	Growth	Growth
“Ecobriz”****	QAC+amines	4	Growth	Growth
“Alphadez”****	QAC+guanidine	4	Growth	Growth
“Chloramine B”*****	Chlorine-based	3	No growth	Growth
“Mirodez-univer”***	QAC+aldehyde	4	No growth	Growth
“Brilliant”**	QAC+aldehyde	4	No growth	Growth
“Aqua-chlor”***	Chlorine-based	3	No growth	No growth

Notes: \* – in the disinfectant instructions for use, the regime is recommended for disinfection of linen, dishes, medical products, janitorial supplies etc.; \*\* - exposure 15 min; \*\*\* - exposure 30 min; \*\*\*\* - exposure 60 min; \*\*\*\*\* - 120 min.

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## CHARACTERISTIC FEATURES OF THE FOCI OF TUBERCULOSIS INFECTION IN RURAL AREAS OF THE EXTREME NORTH

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### Summary

The specifics of conducting antiepidemic work within the foci of tuberculosis infection in the setting of rural extreme northern region are presented. Study of 150 foci of tuberculosis infection showed: remoteness and hard accessibility of rural infection foci to specialized health service delays timely hospitalization of newly identified patients with tuberculosis, complicates examination and isolation of children to sanatoria, and hampers the conduction of antiepidemic measures in new foci of tuberculosis infection by epidemiologists and phthisiologists.

**Keywords:** tuberculosis, children, foci of tuberculosis infection, rural area, extreme north, health services accessibility

Incidence of tuberculosis (TB) in pediatric population from risk groups is what causes most alarm in the current epidemiologic situation for TB in the Russian Federation, although these groups of population are constantly followed-up by phthisiologists (Aksenova V.A. et al., 2011). In 2009 the incidence of TB among children exposed to smear-positive persons was 30 times higher than the incidence in Russian Federation for the same age groups; incidence among adolescents was 25 times higher.

Poor registration and follow-up of children and adolescents exposed to household contacts with active TB is reported (Shilova M.V., 2010). Pediatric TB incidence in children referred to dispensary follow-up group IV with histories of household smear-positive contact was 659.9/100 000 in 2010 (605.7 in 2009; 608.1 in 2008, per 100 000), i.e. grew 8.9% higher.

Detection of TB in rural areas (Punga V.V. et al., 2011) has some specific differences due to often long distances between the patient's place of residence and healthcare facility where examination, diagnosis and treatment are done, more unfavorable social conditions and closer social contacts between people, compared to urban population. In rural regions, pediatric incidence in the foci of infection was characterized by irregular registration of cases and high rates ranging from 3 to 20%. Cases with complicated forms of TB, with involvement of meninges and CNS were present in these regions.

Some authors (Son I.M. et al., 2002) think that intensity of the epidemiologic situation for TB is largely determined by pediatric incidence.

The above said is the reason why today there is a need to improve anti-tuberculosis work in the foci of TB infection, especially in rural areas under hard conditions of the extreme north.

**Aim** of the study was to analyze characteristic features of the foci of TB infection in rural areas of the extreme north.

To determine the characteristic features that influence the conduction of antiepidemic measures in the bacillary foci of infection, we studied 150 foci of TB infection referred by TB Dispensary classification to follow-up group I, where 287 children were residing. To achieve that purpose, we conducted questionnaires in cities and districts (*uluses*) of the Sakha Republic (Yakutia).

The foci of TB infection were divided to 2 groups based on the territory: the study group included 80 foci in rural area located in 20 administrative districts of Yakutia, with pediatric





population of 157 children; control group included 70 foci located in cities and urban-type settlements with pediatric population of 310 children.

Table 1

**Distance and roads between the foci of TB infection and TB Dispensaries**

Distance from TB Dispensary (km)	Group								Total	
	Study group (n=80)				Control group (n=70)					
	Roads				Roads					
	Unsealed		Sealed		Unsealed		Sealed			
	n	%	n	%	n	%	n	%	n	%
0 – 20	20	25.3	-	-	15	53.6	28	66.7	63	42.0
20 – 60	17	21.5	1	100	7	25.0	4	9.5	29	19.3
60 -120	19	24.0	-	-	3	10.7	10	23.8	32	21.3
120 - 180	4	5.1	-	-	3	10.7	-	-	7	4.7
180 - 240	13	16.5	-	-	-	-	-	-	13	8.7
240 - 300	3	3.8	-	-	-	-	-	-	3	2.0
300 or <	3	3.8	-	-	-	-	-	-	3	2.0
Total	79	98.8*	1	1.2*	28	40.0*	42	60.0*	150	100

\* significance of differences between groups ( $p < 0.001$ )

Analysis of remoteness of regional or municipal-level TB Dispensaries from the foci of infection has shown, that 71.3% of the foci are accessible only by unsealed roads; in rural areas up to 98.8% of the foci are accessible only by unsealed roads; most of the roads are inconvenient; automobile transport to the foci of infection is complicated; local animal transport is used depending on season and weather conditions. In urban areas up to 60.0% of the foci can be accessed by sealed roads, the rest 40.0% are accessible by unsealed roads. Distances in urban areas are significantly shorter, than in rural areas: only 21.6% of the foci are located at more than 60 km distances, while in rural areas 53.2% of the foci are even more remote (distances are up to 240 km and more). Inconvenient roads prevail in rural areas: difference between study groups is statistically meaningful ( $\chi^2=63.01$ ;  $p < 0.001$ ).

Table 2

**Seasonal accessibility of the foci of TB infection by road**

Distance from TB Dispensary (km)	Groups								Total	
	Study group (n=80)				Control group (n=70)					
	Trafficability				Trafficability					
	Year-round		Seasonal		Year-round		Seasonal			
	n	%	n	%	n	%	n	%	n	%
0 – 20	5	71.4	15	20.5	43	67.2	-	-	63	42.0
20 – 60	2	28.6	16	22.0	11	17.2	-	-	29	19.3
60 -120	-	-	19	26.0	10	15.6	3	50.0	32	21.3
120 - 180	-	-	4	5.5			3	50.0	7	4.7
180 - 240	-	-	13	17.8			-	-	13	8.7
240 - 300	-	-	3	4.1			-	-	3	2.0
300 or <	-	-	3	4.1			-	-	3	2.0
Total	7	8.8*	73	91.2**	64	91.4	6	8.6	150	100

\* significance of differences between groups ( $p<0.01$ )\* significance of differences between groups ( $p<0.001$ )

Only 8.8% of the foci in study group 1 and 91.2% of the foci in control group were located within the distance of 60 km and were open to visits year-round regardless of the season or weather conditions ( $p<0.01$ ). Most of the remote foci of infection in rural area (57.5%), which are located at 60-120 km and more distances, can be accessed only seasonally depending on the trafficability of the automobile roads.

Seasonal automobile transport is the prevailing one in rural areas, with meaningful difference between study groups ( $\chi^2=102.37$ ;  $p<0.001$ ).

Table 3

**Types of transport providing access to the foci of TB infection**

Distance from TB Dispensary (km)	Groups											
	Study group (n=80)						Control group (n=70)					
	Transport type						Transport type					
	Automobile		Air transport		Specialty transport		Automobile		Air transport		Specialty transport	
	n	%	n	%	n	%	n	%	n	%	n	%
0 – 20	28	50.9	-	-	2	14.3	46	71.9	-	-	-	-
20 – 60	12	21.8	-	-	1	7.1	8	12.5	-	-	-	-
60 -120	11	20.0	-	-	3	21.4	10	15.6	-	-	3	60.0
120 - 180	-	-	3	27.3	1	7.1	-	-	-	-	-	-
180 - 240	4	7.3	3	27.3	6	-	-	-	1	100	2	40.0
240 - 300	-	-	3	27.3	-	-	-	-	-	-	-	-
300 or <	-	-	2	18.1	1	-	-	-	-	-	-	-
Total	55	68.8*	11	13.7*	14	17.5	64	91.4	1	1.4	5	7.2

\* significance of differences between groups ( $p < 0.01$ )

Analysis of the proportions of transport types, by which the foci of TB infection can be accessed, showed that:

- accessibility by automobile transport (mainly UAZ vehicles) was 68.8% for the foci of infection in rural area vs. 91.4% for the foci in urban areas ( $p < 0.01$ );

- accessibility by air transport was 13.7% for rural foci vs. 1.4% for the foci in urban-type settlements ( $p < 0.01$ );

- accessibility by specialty transport (tractor, all-terrain vehicle, animal transport) was 17.5% for rural foci vs. 7.2% for the foci in urban area ( $p < 0.1$ ).

Thus, rural and urban areas have meaningful differences by types of transport ( $\chi^2 = 12.67$ ;  $p < 0.005$ ).

