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SANITARY-EPIDEMIOLOGIC SERVICE IN PERM REGION: 95th ANNIVERSARY *(DEDICATED TO RUSSIAN SANITARY-EPIDEMIOLOGIC SERVICE)*

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The paper outlines the first stages of sanitary activities development in Perm region. We highlight the fact that it was Perm where I.I. Molessson, the first official sanitary inspector in Russia, worked. Here one of the first sanitary inspection of a whole region was performed and "Perm sanitary bulletin" was first published. It was in Perm, where the first sanitary office was established in 1890, and in 1898 the first bacteriological laboratory was organized. Bodies and institutions of Rospotrebnadzor in Perm region are known to be founded on September 15, 1922, when a Decree by Russian People's Commissars Council "On the Republic's sanitary bodies" was issued. A sanitary-hygienic faculty of Perm Medical Institute was set up in 1931 and it gave grounds for preparing qualified sanitary inspectors for state sanitary authorities.

We described basic tasks which were tackled by sanitary inspectors during the Great Patriotic War and just after it. Rospotrebnadzor activities are proved to make for substantial improvements of sanitary-epidemiologic situation in the region. Currently more than 95 % of population are provided with drinking water which fully corresponds to the sanitary legislation requirements. We note constant improvements in catering objects quality and we also see that a quantity of food samples taken at such objects which don't correspond to hygienic standards remains stably low. A share of working places deviating from hygienic standards as per noise, vibration, and illumination, has reduced. Medical examinations are now available to 97.9 % of workers functioning under hazardous (dangerous) working conditions. The lowest occupational morbidity level over the last few years was registered in Perm region in 2016. The Service was among the first in the country to transfer to result-oriented budgeting and risk-oriented surveillance model. Organizational structure is constantly being developed; new legal, economic and organizational approaches are being created and implemented in the activities performed by bodies and institutions of the Federal Service for Surveillance over Consumer Rights protection and Human well-being.

Key words: *Sanitary-epidemiologic Service, Perm region, history, achievements.*

Attitude towards medicine as a tool of providing "internal security of a state" emerged in the first half of the 19th century [9]. Acknowledgement of new concepts on reasons for epidemics evolvement made the greatest contribution into changes in views on a role which medicine played in life of a state. Epidemics at all times were considered to be one of the most dangerous threats for any state. They caused deaths of thousands and hundreds of thousand people, led to economic instability, did enormous and sometimes even irreparable economic harm [4]. Epidemics were viewed as imminent disasters; however, states did very little to fight them. State interference was mostly limited to fighting already existing epidemics by introducing quarantine

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measures which were as cruel as inefficient [2].

And as scientists realized that reasons for epidemics could be cognized and therefore managed (at least partly), it led to working out and implementing a set of activities into a public administration system. Such measures were at first called "medical and police activities" and included:

- introduction of direct public administration of medical activities in the sphere of studying epidemic constitutions, fighting against epidemics and implementation of other national "medical activities on protection and recovery of citizens' health";

- development of specialized medical and sanitary legislation by joint efforts of physicians and lawyers;

- fighting against quacks and provision of population with highly qualified medical personnel via radical reforms in the sphere of medical education;

- creation of a state system for providing assistance to people in need and socially insecure population groups (orphans, elderly and disabled people, low-income families, beggars, etc.);

- implementation of specific activities aimed at creating healthy lifestyle, providing healthy nutrition and safe working conditions.

Each of the above-mentioned activity spheres became a true innovation not only in the history of medicine, but also in the public administration history.

A concept of creating permanently functioning organizations - prototypes of a sanitary service - started to be put into practice in the second half of the 19th century [9]. It was related to the foundation of zemstvo (a regional administration) in 34 provinces of the Russian Empire in 1864. Medicine in a zemstvo should be headed by a physician who could introduce preventive measures protecting wide layers of population (Photo 1). Preventive approach was completely in line with ideas of great N.N.Pirogov who said, "I believe in hygiene. It is there where a true progress of our science lies. Future belongs to preventive medicine" [7].

Perm region can take great pride in the fact that Ivan Ivanovich Molesson (1842-1920), one of our citizens, became the first sanitary inspector in Russia and started his career in our region (Permskaya province back then) (Photo 2). He arrived in Perm in 1871 to work as a doctor in the main province hospital and he was the first to suggest a sanitary examination of the province [1]. In 1874 cattle plague epizooty caused death of practically all cattle in Perm. To fight this dangerous infection, first a sanitary committee was created and later on a permanent sanitary commission was established to "deal with issues related to the city hygiene". In 1886 Molesson introduced the first issue of "Perm epidemiologic bulletin". And it was in Perm in 1890 when the first sanitary office was created and in 1898 the first bacteriological laboratory was set up[1] [1,5].

Photo 1. Doctors from zemstvo examining patients in Kazan

[1]In 1912 it was re-organized into a scientific and research institute (now it is "Biomed" scientific and production association).

Photo 2. I.I. Molesson (1842-1920)

In July 1918 the RSFSR People's Commissariat for Public Health was established and a sanitary-epidemiologic section was a part of it; and in 1920 a sanitary department of Perm regional public healthcare office was organized; its main task was to implement sanitary-epidemiologic activities on the territory of Perm region.

Offices and bodies of Rospotrebnadzor Perm regional office can trace their history back to September 15, 1922, when a Decree "On the Republic sanitary bodies" was signed by the RSFSR People's Commissariat. In 1926 a sanitary and hygienic laboratory headed by K.N. Shapshnev, a professor form the Perm State University, was opened in the city; in 1934 the laboratory was named after him [8].

The first law "On the Republic sanitary bodies" was passed by the RSFSR People's Commissariat on February 1927; and the regulations on them were adopted on October 8, 1927. According to them, sanitary organs received wider functions and rights; they also fixed differentiated standards for providing regions and cities with sanitary personnel, bacteriological laboratories, and disinfection stations, depending on their industrial significance. Preventive sanitary surveillance at all stages of industrial and civil construction became the most important part in the RF sanitary bodies functioning. In August 1929 the RSFSR People's Commissariat listened to the report "On sanitary state in the Republic".

In 1931 a sanitary-hygienic faculty was created in the structure of Perm Medical Institute and it gave grounds for providing state sanitary and epidemic service offices with highly qualified sanitary inspectors. You can see a team of Molotov city sanitary inspection in Photo 3 (1936).

During the Great Patriotic War the sanitary service had peculiar tasks to perform [10]. Epidemic typhus morbidity grew drastically in Perm (Molotov back then) in November-December 1941, and an issue of fighting back pediculosis became truly vital for public healthcare organs and institutions. 5th grade students of the medical institution were assigned to accomplish the task and they did a great job preventing epidemic typhus spread in the city and the region as a whole.

The Regional sanitary and Epidemiologic station was established on April 23, 1942 by a decree passed by Molotov regional deputies council. Later on, in the 50ties last century 41 sanitary-epidemiologic stations and 32 sanitary-bacteriological laboratories were founded all over the region.

70-80ties last century were the period in Perm regional sanitary and epidemiologic service functioning when complex work with enterprises, institutions, and organizations was accomplished in the sphere of health protection, improving working conditions, and lowering workers' morbidity. To fulfill the set tasks, complex plans of sanitary-epidemiologic activities

were created and implemented; such plans were approved by sessions of city and district People's Deputies Councils.

A new RSFSR law "On sanitary and epidemiologic welfare of the population" was passed in 1991 and it opened a new chapter in sanitary-epidemiologic service development. All district and city sanitary and epidemiologic stations ceased to be subordinated to Public Healthcare administrations and were given into subordination to Regional Sanitary-Epidemiologic Service by the Decree of Perm regional executive council No.215 issued on September 12, 1991, and by the Order of Regional Public Healthcare Administration and Regional Sanitary-Epidemiologic Service No. 398/134 issued on September 18, 1991. Overall, 47 offices of the State Sanitary-Epidemiologic Service carried out state sanitary and epidemiologic surveillance in the region.

At the same time laboratory base was equipped with modernized devices and tools and it allowed to substantially enlarge laboratories' capabilities, to increase laboratory research validity, and to make laboratory examinations quite shorter.

Over these years a lot of outstanding state sanitary and epidemiologic service officials and scientists worked in Perm region: B.I. Raikher, A.V. Pshenichnov, V.V. Dianova, V.F. Petrov, G.V. Shaklein, T.M. Lebedeva, M.L. Krasovitskaya, N.V. Zaitseva, N.M. Koza, I.V.Feldblum, A.Ya. Perevalov. Some of them were Chief State Sanitary Inspectors in Perm region, honored scientists, State Prize winners, honored physicians of the USSR and the RF, Doctors and Candidates of Science.

E.N. Belyaev, an outstanding organizer and supervisor, was the head of the Regional Sanitary-Epidemiologic station from 1975 to 1986. Later Evgeniy Nikolaevich was the head of the Central sanitary-epidemiologic administration of the RSFSR Public Healthcare Ministry and the head of the State Committee of the RSFSR sanitary-epidemiologic surveillance.

In the early 90ties Perm regional sanitary and epidemiologic service was one of the first to introduce a new economic mechanism.

Photo 3. Team of Molotov city sanitary inspection, August 1936.

It was at the initial stage of reforms when basic activities of Perm regional sanitary and epidemiologic service activities were optimized; these activities were related to water supply and sewerage in settlements, surveillance over working conditions, food products storage and trade conditions, and organization of educational process.

Later on, State sanitary and epidemiologic service was taking active part in licensing and certification of specific works and services, as well as products which could be potentially dangerous for human health. It carried out radiation control on the region territory and developed a new activity - social and hygienic monitoring which was aimed at assessing population health and environment, at detecting changes in them and predicting their state.

Over those years the organizational structure of the service was continuously reorganized; new departments were created to examine population health in relation to impacts exerted by environmental factors, to introduce automated control systems, to accomplish hygienic certification of laboratories, to perform metrological tasks, etc. Perm Scientific and Research Institute for Children Ecological Pathology headed by the academician N.V. Zaitseva took part in new activities devoted to assessing population health risks caused by environmental factors.

Over the following years the service went on searching for new organizational forms of activity as centralization of administration and funding was widely introduced. In 2002-2003 The Program for Transformation of the Perm regional state sanitary and epidemiologic service organizational structure was successfully implemented. 18 inter-district state sanitary and epidemiologic surveillance centers were created in the region instead of former 47 ones; they fully concentrated staff and material and technical resources, and laboratories were also centralized and consolidated.

Reforms allowed to split surveillance functions from other which didn't belong to a state authority; quality of sanitary and epidemiologic surveillance increased, and funds from the Federal budget were now spent more efficiently.

Foundation of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being in conformity with the Order by the RF President issued on March 9, 2004 No. 314 "On the system and structure of the Federal Executive Bodies" became a new milestone in organizational and legal construction of the state sanitary service. Perm Regional Office of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being was established in Perm region; it comprised 4 territorial departments and Center for Hygiene and Epidemiology in Perm Region and Komi-Permyatskiy autonomous district and its 9 subsidiaries. Their main tasks were to accomplish state surveillance and control over compliance with the RF legislation in the sphere of providing sanitary and epidemiologic welfare of the population and consumer rights protection; to prevent hazardous impacts exerted on people by environmental factors; to prevent infectious and non-infectious diseases (intoxications) of the population. Center for Hygiene and Epidemiology in Perm Region and Komi-Permyatskiy autonomous district provided activities of the surveillance territorial body of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being.

When a new RF region - Permskiy krai - was created on December 12, 2005, bodies and organizations of the Federal Service for Surveillance over Consumer

Rights Protection and Human Well-being in Perm regions were Perm Regional Rospotrebnadzor Office, its 6 territorial departments, Center for Hygiene and Epidemiology in Perm Region and its 6 subsidiaries, and Federal Scientific Center for Medical and Preventive Health Risk Management Technologies which was created by the RF Government decision No. 628 taken on May 8, 2009 on the basis of the Perm Scientific Research Clinical Institute for Children Ecological pathology. The said Center is a truly leading organization of the RF Rospotrebnadzor which has made a substantial contribution into the methodology of state sanitary epidemiologic service optimization, worked out and implemented a risk-oriented approach to surveillance activity, created a number of organizational-administrative, regulative, and methodical documents applied in the activities of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being.

Today, more than 1,000 highly qualified experts work in Rospotrebnadzor bodies and organizations in Perm region; among them there are honored public healthcare workers, people with honorary diplomas granted by the RF Public Healthcare Ministry, Doctors and Candidates of Medical Sciences.

Activities of the sanitary service are quite efficient. Today a share of Perm region population provided with drinking water which conforms to the sanitary legislation requirements amounts to 95.5%. A number of people living within sanitary-hygienic zones of enterprises tends to decrease. Catering objects quality is constantly growing and a number of food samples not conforming to standards remains low (1% over the last years). Over the last years there have been no positive samples of genetically modified products registered in the region [6].

There also have been no mass non-infectious intoxications of population in the region related to consumption of low-quality and dangerous food products. Since 2013, population morbidity related to micronutrient deficiency has leveled off. Over the last 5 years a number of intoxications with alcoholic products has decreased by more than 25%.

Photo 4. Legal consultations on issues related to drugs traffic in Perm region
In the foreground – V.G. Kostarev, Head of Rospotrebnadzor office in Perm region

A set of organizational and surveillance activities in the sphere of providing sanitary and epidemiologic welfare of the regional population made for decrease from 19% to 15% in the number of preschool children facilities with overcrowded groups; a share of working places with artificial luminance not conforming to standards decreased to 7% in comparison with the previous year; with furniture not conforming to standards, to 13%. 90% of school children were provided with high quality nutrition in 2016.

Permanent contacts between the Service and civil society representatives as well as with other administrative bodies are constantly growing; it concerns especially such vital issues as drugs addiction and distribution (Photo 4). Rospotrbnadzor Perm regional office is to implement state policy in this sphere and to make dishonest entrepreneurs and juridical persons to bear responsibility for their products and services' quality. Functions of the State surveillance organization are equally aimed at compliance with hygienic standards both for children and adults, as well as at sanitary and epidemiologic surveillance.

To detect violations in other spheres, the service accomplishes inspections together with other surveillance bodies (Federal Agency of technical Regulating and Metrology, EMERCOM of Russia, Federal Tax Service, etc.)

Due to task-oriented interdepartmental interaction by public administrative bodies, surveillance and control authorities, and employers in 2014-2016 we managed to achieve positive results in providing sanitary-epidemiologic welfare at industrial objects, in communal sphere, in education, and in public healthcare.

A share of working places not conforming to hygienic standards as per noise, vibration, and luminance parameters, has decreased. 97.9% workers employed at hazardous (dangerous) productions had their medical examinations. In 2016 registered occupational morbidity in the region dropped to the lowest level over the last years.

Under massive administrative and budget reforming which state control and surveillance authorities had to undergo, Perm regional sanitary and epidemiologic service managed not only to preserve its authority but also to substantially enlarge its capabilities. Perm experts took a most active part in creating methodological grounds for organization and functioning of the Service under result-oriented budgeting, program-targeted planning, transfer to subsidiary budgeting and risk-oriented control (surveillance).

A history of Perm regional sanitary and epidemiologic service creation and development is not coming to its end today as new solid grounds for future are being formed. To achieve it, organizational structure is being improved, new legal, economic, and organizational approaches in the activities of bodies and organizations of the Federal Service for Surveillance over Consumer Rights Protection and Human Wellbeing are being created and implemented.

Each expert who works in the Service today is fully aware of the responsibility he or she bears; after all they are to protect health and welfare of all the people living in Perm region!

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PREVENTIVE MEDICINE. URGENT ASPECTS OF RISK ANALYSIS

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ON ASSESSMENT OF ROSPOTREBNADZOR SURVEILLANCE AND CONTROL ACTIVITIES EFFICIENCY IN REGIONS: ASSESSMENT CRITERIA BEING PREVENTED ECONOMIC LOSSES CAUSED BY POPULATION MORBIDITY AND MORTALITY AND ASSOCIATED WITH NEGATIVE IMPCATS EXERTED BY ENVIRONMENTAL FACTORS

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The paper outlines the results of calculating actual and prevented economic losses caused by population mortality and morbidity and associated with negative impacts by environmental factors the prevention of which resulted from surveillance and control activities. Rospotrebnadzor bodies and organizations efficiency was assessed in Leningrad region, Bashkortostan, and Chelyabinsk region, and we give the results of this assessment. Not less than 25 environment parameters were examined in each region (air in rural and urban settlements, drinking water, soils in settlements); we examined population morbidity parameters both for children and adults in terms of death causes and morbidity as per 16 diseases categories (as per ICD-10); we also took not less than 20 features of surveillance and control activities. All regions had apparent and measurable risk factors for population health related to environment quality which didn't conform to hygienic requirements and standards. All risks caused additional deaths and diseases among children and adults. in 2015 additional mortality and morbidity cases associated with environmental factors caused economic losses of regional gross product in each region and they were equal to 1-2.5 billion rubles. Surveillance and control activities performed by the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being helped to prevent deterioration of air, drinking water and soils in settlements. As a result, approximately 700 additional deaths and from 70

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to 16 thousand additional diseases among children and adults were prevented in each region. Prevented economic losses in the examined regions varied from 1.0 billion rubles in Chelyabinsk region to 2.3 billion rubles in Bashkortostan. Economic efficiency of surveillance and control activities in the sphere of providing sanitary and epidemiologic safety of the population varies from 18 to 27 rubles per 1 ruble of costs in the examined year.

Key words: *Rospotrebnadzor, surveillance and control activities, population health, environment, efficiency, mortality indexes, losses of regional gross product.*

State authorities in the RF are now being reformed and issues of assessing control and surveillance efficiency are considered to be especially vital in the process. It is proven by regulations which are included into "A concept of increase in efficiency of surveillance and control activities performed by state and local authorities for 2014-2018: a project" [6], "On improving efficiency of surveillance and control activities performed by federal executive bodies: A project of the Presidential Order (worked out by the RF Ministry of Economic Development on October 04, 2016)" [10], and other state strategic documents [12].

A transfer to a risk-oriented approach requires not only lowering administrative barriers for business but above all preventing losses of public values which are protected by the state [4,5]. A trend in improving assessments of surveillance authorities activities in Russia fully corresponds to international practices and proves there is evolution both in getting greater insights into state control (surveillance) efficiency and its role in achieving socially significant results and in state authorities being ready to take on responsibility for risk levels in the spheres under surveillance and their minimization [3, 9,14].

From the point of view of the Federal Service for Surveillance over Consumer Rights Protection and Human Well-being, control and surveillance efficiency first of all entails lowering risks of human environment contamination and improving population health [11,13]. New methodical approaches have been recently created and implemented into Rospotrebnadzor practices; these approaches enable assessing medical and demographic losses which become preventable due to the Service activities and it has become a very important result in solving tasks on assessing efficiency of its activities. "Calculation of actual and prevented economic losses caused by population mortality, morbidity and disability and associated with negative impacts exerted by environmental factors which were prevented due to surveillance and control activities: Methodical guidelines" [8] were created allowing for "The methodology for calculating the economic cost of mortality, morbidity and disability in the working population: Guidelines" (approved by the Order of the RF Ministry for Economic Development, RF Public Healthcare Ministry, RF Ministry of Finance, and Federal Statistics Service on April 10, 2012 No. 192/323n/45n/113) [7] and approved by the RF Chief Sanitary Inspector on October 23, 2014. The documents grants sanitary-epidemiologic surveillance authorities a possibility to assess final results and to show real significance of its functioning to state authorities, business, and civil society.

Methodical guidelines are even more vital as economic efficiency assessment is based on the calculation of prevented GDP losses and GDP growth is one of the state strategic goals. Consequently, assessment results as per actual and preventable losses can be of interest for decision-makers from regional executive bodies, local authorities, territorial authorities, and any other federal executive bodies [16].

Calculation of regional economic losses caused by population morbidity and mortal-

ity which were prevented by control and surveillance activities aimed at providing sanitary and epidemiologic welfare entails sequential consideration and parameterization of several sections in one chain: assessment of correlation between living environment quality and population health parameters; assessment of correlation between measuring environmental objects quality and Rospotrebnadzor control and surveillance activities results; calculation of a number of health disorders prevented due to Rospotrebnadzor bodies and offices control and surveillance activities and economic assessment of such cases based on the detected dependencies.