Table 4

**Description of the foci of TB infection by distance from TB Dispensary and number of smear-positive cases**

Distance from TB Dispensary (km)	Groups							
	Study group (n=80)				Study group (n=80)			
	Smear-positive cases in the focus of infection		MDR		Smear-positive cases in the focus of infection		MDR	
	n	%	n	%	n	%	n	%
0 – 20	-	-	12	41.4	2	100	9	81.8
20 – 60	1	20.0	8	27.6	-	-	-	-
60 -120	-	-	8	27.6			1	9.1
120 - 180	-	-	-	-			-	-
180 - 240	3	60.0	1	3.4			1	9.1
240 - 300	-	-	-	-			-	-
300 or <	1	20.0	-	-			-	-
Total	5	6.2	29	36.3*	2	2.8	11	15.7

\* significance of differences between groups ( $p < 0.01$ )

Number of the foci of TB infection with 2 or more resident smear-positive patients was 6.2% (5 persons) in rural area and 2.8% (2 persons) in urban area; 80.0% of rural patients reside at 180 km from the regional center, i.e. far from TB Dispensary, which extremely complicates timely sanitation of the focus of infection without delays.

Severity and complexity of a focus of infection is determined by the presence of patients, who are positive for multidrug-resistant M.tuberculosis (MDR MTB). In this study 143 (89.9%) out of 159 smear-positive patients were tested for drug sensitivity, of them patients from 79 rural foci of infection (96.3%) and patients from 64 (91.4%) urban foci. MDR MTB were detected in 36.3% of patients from rural areas and in 15.7% of patients from urban areas, i.e. epidemiologically dangerous foci of infection complicated with the presence of MDR MTB occurred twice more often in rural areas ( $p < 0.01$ ).

Delays in isolating the cases by timely hospitalizing patients from the foci of infection were observed in 72.5% of patients from rural areas, which was 1.8 times higher than in patients from urban areas (40.0%;  $p < 0.01$ ). Late case isolation was due to difficult transport system in those districts, where small aircrafts and all-terrain vehicles were the main means of transport. Only 27.5% of patients from rural areas can be isolated to in-patient TB clinics without delays. Study groups significantly differ by timely isolation of patients ( $\chi^2 = 16.12$ ;  $p < 0.001$ ); there is a meaningful prevalence of delayed patient isolation in rural foci of infection.

Of 157 rural children, only 42.0% (66) of children with histories of contact with TB were



examined in time; the same rate for urban children was 88.5% (115) ( $p < 0.01$ ). Among all child contacts, rural children made 54.7%, of which only 58.0% were examined in specialty TB facility without delays; the rest of children were residing in hard-to-access regions of the republic out of the direct service area of TB Dispensaries, where healthcare is provided by the primary level specialists, such as rural practitioners at first aid posts (FAPs) and district physicians. There was significant difference between study groups by timeliness of examination of child contacts ( $\chi^2 = 16.12$ ;  $p < 0.001$ ); delayed phthisiologist's or epidemiologist's visits to the foci of infection were significantly more often in rural foci: 22.5% and 18.8% vs. 80.0 and 48.6% in urban areas.

In conclusion, the specific features of the foci of TB infection in rural areas of the extreme north with its harsh environment are: remoteness from the specialty healthcare clinics and hard accessibility; road trafficability dependent on climate and geographic characteristics; shortage of needed transport. The above said complicates timely hospitalization of new cases with TB, examination and isolation of children to sanatoriums, conduction of antiepidemic activities in the newly detected foci of infection by phthisiologists and epidemiologists.

In view of the challenging climatic and geographic conditions in Yakutia, recommendations need to be developed: 1) to classify the rural foci of TB infection by degree of complexity; 2) to improve antiepidemic measures in the foci of infection, in cooperation with district physicians or rural practitioners (feldshers), registered nurses, local authorities represented by the assigned social worker and community leaders recommended by the phthisiologist.



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## SKIN TEST DIASKINTEST® IN THE DIAGNOSTICS OF TUBERCULOSIS INFECTION IN CHILDREN AND ADOLESCENTS

N.M. Oshchepkova, L.I. Mordovskaya, E.N. Ilyina, A.P. Popova

The specifics of conducting antiepidemic work within the foci of tuberculosis infection in the setting of rural extreme northern region are presented. Study of 150 foci of tuberculosis infection showed: remoteness and hard accessibility of rural infection foci to specialized health service delays timely hospitalization of newly identified patients with tuberculosis, complicates examination and isolation of children to sanatoria, and hampers the conduction of antiepidemic measures in new foci of tuberculosis infection by epidemiologists and phthisiologists.

**Keywords:** tuberculosis, children, tuberculosis infection reservoir, rural area, extreme north, health services accessibility

**Introduction.** Epidemiologic situation for pediatric tuberculosis (TB) remains intense. In 2010 pediatric TB incidence rate in the Sakha Republic (Yakutia) was 21.8 per 100,000 children, and the number of newly identified children (with latent TB infection) was 1.2% of the total pediatric population, while TB incidence in pediatric contacts of smear-positive patients was 642.8 per 100,000 contacts.

TB develops in 12 children and 100 adolescents per 1000 children and adolescents with newly identified infection. These facts point at late diagnosis of TB in some of the children (especially adolescents), and delayed detection of tuberculin test conversion [10].

Current diagnosis of pediatric primary TB infection is performed mainly by tuberculin skin testing. Yet insufficient specificity of tuberculin test, along with the lack of tools to differentiate between primary TB infection and postvaccinal allergy, prevent adequately effective identification of TB infection. [6]. Insufficient effectiveness of primary infection diagnosis in children and adolescents, with the failure to timely deliver preventive chemotherapy courses, leads to development of the forms of local TB, mostly pulmonary TB.

In this context, the improvement of early detection, diagnosis, and TB prevention efforts is an important goal in phthisiatry.

A new skin test preparation Diaskintest® has been developed and registered for use in Russia (Registration number LSR-006435/08, August 11, 2008, Manufacturer: ZAO (CJSC)

“Pharmaceutical company ‘LEKKO’ ”). Diaskintest is an ESAT-6- and CFP-10-based recombinant tuberculosis allergen, produced by genetically modified *Escherichia coli*, and is intended for use as a skin test providing a delayed type hypersensitivity reaction aimed for better TB infection diagnosis. In BCG-vaccinated persons without *M.tuberculosis* infection, Diaskintest®(DST) causes no skin reaction. [1, 3, 5, 9].

**Material and methods.** We examined 351 children and adolescents, who have been followed-up in risk groups for TB at the dispensary department of the State Budgetary Institution of the Sakha Republic (Yakutia) “Research-Practice Center ‘Phthisiatry’ ”, and who received the following skin tests: DST and Mantoux test with 2 TU PPD-L. Patients were divided to 4 study groups:

Group 1: children and adolescents with tuberculin skin test conversion (dispensary follow-up group VI A) – 125 patients;

Group 2: children with a history of past infection and with hyperergic reactions to tuberculin (dispensary follow-up group VI B) – 45 patients;

Group 3: children and adolescents who showed gradual increase of sensitivity to tuberculin (dispensary follow-up group VI C) – 114 patients;

Group 4: children exposed to household contacting with active smear-positive or smear-negative TB cases (dispensary follow-up group IV) – 67 patients.

To examine specific reactivity, Mantoux tests were performed using purified liquid tuberculosis allergen in standard dilution: 2 TU PPD-L per 0.1 mL of solution (Order of the Ministry of Health of the Russian Federation of 21 March 2003 no. 109) [7].

This study complied with the following regulations and guidelines:

- Russian Federation Ministry of Health and Social Development order of 29 October 2009 no. 855 “On introduction of amendment to appendix #4 of the Russian Federation Ministry of Health order of 21 March 2003 no. 109 ‘On improvement of tuberculosis-controlling measures in the Russian Federation’”;

- Guides for physicians: “Skin test with DIASKINTEST® preparation (recombinant tuberculosis allergen 0.2 microg in 0.1 mL intracutaneous solution) for identification of tuberculosis infection” and “Skin test with DIASKINTEST® preparation – new opportunities for identification of tuberculosis infection” [2, 4, 8].

DST is performed in the same technique as Mantoux test with 2 TU PPD-L: 0.1 mL were introduced intradermally into inner surface of mid one-third of the forearm.

Both Mantoux test with 2 TU PPD-L and DST were performed before the initiation of





preventive treatment in risk groups for TB (dispensary follow-up groups VI, IV).

**Results and discussion.** Results of the use of DST in various study groups are presented in Tables 1 and 2.

Group 1 consisted predominantly of preschool children (3-6 years, 85), and included 9 infants (0-2 years), 29 schoolchildren (7-14 years), and 2 adolescents (15-17 years). Most of the children appointed to dispensary follow-up based on their Mantoux test reactions, were aged 3 to 6 years.

Negative results of DST in 31 (24.8%) patients with Mantoux test conversion was found to signify that there was no increased risk of developing active TB. Doubtful reaction to DST was observed in 60 patients (48.0%). Number of children and adolescents who reacted positively to DST (34, 27.2%) was 3.7 times lower, then the number of that to tuberculin skin test, which appears to reflect a lower bacterial burden in a host child. Average sizes of infiltrates (papules) were  $11.3 \pm 0.3$  mm for Mantoux test, and  $5.8 \pm 0.8$  mm for DST,  $p < 0.001$ . Most of the children, who were appointed to follow-up based on their Mantoux reactions, were aged 3 to 6 years. Positive DST results were seen more often in those aged 7 to 14. This suggests the presence of postvaccinal allergy or parallergy in infants and preschool children.

Group 2 (dispensary follow-up group VI B) included mostly children aged 7 to 14 (25), 3 children aged 0 to 2, and 17 children aged 3 to 6.

Larger proportion of children ( $n=27$ , 60.0%) with hyperergic Mantoux reactions tested positive for DST. In this group, average size of the papula following DST ( $13.3 \pm 1.7$  mm) was reliably larger, than that in a group with tuberculin test conversion ( $p < 0.05$ ). Study findings confirm a high risk of active TB in this group of dispensary follow-up.

In group 3 (dispensary follow-up group VI C) most of the children where of school age: 47 children aged 7-14, 18 children aged 15-17, 3 children aged 0-2, 46 children aged 3-6. Positive DST results were seen in 22 (19.3%), doubtful results in 45 (39.5%), and negative results in 47 (41.2%) patients, while average sizes of papules after Mantoux test or DST were almost the same ( $12.4 \pm 0.3$  mm and  $9.9 \pm 1.5$  mm, respectfully,  $p > 0.05$ ). Only 22 (19.3%) children and adolescents with gradually increasing sensitivity to tuberculin tested positive for DST. This could possibly mean that the mycobacteria were in the state of dormant persistence – in this case, reaction to DST turns negative.

Group 4 (dispensary follow-up group IV) comprised mostly infants and preschool children: 14 children aged 0-2, 34 aged 3-6, 19 aged 7-14. DST was positive in 26 (38.8%), children, doubtful in 20 (29.9%), and negative in 21 (31.3%) patients in this group. Children in this group showed almost identical average sizes of reactions to Mantoux test and to DST ( $10.3 \pm 0.6$  and



11.5±1.4mm respectfully,  $p<0.05$ ). Children from dispensary follow-up group IV had positive results of DST more often, than children and adolescents from follow-up group VI A. This leads to suggestion that children exposed to contacting with TB cases showed high risk of developing active TB.

**Conclusions.** Use of DST helped to identify groups of patients with the highest risk of developing TB: dispensary follow-up groups VI B and IV.

Findings from the comparison of diagnostic effectiveness between DST and Mantoux test with 2 TU PPD-L permit recommending DST for use in pediatric practice, to diagnose TB infection in children and adolescents. Doubtful and positive reactions to DST are indications for compulsory dispensary follow-up of these patients. Positive reaction to DST may appear later, then a reaction to tuberculin. Therefore, DST must be repeated 3 months later, if the first reaction was either negative, or doubtful. Positive reaction to DST indicates TB infection and requires an array of diagnostic measures, which must include computed tomography as well.

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Table 1

**Results using Mantoux test with 2 TU PPD-L and Diaskintest®**

Study groups	n=	Mantoux test with 2 TU PPD-L			Diaskintest®		
		Positive abs.n./%	Doubtful abs.n./%	Negative abs.n./%	Positive abs.n./%	Doubtful abs.n./%	Negative abs.n./%
1. Children and adolescents from dispensary follow-up group VI A	125	125/100	-	-	34/27.2	60/48.0	31/24.8
2. Children and adolescents from dispensary follow-up group VI B	45	45/100	-	-	27/60.0	18/40.0	-
3. Children and adolescents from dispensary follow-up group VI C	114	114/100	-	-	22/19.3	45/39.5	47/41.2
4. Children and adolescents from dispensary follow-up group IV	67	53/79.1	6/9.0	8/11.9	26/38.8	20/29.9	21/31.3
Total	351	337/96.0	6/1.7	8/2.3	109/31.0	143/40.8	99/28.2

Table 2

**Results by Mantoux test with 2 TU PPD-L and by Diaskintest®**

Study groups	Mantoux test with 2 TU PPD-L	Diaskintest®	P
	Papule size (M±m), mm, N=patient number	Papule size (M±m), mm, N=patient number	
1. Children and adolescents from dispensary follow-up group VI A	11.3±0.3, n=125	5.8±0.8, n=34	<0.001
2. Children and adolescents from dispensary follow-up group VI B	16.4±0.6, n=45	13.3±1.5, n=27	<0.05
3. Children and adolescents from dispensary follow-up group VI C	12.4±0.3, n=114	9.9±1.5, n=22	>0.05
4. Children and adolescents from dispensary follow-up group IV	10.3±1.4, n=53	11.5±1.4, n=25	>0.05
p		P <sub>1-2,4</sub> <0.05	

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## INTRODUCTION OF NEW DIAGNOSIS AND TREATMENT METHOD FOR TUBERCULOUS COXITIS IN THE RESEARCH-PRACTICE CENTER “PHTHISIATRY”

L.A. Pavlov, S.S. Torduvin, M.V. Sleptsov

### Summary

The study presents epidemiologic indicators for extrapulmonary tuberculosis (EPTB) in the Sakha Republic (Yakutia) for the years 2002 to 2011. We describe the diagnostic methods that can be the most decisive ones, depending on various pathogenesis of EPTB: computed tomography, MRI, trephine biopsy of bones and joints that provides specimens fitting for histological and microbiological examinations. Finally, we present the results of the introduction of total hip replacement, a new high-tech treatment method for tubercular coxarthrosis and its sequelae, successfully performed in 17 patients.

**Keywords:** extrapulmonary tuberculosis, osteoarticular tuberculosis, coxarthrosis, trephine biopsy of bones and joints, total articular replacement

Incidence of extrapulmonary tuberculosis (EPTB) has been observed to decline steadily for the last decade, in the Russian Federation, and in the Sakha Republic (Yakutia) as well. The decline was observed also in the proportion of cases of EPTB within the tuberculosis (TB) incidence structure. Thus for 9 years the incidence of EPTB had decreased by 28%. While in 2002 the incidence was 3.2 per 100 000 population, in 2010 it was 2.5. Although Shilova M.V. noted (2005) that this decrease in incidence of EPTB was calculated based on all disease localizations, except osteoarticular TB. Levashev Yu.N. in 2006 noted that those rates did not reflect the real epidemiological situation for EPTB, and predicted the upsurge of the incidence in the next years.

Likewise, in Yakutia the incidence of EPTB has been tending to decline: 6.3/100 000 in 2002; 4.9/100 000 in 2006; 4.4/100 000 in 2011. Proportion of EPTB in the structure of TB incidence was 8.9% in 2002 and 5.9% in 2011. Thus, epidemiologic indicators for EPTB in Yakutia remain stable overall, and notably exceeding the same indicators in Russia (Table 1).

It should be pointed out, that in Yakutia, as in Russia, incidence of osteoarticular TB has not decreased, but instead has slightly grown, as opposed to decline in the incidence of EPTB of other

localizations. While in the 80-90s of the last century osteoarticular TB ranked 3<sup>d</sup> by detection rate among extrapulmonary forms of tuberculosis, today it persistently ranks the 1<sup>st</sup> place in Yakutia. For example, incidence of osteoarticular TB among the cases of EPTB in Yakutia was 30.6% in 2002, 32.2% in 2005, 42.8% in 2008, and 41.3% in 2010. In 2011 the incidence of EPTB had grown abruptly, which to a large extent was due to increase in osteoarticular TB: 28 (66.6%) cases out of 42 newly identified patients with EPTB had osteoarticular TB. 8 patients with osteoarticular TB have been detected during 2 months in 2012 (Fig. 1).

According to the Order of the Ministry of Health no. 109, only one disease localization must be indicated for registration and recording of newly detected cases of TB. A patient with concurrent extrapulmonary and pulmonary TB will be registered as pulmonary case. Besides that, newly detected cases do not include relapsed cases, cases transferred out from other regions, and patients discharged from imprisonment. Because of this approach to dispensary follow-up of tuberculosis patients [T.N.: regular medical check-up and recordkeeping is termed 'dispensary follow-up'], up to a quarter of detected cases of osteoarticular TB are supposedly "lost".

At the end of 2009, in view of the observed growth of the percentage of osteoarticular TB in the incidence structure of EPTB in Yakutia for the last years, the administration of the 'Phthisiatry' Research & Practice Center had decided to reorient the extrapulmonary TB service to make it meet more fully the needs of patients with osteoarticular TB. So in January 1, 2010, the Inpatient EPTB Department was renamed to the Department For Osteoarticular And Genitourinary TB, with capacity of 50 beds, 30 of which are for patients with the disease of locomotion system. In November 1, 2011, bed capacity has been expanded to 55 beds, after being completed with additional "osteoarticular" beds.

Diagnosis of osteoarticular TB has some specific aspects. The pathogenesis of this disease is such that radiological method is the method of choice for diagnosis, because of its availability and decisive value. And accordingly, wide incorporation of high-end radiological diagnostic methods in Yakutia for the last years, such as x-ray computed tomography and MRI, allows the detection of patients with osteoarticular TB at primary network level.

It is a common knowledge, that in osteoarticular TB, tuberculous etiology of the disease is confirmed usually during the examination of surgical specimens. But in the majority of cases, surgery for osteoarticular TB is preceded by 1-2 months of preoperative anti-TB chemotherapy aimed at stabilization and containment of the pathological process, which makes bacteriological testing of the surgical specimens less diagnostic or nondiagnostic. That is why the use of controlled trephine biopsy of bones and joints becomes increasingly important in terms of histological and

microbiological verification of TB disease at early stage. Besides the above method, the Research & Practice Center 'Phthisiatry' will shortly be adopting arthroscopic interventions for diagnosis and treatment of the TB of major joints.