Our research goal was to assess efficiency of control and surveillance activities accomplished by Rospotrebnador bodies and offices in regions similar as per social and economic development and sanitary-hygienic problems; our assessment criteria were economic losses caused by population mortality and morbidity which were associated with negative impacts exerted by environmental factors and which were prevented due to Rospotrebnadzor activities.

Our research objects were Republic of Bashkortostan, Leningrad region, and Chelyabinsk region, all three being the RF regions with developed industries, apparent problems with environmental contamination and considerable population (totally about 10 million people live in these regions).

Data and methods. We determined calculated economic damage related to population mortality and morbidity as a part of GDP or GRP which was not produced due to a share of economically active population who dropped out of production processes [2,8]. Losses related to mortality were calculated on the basis of 0.5 year of economic activities per each case; losses related to morbidity were calculated on the basis of an average duration of one temporary disability case which was equal to 14 days.

We used the following initial data for our calculations: environment parameters in the regions registered in statistic forms on economic branches accounting No. 18 "Data on sanitary situation in the RF regions" and in databases of the Federal fund for social and hygienic monitoring ("Environment" section); demographic and medical statistics data (forms 1-C; 1-health, 32-health, etc.); "Data on the results of accomplishing Federal state surveillance by Rospotrebnadzor territorial offices" reports; and other data taken from the official statistics (regional population, gross regional products values, etc.).

We allowed for not less than 25 environment parameters as per each region (atmospheric air in urban and rural settlements, drinking water, soils in settlements); adults and children mortality as per causes and morbidity with 16 diseases categories (as per ICD-10); not less than 20 properties of surveillance and control activities.

We applied unified mathematical dependencies in "environment - health - control and surveillance activities" system for all the examined regions; these dependencies were obtained as a result of processing all the aggregated data collected in the whole country over 3 previous years. Thus, for example, relative mortality of children aged 0-17 and retired people was authentically related to a share of atmospheric air samples taken in urban and rural settlements with nitrogen dioxide, suspended substances, and aromatic hydrocarbons contents exceeding MPC ($p<0.05$, $R2=0.233$ for children and 0.249 for retired people). We determined and parameterized correlations between circulatory system diseases both in children and adults and frequency of drinking water taken from communal drinking water supply not conforming to hygienic

standards as per sanitary-chemical parameters ($p<0.05$, $R2=0.118$). We revealed that increased water hardness, increased concentrations of iron, manganese, aluminum, chlorine, and chlorine-organic compounds were related to diseases of digestive organs, circulatory system, skin and subcutaneous tissue, musculoskeletal system, blood, blood-making organs, and certain disorders involving immune mechanisms. Violation of sanitary standards as per microbiological factor is authentically related to infectious diseases frequency, including epidemics ($p<0.05$, $R2=0.102÷0.472$).

If we take the RF as a whole, we can see that the most efficient research is that during which sanitary legislation violations were detected; unscheduled inspections; inspections involving laboratory and instrumental research techniques. Decrease in a share of atmospheric air samples and water samples not conforming to standards is authentically related to frequency of initiated proceedings on administrative offences and passed rulings on administrative punishments imposed on industrial enterprises and water supply facilities etc.

Basic results. Analysis of data on environment quality in the examined regions revealed that there were common problems in all of them related to it being not corresponding to hygienic requirements and standards (Table 1).

Table 1

Basic parameters of environmental quality in the regions and its conformity to hygienic requirements and standards, 2015

Environmental quality parameter	Bashkortostan	Leningrad region	Chelyabinsk region
A share of the examined samples taken from centralized water supply and not conforming to hygienic standards as per microbiological parameters	2,5	4,1	3,0
A share of the examined samples taken from centralized water supply and not conforming to hygienic standards as per sanitary-chemical parameters	6,1	42,5	21,0
A share of the examined atmospheric air samples taken in urban and rural settlements with admixtures in them exceeding MPC, totally	1,1	0,4	1,1
A share of the examined atmospheric air samples taken in urban and rural settlements with suspended substances concentrations in them exceeding MPC	0,9	0,5	1,2
A share of the examined soils samples taken in settlements and not conforming to hygienic standards as per microbiological parameters	0,3	6,8	15,7

The greatest frequency of obligatory requirements violations was registered in all three regions in relation to sanitary-chemical parameters of drinking water quality (from 6.1% in Bashkortostan to 42.5 in Leningrad region). Also we observed increased manganese concentrations in drinking water in all three regions (from 0.8 to 4.3% violations). Increased iron concentrations were detected in Leningrad and Chelyabinsk regions (18.7 and 18.6% of samples not conforming to standards correspondingly). There were certain peculiarities registered in the regions: increased aluminum concentrations in Leningrad region (2.2% samples not conforming to standards); increased nickel concentrations, in Chelyabinsk region

(0.9% violations); sulfates, in Bashkortostan (2.5% samples with concentrations higher than standards). There were peculiarities in atmospheric air contamination which were caused by specific industrial objects located in the regions. Thus, a share of the examined atmospheric air samples taken in rural and urban settlements which contained benzpyrene concentrations higher than MPC exceeded 20% in Chelyabinsk region in 2015. Phenol contents in atmospheric air samples were higher than MPC in 0.9% samples taken in Bashkortostan. The highest level of soils microbiological contamination was detected in Chelyabinsk region and it was certainly due to the fact that this region was more densely populated.

However, all three regions had apparent and measurable risk factors for population health. These risks cause additional death cases and diseases among children and adults and substantial economic losses related to these medical and demographic ones. Thus, approximately 290 additional death cases(mostly among adults) and more than 129,5 thousand morbidity cases were likely to be related to unfavorable environmental quality in Bashkortostan in 2015. Overall, additional death cases and morbidity cases caused economic losses of the gross regional product equal to 1.2 billion rubles. Almost 280 death cases and 43 thousand morbidity cases as well as 900 million rubles of economic losses can be related to poor quality of air, water, and soils in Leningrad region settlements; more than 2.6 billion rubles, in Chelyabinsk region. But still, our analysis of correlation between the results of surveillance and control activities and environmental quality and - indirectly - medical and demographic parameters in the regions proved that these losses could be

Table 2

Environmental parameters not conforming to hygienic standards which were prevented due to control and surveillance activities accomplished by Rospotrebnadzor in 2015

Environmental quality parameter	Bashkortostan	Leningrad region	Chelyabinsk region
A share of drinking water samples not conforming to hygienic standards as per microbiological parameters,%	2,6	2,3	0,8
A share of drinking water samples not conforming to hygienic standards as per sanitary and chemical parameters,%	46,0	31,6	25,1
A share of drinking water samples not conforming to hygienic standards as per aluminum content,%	4,5	3,8	4,3
A share of atmospheric air samples taken in urban and rural areas with contaminations higher than MPC (totally),%	3,7	6,9	2,2
A share of atmospheric air samples taken in urban and rural areas with benzpyrene concentrations higher than MPC (totally),%	14,5	19,7	9,5
A share of atmospheric air samples taken in urban and rural areas with suspended substances concentrations higher than MPC (totally),%	3,1	6,2	1,0
A share of samples taken in settlements and not conforming to hygienic standards as per heavy metals contents, %	2,3	2,5	1,7
A share of the examined samples taken in settlements and not conforming to hygienic standards as per sanitary-chemical parameters, %	7,8	7,5	4,9

considerably higher if there was no sanitary and epidemiologic control.

Thus, Rospotrebnadzor bodies and offices activities prevented a considerable number of violations related to requirements to sanitary and chemical parameters of drinking water quality and soils in urban and rural settlements in Bashkortostan in 2015. If not for controlling activities of the Federal Service for Surveillance over Consumer Rights protection and Human Well-being regional office in Leningrad region, drinking water quality would be much lower, atmospheric air would be gravely contaminated with benzpyrene and suspended substances, and sanitary state of soils would also deteriorate significantly. Table 2 contains only several parameters characterizing potential negative environmental properties which were eliminated due to the Service activities.

Prevented contamination helped to avoid approximately 700-800 additional death cases caused by respiratory organs diseases, cardiovascular diseases, and neoplasms, in all three regions. And here about 35% of all the prevented death cases can be related to economically active population who take part in creation of the gross regional product. A number of prevented morbidity cases amounted to approximately 71 thousand in Leningrad region; 83 thousand, in Chelyabinsk region: and more than 160 thousand, in Bashkortostan. Morbidity structure in the context of diseases prevented by control and surveillance activities was as follows: respiratory organs diseases both among children and adults (from 35 to 50%); digestive organs diseases (about 20% in children and 7.5% in adults); cardiovascular system diseases (about 4% in children and 6-8% in adults), infectious and parasitic diseaes, endocrine system diseases, and other disorders.

Children morbidity in 20-22% cases lead to economically active citizens taking sickness certificates to take care of them [1]; morbidity of economically active population in regions (about 78% of employable population and about 25% people older than this age) directly causes temporary disability of population. It results in direct economic losses in the RF regions and the country as a whole.

Table 3

Economic losses caused by population mortality and morbidity associated with negative impacts exerted by environmental factors which were prevented due to control and surveillance activities in 2015 and efficiency of these activities

Parameter	Bashkortostan	Leningrad region	Chelyabinsk region
Total population, thousand.	4071,99	1778,86	3497,27
Costs on control and surveillance activities aimed at providing sanitary and economic welfare, million rubles.	82,20	54,66	55,79
Gross regional product per 1 employed, million rubles.	0,79	1,06	0,67
Prevented economic losses based on gross regional products values, million rubles:	2 256,66	1 381,12	1 004,47
– due to mortality	65,87	114,40	77,22
– losses from diseases	2 190,79	1 266,72	927,25
Economic efficiency based on prevented GRP losses, rubles per 1 rubles of costs	27,45	25,27	18,01

As per our research results, we determined that prevented economic losses in the examined regions in 2015 ranged from 1.0 billion rubles in Chelyabinsk region to 2.3 billion rubles in Bashkortostan (in 2015 prices) (Table 3).

If we calculate a ratio between prevented economic losses and actual costs which Rospotrebnadzor bore in the regions on surveillance and control activities aimed at providing sanitary-epidemiologic safety it will allow us to assess economic efficiency of these activities as being equal to from 18 rubles/1 rubles of cost in Chelyabinsk region to 27.5 rubles/per 1 ruble of costs in Bashkortostan. The obtained data prove that the Service activities are relevant and highly efficient.

Conclusions:

- assessment of economic efficiency of control and surveillance activities as per their final results, namely lower population morbidity and mortality caused by reasons authentically related to unfavorable environmental factors is a correct and objective criterion for assessing the service activities;

- high efficiency of surveillance and control activities in specific regions should underlie the analysis of the service activities as a whole and should be considered a reference point for other RF regions;

- results of assessing prevented medical-demographic and economic losses should be used as an information-analytical base for working out decisions aimed at minimizing population health risks related to environmental quality.

Further development of the Service activities economic assessments should entail application of these methodological approaches in assessing parameters related to consumer goods quality; in improving data collection and processing techniques for determining correlations within "environment - health" system; in developing systems of detecting, proving and registering cases of damage to population health caused by negative impacts exerted by environmental factors.

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ALGORITHMS, METHODS AND RESULTS OF EVALUATION OF EXPOSITION OF RISK FACTORS

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ON ASSESSING ELECTROMAGNETIC FIELD (300 KMHz – 300MHz) IN A LARGE INDUSTRIAL CITY ON THE BASIS OF 3D MODELING AND INSTRUMENTAL MEASURING

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The article dwells on issues of modeling electromagnetic fields levels (EMF with frequency equal to 300 KMHz - 300 MHz which are created by television and radio broadcasting objects, radiolocation, and mobile communication in a large regional center, in geoinformation system environment. Our task was to estimate EMF levels on areas where apartment blocks were located; to assess energy flows at various floors, to determine zones in a city as per EMF levels; to verify the obtained results with the direct factor measuring. Our calculation included data on 2,011 EMF sources located on a city territory. We allowed for bulk parameters of 31,949 buildings including 17,307 apartment blocks, 3,160 administrative buildings, 307 pre-school children facilities and 105 secondary schools. We performed our calculations in city coordinate system at 109 thousand points. Each calculation created a picture of EMF spread in a plane at a set height which allowed us to determine exposure level at a control point as per "slice" results and to build up a 3D contamination model. Approximately 80% of all the calculated results had EMF parameters within 0.1-10 safety criterion range. We spotted zones with maximum calculated EMF levels at 18-25 meters. Instrumental research proved high factor levels in these zones including those where levels exceeded safety criterion 4-6 times; it makes for certain vigilance in judgments on environmental safety for people who live on the examined territory permanently. The obtained data can be used for foundation of instrumental research points within the frameworks of specific research or social-hygienic monitoring as well as for consequent exposure and health risk assessment. The materials can be used in epidemiologic research for conjugate spatial analysis of energy flows and children and adults mortality.

Key words: *electromagnetic field, health risk factor, spatial modeling.*

Modern technologies based on electromagnetic waves properties are developing quite intensively now and it makes it absolutely necessary to update existing techniques for hygienic assessment of the environment [4, 6, 10]. Base stations of mobile communication, departmental communication (emergency, fire-fighting teams, RF EMERCOM teams etc.), frequency-modulated TV and radio broadcasting, radio relay systems, trace surveillance locators which control situation in the air as well as

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other radiation sources satisfy all the needs of industry and population in constantly increasing scope as they are replacing other processes and devices. Electromagnetic fields levels (EFL) of artificial origin are becoming a significant ecological factor with high biological activity. New technologies are being developed in the sphere of radio- and TV-broadcasting, wireless communication etc. and they are aimed at maximum dense "radio-coverage" of territories where people live permanently. And given the severe competition which exists on the telecommunication services market, we can observe multiple overlapping of electromagnetic fields created by competing companies.

In 1995 the World Health Organization (WHO) officially introduced a concept of "global electromagnetic contamination of the environment" and listed an electromagnetic contamination issue among those being top priority for the mankind. The WHO is implementing the International EMF Project and it highlights the actuality and significance this subject has for the society.

Research on electromagnetic fields levels, including those performed in the context of population exposure to them, has been conducted within a framework of specific scientific projects [1, 7, 12, 15, 16] or complex programs; for example, COST244bis European Scientific program (Bergqvist et al. 2001) [18]. Some authors consider electromagnetic fields to be risk factors for malignant neoplasms evolvement [3, 12], There are some data proving that electromagnetic radiation within radio frequencies range can cause non-carcinogenic risks of population health disorders [11, 13–15,23,24]. We have come across some works containing evidence that certain effects exerted on health still need to be proved [21]. However, all the research in general confirms that it is really vital to study impacts exerted by electromagnetic fields on a human body. In any case, documents issued by the WHO and other international organizations require to adhere to a principle of caution when assessing ionizing radiation objects safety [17, 22, 25–28]. It becomes even more important as some authors believe people in our country tend to underestimate electromagnetic fields danger for health and there is no systemic monitoring of the factor or individual dosage meters for electromagnetic fields measuring.

We should point out that there is very little research on assessing exposure as a measure of contact between this factor and a man when electromagnetic fields are measured. A lot of researchers have noted that it is very complicated to assess this exposure correctly. For example, data on electromagnetic fields levels collected in different countries within COST224bis program network in zones near base stations of mobile communications were within the range from 0.000001 to 48 mW/m2. There was a series of research conducted in Germany, France, and Switzerland, and the data obtained in it also varied greatly: average electromagnetic field level was equal to 0.027-0.09 mW/m2 while its maximum amounted to 3.5 mW/m2 (Vielt et al. 2009, Breckenkamp, 2009) [19, 28]. Some Russian scientists give data on energy flux density from base stations being equal to 0.1 to 5 μW/cm2. Significant dispersion in the results proves it is necessary to search for unified approaches to drawing up observation programs, measuring techniques and reports.

The report issued by Sweden SSM's Scientific Council on Electromagnetic Fields in 2016 contains the most relevant contemporary meta-analysis of research results within "electromagnetic fields - population health" system; it highlights the ne-

cessity to improve overall quality and validity of epidemiologic research [19].

The latter is especially vital when it comes to sanitary-hygienic assessments, research, inspections, and examinations conducted in cities. It is due to the fact that as per data given by some authors electromagnetic contamination issue is deteriorated by complicated interaction between electromagnetic fields and city environment objects (waves reflection and diffraction); by air-wires being multi-directional; by fields vertical volatility etc. [8–11]. But it is hygienic assessment which should underlie city planning and developing and high-rise buildings construction including those aimed for permanent residence [2]. It is also vital to improve techniques for analysis and prediction of sanitary and hygienic situation when choosing a place for a new radiation source location (for example, base stations of mobile communication), and when fixing or eliminating limitations imposed on a height of buildings located near transmitting radio-technical objects and when optimizing a system of electromagnetic fields control points [5]. Here it seems optimal to combine calculations and field observations as it allows to simultaneously decrease costs on the latter and to have a tool for scale assessments and situation modeling [2].

So, given the importance which creation of methodological approaches to design of dynamic 3D maps showing electromagnetic contamination on territories has for urban development tasks, social and hygienic monitoring optimization, and consequent hygienic assessment, we set the goal and tasks of the present work [2, 5].

Our research goal was to create a dynamic 3D vector map of electromagnetic fields in a large industrial center integrated with topical spatial information on places where city population lived constantly and to verify it with instrumental techniques.

We set the following tasks: to perform an inventory of basic electromagnetic fields sources which were located on the city territory; to determine their properties; to calculate electromagnetic fields on the whole city territory at 22 different heights from 2 to 75 meters above a source baseline; to give criteria assessment of the obtained results; to divide the city into zones as per electromagnetic fields levels; to verify the obtained results via direct measurements of the factor.

Data and methods Our research object was the territory and population of Perm, a large industrial center located in the Western Urals. Its total area amounts to 720 square kilometers; population is about 1 million people. To get territorial connection, we applied a vector map of the city in Arc GIS geoinformation system (9.3 version, the total square of the calculated rectangle being 1.085 thousand km2).

Primary processing of all collected data was performed with conventional software, i.e. Microsoft Excel, but we also secured consequent possibility to transfer them into other software packages to calculate electromagnetic fields levels.

Our calculations allowed for volume parameters of 31,949 buildings including 17,307 apartment blocks, 3,160 administrative buildings, 307 pre-school children facilities and 105 secondary schools. Data on 2,011 electromagnetic radiation sources were given by Perm Regional Center for Hygiene and Epidemiology. The database contained information on telecommunication objects, which made for the saturation of the environment with electromagnetic energy in various ranges:

30...300 MHz (10...1 m) was due to mobile communication, frequency-modulated radio broadcasting (ultrashort waves), TV broadcasting, and ambulance;

0,3...3 GHz (100... 10 cm) was due to radio relay lines, mobile communication, radiolocation, radio navigation, and NV broadcasting;

3...30 GHz (10...1 cm) was due to radio location, satellite communication, mobile communication, meteorological locators, and radio relay lines;

30...300 GHz (10...1 mm) was due to radiolocation, satellite communication, radio relay lines, and radio navigation.

Base stations of mobile communication emit electromagnetic energy within the range from 463 to 2,200 Hz. We took into account that base stations aerials are usually located 15-100 meters above the ground on already existing buildings (public, administrative, industrial ones and apartment blocks, on smoke pipes of industrial enterprises etc.) or on specially designed masts.

We applied "PC AEMO 4.0" specialized software package as the basis for assessing the existing impacts exerted by electromagnetic fields; this package conforms to Methodical Guidelines 4.3.1167-02 «Determination of energy flux density at places where radio devices functioning within 300 MHz - 300 GHz range are located" and Methodical Guidelines 4.3.1677-03 "Determination of electromagnetic field created by radiating technical TV devices, frequency-modulated radio broadcasting and base stations of land mobile communication".

Calculations were accomplished within the city coordinate grid in 109,000 points. Each calculation formed a picture of electromagnetic field propagation in plane at a set height and it allowed us to detect exposure level in a checkpoint as per "slice" results and create a 3D model of contamination.

We considered hygienic standards set forth by Sanitary-Hygienic Requirements 2.1.8/2.2.4.1383-03 "Hygienic requirements to location and operation of transmitting radio technical objects" and Sanitary-Hygienic Requirements 2.1.8/2.2.4.1190-03 "Hygienic requirements to location and operations of land mobile radio communication devices" as our criteria of allowable electromagnetic fields levels. According to the above mentioned sanitary-hygienic requirements, maximum allowable electromagnetic fields levels amounted to 10 μW/cm2 within 30 MHz - 300 GHz range.

Instrumental research which verified our calculations was performed by Center for Sanitary and Epidemiology LLC, laboratory-testing center located in Moscow (state certificate No. RA.RU.21ЦСО1 issued on January 29, 2016). Energy flux density was measured according to Methodical Guidelines 4.3.1167-02 «Determination of energy flux density at places where radio devices functioning within 300 MHz - 300 GHz range are located" with PZ-41 electromagnetic radiation gauge. 80 measurements were accomplished during a year at different heights on apartment blocks and public places in zones where calculated energy flux density was the greatest.

Basic results. We detected that 2,011 telecommunication sources created environmental load in the regional center; they caused the saturation of the environment with electromagnetic energy within various ranges. We created a database on electromagnetic radiation sources which included:

– 1,666 base stations of mobile communications with transmitters power ranging from 10 to 20 W which were located evenly on the whole city territory and emitted electromagnetic energy within 400 to 3,000 Hz range; they were placed 15-100 meters above the ground on already existing buildings (public, administrative, industrial ones and apartment blocks, on smoke pipes of industrial en-

terprises etc.) or on specially designed masts;

– 248 radio relay communication line devices which were formed by relay radio stations chains;

– 95 aerials which formed aerial fields of three transmitting radio centers belonging to different state agencies;

– 2 trace surveillance radio locators with transmitters power being equal to 4,100 W functioning at 3,000 MHz frequency, and other radiation sources.

These sources are located unevenly on the city territory. The greatest number of such sources is located on heights in the city center. Practically all sources are located directly in zones where people live or in maximum proximity to such zones.

As per results of all the performed electromagnetic fields calculations at heights ranging from 2 to 70 meters we obtained a considering points array within the calculated parallelepiped boundaries with the results of electromagnetic fields calculation at each separate height. We combined the obtained results with vector layers of buildings allowing for their heights and received a 3D picture of impacts distribution a part of which is given on Figure 1.

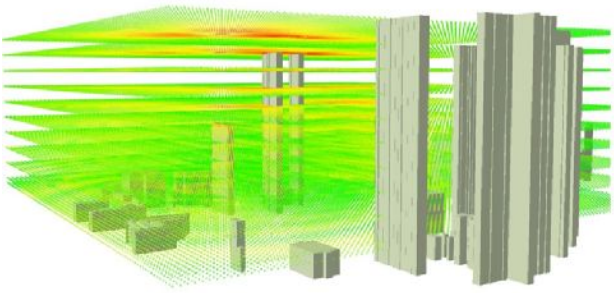

Figure 1. An example of 3D electromagnetic field visualization (heights from 3 to 35 meters above the ground)

Calculations and the consequent mapping of electromagnetic fields on the city territory reveled that their levels didn't exceed maximum permissible ones on the city territory.

The greatest expected electromagnetic field level within the examined range amounted to 15.2 SC (safety criterion) in a zone where the airport radio locator was placed; this locator was for communication between air carriage vehicles and control rooms. It is situated several kilometers away from the city boundaries on Perm district territory. At present there is housing in the area where electromagnetic field levels exceed the existing hygienic standards; so we worked out certain recommendations for the city general design plan.

About 80% of all the considering points were characterized with electromagnetic field parameters lying within 1-10 SC range. Maximum values were within 4-5.5 SC range and were placed at the height of 4-7 floors in various city zones (Figure 2).

As a height grew calculated electromagnetic fields levels increased on the city territory as a whole reaching their peak at 9-18 meters; then they went down gradually but still remained higher than just near the ground.

A square of a territory with 1-10 SC within the calculated rectangle boundaries at 3 meters (first floors) amounted to 5.86 km2; at 12 meters (2-4 floors), 20.9 km2; at 30 meters (9-11 floors), 13,6 km2; at 48 meters, about 14.5 km2.

Approximately 1,000 houses were located in zones where energy flux density amounted to 1-10 SC and where instrumental research was also accomplished; about 145 thousand people live in these houses at present. Quantity of people who permanently live in zones with the greatest calculated electromagnetic contamination (more than 3 SC) amounts to about 15 thousand. Some pre-school children facilities and secondary schools are also located there (Figure 3).

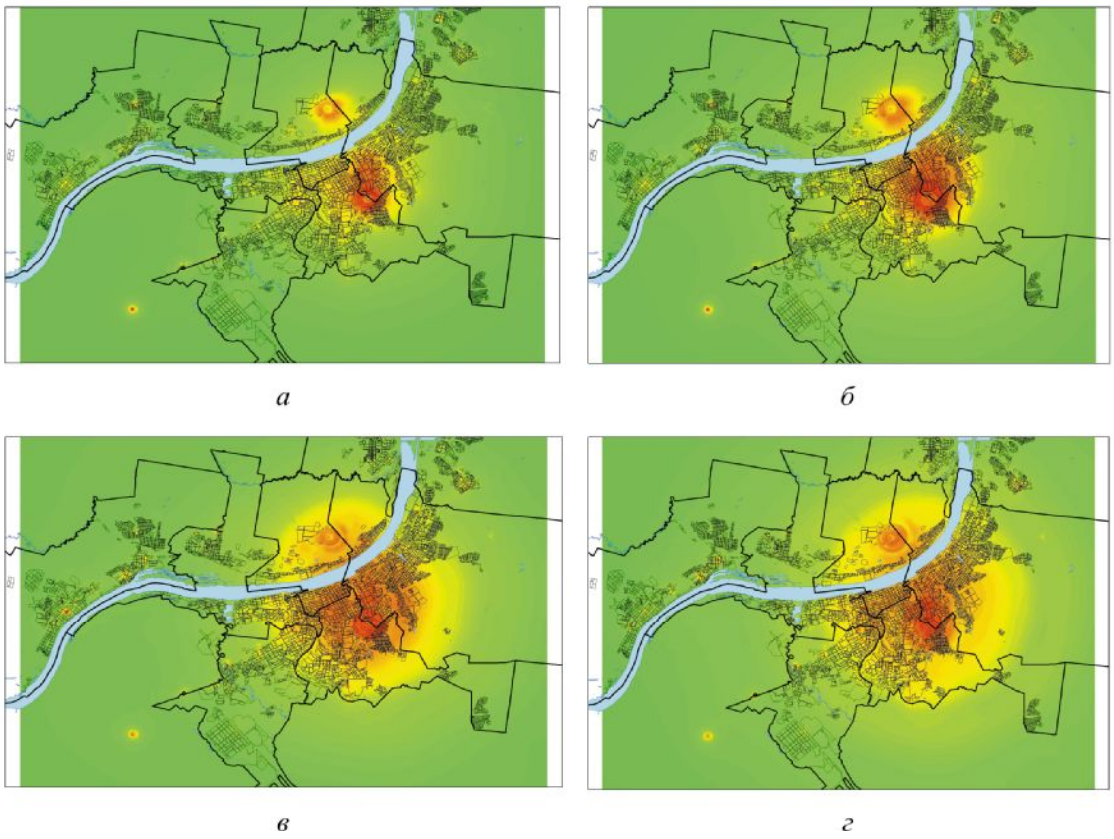

Figure 2. Electromagnetic field levels on Perm city territory at different heights above the ground: a) 3 m; b) 6 m; c) 18 m d) 30 m

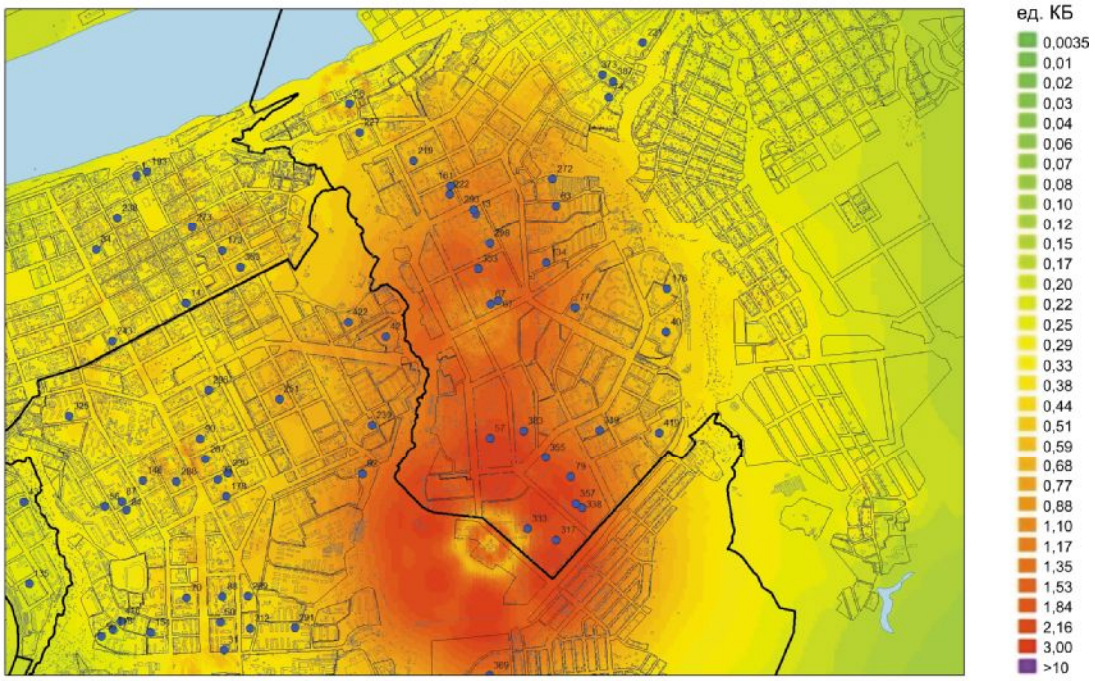

Figure 3. Electromagnetic field levels in the city center and pre-school children facilities located in zones influenced by transmitting radio technical objects (given with dark-blue dots)

Electromagnetic field intensity at different floors of apartment blocks in the central part of Perm in a zone where increased calculated SC values were detected

Parameter	Measuring points				
	Yards	1-2 floors (3-6 m)	3-5 floors (9-15 m)	6-9 floors (18-27 m)	10-14 floors (30-42 m)
Average EFD level, μW/cm2	0,91	0,96	1,58	4,21	1,30
Uncertainty "-" U-	0,45	0,47	0,78	2,07	0,64
Uncertainty "+" U+	0,77	0,82	1,35	3,59	1,11
∑(E/MPL)2	0,04	0,16	0,07	0,13	0,09
SC average	0,20	0,34	0,35	0,87	0,32
Maximum EFD level μW/cm2 sec	1,64	2,56	12,73	**31,29**	4,21
Uncertainty "-" U-	0,81	1,26	6,25	**15,37**	2,07
Uncertainty "+" U+	1,39	2,18	10,85	**26,68**	3,59
∑(E/MPL)2	0,01	0,57	–	**–**	0,25
SC max	0,31	1,05	2,36	**5,80**	1,03

Instrumental research had quite high convergence with the calculated parameters. Electromagnetic fields levels as per data obtained via field observations in "red-orange zone" which was considered to have electromagnetic field ranging from 0.3 to 3.0 SC as per situation modeling via calculation were characterized with average measured energy flux density being equal to 0.52 μW/cm2.

We also fully confirmed that energy flux density changed as per heights. 18-25 meters above a building baseline were "critical" for Perm on the examined area (Table). The highest electromagnetic fields levels were detected exactly at such heights (Table).

Due to the fact that instrumental research was purposely performed on areas where electromagnetic fields levels were potentially the highest, it revealed a number of cases when they exceeded the safety criterion. It was higher than 1.0 in 9 out of 80 samples; excess multiplicity was almost 6 times. Maximum level of energy flux density (31.29 μW/cm2) allowing for "+" U+ uncertainty (26.68 μW/cm2), which amounted to 5.8 SC, was detected at about 18 meters above the ground. 2.35 SC was detected in the same apartment block at the top 5th floor during the next measuring with maximum energy flux density being 12.73 μW/cm2, allowing for "+" U+ uncertainty, 10.85 μW/cm2. Further violations of hygienic standards prove it is necessary to perform systemic monitoring of electromagnetic fields level, to assess population health risks, and to give grounds for consequent solutions aimed at their minimization.

Conclusions:

Overall, the performed research allowed us to conclude that the total assessment of the situation on the basis of calculations within a geoinformation system medium was quite relevant. Creation of a maximum full and correct database on sources of electromagnetic contamination in a city is the primary condition for a qualitative assessment; it is also necessary to geocode these sources with the use of a territory vector map.

Our research revealed that the highest electromagnetic contamination levels on the examined territory of a regional center evolved at 18-25 meters above the ground and it was due to peculiarities of radiating and receiving air wires location.

We detected that electromagnetic field levels were 4-6 times higher than maximum permissible ones in zones with the highest calculated energy flux density at 18-25 meters above the ground; it makes it quite difficult to assume such environment is safe for people who permanently live on the examined territory.

The obtained data are to be applied in giving grounds for field observation points within specialized research framework or social-hygienic monitoring as well as in consequent assessment of exposure and health risks. These materials can be used within epidemiologic research for conjugate spatial analysis of energy flux density and adults and children morbidity with diseases which are proved or considered to be associated with electromagnetic radiation (leukemia, meningioma, hemopathy etc.).

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APPLICATION OF REGRESSION ANALYSIS AND CLASSIFICATION TREES IN CALCULATING ADDITIONAL POPULATION RISK OF ISCHEMIC HEART DISEASE

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Our research goal was to perform a comparative analysis of regression analysis application and tree classification application in calculating additional population risk on the example of ischemic heart diseases (IHD). Our research object was a random population sample comprising both male and female population aged 25-64 in Kemerovo region (1,628 people) within ESSE-RF multi-centered epidemiologic research. We considered the following IHD risk factors: lipid metabolism parameters, arterial hypertension, lifestyle factors, psychoemotional peculiarities, and social parameters. IHD occurrence was assessed as per sum of 3 epidemiologic criteria: on the basis of ECG changes coding as per Minnesota code, Rose questionnaire, and cardiac infarction in case history. We calculated additional population IHD risk determined by risk factors as per unified original algorithms, but with various statistic analysis techniques: logistic regression analysis and classification trees.

We built up mathematic models for IHD probability as per risk factors, with predictive significance equal to 83.8% for logistic regression analysis and to 71.9% for classification trees. The applied statistical analysis techniques show different contributions made by risk factors into IHD prevalence which results from absence of correlation between them.

IBD risk additional to population one and determined by risk factors as per both statistical analysis techniques in sex-age groups changed from negative values in age groups younger than 45 to positive values in older people. Increase in additional IHD risk in aged groups as per both techniques was practically linear with slight deviations. Difference in additional population risk calculated as per two statistical analysis techniques was insignificant and as a rule it didn't exceed 1.5%. Consequently, both techniques give similar results and can be equally used in calculating IHD population risk.

Key words: *regression analysis, risk factor, ischemic heart disease, population risk, predictive models, statistical analysis techniques.*

Cardiovascular diseases etiology is determined by a lot of factors and it makes it necessary to consider probability of their evolvement and unfavorable outcomes with integral risk assessment models. Such models should include several basic factors. In most cases one respondent can have a combination of two and even more risk factors and a forecast for development and clinical course of cardiovascular diseases is much worse when several, even moderately apparent, risk factors are combined [8, 9,12,]. In particular, PROCAM research revealed that a combination of two or more factors of cardiovascular system disorders risks led to significant in-

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crease in number of sudden deaths and cardiac infarctions [11, 13]. It made for a creation of "summary cardiovascular risk" notion [8]. Models for predicting individual risks have been widely used in everyday cardiologists' practices as they help to make decisions on prevention techniques and remedies, and on prescribing, giving up, or intensifying drug therapy [11, 13, 14]. Up to now, a great number of individual risks prediction models have been developed including such well-known ones as Framingham Risk Score, SCORE, PROCAM etc., as well as their numerous modifications [1, 2, 10, 11, 13, 14].

Population cardiovascular diseases risks are usually assessed when epidemiologic research takes place; such assessments are mostly aimed at modeling and predicting risks at population or subpopulation level (regions or population groups) [4]. Population regularities modeling is frequently used in practice to solve tasks set before a public healthcare system, for example, assessing efficiency of various approaches to treatment and prevention [3, 4, 15].

Approaches to population risk assessment which we have created are methodologically in line with individual cardiovascular risks scores [5]. In the latter case individuals are an object of analysis; and risk factors which they have (for example, smoking) and quantitative characteristics describing them (for example, age or blood pressure) are integrated into a final predictive cardiovascular risk value. When a population risk is assessed, research focuses on population groups and cardiovascular risk factors prevalence can differ significantly among them due to their heterogeneity as per medical-demographical, national, geographic, and social-economic, and other peculiarities. In this case population risk integration is based on analyzing both discrepancies in risk factors prevalence and assessing their contribution into examined cardiovascular events.

Application of methodical approaches which we created allowed to derive a complex characteristics for a cardiovascular risk factors burden (17 factors) in 14 occupational groups with different working conditions [6]. Population risk analysis of ischemic heart disease (IHD) based on integral assessment of 12 risk factors enabled detecting sex-age and social-economic regularities of the examined disease [5, 7]. To assess contributions made by various risk factors into the examined diseases prevalence, we applied a decision tree technique in our research. But as this statistical analysis techniques is rather complicated when applied and is not so widely spread in biomedical research, we thought it necessary to assess possibility of other techniques application.

Our research goal was to perform a comparative analysis of regression analysis application and decision trees application to calculate additional population risk on the example of IHD.

Data and methods. This work is completed within the frameworks of multicentered epidemiologic research "Cardiovascular diseases etiology and their risk factors in the RF" (ESSE-RF) in Kemerovo region. We chose a random population sampling, both male and female, as our research object; people were 25-64 and they all lived in Kemerovo region. Our sampling was made of 1,628 people, 700 males (43.0%) and 928 females (57.0%).

The research was performed in full conformity with Good Clinical Practice standards and Helsinki Declaration principles. The research protocol was approved by the Ethical Committee of the Scientific Research Institute for Complex Issues of Cardiovascular Diseases. All the partici-

pants gave their written informed consent to take part in it.

We studied such IHD risk factors as lipid metabolism parameters, arterial hypertension, lifestyle factors, psychoemotional peculiarities, social parameters (low incomes, poor education, having no family, being unemployed).

According to WHO classification, we considered body mass index being more than 30 kg/m2 being a proof of obesity. Arterial hypertension was classified as per WHO/ISoH criteria (1999) when systolic blood pressure was not lower than 140 mm Hg, and diastolic one, not lower than 90 mm Hg, as well as when both these parameters were equal to a standard but under hypertensive drugs.

Hypercholesterolemia was classified when crude cholesterol concentration was higher than 5.0 mmol/l; hypertriglyceridemia, when triglycerides were higher than 1.7 mmol/l; high low density lipoproteins level was registered at their values exceeding 3.0 mmol/l; low high density lipoproteins level, lower than 1.0 mmol/l; hyperglycemia on an empty stomach was registered when dextrose level was higher than 5.6 mmol/l.

We applied Hospital Anxiety and Depression Scale (HADS) validated in the RF to assess depression; susceptibility to stress was assessed as per Perceived Stress Scale. We calculated 75-percentile on the basis of the obtained ordinal series, and values higher than 8 scores and more as per depression scale and 5 scores and more as per stress scale were considered to be a risk factor.

IDH occurrence was assessed as per a sum of three epidemiologic criteria: on the basis of coding of ECG changes as per Minnesota code, Rose questionnaire (pectoris) and cardiac infarction in a case history.

Additional population IHD risk caused by risk factors was calculated as per unified algorithms but with application of different statistical analysis techniques.

At the first stage, we calculated a contribution made by the examined risk factors into IHD prevalence values for the whole sampling. To do this, we first applied logical regression analysis, and then, decision trees. To remove possible modifying influence exerted by sex and age in the course of logical regression analysis, we introduced them into it as well. B-coefficient values were used as a value describing a contribution made by a risk factor into IHD prevalence.