Introduction of newer diagnostic and treatment methods for osteoarticular TB, including high-tech methods, has been a long-standing need. This has become possible, when the new building of the 'Phthisiatry' Research & Practice Center, which is equipped to fit the modern requirements, has started to work.

In June, 2010 we have started to implement total hip replacement – new high-tech surgical treatment method for tuberculosis of the hip joint and its sequelae. Surgical operations were performed in assistance with the Traumatology Department of the Republican Hospital No.2 (Center for Emergency Medical Care).

During the next two years 17 total hip replacement procedures have been performed in the Department for Osteoarticular and Genitourinary TB. Out of 17 surgical patients, 8 (47.0%) had quiescent (inactive) tuberculous coxitis, the outcome of which was meta-tuberculous coxarthrosis; 4 (23.5%) patients who had TB of other localizations were operated for concurrent non-TB hip joint disease (1 (5.8%) patient with femoral neck fracture, and 3 (17.6%) with coxarthrosis deformans); 5 (29.4%) patients were non-TB cases who had nonspecific arthropathy.

Non-TB diseases of hip joint included: 5 (29.4%) cases of coxarthrosis deformans in parallel with Perthes' disease; 2 (11.7%) cases of non-consolidated femoral neck fracture; 1 case (5.8%) of coxarthrosis deformans in parallel with congenital dislocation; 1 case (5.8%) of coxarthrosis deformans due to past history of traumatic hip dislocation.

The majority (n=13; 76.4%) of the operated patients were male. By age-groups, patients were predominantly above 50 years old, although patient age ranged from 28 to 70 (mean age was 53.5). The majority of patients were aboriginal residents (n=12; 70.5%). By rural/urban residence, patients were distributed to almost equal groups: 9 (52.9%) and 8 (47.1%), respectfully.

Duration of the disease varied from 1.5 years (tuberculous coxitis) to 69 years (congenital hip dislocation).

Absolute majority of the patients (n=16; 94.1%) had an assigned disabled status by the time of surgical intervention. Of them, 2 patients had grade III disability (11.7%), 13 patients had grade II disability (76.4%), and 1 patient had grade I disability (5.8%). All personal rehabilitation programs of the patients included total hip replacement as the recommended operative treatment. Henceforth, Federal Social Insurance Fund reimbursed expenses for purchase of prostheses from the suppliers. Multimodality in-patient treatment (preoperative examination, operation, postoperative care) was



kept on budget of the institution. Later and in the future, the treatment should be at the expense of federal budget, provided that the 'Phthisiatry' Research & Practice Center receives the federal quotes of high-tech medical care (the appropriate license was granted to our institution in 2011).

All surgical interventions were performed under x-ray image guidance using Ceraver and Smith&Nephew surgical instruments. 7 (41.2%) joint implants by Ceraver and 10 (58.8%) by Smith&Nephew were fitted. Of the 17 prosthetic implants, 4 (23.5%) were metal-on-polyethylene, 3 (17.6%) metal-on-ceramic, 5 (29.4%) ceramic-on-ceramic and 5 (29.4%) were titanium nickellide implants.

Most of the patients (n=13; 76.5%) were operated under spinal anesthesia, and 4 (23.5%) – under general anesthesia. In early postoperative period all patients had been observed in the Department of Anesthesiology and Emergency Care for 1-5 days. All patients received prophylactic low molecular heparin, with coagulogram monitoring, and were treated by antibacterial therapy with cephalosporin. Surgical wounds in all cases healed by first intention. Within 3 to 7 days all patients started to use crutches to walk. In late postoperative period patients were prescribed physical therapy (ultrasonic therapy in combination with lidase; magnetic laser therapy) and massage.

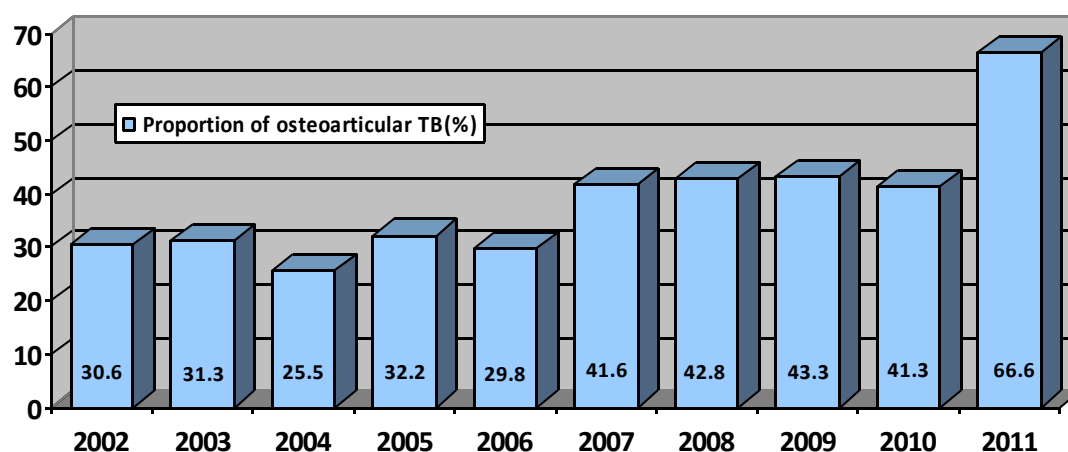
In 1 case a complication occurred in late postoperative period (2 months after the surgery): dislocation of the femoral component of the prosthetic implant. The patient I., 51 years old, underwent total hip replacement with metal-on-polyethylene Ceraver implant on July 14, 2011. Wounds healed by first intention, and stitches were removed on day 10. On July 27, 2011 the patient was discharged at his own wish, and was prescribed further out-patient treatment at the place of his neighborhood. In his own words, the patient did not comply with the recommendations on weight-bearing limitations and the use of additional support, which 2 months after the surgery resulted in pain and movement restriction in the operated joint during wrong bodily movement made by the patient. After x-ray examination the patient was diagnosed with dislocation and was hospitalized again. In October 2011 replacement of the acetabular cup of the patient's prosthesis was performed with additional myotomy. The outcome was satisfactory.

In conclusion, introduction of high-tech surgical interventions for total hip replacement to the work of the specialty department of the 'Phthisiatry' Research & Practice Center can be acknowledged as successful. The further work to be done is staff training, surgical skill improvement and solving organizational issues. The current work on appointing patients from population groups followed-up in TB Dispensary for tuberculous coxitis, to surgical treatment is going on.

Table 1

**Annual trends in the incidence of extrapulmonary TB per 100 000 population**

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
<b>Sakha-Yakutia</b>	6.3	5.3	5.4	3.3	4.9	3.8	3.7	3.2	3.0	4.4
<b>Far East Federal District</b>	н/д	3.0	3.3	3.0	3.1	3.4	2.6	2.7	2.8	n/a
<b>Russian Federation</b>	3.2	3.2	3.1	3.0	2.9	2.8	2.7	2.6	2.5	n/a



**Fig. 1. Proportion of osteoarticular TB in the incidence structure of extrapulmonary TB, Sakha Republic (Yakutia), 2002-2011**

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## INCIDENCE OF TUBERCULOSIS IN THE STAFF OF HEALTHCARE ORGANIZATIONS AND RESPONSIBILITY OF REGISTERED NURSING STAFF IN CONDUCTING ANTIEPIDEMIC MEASURES

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**Summary.** We comparatively analyzed the incidence of tuberculosis in the staff of various specialty healthcare organizations, through the case of the Sakha Republic (Yakutia), and monitored clinical *M.tuberculosis* strains for susceptibility/resistance to disinfectants. Incidence of tuberculosis among the staff of anti-tuberculosis institutions was 3 to 4 times higher ( $p<0.05$ ), than in the staff of other healthcare organizations; among them, tuberculosis occurred mostly in registered nursing staff and in nurse assistant staff.

Disinfectants types that played main role in the control of nosocomial transmission of *M.tuberculosis* were chlorine compounds, and quaternary ammonium compounds (QAC) in combination with aldehydes.

**Keywords:** tuberculosis, *Mycobacterium tuberculosis*, incidence, antiepidemic measures, medical staff, disinfectants

**Background.** Overall epidemiologic situation with tuberculosis (TB) in Russia, and in Sakha Republic (Yakutia), is still stressful, despite recent stabilization in some indicators of TB prevalence and despite organization of anti-TB activities for population protection [1,5]. Incidence of nosocomial TB keeps growing, and has increased twice over the last 10 years [4]. Intrahospital non-specific antiepidemic measures start to play increasingly important role in today's unfavorable epidemiologic situation with TB; these measures consist essentially in decontaminating various inanimate objects by means of disinfecting agents [2,3], and in preventing nosocomial transmission of *M.tuberculosis* (MTB) [9].