When we applied decision trees we chose on a discriminant one-dimensional branching technique for categorical and ordinal predictors. We took equal costs of wrong objects classification and a priori probabilities proportionate to sizes of dependent variable classes as fidelity criteria. Branching was stopped according to a pruning rule as per an error in classification, minimal number of incorrectly classified objects being equal to 12, and a standard error, equal to 1.0. We used values of predictors significant ranks as parameters of contributions made by risk factors into IHD prevalence.

Further on, calculation was made as per the same scheme. We calculated risk factors prevalence in sex-age groups and in the whole sampling. Load with IHD risk factors was calculated as a sum of multiplying risk factors prevalence by their contribution into IHD risks as per the following formula:

$$P = \sum(RC)_n, \quad (1)$$

Where P is IHD risk factors load; R is a risk factor prevalence, %; C is a risk factor contribution into IHD prevalence values.

Then we calculated a difference between risk factors load in age-sex groups in comparison with the overall sampling as per formula:

$$\Delta P = P_{\text{гр.}} - P_{\text{в.}}, \quad (2)$$

Where ΔP is a difference between risk factors load in age-sex groups in comparison with the overall sampling as per formula; Pgr is a risk factors load in age-sex groups; Ps. is a risk factor load in the overall sampling.

On the next stage we applied linear regression analysis to determine frequency of IHD association with the risk factor loads values in age-sex groups. B-coefficient which was obtained in the course of linear regression analysis was used to recalculate difference in risk factor loads in age-sex groups into population risk values as per formula:

$$P\% = \Delta PB, \quad (3)$$

Where P% is IHD risk which is additional to population one and caused by risk factors, %; B is B-coefficient showing a correlation between IHD frequency and risk factors load in linear regression analysis.

Critical level of statistic significance and p-level for a choice on a branching variable (for decision trees) was considered equal to 0.05.

Results and discussion. As per logistic analysis results statistically significant (or very close to such, $0.1>p>0.05$) associations with IHD allowing for age and sex are observed as per following risk factors: hypertension, hypertriglyceridemia, hyperglycemia, obesity, pancreatic diabetes, smoking, stress, depression, absence of high education, and being unemployed (Table 1). We used only these risk factors in our further analysis.

Table 1 contains B-coefficients as per regression analysis (from 0.046 hyperglycemia to 0.491 pancreatic diabetes) and ranks as per decision trees (from 20 for smoking to 100 for obesity) which describe the selected risk factors and which were further used in risk factors load calculations (formula 1) as per two techniques. We should note that predictive significance of a mathematical model for IHD probability as per risk factors sum was equal to 83.8% when this model was designed via logistic regression analysis, and to 71.9% in case when decision trees were applied.

We didn't detect any statistically significant correlation between B-coefficient values and risk factors significance ranks as correlation coefficient was equal to -0.32 at $p = 0.37$. Therefore, different statistic analysis techniques gave different values of contributions made by the examined risk factors into IHD prevalence parameters.

Tables 2 and 3 contain information on IHD and risk factors prevalence in age-sex groups and in the overall sampling. Risk factors prevalence in the overall sampling varied from 3.9% (pancreatic diabetes) to 60.7% (absence of high education). IHD prevalence in the overall sampling reached 16.8%; 13.5% in males; 19.2%, in females.

Risk factors load (as per formula 1) and difference in loads in sex-age groups in comparison with the overall sampling (as per formula 2) calculated via two techniques is given in tables 2 and 3. Risk factors load calculated with logistic regression analysis amounted to 71.8 for the overall sampling; 72.0, for males; 71.7, for females. This load naturally grew with age and increased from 49.6 to 93.8 for males, and from 45.6 to 97.0 for females.

The same regularities were observed for risk factor load calculated with decision trees. The load amounted to 19,459.6 for the overall sampling; to 18,831.7, for males;

Table 1

Influence exerted by risk factors on IHD probability as per regression analysis data (allowing for age and sex) and rank values as pre decision trees data.

Risk factors	OR	95% CI	*p-level*	B-coeff.	Ranks
Hypertension	1,28	0,97–1,70	0,082	0,118	68
Hypercholesterolemia	0,89	0,67–1,18	0,41	–	–
Hypertriglyceridemia	1,66	1,22–2,25	0,0013	0,355	80
High LDL levels	0,92	0,68–1,24	0,58	–	–
Low HDL levels	0,72	0,21–2,49	0,61	–	–
Hyperglycemia	1,37	0,99–1,90	0,060	0,046	85
Obesity	1,49	1,13–1,97	0,0048	0,260	100
Pancreatic diabetes	1,96	1,13–3,41	0,016	0,491	81
Smoking	1,59	1,16–2,16	0,0036	0,359	20
Low physical activity	0,97	0,70–1,34	0,83	–	–
Stress	1,56	1,15–2,11	0,0042	0,311	74
Depression	1,88	1,39–2,55	0,000049	0,402	47
Income	0,98	0,65–1,47	0,91	–	–
Education	1,57	1,17–2,11	0,0026	0,292	71
Employment	1,40	1,04–1,88	0,028	0,170	83
Family	1,02	0,76–1,37	0,89	–	–

Table 2

IHD and risk factors prevalence and risk factors load in male age groups and in the overall sampling

Risk factors	Age groups, number of observations								All men (700)	Over-all sam-pling
	Younger than 30 (86)	31–35 (85)	36–40 (88)	41–45 (65)	46–50 (98)	51–55 (94)	56–60 (107)	61–65 (77)		
Hypertension, %	20,9	37,6	44,3	56,9	51,0	69,1	61,7	71,4	51,7	43,3
Hypertriglycer-idemia, %	14,1	17,6	21,8	24,6	25,5	25,5	27,4	23,7	22,7	20,3
Hyperglycemia, %	8,2	7,1	11,5	7,7	17,3	28,7	22,6	43,4	18,5	17,2
Obesity, %	12,9	22,3	21,6	35,4	36,7	35,5	34,6	37,7	29,7	35,2
Pancreatic diabetes, %	1,2	0,0	0,0	0,0	4,1	5,3	4,7	14,7	3,7	3,9
Smoking, %	47,7	47,1	46,6	47,7	50,0	48,9	43,0	33,8	45,7	30,5
Stress, %	10,5	15,3	12,5	9,2	13,3	11,7	14,0	16,9	13,0	22,6
Depression, %	8,1	11,8	10,2	9,2	13,3	13,8	16,8	27,3	13,9	19,0
Education, %	43,0	51,8	61,4	55,4	70,4	71,3	63,6	63,6	60,6	60,7
Employment, %	9,3	9,4	9,1	7,7	16,3	26,6	32,1	64,9	22,0	25,4
IHD, %	3,5	3,5	5,9	9,2	10,3	22,3	21,5	30,3	13,5	16,8
Load 1	49,6	59,9	63,3	66,2	78,2	82,4	79,9	93,8	72,0	71,8
Difference 1	–22,2	–11,9	–8,5	–5,6	6,4	10,6	8,1	22,0	0,2	0
Load 2	10570	13885,1	15345	16671,4	19941,2	22920,1	22014,8	28512,9	18831,7	19459,6
Difference 2	–8889,6	–5574,5	–4114,6	–2788,6	481,6	3460,5	2555,2	9053,3	–627,9	0,0

Table 3

IHD and risk factors prevalence and risk factors load in female age groups

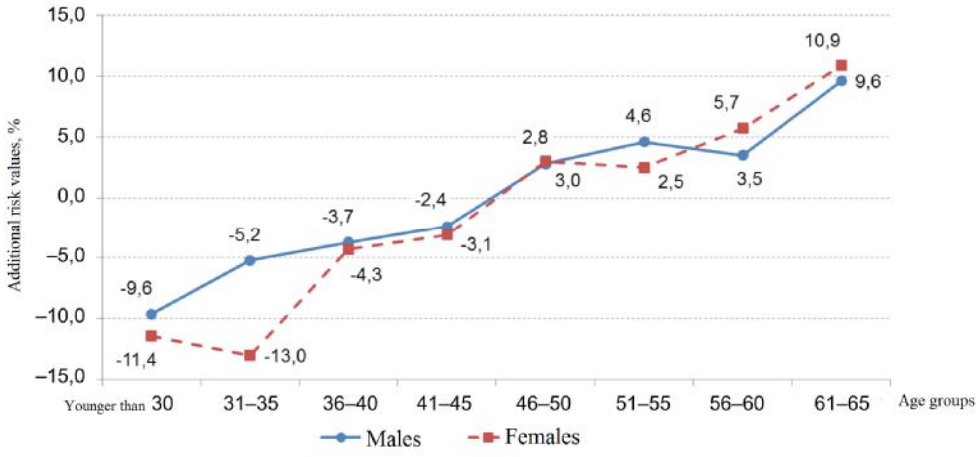
Risk factors	Age groups, number of observations								All women (928)
	Younger than 30 (97)	31–35 (97)	36–40 (86)	41–45 (91)	46–50 (112)	51–55 (159)	56–60 (170)	61–65 (116)	
Hypertension, %	10,3	8,2	18,6	30,8	42,0	50,3	52,3	57,8	37,2
Hypertriglyceridemia, %	5,2	9,3	9,3	17,6	26,4	23,4	20,4	28,1	18,5
Hyperglycemia, %	0,0	2,1	12,8	13,2	15,5	15,8	26,9	32,5	16,2
Obesity, %	9,3	14,4	27,9	41,8	46,4	44,9	50,6	61,2	39,4
Pancreatic diabetes, %	0,0	0,0	1,2	2,2	2,7	5,1	6,5	10,6	4,0
Smoking, %	26,8	29,9	29,1	26,4	17,9	17,0	10,0	6,9	19,0
Stress, %	26,8	26,8	29,4	27,8	36,6	28,9	31,4	29,3	29,8
Depression, %	11,3	7,2	17,4	17,6	23,2	28,9	31,8	31,9	22,8
Education, %	48,5	33,0	59,3	51,6	71,4	63,5	69,4	76,7	60,9
Employment, %	20,6	12,4	24,4	11,0	14,3	18,9	44,7	63,7	27,9
IHD, %	4,1	14,6	13,2	15,4	18,0	25,2	26,5	25,2	19,2
Load 1	45,6	41,8	62,0	64,6	78,8	77,6	85,0	97,0	71,7
Difference 1	–26,2	–30,0	–9,8	–7,2	7	5,8	13,2	25,2	–0,1
Load 2	10250	9211,9	15794,9	16971,6	21557,3	21452,6	25717,1	30457,8	19947
Difference 2	–9209,6	–10247,7	–3664,7	–2488	2097,7	1993	6257,5	10998,2	487,4

to 19,947.0, for females. The load grew with age from 10,570.0 to 28,512.9 for males and from 10,250.0 to 30,457.8 for females.

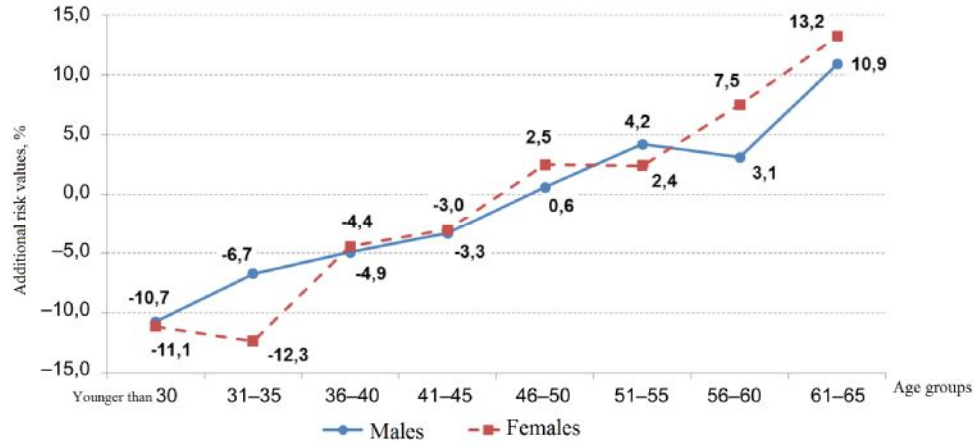
Mathematical models created with linear regression analysis showed that risk factor load could account for IHD prevalence in age-sex groups by 62.6% (logistic regression) and by 71.7% (classification trees). Regression B-coefficients calculated as per these models were used to recalculate differences in risk factors loads into population risk values as per formula 3.

B-coefficient was equal to 0.4345 when logistic regression analysis was applied, and to 0.0012, when decision trees were applied.

IHD risk, additional to population one, caused by risk factors, and calculated as per formula 3, is shown on Figure 1 (regression analysis) and on Figure 1 (decision trees). Additional risk in younger age groups (younger than 46) calculated as per both techniques was lower than population one, from -2 % to -11 %; but it reached values higher than population one, from 0.5% to 13%, in age groups older than 45. IHD additional risk increase in age groups was practically linear with slight deviations: lower risk for females aged 31-35 and 51-55; and for males aged 56-60 in comparison with the previous age group (Figure 2). Here deviations from linearity of IHD additional risk growth with age are observed as per both techniques, logistic regression analysis and decision trees.

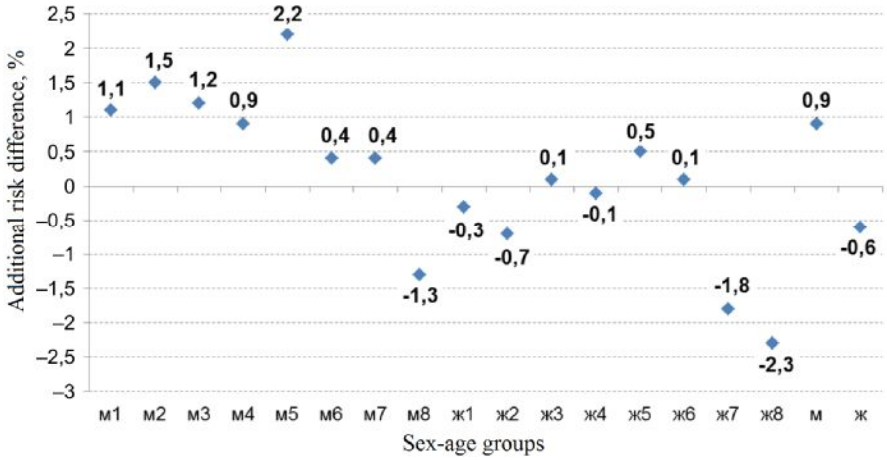


a



b

Figure 1. IHD risk additional to population one, caused by risk factors, %:
a – regression analysis; *b* – decision trees



Note: м – are males, ж – are females, 1 – younger than 30, 2 – 31-35,
3 – 36-40, 4 – 41-45, 5 – 46-50, 6 – 51-55, 7 – 56-60, 8 – 61-65.

Figure 2. Difference between additional population risk calculated as per two statistical analysis techniques

Data which are obtained via these techniques allow calculating load with risk factors. And here, as per both techniques (regression analysis and decision trees) difference in load in age-sex groups in comparison with the overall sampling changes from negative values in age groups up to 45 years (inclusive), to positive values in people older than 45. IHD risk additional to population one and caused by risk factors changes similarly. Increase in additional IHD risk in age groups as per both techniques is practically linear, with slight deviations. Additional IHD risk in age groups younger than 30, both sexes, is lower than population one by 9.6–11.4 %; it becomes higher than population one in age groups closer to 50 (by 0.6–2.8 %); and it reaches its maximum values by 65 (by 9.6–13.2 %).

Despite different statistical analysis techniques giving different values of contributions made by the examined risk factors into IHD prevalence parameters, the correlation between values of additional population risk calculated with regression analysis and with decision trees is strong and statistically significant. Difference of additional population risk calculated as per different statistical analysis techniques is slight and, as a rule, doesn't exceed 1.5%. Therefore, both techniques give similar results and can be equally applied to calculate population IHD risks.

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NEW TECHNIQUES AND MODELS FOR ASSESSING ISCHEMIC HEART DISEASE RISKS

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The paper focuses on tasks of creating and implementing a new technique aimed at assessing ischemic heart diseases risk. The techniques is based on a laboratory-diagnostic complex which includes oxidative, lipid-lipoprotein, inflammatory and metabolic biochemical parameters; s system of logic-mathematic models used for obtaining numeric risk assessments; and a program module which allows to calculate and analyze the results. we justified our models in the course of our research which included 172 patients suffering from ischemic heart diseases (IHD) combined with coronary atherosclerosis verified by coronary arteriography and 167 patients who didn't have ischemic heart diseases. Our research program included demographic and social data, questioning on tobacco and alcohol addiction, questioning about dietary habits, chronic diseases case history and medications intake, cardiologic questioning as per Rose, anthropometry, 3-times measured blood pressure, spirometry, and electrocardiogram taking and recording with decoding as per Minnesota code. We detected biochemical parameters of each patient and adjusted our task of creating techniques and models for assessing ischemic heart disease risks on the basis of inflammatory, oxidative, and lipid biological markers. We created a system of logic and mathematic models which is a universal scheme for laboratory parameters processing allowing for dissimilar data specificity. The system of models is universal, but a diagnostic approach to applied biochemical parameters is specific. The created program module (calculator) helps a physician to obtain a result on the basis of laboratory research data; the result characterizes numeric risks of coronary atherosclerosis and ischemic heart disease for a patient. It also allows to obtain a visual image of a system of parameters and their deviation from a conditional «standard – pathology» boundary. The complex is implemented into practice by the Scientific Research Institute for Therapy and Preventive Medicine.

Key words: *risk assessment, ischemic heart disease, laboratory and diagnostic complex, biochemical parameters, logic and mathematic model, program module, questioning as per Rose.*

According to statistics, each thirteenth RF citizen suffers from cardiovascular pathology; ischemic heart disease plays a leading part among mortality causes related to circulatory system diseases (55.7%) [1]. Mortality as per ischemic heart disease (IHD) in Novosibirsk region amounts to more than 35 people per 1,000 adults [6]. In relation to that, any research aimed at improving diagnostics and making it timely as well as secondary ischemic heart diseases prevention is of specific importance within strategies of providing medical assistance to cardiologic profile patients [1, 8, 11]. The

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urgency to study factors and biological markers of key pathophysiological mechanisms of cardiovascular diseases evolvement in West Siberia region is determined by its specific climatic and geographical conditions, nutrition peculiarities, and extremely high prevalence of ischemic heart disease risk factors; therefore, it is necessary to obtain new data on risks of the disease complications and on ways of improving its early diagnostics [9].

Cardiovascular risk is a probability of any unfavorable event occurrence in cardiovascular system (including death caused by a cardiovascular disease or its complication) within a certain period of time (for example, within the next 19 years) [15]. Risk stratification in IHD diagnostics is performed on the basis of clinical data, stress-tests results, heart ventricles functioning assessment, coronary arteriography results, and other parameters [7, 10, 14, 18].

SCORE scale is widely known among risk meters which are used in cardiology; this scale is aimed at assessing absolute risk of a fatal cardiovascular disease within the next 10 years. When risk is assessed as per SCORE scale, its assessment allows for the following parameters: sex, age (40-65 years), blood pressure, crude cholesterol level, and smoking state [13]. Cardiovascular risk is also assessed depending on optimal values of lipid parameters, body mass index, and metabolic syndrome diagnostics results [4, 16].

As a rule, assessment of a fatal cardiovascular disease risk is made via summing points received as per each risk meter scale parameter. The obtained result is then converted into per cents or remains in numeric values. After that, to determine risk degree, it is necessary to use look-up tables containing values obtained as per a risk meter scale and probability of fatal cardiovascular diseases occurrence or evolvement given in per cents. Such techniques and procedures for analyzing values of parameters which are included into risk scales are present in most well-known scales such as HAS-BLEND, CHA2DS2-VASc, GRACE, CRUSADE, and TIMI. Risk assessment can also be performed by assessing a parameter occurrence within a range which a certain risk degree corresponds to. A fatal cardiovascular disease risk is assessed as per this principle depending on the following factors: body mass index, lipid parameters values, criteria of metabolic syndrome diagnostics, blood pressure etc. [4, 8]. Such procedures for determining numeric risk assessment sometimes can't be easily applied in clinical practice due to complicated calculations required for their obtaining. Automated calculators which make this process much more simple as a rule allow to process data obtained via screening research and can't provide systemic assessment which allows for not only clinical parameters but also biochemical ones [5].

We set the following tasks within the framework of the present research:

- to work out efficient screening laboratory and diagnostic techniques for early detection of IHD risk factors based on biochemical parameters analysis;
- to apply logical and mathematical models for obtaining numeric values of the disease risk;
- to work out a user-friendly program module which would allow to assess IHD risk on the basis of biochemical parameters analysis.

Data and methods. We performed our research on 172 patients suffering from ischemic heart disease together with coronary atherosclerosis verified by coronary arteriography data; and on 167 patients without IHD according to the research data. Our research program included demographic and social data, questioning on tobacco and alcohol addiction, questioning

on dietary habits, chronic diseases case history, medications prescriptions history, cardiologic questioning as per Rose, anthropometry, triple blood pressure measuring, spirometry, and electrocardiogram taking with decoding as per Minnesota code. Biochemical parameters of each patient were also determined. Assessment of coronary atherosclerosis risk was performed with a logical and mathematical technique. Our logical and mathematical model was based on a laboratory and diagnostic complex which had been previously worked out in Scientific Research Institute for Therapy and Preventive Medicine. This complex included the most informative oxidative, lipid-lipoprotein, inflammatory, and metabolic biochemical parameters which characterized basic pathogenetic reasons for coronary atherosclerosis: initial level lipid peroxidation products in low density lipoproteins (LP0), low density lipoproteins resistance to oxidation (LP30), insulin concentration in blood (Insulin), C-reactive protein concentration (CRP), apoprotein A1 (apoA1) and B (apoB) concentration, triglycerides (TG) concentration, and cholesterol - high density lipoproteins concentration [2, 3, 17]. The model allowed for the weight of each parameter characterizing different contribution made into the overall diseases clinical picture, "standard - pathology" boundaries revealed for each parameter, and a standardization technique.

Algorithm of calculating IHD risk values for the obtained laboratory-clinical panel consists of three main stages. First, nxi interval values "standard - pathology" are set for each xi parameter. Second, a standardization technique is set for each xi depending on a measuring scale and value analysis logic. Third, αi weighted average assessment of a contribution made by each parameter into the overall integral IHD risk assessment is made via Delphi method. After that an integrated model is formed; it allows to calculate a uniform overall assessment allowing for contribution made by each xi standardized value by their "standard - pathology" interval values:

$$_{n}x_i : y = \sum_{i=1}^{8} \alpha_i f(x_i),$$

where αi is a weighing coefficient which allows for a parameter contribution obtained via Delphi method;

f (xi) is a logical-mathematical function for recalculating an initial value of each of all 8 x parameters, allowing for the logic of initial parameter analysis and a way of its recalculation relative to nxi "standard - pathology" set by an expert for each xi, for .

To obtain the integrated model, we tested it on actual data and assessed it with calculating such characteristics as diagnostic accuracy, specificity, and sensitivity [12].

Sensitivity (Se) is a diagnostic technique capacity to give a correct result which is determined as a share of true positive results among all the conducted tests.

Specificity (Sp) is a diagnostic technique capacity not to give any false positive results in case there is no disease; it is determined as a share of true negative results among healthy people in the examined group.

Diagnostic accuracy (Ac) is a share of correct test results (i.e. sum of true positive and true negative results) among all the examined patients.

Results and discussion

The result of the conducted experiment (Figure 1) for the created model support on the total database on patients with diagnosed IHD (1) and without the diseases (0) allows to determine ranges of models threshold values which can be changed de-

pending on a task being performed (screening, prediction, etc.). Optimal threshold value for Ac-Sp-Se three parameters ratio is 0.6 when it concerns screening task or IHD risk assessment. This threshold coefficient allows to obtain calculated risk assessment values within 0 - 200 points range (standard reduced units of risk evidence); here 0-80 points range of IHD probability assessment means there is no IHD risk; 81-150 points range proves there is IHD risk; when a range lies beyond 150 points, it means IHD risk is very high.

Let us consider peculiarities of the created technique application on the example of three patients whose data are given in Table 1. To calculate risk assessment, we apply parameters values obtained on the logic of laboratory research results analysis and techniques used for their recalculation relative to "standard - pathology" interval value set by an expert.

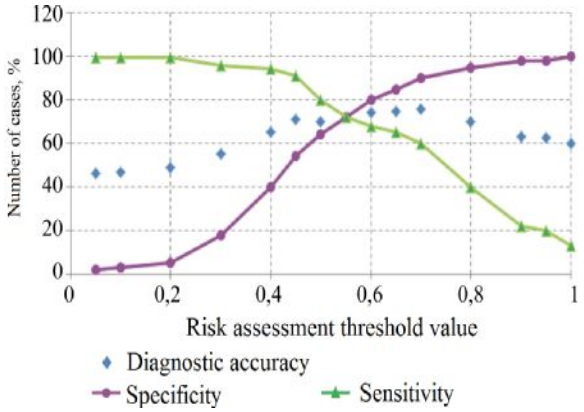

Figure 1. Results of the conducted experiment

Example of three patients

Parameters	Параметр								
	LP0	LP30	Insulin	CRP	apoA1	apoB	CS-HDL	TG	IDS
Initial values									
Patient A	0,5	31,7	6,8	2,21	186,99	83,69	70	105	0
Patient B	1,8	23,2	1,74	9,07	133,3	169,1	38	195	1
Patient C	1,3	24,1	3,46	4,98	132,7	93,87	70	59	0
Recalculated values									
Patient A	0,00	1,40	0,08	0,11	0,12	0,18	0,00	0,00	22
Patient B	0,20	0,43	0,00	1,10	1,30	1,50	1,20	1,40	171
Patient C	0,00	0,51	0,00	1,10	1,30	0,69	0,00	0,00	88

Values calculation algorithm allows to obtain assessment of deviations from conditionally permissible standard. As we interpreted results as per 8 considered parameters, we made all the initial scales and different "standard - pathology" boundaries ranges to look similar to achieve uniformity and convenient interpretation. It allowed us to assess how close this or that parameter was to a standard (close to 0). When IHD risk is assessed, all the recalculated values for each parameters are taken into account with their weighing coefficients obtained via Delphi method. When results are visualized (Figure 2) one can see pathogenetic picture peculiarities which become apparent through deviations in s standardized parameter from a conditional "standard - pathology" boundary which is represented by a red line on the graph.

To make IHD risk assessment easier, a program module has been developed (state registration certificate for software No. 2017612582 dated March 01, 2017); it allows to get an assessment value with the use of the created logical and mathe-

matical model. This program module window is given in Figure 3; it is used for data input and risk assessment calculation. A user can input research data and press a "Calculate" button to get the result. On the basis of this result a physician can prescribe additional examinations if IHD risks for a patient are average or high.

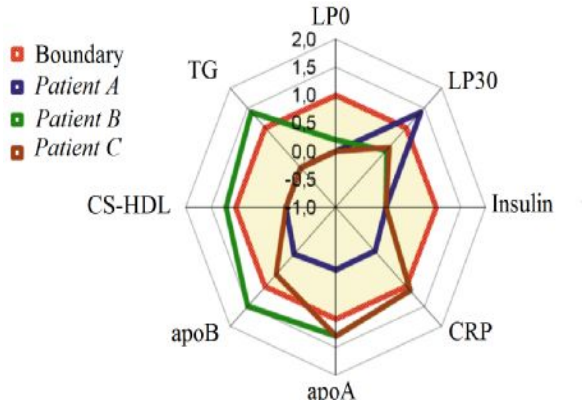

Figure 2. Visualization of the results obtained for three patients

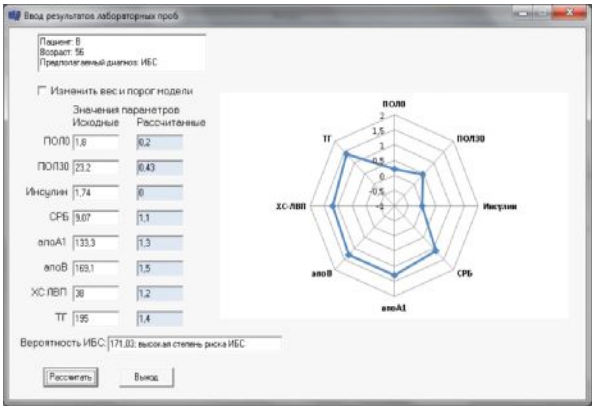

Figure 3. An example of the program module interface

The obtained integrated model was tested with the use of actual data; diagnostic accuracy, specificity, and sensitivity were also calculated for all the examined patients. One of the testing results which illustrates the model verification is given in Figure 4.

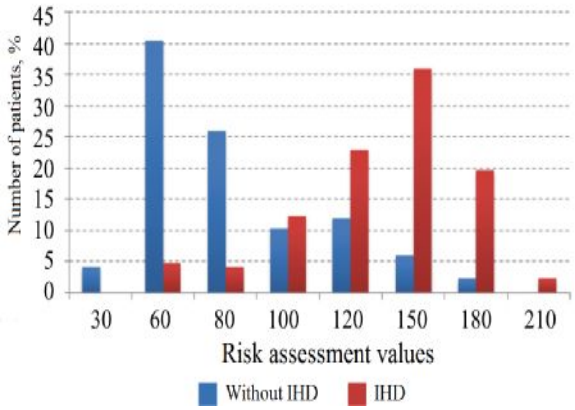

Figure 4. The result of assessing the model accuracy

Conclusions

So, we obtained the following results and came to the following conclusions in the course of our research:

Analysis of risk meters and scales which are widely used in cardiology allowed us to reveal that when risks were calculated, such assessments practically never included a set of oxidative, lipid-lipoprotein, inflammatory, and metabolic biochemical parameters.

Techniques aimed at obtaining numeric assessments as a rule require human processing of various parameters values and allow to form a set of assessments in different scales or one consolidated risk assessment.

As per results of the performed analysis we refined our task of creating techniques and models for IHD risk assessment on the basis of inflammatory, oxidative, and lipid biomarkers.

We developed a system of logical and mathematical models which is a universal scheme for laboratory parameters processing as it allows for heterogeneous data peculiarities. When we tested this developed model support, we obtained results which proved our models were highly accurate and their parameters gave a lot of

possibilities to increase specificity or sensitivity which are very important in screening or individual examinations of patients.

Our developed system of logical and mathematical models is universal, but diagnostic approach to applied biochemical parameters is specific.

The developed program module (calculator) allows a physician to obtain a result based on laboratory examinations data; this result characterizes numeric risk of coronary atherosclerosis and IHD for a patient. A physician can also see a visualization of a set of parameters on a screen and to detect their deviations from "standard - pathology" conditional boundary.

The developed laboratory-diagnostic complex is implemented into practical activities of the Scientific Research Institute for Therapy and Preventive Medicine.

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RISK ASSESSMENT PRACTICE IN HYGIENIC AND EPIDEMIOLOGICAL STUDIES

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RESULTS OF PHYSIOLOGICAL ADAPTATION ASSESSMTN AND HEALTH RISKS FOR LABOR MIGRANTS FROM TAJIKISTAN

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The paper focuses on the results of physiological research performed on 9 occupational groups of migrants who came to Moscow region of Russia from southern Central Asia republics. We studied adaptation processes characteristics in labor migrants as per cardiovascular system parameters and neuromuscular apparatus parameters. We revealed peculiarities in heart rate variability (changes in stress index S1, values of AMo, VLF spectrum power, PARS parameter) in migrants depending on neuro-emotional nature of working activity and muscular loads intensity. We detected apparent decrease in dynamometric parameters of endurance and maximum working capacity of arms muscles and backbones and legs muscles by the end of their working day. We created a procedure to determine an adaptation process stage under combined effects exerted by labor physical hardness and neuro-emotional intensity; unsatisfactory adaptation increases health disorders risks. We showed that long-term and intense impacts by factors determining labor process hardness caused occupational diseases of musculoskeletal system and peripheral nervous system. We revealed that as labor intensity grew working stress in a body also increased and it could transform into overstrain and occupational diseases evolvement (primary hypertension, ischemic heart diseases, and neurotic disorders). A distinctive feature is that men suffer from cardiovascular system pathologies more frequently while women tend to suffer from nervous system pathologies. In this relation, we should make separate predictions of occupational pathology probability depending on labor intensity level for males and females.

Adaptation processes optimization should include organization of rational work and rest regime, healthy lifestyle formation, improvements in medical aid for migrants.

***Key words**: migrants, neuro-emotional nature of labor, muscular loads, адаптация, heart rate variability, healthy lifestyle.*

An issue of labor migration in Russia is determined, on the one hand, by necessity to at-tract additional labor force required for post-perestroika development of Russian economy and efficient use of human resources in all brunches of industries, agriculture, and communal services. On the other hand, citizens from former USSR republics (Central Asia) need to come to Russia searching for paid jobs; they come to various regions, including Moscow and Moscow region [12, 13] .

A concept of adaptation as a process of a

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body getting adapted to the environment is widely used in biology and medicine. Examination of human adaptation to new environmental factors and health disorders have attracted attention of many researchers. A theory on sequence of adaptive shifts in a body under influence exerted by increased loads has been developed with-in general physiology and occupational physiology [1]. Sequence in adaptation processes evolvement involved sequencing of a certain stages in functional state; adaptation failure led to increased risk of pathologic disorders. N.A. Agadjanyan observed adaptation processes peculiari-ties occurring in adaptation to highlands and hypoxia, which became apparent in more efficient cardiovascular system responses in native Tadjiks in comparison with visitors [2]. S.G. Krivoshchekov studied how healthy migrants adapted to conditions in sub-polar regions (Middle Priobye) under ordinary and shift working regimes; as a result, a concept of human adaptation in the North was created [10]. Adaptation to a new place of living is known not to pass without consequences for one's health; adverse environmental factors and working process factors influ-ence bodies of labor migrants working in various RF regions. Yu.V. Moikin et al revealed chronic diseases exacerbation in Baikal-Amur Railroad builders who came from the south of Ukraine and Moldavia during their first months of staying on ecologically adverse territories of Siberia [8]. Substantial physical loads, both local and overall, which builders had to undergo were shown to result in occupational diseases of musculoskeletal system and neuromuscular system.

Adverse social and psychological conditions labor migrants work in are related to exces-sive requirements at a working place, to absence of any possibilities to participate in labor process adjustment (low control at a working place), and insignificant (very small) social support for labor migrants [7]. It can lead to stress at a working place [4, 17,18], and increased cardiovascular system diseases risk [14, 16, 19]. Occupational stress related to overexhaustion, central nervous system depletion, as well as functional overstrain, can cause neurotic disorders evolvement which are a significant part of psychological health issues [5].

Peculiarities of adaptation among various occupational groups of labor migrants have been attracting more and more attention in recent years; a new research trend in occupational physiology and occupational medicine is being formed and it is related to more profound insight into adaptation process which all aspects of our everyday life are involved in. Analysis of scien-tific literature has revealed that today there are not enough data on research on adaptation re-sponses to working processes peculiarities and to new social and psychological conditions in labor migrants as well as on their health risks analysis. And here labor intensity and peculiarities of specific working loads play a very important role in formation of a body functional state as they can vary greatly in case of each specific occupational group of labor migrants. It is especially vital in case of young people who come to Russia both as labor migrants looking for a job and as students who come from various Tajikistan regions to start their studies in HEE in the country capital.

Our research goal was to give scientific grounds for physiological peculiarities of Tadjiks migrants adaptation to industrial, social and psychological, and climatic and natural conditions in Moscow region; another goal was to work out activities aimed at providing social and medical support for labor migrants.

Data and methods. Research in industrial environments was performed on 6 occupational groups of men (builders-steelmen, builders-erectors, subway builders, road builders, vegetable warehouse workers, and vegetable market workers) and 3 groups of women employed in social sphere (housemaids, nurses, and child-minders) which were selected allowing for physical and neuro-emotional loads.

Students from Moscow Mining University and Tajikistan State Medical University who went into various sports (volleyball, futsal, free-style wrestling, box, taekwondo, and field shooting with handguns) took part in the research; they were 18-25 (21.5± 0.9). Our basic research periods were a training one and a period of competitions. Totally 139 people were examined.

Job analysis as per labor hardness and labor intensity was performed in conformity with Guidelines P 2.2.2006-05 [11]; physiological examinations included arm and backbone dyna-mometry, tremor measuring, determination of index of functional changes in circulatory system [9], and heart rate variability analysis as per conventional techniques [3,6,15].

Results and discussion. Physiological examinations of labor migrants were aimed at studying functional state of neuro-muscular system as being occupationally significant and making great contribution in providing reliability of work performed by the examined occupational groups. We detected decrease in dynamometric parameters of steelmen in a shift dynamics which became most apparent by the end of their working day. Thus, if hand muscles endurance lowered by 11.2% by a lunch break, then by the end of a shift that decrease became more drastic and amounted to 28.5% ($P \leq 0/05$), which was higher than physiological standards of a body strain in case of physical efforts; such physiological standards are equal up to 20% in case of general muscular loads.

The performed research revealed that a lunch break was not enough for the examined pa-rameters to recover. An integral dynamometry parameter, maximum muscular efficiency, also went down over a shift dynamics and this decrease amounted to 31.8% by the end of work in comparison with the data obtained when a shift just began. Such changes in dynamometry pa-rameters can be evidence that strain evolves in a neuro-muscular apparatus of arms and it is caused by physical hardness of work done. Together with decrease in dynamometry parameters hand tremor grew drastically (2.5 times). Thus, when a shift began a number of touches per 30 seconds amounted to 9.7± 1.16, but by a shift end it grew to 29.8 ± 2.13 touches ($P \leq 0.05$).

We should also note that work done by steelmen involves frequent maintaining uncom-fortable working postures (up to 50% of a shift), namely deep bendings; therefore, it was inter-esting to trace changes in dynamometry parameters of muscles supporting such postures. Strength reduced by 15.9%, endurance, by 25.6%, and integral parameter of maximum muscular efficiency, by 37.9%, by the end of work (Figure 1). So, we can conclude that strain and over-strain of neuro-muscular system caused by work evolves in steelmen (binders) over a shift dy-namics.

Data obtained via physiological research show that natural decrease in maximum efficiency of hand muscles develops in erectors over a shift dynamics; it reached 6.2% to static ef-forts by the end of work. Together with this decrease in maximum efficiency there was a fall in endurance by 9.0% by a lunch break, and by 14.5%, by the end of work. Calculated integral pa-rameter of maximum muscular efficiency also went down during a shift: by a lunch break it fell by 22.4%, and by the end of work, by 21.6% ($P \leq 0.05$). the described changes in dynamometry parameters can be evidence that strain evolves in neuro-muscular apparatus of erectors (binders)' arms and it is caused by a great number of local movements required in fastening building struc-tures with wire (binding).

Erectors' work involves preparing base surfaces, carrying panels over to a place of erec-tion, panels' strapping at storage places and other operations which require efforts by substantial groups of muscles. Research on efficiency and endurance of backbone muscles and legs muscles in a shift dynamics revealed there was decrease in backbones efficiency and endurance over a shift. Efficiency went down by 9.2%, endurance, by 21.8%, and in-

tegral parameters of maximum muscular efficiency, by 28.9%, by the end of work ($P \leq 0.05$), i.e., strain and overstrain devel-oped in workers' neuro-muscular system in a shift dynamics.

Such changes in dynamometry parameters can be evidence that strain and overstrain evolves in neuro-muscular apparatus and it is caused by physical hardness of work done. Mi-grants complained on pains in various parts of their bodies, including legs and arms muscles, and on overall fatigue, by the end of their working day.

Research of functional state of female migrants' neuro-muscular apparatus in a working day dynamics revealed that maximum efficiency of their right working arm tended to go down by the end of their work in comparison with the working day beginning. Endurance to static ef-forts decreased authentically by the end of a working day in comparison with its level at the be-ginning of it; decrease amounted to 29.3% in housemaids and nurses, and to 28.2% in child minders ($P \leq 0.05$).Statistically significant decrease in maximum muscular efficiency was detected already after 4 hours of work; by the end of a working day this decrease amounted to 31.0%, 28.9%, 31.0% of the initial level correspondingly.

Apparent static strain in lumbar muscles caused by performing work tasks in an uncom-fortable posture which involved bending by 45º was confirmed by negative dynamics in back-bone muscles dynamometry parameters in female migrants employed in social sphere. Maximum efficiency of backbone muscles in migrants working as housemaids decreased by 49.7% by the end of work; nurses, by 35.3%; child-minders, by 32.7% from the initial level ($P \leq 0.05$).