To prevent possible emergence of strains with resistance to disinfectants, hospital strains must be monitored for resistance to disinfectants currently in-use in the hospital, and disinfectants must be rotated subsequently, i.e. disinfectant of one chemical type must be systematically replaced by disinfectant of another chemical type, when necessary [7]. Sanitation measures aimed at

prevention of nosocomial infection, including TB, are largely defined by antiepidemic schedule [10], while registered nursing staff plays the key role in effective conduct of this schedule [6,8].

**Aim.** To comparatively analyze the incidence of TB in the staff of healthcare organizations of diverse specialties, through the case of Sakha Republic (Yakutia); to conduct monitoring for susceptibility/resistance to disinfectants in clinical MTB strains.

**Materials and methods.** The study was held from 2007 to 2011; the subjects and materials included:

Patients (staff) with occupation in healthcare organizations, newly diagnosed with TB, of them, 57 working in healthcare organizations and 23 working in anti-TB institutions. Patient groups were randomized according to job positions held by medical staff in various healthcare organizations.

Disinfectants used in anti-TB institutions, grouped by chemical composition of their main active substances.

Tuberculocidal properties of disinfectants were tested using the techniques [11,12] based on procedures adopted from the widely known method accepted in disinfectant testing practice, i.e. submerging coarse calico test-objects contaminated with the test-microbes into a disinfectant.

The following test strains were used to assess the effectiveness of disinfectants: 1. Clinical strain *M.tuberculosis* No.255, resistant to streptomycin at 10 mcg/mL MIC, to isoniazid at 1 mcg/mL MIC, to rifampicin at 40 mcg/mL, and to capreomycin at 30 mcg/mL; 2. Drug-susceptible clinical strain of *M.tuberculosis* № 258.

More than 500 control samples were collected and tested to study the effectiveness of 9 disinfectants used in anti-TB institutions: 1. "Chloramine B" (0.5% concentration); 2. "Sulphochlorantine D" (1.0%); 3. "Chlormisept-R" (0.2%); 4. "Slavin" (1.2%); 5. "Brilliant" (2.0%); 6. "Aqua-chlor" (0.1%); 7. "Mirodez-univer" (1.0%); 8. "Ecobriz" (2.0%); 9. "Alphadez" (1.0%).

The study findings were summarized using statistical methods: calculation of the median, with minimum and maximum values; calculation of mean square deviation; Student's test (t); Pearson's/Fisher's  $\chi^2$  tests with correction factors (Yates, McNemar) to check the reliability of differences (p), with at least 9% confidence interval.

**Results and discussion.** TB incidence rate in medical personnel (Table 1) was lower (median 56.84; min 53.1; max 56.9), than in civil population of Yakutia (median 68.8; min 65.7; max 73.9), ( $p>0.05$ ). Low min/max amplitude indicated that incidence level in medical staff tended to be more stable. Comparison of the incidence (per 100 000 employees) rates between healthcare



organizations and anti-TB institutions showed statistically meaningful difference: incidence among the staff of anti-TB service was 3.5-4 times higher, than in the staff of other healthcare organizations: 12 (46.7) and 3 (163.3) cases, respectfully ( $\chi^2=24.22$ ;  $p<0.001$ ).

The highest TB incidence was revealed among the staff of the “Phthisiatry” Research-Practice Center: 513.7/100 000 pop., 7.5 times higher than the incidence among civil population of Yakutia ( $\chi^2\text{-Pearson}=332.0$ ;  $p<0.001$ ) (Fig.1).

Among the rest of healthcare organizations, high TB incidence was documented in the staff of the Center for Emergency Care (Republican Hospital No.2): 459.4/100 000 pop., 6 times higher than the incidence (68.2/100 000 pop.) among civil population of Yakutia. ( $\chi^2\text{-Pearson}=282.7$ ;  $p<0.001$ ).

Patients are hospitalized to the Center for Emergency Care (Republican Hospital No.2) by emergency ambulance – unexamined patients seeking emergency care. Such high incidence may be predetermined by the absence of infection control system, low effectiveness of antiepidemic measures or disinfectants.

We analyzed TB case detection methods in 80 patients, of them, 23 employees of anti-TB institutions and 57 employees of other healthcare organizations (Table 2). In personnel of healthcare organizations, TB disease cases were detected more often on visit to a doctor due to feeling unwell, while in the staff of anti-TB institutions, TB cases were detected via occupational health examinations, and this difference was highly significant ( $\chi^2\text{-Pearson}=9.03$ , with Yates correction  $\chi^2\text{-Yates}=7.61$ ;  $p\leq 0.027$ ). Analysis of the time to case detection showed that TB cases detected in other healthcare organizations were significantly more often bacillary-positive ( $\chi^2\text{-McNemar}=6.88$ ;  $p<0.05$ ) or had destructions in lung tissue at the time of detection ( $\chi^2\text{-Fisher}=0.58$ ;  $p>0.05$ ). Hence TB disease in the staff of healthcare organizations was detected in the late stage, when bacterial expectoration and lung destruction were already present; this is confirmed also by generalized indicator of delayed detection ( $\chi^2\text{-McNemar}=9.85$ ;  $p<0.01$ ).

Study of the incidence of TB among healthcare workers in relation to different job positions (Table 3) showed more frequent incidence among registered nursing staff (36; 45.0%), followed by nursing assistants (32; 40.0%), with rarer incidence among doctor staff (12; 15.0%) ( $\chi^2\text{-Pearson}=27.64$ ;  $p<0.001$ ). This may be explained by direct exposure to patients with TB and spending much time near the patients, some of whom are bacillary-positive, as well as by low level of hospital infection control and low effectiveness of antiepidemic measures.

Decontamination of indoor spaces and inanimate objects is an important component of antiepidemic measures against TB infection in healthcare organizations. We analyzed the activity of

several disinfectants with different chemical compositions, to determine the effectiveness of disinfectants recommended for use against MTB strains (Table 4). All disinfectants tested are widely used in healthcare practice, and none of them (used in recommended regimes) demonstrated 100% tuberculocidal effect on test strains of MTB, both multidrug-resistant (MDR), and drug-susceptible. Overall, of 9 disinfectants recommended for accepted practice, 5 (55.5%) disinfectants were effective against drug-susceptible MTB, and 2 (22.2%) were effective against MDR MTB. Tuberculocidal effect on clinical MTB strains was demonstrated by the following types of disinfectants: chlorine compounds, quaternary ammonium compounds (QAC)+aldehydes.

The study showed that, because nursing and nurse assistant staff is most vulnerable to TB infection, new approaches are needed to improve the performance of these groups of anti-TB service personnel. The key measures to achieve this should include: ensuring safe working environment; staff education on principles and methods of infection control; creating the quality management system for nursing care that would help to shape the body of knowledge and skills to remain up-to-date with contemporary requirements. To conduct effective antiepidemic measures, essential emphasis must be made on monitoring for microbial susceptibility/resistance to disinfectants used in the hospital.

### **Conclusions:**

5. Incidence of TB among the staff of anti-TB institutions was 3.5-4 times higher than in the staff of other healthcare organizations. Among the staff of anti-TB institutions, TB occurred mostly in registered nursing staff and in nurse assistant staff ( $p < 0.001$ ).

6. In the staff of anti-TB institutions, preventive health examination was the chief TB detection method in 74% of cases; in the staff of other health organizations, 63% cases were detected on visit to a doctor due to feeling unwell ( $p < 0.05$ ).

7. The personnel of emergency care was 6 times more ( $p < 0.001$ ) predisposed to TB infection, than civil population of Sakha Republic (Yakutia).

8. Among disinfectants, chlorine compounds and QAC+aldehydes had tuberculocidal effect on clinical strains of MTB isolated in the territory of Sakha Republic (Yakutia).

### **Proposals:**

4. Medical staff must be continuously educated on issues relating to high risk of nosocomial transmission of TB infection.

5. Personnel of emergency healthcare organizations must undergo mass fluorographic examination twice a year, with the purpose of early detection of TB.

6. Uniform procedure of disinfection processes (routine and final disinfection in TB infection



reservoir) for TB prevention must be developed, taking into account also data from hospital MTB strain monitoring for resistance to disinfectants in-use.





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Table 1

**Incidence of tuberculosis in the staff of healthcare organizations, Sakha Republic (Yakutia), per 100.000 pop.**

Year	Total		Of them:			
	Absolute number	Rate per 100 000 pop.	Healthcare organizations		Anti-TB institutions	
			Absolute number	Rate per 100 000 pop.	Absolute number	Rate per 100 000 pop.
2007	16	56.2	8	30.1	8	415.3
2008	18	63.5	14	53.0	4	205.9
2009	15	53.1	10	37.9	5	259.8
2010	16	56.9	13	49.5	3	160.5
2011	15	55.5	12	46.7*	3	163.3**
Total	80		57		23	

Note: \*/\*\* -  $p < 0.001$

Table 2

**Tuberculosis detection methods in the staff of healthcare organizations (absolute number, %)**

Year	Total		Detection method				MTB (+)		CV (+)	
	Anti-TB institutions	Other healthcare organizations	Occupational examination		On visit		ATB I	OHO	ATB I	OHO
			ATBI	OHO	ATBI	OHO				
2007	8	8	7(87.5)	3(37.5)	1(12.5)	5(62.5)	4(50)	3(37.5)	2(25)	4(50)
2008	4	14	2(50)	6(43)	2(50)	8(57)	1(25)	9(64)	1(25)	7(60)
2009	5	10	4(80)	4(40)	1(20)	6(60)	4(80)	6(60)	2(40)	1(10)
2010	3	13	2(67)	5(38.5)	1(33)	8(63)	1(33)	7(53)	1(33)	7(37)
2011	3	12	2(67)	3(25)	1(33)	9(75)	1(33)	5(42)	1(33)	2(17)
Total	23	57	17(74)*	21(37)*	6(26)*	36(63)*	11(48)	30(53)	7(30)	21(36)

Note: \*/\*-  $p < 0.01$

Table 3

Occurrence of tuberculosis in the staff of healthcare organizations in relation to job positions (absolute number, %).

Year	Total	Job positions					
		Doctors		Registered nursing staff		Nursing assistants	
		abs.n	%	abs.n	%	abs.n	%
2007	16	4	25	7	43.75	5	31.25
2008	18	1	5.5	14	77.8	3	16.7
2009	15	3	20	4	26.7	8	53.3
2010	16	3	18.75	6	37.5	7	43.75
2011	15	1	6.7	5	33.3	9	60
<b>Total</b>	<b>80</b>	<b>12*</b>	<b>15.0</b>	<b>36**</b>	<b>45.0</b>	<b>32**</b>	<b>40.0</b>

Note: \*/\*\* -  $p < 0.001$

### Incidence

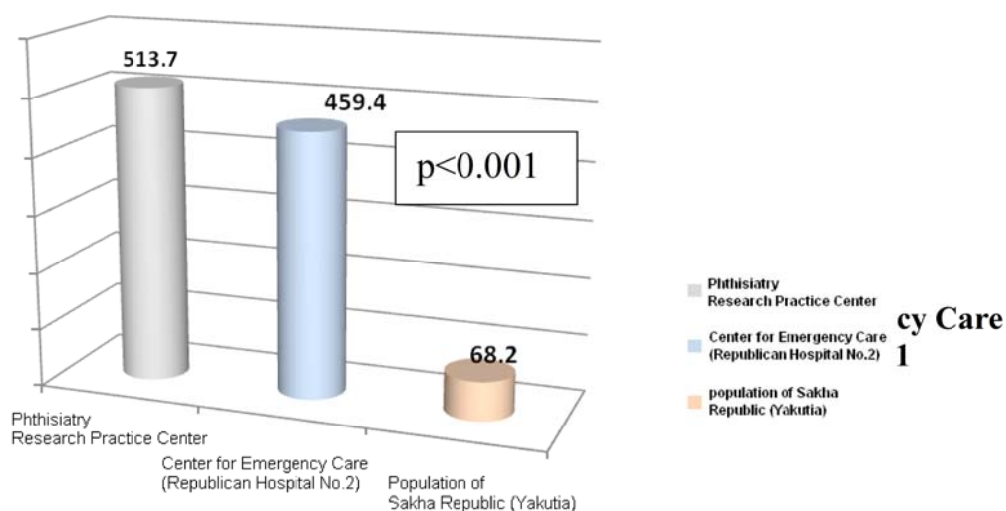


Fig.1. 1

Table 4

**Control of the effectiveness of disinfectants against clinical strains of *M.tuberculosis* circulating in the territory of Sakha Republic (Yakutia)**

Disinfectants	Disinfectant type and class		Clinical strains of <i>M.tuberculosis</i>	
	Disinfectants grouped by active substances	Toxicity class	<i>M.tuberculosis</i> strain No.258, susceptible	<i>M.tuberculosis</i> strain No.255, MDR
“Slavin”**	guanidine+aldehyde	3	Growth	Growth
“Sulphochlorantine D”****	Chlorine-based	3	No growth	No growth
“Chlormisept-R”****	Chlorine-based	3	Growth	Growth
“Ecobriz”****	QAC+amines	4	Growth	Growth
“Alphadez”****	QAC+guanidine	4	Growth	Growth
“Chloramine B”****	Chlorine-based	3	No growth	Growth
“Mirodez-univer”***	QAC+aldehyde	4	No growth	Growth
“Brilliant”**	QAC+aldehyde	4	No growth	Growth
“Aqua-chlor”***	Chlorine-based	3	No growth	No growth

Notes: \* – in the disinfectant instructions for use, the regime is recommended for disinfection of linen, dishes, medical products, janitorial supplies etc.; \*\* - exposure 15 min; \*\*\* - exposure 30 min; \*\*\*\* - exposure 60 min; \*\*\*\*\* - 120 min.

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## Fluctuation of suicidal behavior of the North population of the Russian Federation

M.P. Dutkin

The article presents the research of dynamics of suicide in the Russian Federation and Republic Sakha (Yakutia). In the Russian Federation, now there is a pronounced downward trend in suicides, since 1996 year. Reducing mortality from suicide for the Russian Federation as a whole amounted to 35.4%. In Republic Sakha (Yakutia) in recent years the suicide rate is 47-48 per 100 thousand people that is not a steady downward trend. Archaic Pagan beliefs and Archetypes of the “collective unconscious” (K. Jung) as an ethnocultural factor in the origin of the suicides were researched.

**Keywords:** suicide, socio-economic factor, ethnocultural factor of suicide, the indigenous peoples of the North, the archaic Pagan beliefs, the Archetypes of the “collective unconscious”, K. Jung terminology.

French philosopher, founder of existential direction of modern psychology and philosophy, Camus A. believed that there is only one truly serious philosophical problem – the problem of suicide. Decide whether or not life is worth to survive means to answer the fundamental question of philosophy [5].

Recently, in many countries there has been an increase in the number of suicides (especially among young people). In the developed countries among the causes of death of adult suicide has one of the highest and second place among the causes of death of children, adolescents and young people. According to incomplete data from WHO (World Health Organization) in the world takes place each year more than 500 000 suicides and about 7 million. attempts. The highest rate of suicide in economically developed countries – Hungary – 46 cases per year per 100 000 population in the year 1984 in Denmark in 1980, 31.6, Finland-29 in 1992, the United States, in 1984, 12.4 [3]. In the Soviet Union after the Russian Revolution and civil war, the number of suicides increased dramatically. In the 1926 years in Moscow and Leningrad suicide rate reached 41.8 – men's, women's-19.5 [3].

Further, there were two jump suicides in 1937 (the consequences of political repression) and 1947 (the consequences of the great patriotic war), then some recession during Khrushchev's "thaw", and dramatic growth during the economic well-being of the "stagnant" years until 1984, (38.7 cases per 100 000 population), when the Soviet Union occupied the second place in the world in terms of the number of suicides, second only to Hungary.

During the "perestroika" suicide rate fell sharply to 23.1 (affected by psychological expectations of Soviet citizens to improve the life and impact of the public campaign for sober lifestyle "), but, since 1988, he begins to grow, and in 1995, rising to almost half (41.1 per 100 thousand of population). The extraordinary growth in the number of suicides (especially in our country) highlights the importance of essential deepening for suicide studies and at the same time, notes the lack of their theoretical level and their influence on the situation. There is a need to analyse the issue of suicide in modern material to effectively combat this scourge. Most suicide researchers, starting with E. Durkheim, the main cause of suicide is called the social factor.

Founder of sociological theories of origin E. Durkheim suicide considered suicide as a result of an individual's interpersonal gap, its exclusion from the social group to which he belonged for quite some time as a result of the socio-economic turmoil in the country [4].

The famous Russian psychiatrist Behterev V. article "on the causes of suicide and a possible fight with them», published in Saint Petersburg in 1912, has identified the following conditions contributing to suicides: rapid change in usual conditions of life for the worse; a large migration of people from rural to urban areas; alcoholism; frustration in the society; availability of guns of suicide; heredity; mental illness; loss of loved ones; sharp contradictions in their views and needs between spouses, senior and junior members of the family [cited by: 1].

This study served as a Material "Statistical Yearbook of the Russian Federation" of 2010, [11]. Methodological bases served as such methods are empirical research, observation, comparison, measurement, analysis and synthesis.

In the Russian Federation since 1996, there has been a tendency to reduce the number of suicides (peak of suicides took place in the year of 1995 on 100 thousand population, 41.1). In 2009 year that figure had decreased to 26.5 (table 1). Thus, the decline in deaths from suicide in the whole Russian Federation amounted to 35.4% (compared to 1996) in the Republic of Sakha (Yakutia), the number of suicides has no steady downward trend (Figure 1). The peak of suicides



took place in the year 2001-50.4. In 2007 and 2008, the rate of suicides was 48.3 and 48.5 respectively. In the year 2009 – 46.9. Suicide rate in three years in the Republic of Sakha (Yakutia) (2007, 2008 and 2009) exceed similar indicator in the all about 1.6 times. In 2010, there is a slight downward trend in the number of suicides is 40.8. Went down for the year-5.3%.

Analysis of suicide rates by place of residence revealed a trend of higher suicide rate of rural population compared to urban populations. Coefficient of suicidal behavior of villagers in "post-Soviet" period was 1.2 lower than city dwellers (table 2 and Figure 2). Since 2007, the death rate from suicide among rural population began to exceed the suicide rate of urban population (in 2009, in 1.03 times higher). This phenomenon is explained by socio-economic factors: high and growing gap in the level and quality of life of the urban and rural population, high unemployment and rapid urbanization (in most countries, more die from suicide than urban population rural population).