Detected changes in dynamometry parameters in a shift dynamics and graveness of phys-iological shifts prove that strain and overstrain evolves in neuro-muscular apparatus of arms and backbone muscles of labor migrants. First signs of strain occur already after 4 hours of work. By the end of work strain in neuro-muscular apparatus becomes quite apparent. The research results allowed us to determine a correlation between labor hardness and intensity and nature of changes in blood pressure and heart rate. Index of functional changes as-sessment and its average values over a shift proved that higher values of it were detected among steelmen who had greater workload. Thus, average values of functional changes index were equal to 3.09±0.07 for steelmen; 3.31±0.06 for erectors; 3.20±0.08 for subway builders; and 2.69±0.10 for vegetable market workers. We detected significant discrepancies between groups ($p \leq 0.05$). There was clear decrease in functional capabilities of a circulatory system and unsatisfactory adaptation evolvement in builders during stressful working hours. As market workers had significantly smaller workload we detected only functional strain evolvement in them.

Research on heart rate variability revealed authentic discrepancies in stress index (SI) pa-rameters in workers from various occupational groups depending on labor hardness category. As we can see from Figure 1, its values grew from 201.0±14.9 st.units in case of labor hardness cat-egory 3.1 (vegetable market workers) to 511.4±13.6 (steelmen) and 611.9±25.7 st.units (subway builders - tunnellers) in case of category 3.3. Seemingly, central regulation mechanisms became more active when autonomous circuit was suppressed in workers with labor of category 3.3 which indicated body physiological reserves were strained.

It was confirmed by significant decrease in summary cardiac intervals variability - SDNN - in subway tunnellers whose labor had 3.3 category of hardness. The parameter amounted to 41.6±2.01 msec against 59.87±1.55 msec y in market workers (labor hardness category 3.1). According to R.M. Baevskiy, the obtained data prove that parasympathetic section of vegetative nervous system becomes less active.

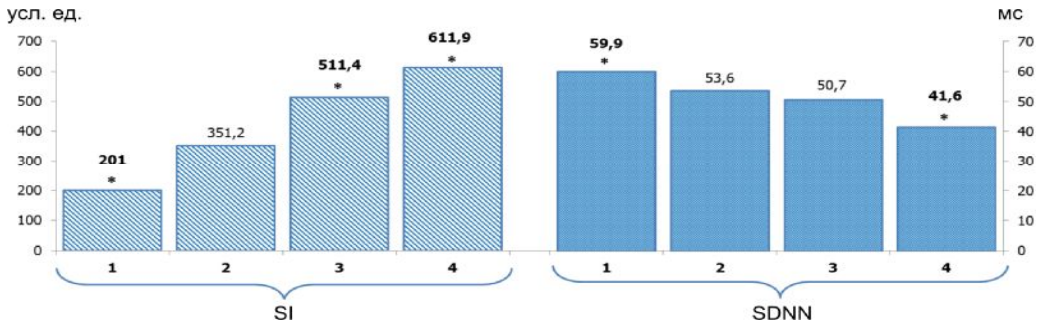

Figure 1 - Stress index parameters (SI) and total heart rate variability (SDNN) in labor migrants from various occupational groups depending on labor hardness category: 1 – vegetable market workers (category 3.1); 2 – road builders (category 3.2); 3 – steelmen (category 3.3); 4 – subway-builders - tunnellers (category 3.3). * $p<0.05$ – statistically significant changes in comparison with group 1

Index of centralization - IC - was also quite informative as we analyzed research results for workers with different physical loads (Figure 2). The obtained results coincide with changes in autocorrelation function parameter and prove there is increase of central mechanisms in heart rate regulation when labor hardness is high. Analysis of heart rate frequency characteristics re-vealed apparent increase in spectrum power of very low frequency (VLF) component in builders and subway builders with simultaneous increase in heart rate (to 91.5 beats/min), which proved sympathetic activation was high.

Regulatory systems activity parameter (PARS) revealed substantial strain in adaptation mechanisms of labor migrants. Thus, it varied from 4.74±0.54 – 5.85±0.64 st.units in female migrants employed in social sphere. It indicated that apparent strain in regulatory systems evolved and it was related to active mobilization of protective mechanisms including increased activity of sympathico-adrenal section. The obtained PARS values in Mosmetrostroy (subway) builders (6.21±0.82 points), and erectors (6.0±0.90) allowed to rank body functional state among regulatory systems overstrain (Table1).

This state is characterized with inefficient protective mechanisms unable to provide ade-quate body response to impacts exerted by working process factors and working environment. In this case excessive regulatory systems activation in not supported by relevant functional reserves.

To determine circulation regulation type (hypokinetic, hyperkinetic, or eukinetic one), we compared obtained values of blood minute volume and peripheral resistance with the standard values of the said parameters [2]. Our research results allowed us to reveal prevalence of hyper-kinetic circulation type in labor migrants. And here minute volume was higher than proper minute volume by more than 10%; peripheral resistance was more than 10% lower than its standard value. Hyperkinetic (cardiac) circulation type means greater heart output (blood minute volume) together with lowered peripheral resistance. Some migrants had eukinetic regulation type which was accompanied with certain decrease in peripheral vascular resistance. And in this case devia-tions of blood minute volume and peripheral resistance from their standard values were within ±10.0%.

Individual analysis of peculiarities in hemodynamics allowed us to determine per cent distribution of people with different circulation types as per examination groups (Table 2). The biggest share of people with unfavorable hypokinetic type of hemodynamics was detected in mi-grants working at big construction sites in Moscow and in Mosmetrostroy (subway construction): 36.9 ± 6,8% and 39.3 ± 9.2% correspondingly.

There were a lot of people with hyperkinetic type of circulation regulation in these migrants groups; their number in group I amounted to 34.2 ± 6.5%; in group II, 32.1 ± 8.8%. The obtained results prove there is more apparent instability in cardiovascular system functioning in migrants and it coincides with heart rate variability results.

So, performed research revealed that adverse functional changes evolved in labor migrants and they proved there was overstrain in neuro-muscular apparatus in workers; bodies. As working period grows longer, evolving stress in certain body system can cause risks of patholog-ical disorders. Basing on big database containing information on examined workers with various occupations, including builders, we calculated probability of occupational pathologies evolve-ment in musculoskeletal system and peripheral nervous system depending on working process hardness. It was detected that if labor had 3.2 or 3.3 hardness category, pathologies evolvement probability amounted to 17.1-37.0% cases which meant physiological-hygienic optimization of labor was required.

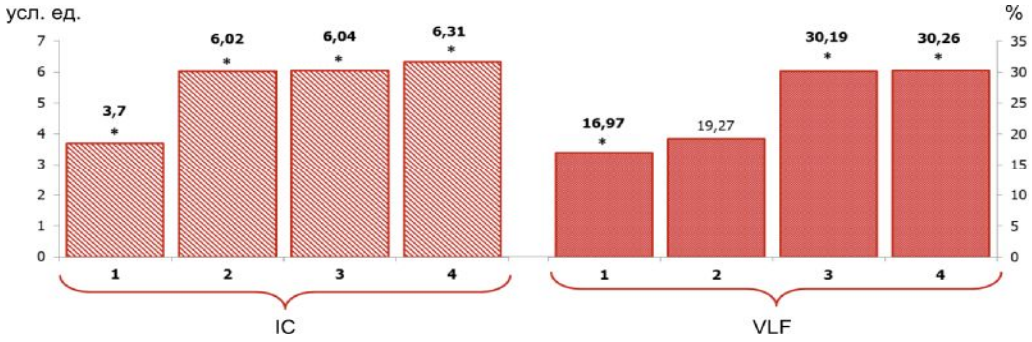

Figure 2 - Centralization index parameters (IC) and relative spectrum power of very low fre-quency component (VLF%) of heart rate variability in labor migrants from various occupational groups depending on labor hardness category: 1 – vegetable market workers (category 3.1); 2 – road builders (category 3.2); 3 – steelmen (category 3.3); 4 – subway builders - tunnellers (cate-gory 3.3). * p<0.05- statistically significant changes in comparison with group 1

Table 1

Certain parameters of heart rate variability in migrants from various occupational groups

Parameters	Groups									$p < 0,05$
	Steelmen	Erectors	Subway builders	Road builders	Vegetable warehouse workers	Vegetable mar-ket workers	Employed in social sphere			
							Housemaids	Nurses	Child-minders	
	1	2	3	4	5	6	7	8	9	
SDNN, мс	50,70 ± 1,61	41,72 ± 1,86	41,60 ± 2,01	53,56 ± 1,91	56,81 ± 1,57	59,87 ± 1,55	52,52 ± 1,65	48,88 ± 152	50,44 ± 2,17	$p_{2-6,3-6}$
SI, conv. units	511,4 ± 13,6	546,4 ± 23,5	611,9 ± 25,7	351,2 ± 25,8	255,9 ± 17,9	201,0 ± 14,9	389,0 ± 15,6	451,5 ± 19,6	357,7 ± 20,4	$p_{1-6, 2-6, 3-6, 4-6, 5-6, 6-7, 6-8, 6-9}$
CCO	6,85 ± 0,24	6,29 ± 0,81	5,68 ± 0,92	5,50 ± 1,80	5,99 ± 1,42	2,98 ± 0,31	4,36 ± 0,79	4,62 ± 0,92	5,39 ± 1,03	$p_{1-6, 2-6, 3-6, 6-9}$
TP, мс^2	1946,9 ± 147,5	1188,9 ± 155,6	1468,0 ± 175,3	1853,9 ± 250,3	2339,8 ± 176,1	2739,6 ± 197,7	2122,7 ± 202,1	1829,8 ± 219,4	1978,0 ± 179,1	$p_{1-6, 2-6, 3-6, 4-6, 6-8, 6-9}$
HF, %	17,20 ± 1,95	18,46 ± 1,60	17,15 ± 0,90	23,45 ± 2,11	21,89 ± 2,44	50,22 ± 4,50	39,0 ± 2,86	27,15 ± 2,27	29,31 ± 1,27	$p_{1-6, 2-6, 3-6, 4-6, 5-6, 6-8, 6-9}$
VLF, %	30,19 ± 2,42	30,69 ± 1,78	30,26 ± 2,04	19,27 ± 1,25	28,39 ± 2,58	16,97 ± 1,89	22,14 ± 2,17	20,78 ± 1,50	21,80 ± 1,92	$p_{1-6, 2-6, 3-6, 5-6}$
IC, conv. units	6,04 ± 0,61	7,58 ± 1,11	6,31 ± 0,95	6,02 ± 0,85	6,0 ± 1,02	3,70 ± 0,91	5,18 ± 0,60	5,29 ± 1,01	5,59 ± 0,70	$p_{1-6, 2-6, 3-6}$
PARC, conv. un	5,57 ± 0,79	6,0 ± 0,90	6,21 ± 0,82	5,56 ± 0,69	4,88 ± 0,42	4,05 ± 0,62	4,74 ± 0,54	5,29 ± 0,71	5,85 ± 0,64	p_{3-6}

Table 2

Results of research on circulation type in migrants from various occupational groups

Circulation type	Examined group				
	Steelmen and erec-tors	Subway tunnellers	Road build-ers	Vegetable warehouse workers	Market workers
	1	2	3	4	5
Hyperkinetic	34,2 ± 6,5	32,1 ± 8,8	49,0 ± 8,7	42,8 ± 6,1	54,1 ± 7,4
Eukinetic	28,9 ± 7,1	28,6 ± 8,5	27,2 ± 11,5	40,8 ±11,1	37,0 ± 12,4
Hypokinetic	36,9 ± 6,8*	39,3 ± 9,2*	23,8 ± 9,9	16,4 ± 4,4	8,9 ± 9,2*

*p ≤0.05 in comparison with the 5th group (market workers)

Functional sample with fixed respiration rate (FRR6, FRR12) was aimed at detecting physiological reserves of cardiovascular activity and adaptation reactions of a human body. When respiration frequency was equal to 10 cycles per minute (FRR6), there was increase in power of high frequency waves (HF) within 0.15 - 0.25 Hz range, and it was shaped as a narrow high-amplitude wave. Most researchers considered it an effect of vagus nerve stimulation.

When respiration was less frequent and deep - 5 cycles per minute (FRR12), we detected authentic fall in heart rate variability, mode amplitude, S1 and parameters with characterized respiration waves. And at the same time authentic increase in SDNN appeared. Growth in power of low frequency waves (LF) with respiration which was 5 cycles per minute frequent was shaped as high amplitude peak within 0.05 - 0.15 Hz range.

We used samples with fixed respiration rate and revealed 2 basic reaction types which didn't depend on sex or place of permanent residence. The first type reaction was characterized with the situation in which increase in body regulatory systems stress occurred at FRR6 with the following decrease at FRR12. The second reaction type was characterized with gradual decrease in stress level at FRR6 and FRR12.

The performed spectral analysis revealed that changes in relative values of spectrum components during sampling of cardiorespiratory system with FRR were characterized with au-thentic increase in a spectrum high frequency component (HF) at FRR6 and its suppression at FRR12; decrease in low-frequency spectrum component (LF) at FRR6 and increase at FRR12.

Cardiovascular system response to a functional sample with fixed respiration rate in Tadjiks migrants is lowered in comparison with Russians living in Moscow region. It also proves that their adaptive reactions have certain physiological peculiarities depending on climate and geographic conditions of highlands in a donor country which make for increase blood saturation with oxygen and increase in cardiac muscle contractility.

We analyzed the results of research on competition stress as per heart rate variability in students representing various groups of professional sportsmen. Comparative analysis of heart rate variability parameters obtained before and after competition loads revealed slight changes in cardiovascular system responses in all the examined groups.

The greatest changes occurred in stress index SI in all groups except shooters; responses to competition loads were similar but with excessive appearance. Pre-start level of regulatory system stress was different both in individual sportsmen and in different kinds of sports.

The lowest SI before competitions was detected in volleyball players and football players, i.e. sportsmen from team sport games. But in case of sports where success depended on a sportsman' individual efforts, i.e. in fighting, SI before competitions was substantially higher.

The highest SI values, both before and after competitions, were detected in boxers

which probably was due to this kind of sport being rather extreme.

We gave grounds for a body adaptation under joint impacts exerted by labor hardness and intensity as per results of physiological research on representatives from various social groups (labor migrants, male and female students - professional sportsmen). The obtained results allowed us to justify determination of stages in adaptation as per results of analyzing correlations between working process factors and physiological parameters (dynamometry parameters and parameters of body vegetative provision).

Analysis of correlations between physical hardness of labor and its neuro-emotional in-tensity and physiological parameters of neuro-muscular system and cardiovascular system al-lowed us to rank them. Central place in this system belongs to labor hardness; other parameters as per their ranks are set as follows: working posture (is statistically significantly related to physiological parameters in 93.3% of cases), static load (80.0%), labor intensity (73.3%), and emotional load (66.7%).

Research results helped us to give grounds for quantitative assessment of strain evolving in body adaptation responses due to physical labor and neuro-emotional labor which included calculation of decrease in neuro-muscular apparatus parameters (% of shift from initial state), and changes in average monthly values of cardiovascular system parameters (deviations from standard and proper values in %).

We applied regression analysis of data on changes in adaptation which occurred in great number of workers by the end of their working shift as per neuro-muscular system and cardio-vascular system parameters; it allowed us to derive a formula for determining level of strain in body adaptation responses (an application for a patent is completed). we determined stages in adaptation process of a worker's body in working process: self-regulation (optimal strain), activa-tion (allowable strain), mobilizations of 1,2, or 3 degree (overstrain of 1, 2, or 3 degree).

Long-term and intense impacts of factors determining labor hardness causes occupational diseases of musculoskeletal system and peripheral nervous system. Analysis of data obtained during physiological-clinical research allowed to reveal dependence between frequency of occu-pational diseases evolving in peripheral nervous system and musculoskeletal system of workers from the examined occupational groups and labor hardness (in conformity with working condi-tions class as per P 22.2006-05); the dependence is described with a log0linear regression equation.

Physical labor with local muscular loads, for example, erectors' work, involves completing a great number of small stereotype hands movement (from 4,000 to 130,000 per a shift), and it determines nature and depth of functional shifts and pathological disorders. Multiple regression analysis revealed there was a positive correlation ($P < 0.01$) between: a) a number of movements per shift and neuromuscular system fatigue in workers ($r = 0.96$); b) a number of movements per shift and frequency of occupational diseases evolving in peripheral nervous system and musculoskeletal system ($r = 0.92$); c) neuro-muscular apparatus fatigue and occupational pa-thology frequency ($r = 0.72$).

We calculated dependence between occupational diseases frequency and labor hardness category allowing for local muscular load; our calculation revealed that if labor hardness category was 1 (optimal) and a number of local movements per a shift didn't exceed 20,000, occupational diseases (pathological disorders in peripheral nervous system and musculoskeletal system) occurred in rare cases (up to 2%); if labor had 2 category (40,000 movements), pathologies oc-curred in 2-13% cases. But if labor category was 3 (hard labor, up to 60,000 movements) occupational diseases occurred in 13.1-20.0% cases; category 3.2. (more than 60,000 move-

ments), 20.1-28% cases; category 3.3, more than 28% cases.

Examination of physical labor related to regional and overall muscular loads revealed that labor process factors determining labor hardness (weight of cargos which workers had to lift and move, dynamic and static loads, number of movements, period of staying in physiologically non-rational postures etc.), were different in different occupational groups. Complex physiological-clinical research revealed close correlation between evolving neuro-muscular system fatigue as well as nature and depth of pathological disorders in peripheral nervous system and musculo-skeletal system and physical loads. Results of multiple linear regression analysis revealed there was an authentic ($P< 0.001$) correlation between examined physiological parameters and impacts exerted by above-mentioned labor process factors; correlation coefficient with muscular endur-ance amounted to + 0.79; electrobiological muscular activity during work + 0.92; heart rate + 0.88.

We calculated dependence between occupational diseases frequency (retrospective analy-sis of 2,318 cases) and labor hardness category allowing for regional and overall muscular loads; it helped us to derive a regression equation. We can see from this equation that if labor category is 1 (optimal) occupational diseases probability didn't exceed 6%. If labor category was 2, patho-logical disorders frequency didn't exceed 17.0% of cases. In case of hazardous (hard) labor (category 3.1) occupational diseases occurred in 17.1-28% cases; category 3.2, 28%: category 3.3, more than 36% cases.

As integral parameter of labor intensity grew, overall working strain in workers' bodies increased substantially and it could result in overstrain and consequently in occupational diseases. We performed correlation analysis on the example of several occupational groups searching for correlations between a share of workers who had certain general somatic pathologies and labor intensity. We revealed high direct correlation between integral parameter value and a share of people with the following pathologies: primary hypertension, ischemic heart diseases, and neurotic disorders (total number); i.e., the higher labor intensity was the greater risk of the said pathologies evolvement occurred. Regression analysis performed by us revealed that this de-pendence was given as a logarithmic equation regardless of a pathology detected.

Results of clinical examination performed on these occupational groups proved that the higher labor intensity was the greater share of people with this or that pathology was detected. Thus, primary hypertension was detected in 6.0-6.6% of women with 2 category of labor intensi-ty; in 9.77-13% of women with 3.1 labor intensity (in 10.77-18.9% of men); in 17.3-21.6% in women with 3.2 labor intensity (in 27.0-27.3% of men). Ischemic heart disease was correspond-ingly detected in 0.9-3.2% of women with 2 labor intensity; in 1.1-4.3% women with 3.1 labor intensity (in 8.0-8.4% of men); in 10.3-11.2% of women with 3.2 labor intensity (up to 32.5% of men). the same regularity was detected as per total number of neurotic disorders: 18.9-31.7% in case of 2 labor intensity; 44.7-45.4% in case of 3.1 labor intensity (12.1-24.2% males); 50.9-69.6% in case of 3.2 labor intensity (up to 34.3% males). A distinctive peculiarity is that men tend to have higher % of cardiovascular system pathology, and women, nervous system patholo-gy, and it coincides with data taken from literature. In this respect, prediction of occupational pathology evolvement depending on labor intensity should be done separately for women and men. Calculated probabilities (in %) of occupational pathologies practically fully coincide with the data of complex occupational analysis and physiological-clinical research.

We created scientifically grounded recommendations on medical and social support for la-bor migrants: educational activities, occupational selection and occupational orienta-

tion; rational work and rest regimes; motivation to pursue healthy lifestyle; medical and diagnostic activities; additions to legal regulations for labor migrants.

Conclusions. We proved that a heart rate variability parameter when combined with functional samples was quite informative for characterizing peculiarities of regulation by vegetative functions and stress level. Nature of strain in body regulatory systems as per heart rate variability parameters depends on working process peculiarities, climatic and geographic conditions, stressful situations of social and occupational genesis related to social and psychological life of labor migrants.

Activity of sympathetic section of regulation in labor migrants revealed that adaptation strain syndrome as per physiological parameters became apparent through changes in heart rate variability: various levels of SI stress index related to great physical (muscular) loads and neuro-emotional loads; evident increase in spectrum power of very low-frequency component (VLF) with simultaneous increase in heart rate. We determined stages in a body functional state and adaptation stages as per regulatory systems activity parameter (PARS) (optimal strain was equal to 1.19±0.28 points; allowable strain was equal to 40.5±0.62 points; overstrain was equal to 6.21±0.82 points).

Detected discrepancies between native Russians and Tadjiks migrants in the following parameters: overall heart arte variability parameter SDNN, correspondingly: (63.76± 2.80) and (56.25±1.62) msec; very low frequency spectrum component VLF: (14.51± 0.81) and (19.54±2.94) %; low frequency spectrum component LF: (50.61±1.72) and (35.38±2.10) % con-firm that biological adaptation is directly determined and it was formed as a result of long-term historical process.

Our comparative and physiological research allowed us to reveal that adaptation process developed basing on various mechanisms: increase in spectrum components power or increase in information processing period or information transfer rate; it is proved by data on dynamics of periods of waves with different frequency during a test with fixed respiration rate. We applied functional samples with fixed respiration rate and it allowed us to reveal that Tadjiks migrants regardless of their sex tended to have smaller range of fluctuations in heart rate variability pa-rameters during respiratory testing which was the evidence of efficiency of cardiovascular system response to a test with fixed respiration rate.

The created standards of physical development allowing for sex and age helped to give physiological grounds for standard requirements to organization of a student's workplace under contemporary conditions involving educational process computerization as it could increase effi-ciency and preserve students' health. Our examination of personal features and temperament peculiarities revealed discrepancies in heart rate variability parameters in students with different extroversion and introversion levels. These discrepancies were authentic increase in SI and mode amplitude and decrease in SDNN, TP, and LF as extroversion grew. We created and gave scientific grounds for quantitative assessment of 5 strain stages in a worker's adaptation to a working process which were related to combined impacts exerted on a body by labor physical hardness and neuro-emotional intensity: self-regulation stage (optimal strain), activation (allowable strain), mobilization of 1,2, or 3 degree (overstrain of 1,2, or 3 de-gree).

Health disorders prevention aimed at preserving migrants labor potential requires devel-oping medical and social support program which allows for functional restructuring of body physiological regulatory mechanisms which corresponds to a stage of 2- and 3- adaptation pro-cess mobilization degree.

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ASSESSMENT OF CORRELATION BETWEEN LEUCOCYTES MIGRATION REACTION AND LEVEL OF INHALATION EXPOSURE TO PRIORITY AIR CONTAMINANTS

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Nowadays each forth person suffers from allergic diseases and allergic pathology prevalence is constantly growing. There are compounds in air which are generally toxic, or have sensitizing or allergenic effects on a body. For example, we can name formaldehyde and nitrogen dioxide. Our research goal was to reveal a correlation between reaction of leucocytes migration inhibition to formaldehyde and level of inhalation exposure to the examined chemicals. We examined 410 teenagers who permanently lived in industrial cities in Irkutsk region. We studied individual load as per formaldehyde and nitrogen dioxide. We estimated eosinophils content in nasal mucus and determined indexes of leucocytes migration inhibition to formaldehyde. Index of formaldehyde effects danger was detected to exceed 1 in 54% teenagers. The greatest value of danger coefficient in terms of exposure to this substance was equal to 1.76. anger index in terms of exposure to nitrogen dioxide didn't exceed 0.7 in the examined teenagers. The obtained results prove that inhalation formaldehyde load influences teenagers from industrial centers as sensitization to this substance evolves in them. We found out that true inhibition reaction of leucocytes migration in a reaction with formaldehyde more frequently occurred in people with danger index in terms of exposure to this substance being lower than 1. We obtained models which described correlation between level of sensitization to formaldehyde and a number of eosinophils in nasal mucus and it allowed us to detect that sensitization depended on the examined contaminants content in the air. The sensitization to chemical air contaminants which we revealed in teenagers calls for necessary activities aimed at reducing risks of allergenic pathology evolvement in them.

Key words: *teenagers, formaldehyde, nitrogen dioxide, inhalation load, reaction of leucocytes migration inhibition, rhinocytogram, eosinophils.*

Allergic diseases prevalence has been growing over the last decades; nowadays each fourth person suffers from them [11, 14]. Allergic pathologies are proved to be more frequent in industrial cities and territories with adverse ecological situation [5, 7, 11, 15, 17, 18]. At the same time allergenic intolerance to various chemicals, including inert ones [4], occurs more often; and it is also detected that ecological pollutants are able to act as allergens and sensitizers [2, 12]. Formaldehyde is undoubted-

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ly one of such pollutants as it exerts overall toxic, sensitizing, and allergenic impacts on a body [5, 13, 16, 18, 19]. It was revealed that 28 - 36% of children living in industrial cities located in East Siberia where 14% of the total inhalation exposure danger index belonged to nitrogen dioxide, and 9 - 18% to formaldehyde [6], suffered from allergic rhinitis or bronchial asthma [1]. We should also take into account that nowadays there are no data which can prove that nitrogen dioxide as one of priority ecological pollutants has any sensitizing effects; however, when sensitivity to it evolves it can be determined by oxidation stress development and consequent variety of pro- and anti-inflammatory processes caused by the impacts exerted by the substance. The earlier research revealed that sensitization to formaldehyde and sodium nitrite occurred quire frequently in children living in industrial cities where allergenic pathologies prevailed [3]. At the same time, there are no proofs that such ecological factors play any important role in the evolvement of such diseases.

In relation to that our research goal was to detect correlation between reaction of leucocytes migration inhibition to formaldehyde and level of inhalation exposure to chemicals.

Data and methods. Our research was performed on 410 teenagers aged 14-17 who permanently lived in industrial cities located in Irkutsk region (Angarsk and Sayansk), after their parents (legal representatives) gave their informed consent.

Atmospheric air quality was assessed as per data collected at Hydrometeorological service stationary posts located in Angarsk and Sayansk. Air samples in houses and educational establishments were taken by experts from East-Siberian Institute of Medical and Ecological Research (Candidates of Biological Sciences L.G. Lisetskaya and N.A. Taranenko); contents of sulfur dioxide and nitrogen dioxide, carbon monoxide, formaldehyde, and suspended substances, were examined in the samples. When calculating individual chemical load exerted by formaldehyde and nitrogen dioxide on teenagers' bodies, we used data on admixtures content in atmospheric air, in the air in houses and educational establishments, information on educational processes organization and students' rest (questioning was performed by an expert from East-Siberian Institute of Medical and Ecological Research, Candidate of Medical Sciences I.V. Melnikova), anthropometric and spirometric parameters (as per data obtained via medical examination performed by physicians in the clinic of East-Siberian Institute of Medical and Ecological Research) [8]. Individual danger coefficients of inhalation exposure to chemicals were calculated in conformity with Guide to health risk assessment when exposed to chemicals polluting the environment 2.1.10.1920-04 [8, 10].

Nasal mucus examination (rhinocytogram) was accomplished via microscopy, a conventional examination technique. Eosinophils quantity in swabs was calculated per 100 calculated cells. Reaction of leucocytes migration inhibition was performed with the use of Costar pads as per a procedure described earlier when a chemokinetic factor, formaldehyde, was added [9]. Concentrations of a chemical mitogen to perform reaction of leucocytes migration inhibition were adjusted via experiments. Migration index (MI) was calculated as per ratio of tested samples colonies size to intact control and given in per cents. MIs which were beyond (-20% - +20%) range were considered to be positive.

Research results were analyzed with «STATISTICA 6.0» program software, and such non-parametric techniques as

Spearman's rank correlation and U-criterion by Mann - Whitney were applied. We compared frequencies of deviations from standards in the examined parameters with the use of abundance of a character in a sampling. To assess influence exerted by chemical factors on MI value in the reaction of leucocytes migration inhibition we applied non-linear regression with step-by-step introduction. Discrepancies were considered to be statistically significant in all cases when $p<0.05$.

Results and discussion. There had previously been research performed on the territories of the examined cities and as a result it had been revealed that formaldehyde and nitrogen dioxide made the greatest contribution into immune system disorders risk [6, 8]; allowing for the results of the above-mentioned research we calculated individual exposure load exerted by the said substances on teenagers' bodies.

Danger coefficients (HQ) of formaldehyde effects varied from 0.6 to 1.76, nitrogen dioxide, from 0.05 to 0.59. The examined teenagers were divided into groups as per HQ values for air pollutants impacts. Teenagers with HQ value for formaldehyde effects being lower than 1 made up the IFA group (190 teenagers), with value being 1 and higher, IIFA group (220 teenagers).

We detected that quantity of eosinophils in nasal mucus increase in which was the evidence of a body allergic orientation didn't have any discrepancies between groups of teenagers with different level of inhalation formaldehyde load (Table 1). It is quite interesting that a body reaction to formaldehyde was detected in 40% of the examined teenagers which indicated there was sensitization to the substance in them. At the same time average group value of MI to formaldehyde in teenagers with HQ of the exposure to the toxicant being ≥1 was statistically significantly higher than in teenagers with HQ being lower than 1. We should note that leucocytes migration inhibition occurred statistically significantly more frequently (33.9%) and activation occurred two times more rarely (10.7%) in group IFA than in group IIFA (17.0%, p=0.01 and 21.8%, p=0.08 correspondingly).

The examined teenagers were divided into two groups as per HQ value of nitrogen dioxide (NO2) effects in the following way: 104 teenagers with the said parameter value being lower than 0.3 made up the group INO2, 306 teenagers with inhalation nitrogen dioxide load being 0.3 and higher made up the group IINO2.

As we analyzed relative content of eosinophils in nasal mucus taken from teenagers with different HQ values of nitrogen dioxide effects, we revealed that their quantity in teenagers from group IINO2 was higher than in another one (Table 2).

It is quite noticeable that when the examined teenagers were divided into groups depending on HQ values of nitrogen dioxide effects, the nature of leucocytes response to formaldehyde in inhibition reaction had opposite orientation in comparison with groups IFA and IIFA.

Table 1

Parameters of a body allergic orientation and sensitization in teenagers with different inhalation formaldehyde load, Med (LQ-UQ)

Parameters	Group I_{FA}	Group II_{FA}	*p*
Eosinophils content in nasal mucus, %	2,00 (0,00– 10,00)	1,00 (0,00 – 10,00)	0,082
Leucocytes migration index in reaction to formaldehyde, %	–9,13 (–26,55 – – 1,93)	0,00 (–13,78 – 18,15)	0,001

Table 2

Parameters of a body allergic orientation and sensitization in teenagers with different inhalation nitrogen dioxide load, Med (LQ-UQ)

Parameter	Group I_{NO_2}	Group II_{NO_2}	*p*
Eosinophils content in nasal mucus, %	0,00 (0,00–8,00)	2,00 (0,00–11,00)	0,004
Leucocytes migration index in reaction to nitrogen dioxide, %	3,36 (–8,16–18,15)	–6,62 (–20,09–8,00)	0,006

Thus, increase in exposure to nitrogen dioxide led to changes in MI to formaldehyde from values proving leucocytes migration activation (INO2 group) to values which characterized the reaction as being inhibition one (IINO2 group).

Correlations analysis allowed us to detect a weak association between HQ of formaldehyde effects, HQ of nitrogen dioxide values, and MI to formaldehyde (R=0.18, p=0.01 and R=-0.19, p=0.01 correspondingly). Regression analysis helped to reveal that eosinophils content in nasal mucus taken from teenagers depended on inhalation load both with formaldehyde and nitrogen dioxide. The equation giving this dependence was as follows: EOS =71.57 – 0.13*HQNO2– 2.86*HQFA+ 2.68*(HQNO2)2, where EOS was relative eosinophils content in nasal mucus, HQNO2 was HQ of nitrogen dioxide effects, HQFAwas HQ of formaldehyde effects. Other parameters for this model were: F(3.353)=4.923, p<0.002, R=0.20, R2=0.04, adjusted R2=0.03.

We also obtained models which described dependence between sensitization to formaldehyde and chemical inhalation load with the examined compounds. MIFA = 56.29 + 2.00*(HQFA)2– 0.32*(HQNO2)2 – 1.55*HQFA, where MOFA was MI to formaldehyde, HQNO2 was HQ of nitrogen dioxide effects, HQFAwas HQ of formaldehyde effects. Parameters for the determining model were MIFAF(3.197)=3.921, p<0.009, R=0.24, R2=0.06, adjusted R2=0.04.

Conclusion. The results we obtained prove than inhalation formaldehyde load influences sensitization to it in teenagers living in industrial cities. True reaction of leucocytes migration inhibition to formaldehyde more frequently occurs in people with HQ of the toxicant being <1; to sodium nitrite, in teenagers with HQ of nitrogen dioxide effects being higher than 0.3. Determinacy of leucocytes migration index in reaction to formaldehyde and eosinophils content in nasal mucus are not of linear nature and depend not only on load with formaldehyde but also on nitrogen dioxide introduction into a body; it proves that this pollutant has only indirect effects on a body sensitization and allergization.

The revealed sensitization of teenagers' bodies to chemicals polluting both air indoors and atmospheric air makes it necessary to carry out activities aimed at lowering chemical inhalation load and allergenic pathology risks caused by a lifestyle, nutrition, etc.

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GIVING GROUNDS FOR PHYSIOLOGICAL-ERGONOMIC ACTIVITIES AIMED AT REDUCING EYE FATIGUE CAUSED BY WORK WITH VISUAL DISPLAY TERMINALS

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The research was performed on occupational groups which combined visual display terminals (VDT) users. Basic occupational activity of such workers was information input and information read-out from a screen. Constant visual work with a display is a risk factor which can cause health disorders. It makes for visual analyzer strain which becomes apparent through decrease in accommodation as a result of changes in the closest and the farthest point of clear vision. As period of work with a screen becomes longer, fatigue grows, and visual analyzer performance decreases. There are other signs proving eye fatigue; they are changes in temporary characteristics of clear vision stability which are determined by a period of successive contrast perception, and critical fusion frequency which reflects the central nervous system instability.

Long-term visually stressful work with VDT causes strain in the body systems which provide visual process. Non-mobile forced "sitting" position can also cause decrease in physical efficiency. Research which was conducted on workers who had to spend more than 4 hours a shift at VDT in their working environment helped to reveal a dependence between their overall physical efficiency and changes in visual analyzer during a shift. The lower workers' physical efficiency was (both male and female), the greater accommodation decrease was detected in them. It is shown that visually stressful work performed by people with low physical efficiency can make for transfer of strain evolving during a shift into overstrain.

To prevent eye fatigue as well as overall one in VDT users, it is necessary to work out complex preventive activities which include work and rest regimes; preventive measures aimed at vision strain relieving; correction techniques which help to improve physical efficiency; rational workplace organization.

***Key words**: professional user, visual display terminal, visual analyzer, vision strain, accommodation, overall physical efficiency.*

Nowadays computers are widely used in various spheres of economic activities; notably, they are required to perform design and technological works, managerial tasks, to do accounting, and so on. Apart from their industrial use, computers are also a part of our everyday life. 3 billion people are known to not only use a computer for a bigger part of their working activities, but also spend hours looking at a visual display terminal (laptops, smartphones, and TV sets) in their free time. In relation to that, it has become necessary to perform comprehensive research on impacts exerted by visual display units on users' health as it is pointed out in the WHO Decision No. 99 dated 1989 [2].

Work with a visual display terminal

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(VDT) is multi-functional and it involves loads on various systems of an operator's body [5,20,21,23]. Work tasks of VDT users are quite different in terms of intensity and duration of impacts exerted by intellectual, emotional and sensory loads depending on their occupational activity (from information input to operators who control complicated technological processes); these loads determine various labor intensity categories.

We analyzed performed research in the sphere of occupational activities which VDT users tend to have [11,13,15] and revealed that an image on a VDT screen was a leading factor causing visual strain evolvement as such an image differed from an image on paper greatly. Strain which professional VDT users suffer from has certain peculiarities [4,7,14,22]. However, long-term and intensive work with a VDT screen leads to visual analyzer overstrain which is viewed as "computer visual syndrome" with occupational ophthalmopathy evolvement in PC operators [6,16,24]. We can spotlight three similar but not identical states which occur during work with VDT and make for decrease in work efficiency: they are fatigue, monotony, and mental satiety. Fatigue can be described as a natural reaction related to growing strain caused by performing visual-strained work. Here we should particularly highlight that such occupational activity is mostly performed in a non-mobile "sitting" position. Simultaneously low physical activity (hypokinesis) is well-known to result in substantial decrease in overall physical efficiency (OPE) which has a number of negative consequences for central nervous system, cardiovascular system, peripheral nervous system, and for a functional state of a visual analyzer [3,12,17,18]. It is shown that if workers performing visual-strained activities with precise labor (with a hand lens, magnifying glass, or a microscope) increase their overall physical efficiency via training on a cycle ergometer, it improves their subjective estimation of their own health and restores functional capabilities of their bodies including their visual analyzer [8,19]. And here we should note that there haven't been any similar studies on professional VDT users involving estimation of their overall physical efficiency and nature of negative changes in their visual analyzer allowing for gender differences, or in a working shift dynamics; so it made us to choose our research goal.

Research goal. Our goal was to study peculiarities of physiological changes in a visual analyzer occurring during work with VDT in male and female workers allowing for their overall physical efficiency and to give grounds for physiological and ergonomic activities aimed at reducing risks of visual fatigue evolvement.

Techniques and scope. We applied techniques which allowed us to obtain comprehensive characteristics of a visual analyzer state in working conditions. Our set of techniques included determination of accommodation volume, period of successive contrast perception (PSCP), and critical fusion frequency (CFF).

We determined overall physical efficiency (OPE) as per PWC170 test with a cycle ergometer. An examined worker was offered to have two training sessions, 5 minutes each, with a 3-minute rest between them (the first session was 23 W (150 kg·m/min), the second one was 75-100 W (450-600 kg·m/min), heart rate was registered during the last 30 sec. PWC170 was calculated as per conventional formula [10].

We examined various occupational groups which comprised VDT users who had to either input information into a PC (accountants, designers, editors, telegraphers, bank clerks etc.) or to read infor-

mation shown on a screen (production engineers, call centers operators, TV broadcasting centers workers etc.). All the examined workers were practically healthy people aged 25-30 with their working experience being not less than 3 years. Overall, we examined 175 people in a working shift dynamics. To assess overall physical efficiency, we examined 184 professional VDT users (113 males and 71 females aged 25-39).

Primary results. On the basis of the performed research we revealed that the bigger part of a working shift was spent near a VDT screen the more intensive a user's working activities became. We determined that if work on a PC amounted to 67.5% of a working shift than a coefficient of correlation between time spent near a screen and evolving visual analyzer strain was equal to $r = 0.67$ ($P<0.05$), but if that period of work on a PC grew to 87.4% of a working shift, correlation coefficient increased substantially up to $r = 0.92$ ($P< 0.001$).

Constant visual work with a VDT screen makes for visual analyzer strain which becomes apparent through lower accommodation volume caused by changes in the near and far points of accommodation (Table 1).