According to federal State statistics service for the 2009 year, leaders on the frequency of suicide among children-Tuva, Yakutia and Buryatia. At 100 thousand children aged 10 to 14 years there have consequently 15.6; 13.4 12.6 and suicides. These indicators are extremely high (3 times the Russian figures). In these same regions, there is the most unfavorable situation among teenagers 15-19 years: in Tuva-120.6 on 100 thousand, Buryatia-86.6 and Yakutia-74.2 (table 3). The high number of suicides in the national republics of the North of RUSSIA, particularly the adolescent and child suicides, reveal, apart from socio-economic factors, the so-called "itnokultural" factor in the origin of the suicide.

Itnokultural factor in the origin of the suicide in the first place there is the example of Hungary, which for a long time, until 1994, was leading by the number of suicides in the world. Hungarian language belongs to the Finno-Ugric language group. In terms of socio-economic development in Hungary was not behind its neighbors in "Kommunismus camp" – Poland, Romania and Czechoslovakia, where the suicide rate was much lower. In the Russian Federation regions, where mostly people related to the Finno-Ugric language group (Komi, Udmurt Republic, the Republic of Mari-El), have always been a high rate of suicide. Other foreign countries with Finno-Ugric population also give similar high rates of suicides: Finland – 100 thousand population at 20.3 (2004), Estonia – 20.3 (2005 year).

Doctor of medicine, psychiatrist Polozhy B. in his article "Suicide in the context of





«nukultural Psychiatry» writes that the study of the frequency of suicide in the Komi Republic found that persons of Finno-Ugric nationalities at 94.9 per 100 000 population, 2.2 times higher than the rate among the Slavs (41.5) at 100 thousand of population and 1.7 times the average for the Republic [9]. The prevalence of suicide among Finno-Ugric tribes has increased in recent years, 1.6 times, and among the Slavs remained stable. These figures, according to Polozhy B., convincingly show a great predisposition to Finno-Ugrians suicide response. The frequency of suicide in Finno-Ugric subpopulation higher among men (in 2.5 times) and women (in 2.7 times).

This confirms another researcher with suicidal behavior Terebihin V.: in 2008, the rate of mortality from suicides in the Russian Federation (number of deaths per 100 thousand of population) stood at 27, in the Komi Republic 42 [12]. For comparison: in the Republic of Sakha (Yakutia), the ratio amounted to 48.5 in 2008 year. Level of suicidal behavior in the Republic of Sakha (Yakutia) is higher than the average in the Russian Federation more than 1.8 times and nearly 2.5 times higher than the maximum thresholds, critical incidence of suicide, some experts from the World Health Organization (20 suicides per 100 000 population).

Consequently, suicidal behavior is widespread not only in those regions of the Russian Federation, where the population to Finno-Ugric origins, but also in the regions of the far North in particular, in the Republic of Sakha (Yakutia). The Republic of Northern Caucasus always show low rates of suicide, regardless of religious belief (the population of North Ossetia, mostly confessing Christianity, gives the same low rates of suicidal behavior, like the neighbouring republics, Muslim).

It is noteworthy that the Republic of the Caucasus (Azerbaijan, where the population profess Islam, Armenia and Georgia, whose population professes Christianity) have always differed from the Russian Federation incomparably low rates of suicide, even when they were part of the Soviet Union. For example: in 2002, Azerbaijan gave 1.1 suicides per 100 000 population in 2003 year – the Armenia 1.8 and Georgia in 2001, 2.2 case.

Suicide researcher in pre-revolutionary Yakutia Dmitri Shepilov in 1928, by analyzing the historical data of the Yakut, wrote in his Suicide in Yakutia (study): "in Yakutia in the early 19th century, the number of suicides in 1809 and 1810, respectively 23 and 17, that is about three times higher than in Russia» [13]. According to Polozhy B., of the indigenous peoples of the North of the country, despite the influence of the Orthodox faith, still strong remain archaic Pagan beliefs

that belong to the этнокультурал factor of suicidal behavior. They (the archaic ancient beliefs) are expressed in national traditions and customs [9]. It's symptoms. But, says Polozhy B., "remain the internal psychological or historical memory of the people." In our view, these "internal mental facilities are Archetypes of" collective unconscious "in the terminology of K. Jung.

In the foreword to the book by K. Jung's analytical psychology known Russian philosopher, psychoanalyst Rutkiewicz A. explains the essence of the teachings of ... the eminent psychologist, Jung gradually coming to the central point of his teachings, which he later would call teachings about archetypes collective unconscious: beyond the threshold of consciousness is eternal praformen, manifested at various times in various cultures. They are stored in the unconscious and passed down from generation to generation "[14].

K. Jung reveals the essence of the instincts "specifically designed motivating force that long before consciousness was inherent goal and continue to do so, despite any later than the achieved level of consciousness. Consequently, they are in a close analogy with Archetypes, so close that there are sufficient grounds to assume that the unconscious fantasies of archetypes instincts" [14].

K. Jung suicide problem was communicating with the unconscious desire for Spiritual rebirth. This is due to the updating of the collective unconscious. The archetype of the Renaissance is a mental image of the reward awaiting a person in the face of unbearable existence, and is associated with the archetype of the "Mother", which leads to metaphorical return into the womb the mother, where you can feel a welcome sense of security [15, 16].

Thus, when the problems of life impeded the realization of the personality of its actual capabilities are regressing the psyche with the revival of more ancient archaic archetypes collective unconscious, which in the past ensured the survival of the population. It is known, for example, that until the beginning of the 20th century old chukchi left voluntarily to die in the tundra to more food got its other brethren [2].

Famous ethnographer in the same custom Seroszewski W. suicide stated and Yakuts, "the old man and old woman Earlier if became too old or if someone very ill without hope of recovery, the people asked their children to be buried, and then transferred him to the forest's relative and suddenly pushing in advance prepared hole and dug it out alive" [10].

Old yakut Modžukan, says another famous Yakut researcher Kulakowski A., edge made his



coffin, dug a grave and says to his wife: "I grew old, and I have no previous mighty forces. Will my enemies and win me old man fainted. Then my glory is gone. So I decided to avoid that embarrassment, giving himself or herself voluntarily death "[6].

Platon Oyunsky, famous Yakut poet and philologist, noted: "cases of voluntary death in Yakut tales are also often" [8]. Describes the two types of suicide. In the first form, the elderly already have lived their working age, leaving behind an offspring, considered its existence unnecessary and disadvantageous to the family, so they went away from life, but without the hand. Their children were to bury them and make them a grave mound. Dying is usually given voluntarily swallow heart of cattle, and at a time when the heart is in my throat, the old stalls at throwing in a pit and buried. People who out of fear and pity couldn't do this over their fathers, raised to laughter: "coward has not executed the will of his father, gave him die like a beast." Another example of a voluntary death is the threat to be disgraced, desire to die is not defeated; the famous strongman, having reached old age, forced his wife and son to bury in prepared in advance the Tomb alive [ibid.].

Ancient archetypes, which in the recent past to ensure the survival of the population, create in the minds of modern people irrational thinking and mystical experiences. According to the doctor of sociological science Nemyrivsky V. archaic ancient beliefs. Provide fertile breeding ground for the emergence and growth of the so-called magic mass consciousness [7]. He writes that the modern national ideology should be based on national mentality, socio-cultural traditions, sustainable, centuries manifestations in popular consciousness and behavior, motivations and values the archetypes in the depths of the mass unconscious of Russia. Nemirovsky V. notes that different levels of mass consciousness rises "magic" to the detriment of "realism". Monitoring studies indicate that over the past 16 years, the number of holders of the magic of mass consciousness, that is, the collective unconscious, has increased by about a quarter: currently, about 90 per cent of the population of Krasnoyarskiy State are native magical consciousness [7]. They believe the psychics, fortune telling, in the so called "corruption" in the horoscope. Speaking the language of psychoanalysis, in mass consciousness (unconscious) of our nation continues to dominate, and indeed strengthened, "tanatofilib" – desire for death, writes Nemirovsky V.

An important element of this magical mass consciousness is the attribution of responsibility for everything that happens with the person or the society on external factors. It is actively

seeking an external enemy, xenophobia, paternalism. In a social setting these people hold passive behavior strategy, hoping for State assistance in solving any of life's problems, then there is a good ground for social apathy (it is well known that the income of the rural population in the North is several times smaller than the incomes of industrial districts). If it doesn't come, then the individual is often depressed.

This primitive form is schizophrenia and human behavior, when he knowingly or unknowingly is committed to its final end is death.

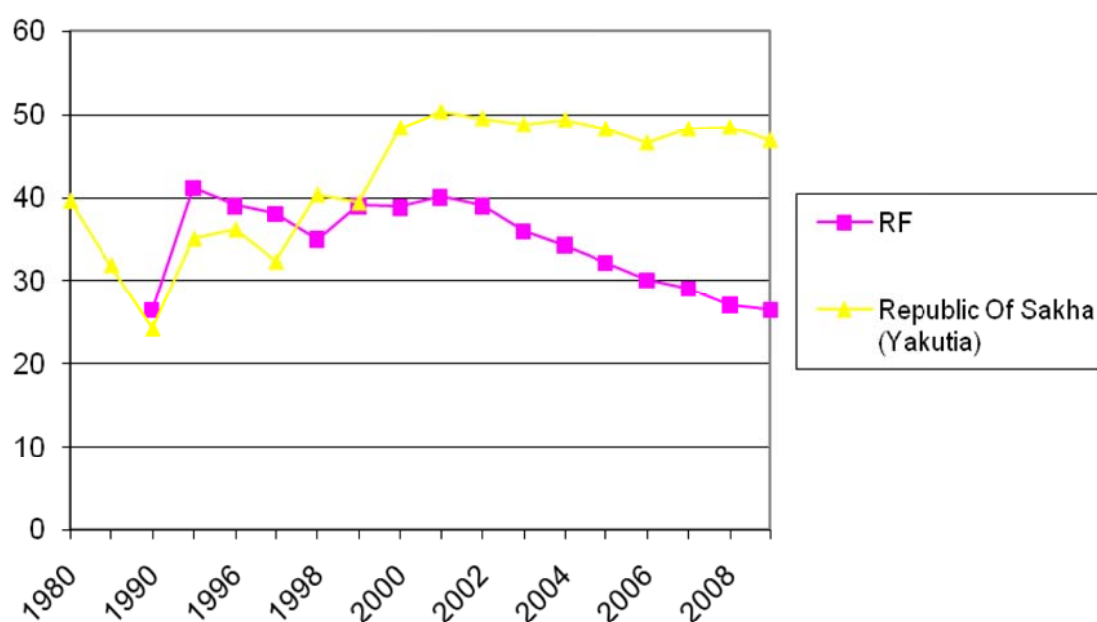
Diverse stress, trauma leads to a violation of the dynamic balance between the conscious and the unconscious in the form of neurosis. This results in the actualization of the archetypes of the collective unconscious, which the recent past, ensures the survival of the North Asien. Ancient archetypes, penetrating mind, his unusual appearance upset psyche. They generate awe, depression, and mystical experiences. Thus, according to K. Jung, there are “mystical” neuroses. And with a weak form of a person experiences unpleasant experiences, and with the strong form of neurosis appears mysterious fear. Consciousness is filled with mythological images, thinking becomes archaic, background mood down – depression begins.

Depression, explicit or scrambled is a major psychological factor in the origins of suicidal behavior.

**Table 1.** Mortality from suicide in RUSSIAN and Sakha Republik (number of deaths per 100000 inhabitants)

	1980	1985	1990	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
R F			26,5	41,1	39	38	35	39	38,8	40	39	36	34,3	32,2	30,1	29,1	27,1	26,5	
R S I	39,6	31,9	24,2	35,1	36,2	32,3	40,4	39,4	48,4	50,4	49,6	48,8	49,4	48,3	46,6	48,3	48,5	46,9	40,8

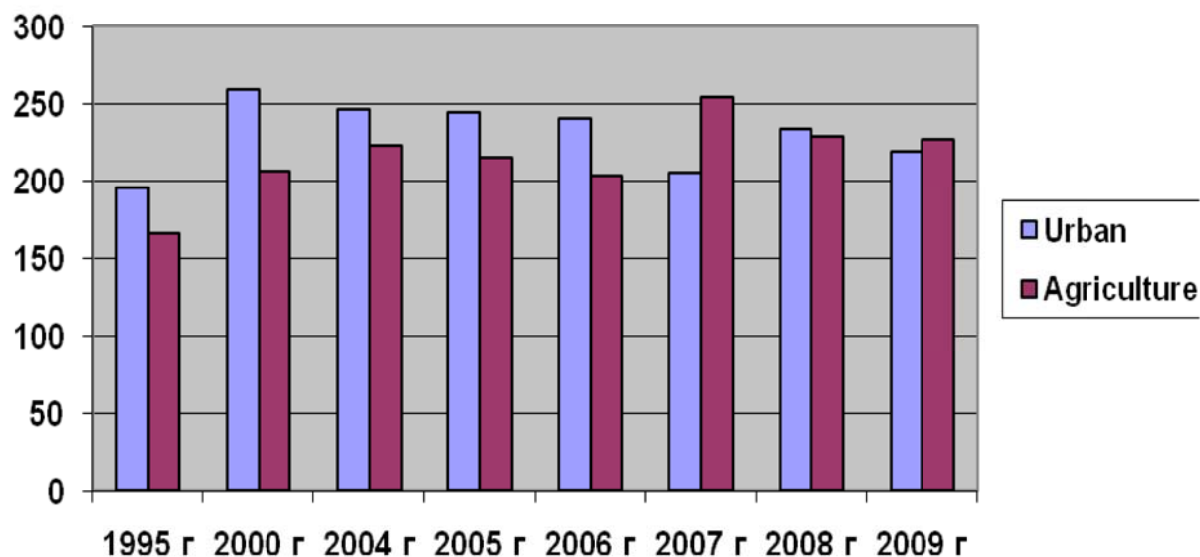
**Figure 1.** Mortality from suicides in the Russian Federation and the RS (I) (number of deaths per 100000 inhabitants)



**Table 2.** Mortality population of suicides in the Republic of Sakha (Yakutia)

	1995 г	2000 г	2004 г	2005 г	2006 г	2007 г	2008 г	2009 г
Urban	195	259	246	244	240	205	233	219
Agriculture	166	206	223	215	203	254	228	226

**Figure 2.** Rural and urban population, mortality from suicides in the Republic of Sakha (Yakutia)



**Table 3.** Teen suicide, 15-19 years (100 thousand) for the 2010 year:

The Subject Of The Federation	R. Sakha Yakuti a	R. Tuva	Rep. Buryatiya	Republic Of Khakassia	Respublik a Kalmykiy a	In RUSSIAN FEDERAT ION
Teenagers 15-19 years	74,2	120,6	86,6	50,3	51,2	19,8
Children up to 15 years	13,4	15,6	12,6	7,3	5,6	3,5

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### Modern etiological and pathological aspects of dental caries

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**Abstract.** The subject of this article is the survey of evolution and factor mechanisms effecting formation of firm dental tissue pathological process of demineralized character. There is a description of clinical and epidemiological features of dental caries and also its connection with organs and systems of the whole organism. Different factors of this pathology from the medical point of view are given here in details.

**Keywords:** spreading, clinical impression, epidemiology, pathogenesis, dental caries etiology.

At present, the frequency of dental caries among the different age groups reaches to high levels [18, 20, 25]. It should be noted that one of the main causes of tooth loss are the complications of tooth decay. Besides, carious teeth can be a source of focal-related diseases of the musculoskeletal system, internal and other organs [5, 28]. Dental caries is the most common in the structure of pathological processes, which is why the studying from theoretical and practical point of view is very important. [29]. However, many studies have found multifactoral origin of pathological processes of dental hard tissues with their demineralization [2, 13].

According to I. Ushnitsky with co-authors [29], on conditions that biogeochemical lack of fluoride the level of dental caries in preschool and school-age children is much higher in the North compared with regions with normal content of these elements in the main sources of drinking water [29]. The people of South climatic zones have lower prevalence to caries.

When there is demineralization of dental hard tissues the manifestation of defense mechanisms of the pulp has observed in the form of mineral deposit crystals, as in the lumen of the dentinal tubules and intertubular dentin [4]. It should be noted that when the tooth spot is white it can restore the enamel structure spontaneously or in the process of remineralizing therapy, but the pigmented tooth spot, especially dark one, does not provide restoring of enamel structure in the process of remineralizing therapy [37]. However, this author argues that if the source of demineralization pigmented spots sums up to 4 mm I the dynamic monitoring is possible, and if the damaged area is 4 mm I or more, especially in extensive lesions, the preparation and sealing are necessary.

Age-related changes in the body affect the rate of occurrence, location, nature of the current decay, which exactly determines the tactics of prevention and treatment materials. According to researchers of different countries, the problem of the prevention and treatment of dental caries in primary teeth of young children from 1 to 3 years is the most acute and almost unresolved [47].

The certain health condition of organism affects the level of dental caries. Thus, there is a high level of susceptibility of hard tissue teeth caries and its complications among children with cerebral palsy [12]. Epidemiological studies show that 2-2.5 people per 1000 population suffer from cerebral palsy in industrialized countries [3]. Among adults with cardiovascular disease and systemic osteoporosis, kidney disease one can observe unfavorable clinical and epidemiological situation of basic dental disease [34]. According to M. Simonova with co-authors [35], the dental complications status among patients with Shegren syndrome is much higher than the average age values. Besides, all patients are characterized by rapid tooth decay through cervical caries, tooth cutting edge, fragility and pathological abrasion of enamel [35]. Significant impact on the frequency and severity of dental caries susceptibility contributes to the presence of several somatic diseases [33].

Thus, the frequency and severity of the pathological processes of teeth hard tissue happen





because of specific regional influence, health and socio-economic factors that require research considering environmental and biological reasons in the formation and development of dental caries to improve treatment and preventive care for different age groups.

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