Table 1

Changes in accommodation parameters in VDT users depending on time spent working with a screen

Period of work with a screen	Time of measuring	Accommodation volume (diopter)	Near point (diopter)	Far point (diopter)
Up to 2 hours	Beginning of a shift	7,05 ± 0,26	7,5 ± 0,30	0,45 ± 0,02
	End of a shift	6,8 ± 0,23	7,1 ± 0,23	0,30 ± 0,05
	% of changes	3,6	5,4	33,4
Up to 4 hours	Beginning of a shift	7,1 ± 0,40	7,8 ± 0,30	0,76 ± 0,06
	End of a shift	6,6 ± 0,35	7,2 ± 0,28	0,56 ± 0,04*
	% of changes	7,1	7,7	25,5
More than 4 hours	Beginning of a shift	7,6 ± 0,35	8,4 ± 0,37	0,80 ± 0,05
	End of a shift	6,3 ± 0,27*	6,7 ± 0,28*	0,50 ± 0,03*
	% of changes	17,2	20,3	37,5

Note: * – validity of discrepancy between a shift beginning and end ($P<0.05$)

As we can see from this table, as a period of time spent working with a VDT screen grows, per cent of decrease in accommodation volume also rises; here contribution made by a period of time spent working with a screen into decrease in accommodation volume amounts to 68.6-69.4%, correlation coefficient being 0.83 ($P<0.01$). There are other signs of visual fatigue, for example, changes in temporary characteristics of clear vision which are determined as per period of successive contrast perception (PSCP) which drops by 11.4-22.9% over a shift in dynamics, and critical fusion frequency (CFF) which reflects central nervous system instability and also goes down by 6.5-15.0%.

Besides, long work with a VDT screen as a rule is combined with subjective sensations, the most typical being "eyes and eye balls reddening" (48.4%), "lacrimation" (36.2%), "visual blurring in the dis-

tance" (34.2%) and "unclear vision near" (29.8%), "burning or pain in the eyes" (31.9%), "acute pain in the eyes" (43.8%), "visual fatigue" (70.3%), "overall fatigue" (52.4%). Occurrence of such complaints can on the one hand be caused by peculiarities which screen images have - low contrast, screen flicker, frequent brightness jumps, etc; on the other hand, it can be caused by a period of time spent near a VDT: long-term fixation of a sight on a screen, frequent need to readapt ones' eyes from a screen to a sheet of paper and vice versa. When performing their work functions, VDT users often have to shift their sight from a screen to a keyboard, and then to a paper document. Frequent readaptation of an eye to different brightness levels and distance is one of major negative factors which work with a screen involves. Such work leads to rapid fatigue evolvement, visual blurring, and double imaging. A set of detected disorders is described in literature as "computer visual syndrome". As per data taken from literature, frequency of this syndrome occurrence in professional VDT users amounted to 28.5%; people who had to work on a PC for more than 4 hours a shift mentioned having it in 96.0% of cases as they suffered from decrease in visual acuity, accommodation cramp, and other changes in their visual analyzer [1, 9,].

To prevent visual and overall fatigue in VDT users, it is necessary to implement complex preventive activities which include periodical medical examinations, work and rest regimes, and rational organization of a working place.

To maintain efficiency at an optimal level during the whole working shift, it is necessary to introduce scheduled breaks; here we should remember that if work involving information input (up to 20,000 characters), or in a dialogue regime is performed for a period of time up to 2 hours per shift, an overall scheduled break should last not less than 30 minutes. Work involving information input in volume up to 40,000 characters or in a dialogue regime up to 4 hours per shift causes such visual fatigue that scheduled breaks with overall duration not less than 50 minutes are required to eliminate it. Even stricter requirements are to be fixed in case of work involving information input in volumes up to 60,000 characters or work in a dialogue regime up to 6 hours per shift. Such work together with visual and overall fatigue causes visual analyzer overstrain; so, scheduled breaks lasting for not less than 70 minutes per shift are to be introduced.

Workers should not perform any functions during their scheduled breaks; they are recommended to leave their working place and, if possible, to go to a rest room or outdoors; or they should try to stop working with a PC for a while and switch to other activities. During breaks it is advisable to do exercises which improve circulation in eye balls; to do relaxing exercises for body and arms muscles, and to do self-massage of a pilary part of a head. We also recommend to take "a live cell" vitamin and mineral complex to prevent computer visual syndrome evolvement [1].

We should note though that workers having to perform visually strained activities do it in a non-mobile sitting position and it can consequently lead to decrease in their physical efficiency. Research performed in industrial environment on people who had to work with VDT for more than 4 hours per a shift allowed to reveal a dependence between their overall physical efficiency (OPE) and changes in their visual analyzer in shift dynamics. Table 2 contains data on three levels of overall physical efficiency in workers (males and fe-

males aged 25-39) and character of their distribution (in %).

Assessment of overall physical efficiency which professional users of VDT tended to have revealed that 37% males had low OPE, 46% had average OPE, and only 17% had high OPE. 54% of the examined females had low OPE, 37% had average OPE. And only 9% had high overall physical efficiency.

Table 2

Parameters of 3 levels of OPE in males and females aged 25-39, working with VDT

Parameters	Work with a PC					
	Females			Males		
	Low level	Average level	High level	Low level	Average level	High level
MOC ml/min·kg	< 28,0	29,0–36,0	> 37,0	< 33,0	34,0–40,0	> 40,0
PWC170 kg·m/min·kg	< 14,0	15,0–17,0	> 18,0	< 15,0	16,0–19,0	> 20,0
% of examined	54	37	9	37	46	17

Table 3

Changes in accommodation volume, PSCP and CFF in professional VDT users depending on their OPE in shift dynamics

OPE level	Time of measuring	Accommodation volume (diopter)	PSCP (sec)	CFF (Hz)
Females				
Low	Shift beginning	7,6 ± 0,35	8,3 ± 0,69	42,4 ± 1,14
	Shift end	6,3 ± 0,27*	6,4 ± 0,52*	34,1 ± 0,63*
	% of changes	17,2	22,9	19,4
Average	Shift beginning	7,1 ± 0,40	9,6 ± 0,48	39,9 ± 1,08
	Shift end	6,6 ± 0,35	8,4 ± 0,56	34,9 ± 0,64*
	% of changes	7,1	12,5	12,6
High	Shift beginning	7,05 ± 0,26	8,8 ± 0,69	40,2 ± 1,04
	Shift end	6,8 ± 0,23	7,8 ± 0,71	37,6 ± 0,67
	% of changes	3,6	11,4	6,5
Males				
Low	Shift beginning	6,44 ± 0,31	7,5 ± 0,39	43,4 ± 1,04
	Shift end	5,60 ± 0,29*	6,4 ± 0,42	36,2 ± 0,93*
	% of changes	13,1	16,7	16,3
Average	Shift beginning	6,93 ± 0,24	8,7 ± 0,28	40,9 ± 1,08
	Shift end	6,40 ± 0,28	7,8 ± 0,32	36,6 ± 0,84*
	% of changes	7,7	10,4	10,6
High	Shift beginning	7,02 ± 0,26	8,4 ± 0,42	41,6 ± 0,94
	Shift end	6,81 ± 0,34	7,9 ± 0,51	38,4 ± 0,62
	% of changes	3,0	6,0	7,7

Note: * is validity of discrepancy between a shift beginning and a shift end ($P<0.05$).

The performed research allowed to detect discrepancies in visual fatigue evolvement in professional VDT users in shift dynamics; such discrepancies depended on OPE level (table 3).

As we can see from the data presented in Table 2, accommodation volume decreased in female VDT users in shift dynamics; this decrease amounted to 0.25 - 1.3 diopter or 3.6-17.2% in various occupational groups. We should note that decrease in accommodation volume was caused by the near point moving farther by 0.4-1.7 diopter or 5.4-20.3%. The far point moved closer to eyes by 11.6-37.5% during a shift. As we analyzed the obtained data, we revealed that changes in accommodation volume were closely related to overall physical efficiency of VDT users. The lower OPE female workers had the greater decrease in accommodation volume occurred in them; thus, if OPE was low, accommodation volume went down by 17.2% while in case of people with high OPE the reduction was only by 3.6%. Similar parameters of decrease in accommodation volumes were detected among male VDT users; however, allowing for usually better physical abilities of men, changes in shift dynamics were less apparent in them in comparison with females even if their overall physical efficiency was low.

The multiple regression analysis which we performed revealed that contribution made by OPE level into changes in accommodation volumes among males and females was quite similar and amounted to 68.6-69.4% with correlation coefficient being equal to 0.82-0.83; i.e. the lower overall physical efficiency was, the more apparent changes in accommodation volumes occurred, and, consequently, the greater decrease in visual analyzer efficiency was detected.

We can also judge on decrease in visual analyzer efficiency both in males and females as per changes in temporary properties of a visual organ, PSCP and CFF, which are the evidence of visual fatigue evolvement. Here most apparent and hazardous decrease in all parameters was detected in people with low overall physical efficiency regardless of their sex.

Decrease in overall physical efficiency makes for growing number of people who tend to have various complaints. Thus, a share of female professional VDT users with low OPE who had complaints ranged from 9.2% to 12.8% when a shift started; when a shift ended, the share grew to 34.9-70.5%. Only 2.5-6.3% of females with high OPE had complaints at the beginning of a shift and 3.7-28.6% of them had complaints when a shift ended. A share of male users complaining on visual discomfort was a bit lower. Thus, 7.2-10.8% of males with low OPE had complaints when starting work; 23.8-60.9% of them had complaints when their shift ended. 1.2-5.1% of males with high OPE complained at the beginning of a shift and the share grew to 7.0-25% by the end of a shift.

Consequently, to maintain efficiency at an optimal level during visually strained work with a VDT screen, it is necessary, on the one hand, to apply correction techniques which make for increase in OPE level, and, on the other hand, to perform prevention activities aimed at visual fatigue elimination. To achieve this, we developed specific training exercises on a cycle ergometer; these exercises became a part of a working day and were done during scheduled breaks.

Exercises were done on an electric cycle ergometer during 3 months 5 times a week. A load was chosen individually and amounted to 75-100 Wt. Each load stage was performed during 3 minutes. Frequen-

cy of pedaling was set by a metronome and amounted to 60 rpm. One training session lasted for 10-15 minutes. Heart rate was registered at the end of each load stage.

As a result of performed training period, decrease in heart rate under the same load was detected. Thus, we revealed that heart rate of people with low OPE amounted to 159±2.3 beats/min at the end of cycle ergometer load, while the same load led to 125±2.0 beats/min in people with high OPE; i.e., when the same load was offered to different people, physiological costs of training were authentically higher for people with low OPE than for those with high one. The same data were obtained as per results of assessing a visual analyzer functional state. Thus, as we analyzed the obtained data, we revealed that accommodation volume in people with low OPE decreased by 12% by a shift end, but when their OPE grew due to training, this decrease amounted to only 4%. If OPE was low, PSCP decreased by 22.9%, and CFF, by 19.4%, among females, and by 16.7% and 16.3% correspondingly among males. A percent of decrease in temporary properties in shift dynamics both among males and females proves that visual fatigue evolves in them by a shift end. PSCP dropped by 11.4% and CFF, by 6.5% in females with high OPE, and by 6.0% and 7.7% correspondingly in males with high OPE, i.e., by a shift end visual fatigue was quite insignificant as the obtained parameters of decrease in temporary properties were lower than those which could prove that visual fatigue really evolved (15%). Also a number of people complaining on subjective sensations of fatigue and visual discomfort fell after training exercises.

Our research gave grounds for "standard" levels of overall physical efficiency which was required for work with VDT for males and females as per PWC170 parameters (females $\geq$ 15.0, males $\geq$ 16.0 kg·m/min·kg) and maximum oxygen consumption (females $\geq$ 29.0, males $\geq$ 34.0 ml/min·kg).

When working with VDT, it is also very important for a working place to conform to ergonomic requirements. Working furniture design (desks and arm-chairs) is to provide possibility of individual adjustment according to a user height so that a comfortable working posture could be maintained. When a working place for a PC user is organized, a VDT is to be placed on a desk in such a way that its back panel is against a wall; a screen is not to be placed opposite a window or any other light sources which could produce patches of light on it. A desk is to have such a size that a distance between a user and a screen is not less than 60-70 cm, and between a user and a keyboard, 30-40 cm. Luminance at a working place matters greatly in work with a VDT as it is required for visual comfort maintenance. Overall luminance in a room where VDTs are placed should be within 300-500 meter-candela. And here, apart from lamps lighting a whole room, there should be an individual one (not less than 60 Wt) with a solid lampshade which lights up only a text a user works with.

Conclusions. We detected that if there were no specific preventive activities, level of functional overstrain in a visual analyzer grew and it caused decrease in its efficiency. Preventive activities in case of work with VDT should above all be aimed at visual overstrain prevention and a working day regime should include visual gymnastics which is aimed at accommodation recovery and eye muscles training as well as better circulation in the eyes.

Workers should take "a live cell" vitamin and mineral complex during their scheduled breaks as it helps to prevent computer visual syndrome evolvement.

And allowing for VDT users work being performed in a non-mobile working posture, i.e. under working hypokinesis, we should provide for greater and more intense motor activity, both during a working day, and leisure hours.

To increase overall physical efficiency to "standard" levels and to achieve resistance to working process factors, we developed specific programs based on integrated approach to application of physical training and education techniques.

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RISK OF ARTERIAL HYPERTENSION IN WORKERS EMPLOYED AT COAL-MINING ENTERPRISES: SOCIAL AND HYGIENIC ASSESSMENT

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We analyzed risks of arterial hypertension development in occupational groups employed at coal-mining enterprises in Kemerovo region (1,915 workers). We used data on arterial hypertension development in Kemerovo region as our reference group; these data were obtained within the framework of ESSE-RF epidemiologic research (700 people aged 25–64 were examined). We noted that work at coal-mining enterprises involved several factors which could have negative influence on workers' health. Working conditions for those workers who had to stay in a mine during the whole working shift meant that workers were under negative impacts caused by unfavorable microclimate and heavy dust loads. To eliminate age discrepancies between workers employed at coal-mining enterprises and the reference group, we performed standardization as per age (data on the reference group were taken as our standard). We calculated arterial hypertension frequencies in the chosen occupational groups and determined relative risks of arterial hypertension via creation of contingency tables. To exclude any influence that might be exerted on relative risks of arterial hypertension by occupational selection, we corrected the obtained results as per "health recruitment effect". Miners had lower arterial hypertension prevalence among them than unorganized sampling made of ordinary Kemerovo region population, 28.46 % and 53.29 % (p<0.001). We showed that statistically significant low risks of arterial hypertension among workers were due to occupational selection they had to undergo when being recruited. As we performed this correction as per "healthy recruitment effect" arterial hypertension risks for miners and drifters changed from statistically significant low to statistically significant high, from 0.55 (95 % CI 0.48–0.64) to 1.14 (95 % CI 1.04–1.26). So, if we want to assess arterial hypertension prevalence and risks in occupational groups where occupational selection can't be excluded we should perform this additional correction to remove "healthy recruitment effect".

Key words: *risk assessment techniques, arterial hypertension, working population, occupational selection, a healthy worker effect, healthy recruitment effect, hygienic assessment of working conditions, ESSE-RF.*

Nowadays arterial hypertension (AH) is considered to be a primary factor of cardiovascular diseases risk as well as most frequent reason for temporary disability which causes great employers' losses [11, 13, 17]. Arterial hypertension is known to be a multi-factor disease with genetic predisposition. Today occupational factors

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apart from conventional ones are more and more frequently considered as AH predictors [11, 14].

Work at coal-mining enterprises involves several conditions which have adverse effects on people health. We can mention such adverse factors as industrial microclimate (drastic thermal gradients and increased air humidity), mine dust, vibration, apparent physical and emotional loads [1]. All the mentioned factors exist at miners' workplaces in most cases and their levels exceed any permissible values. 58.4% of workers employed in coal industry have to work under excessive dustiness; 14.9%, increased humidity; 15.0%, adverse temperature conditions; 14.5% workers have to contact toxic chemicals [10]. There are high requirements to body functional reserves in occupational selection. It in its turn leads to the situation when only people who are fit in terms of health are allowed to occupy workplaces in this industry. In literature, this organized or unorganized occupational selection of more healthy employees among people working under adverse working conditions is called "a healthy worker effect" [3, 6, 19]. This effect becomes apparent via better health parameters of such workers in comparison with those working in more favorable conditions; thus, it creates an inadequate impression that adverse industrial factors may have protective influence on a body [6]. "Healthy recruitment effect" is a significant components of "a healthy worker effect". "Healthy recruitment effect" characterizes "a healthy worker effect" during an initial period of workers' occupational activities due to the fact that healthier people apply for a job with adverse industrial conditions or for a job in general in comparison with people who have poorer health or lower functional capabilities [6, 15]. Examination of morbidity in junior age groups allows to detect occupational selection occurrence and assess impacts exerted by adverse factors - AH predictors - on workers' health. So, it seems vital to analyze AH prevalence in miners' occupational groups as well as to calculate AH risks allowing for "healthy recruitment effect".

Our research goal was to assess arterial hypertension prevalence and risks of its evolvement among coal-mining workers.

Data and methods. We performed our research on workers employed at two large coal mines in Kemerovo region (2009-2011). Data on health state of 1,915 male workers were obtained in the course of annual preventive examinations. Working conditions were assessed as per workplaces certification results [9]. 3 separate groups to be examined were created as per hygienic characteristics. The first group was made up of middle and senior management, controllers, fitters, and other employees who worked "on the surface" (43.08%). The second group included mining devices drivers and underground devices drivers as well as electricians-fitters and underground mounters (25.9%). The third group was made up of underground miners and drifters (31.02%). Adverse factors had only slight influence on workers from the first group; their working activity involved only emotional loads. Occupational activities of workers from the second and the third group directly involved staying in a mine during the whole working shift and they had to undergo adverse impacts by unfavorable microclimate, heavy dustiness, noise, vibration, as well as labor hardness and intensity [2, 18]. Workers from the second group had to maintain mining devices and electrical equipment. The third group comprised occupations with unskilled labor as well as occupations which involved a worker's staying in a forced posture during his working shift [7].

We used data obtained during ESSE-RF research (Epidemiology of cardiovascular diseases in the RF regions, 2012-2013) as our reference group (the fourth group) [12]. We chose 700 men aged 25-64 out of a population sampling which was randomly created among working population of Kemerovo region. Occupational structure of our reference group was as follows: 32.38% workers with physical labor, 36.93%, with mental work, 23.44% were operators, and 7.25% were retired.

We measured blood pressure, put a diagnose and determined AH degree of people with blood pressure ≥ 140/90 mmHg or those who took anti-hypertension drugs during our research as they suffered from previously diagnosed AH in conformity with the recommendations by Russian Medical Society on Arterial Hypertension / Russian Scientific Society of Cardiologists.

The age of men was different in different groups: it was equal to 40.22±10.82 in the first group; 39.87±9.51, in the second group; 37.75±9.76 in the third group; 45.87±11.45 in the fourth group ($p<0.001$). We determined the following age structure among miners: 36.61% were younger than 35 (24.43% in the fourth group); 30.34% were 36-45 (21.86% in the fourth group); 33.05% were older than 46 (53.71% in the fourth group).

Data were statistically treated with descriptive statistic techniques and distribution-free statistics (Pearson's X^2 criterion). Critical level of statistic significance was set as being equal to 0.05. We compared actual AH prevalence among miners with the same parameters in the reference group, calculated relative risk (RR) and 95% confidence interval (CI). To eliminate age discrepancies between miners and the reference group, we performed direct standardization as per age (reference group data were taken as standard) [4, 5]. We calculated AH frequencies in the examined occupational groups; to calculate relative AH risk, we drew up contingency tables [8]. It is known that decrease in cardiovascular diseases risks occurs in occupational groups with working conditions involving adverse factors influence due to "healthy recruitment effect" and it leads to inadequate conclusions on good health state. To identify and eliminate "healthy recruitment effect" influence, we applied a technique created by experts from Scientific Research Institute for Complex Issues of Cardiovascular Diseases (S.A. Maksimov et al) [3, 8]. We determined if there was "healthy recruitment effect" and how apparent it was at the first stage; to do that, we studied AH prevalence in the youngest age group (younger than 35). At the second stage AH prevalence parameters standardized as per age were adjusted by a ratio between AH frequency in the youngest occupational age groups (younger than 35) and the youngest age group in the reference one (younger than 35) [3].

Results and discussion. Workers employed at mining enterprises really have lower AH prevalence in comparison with non-organized sampling of Kemerovo region population, 28.46% and 53.29%, correspondingly ($p<0.001$). The specific weight of people with AH in the occupational groups was as follows: 33.82% in the first group; 24.6%, in the second one; 24.24%, in the third one. Statistically significantly low AH risks were detected for miners in comparison with the reference group. Thus, RR was equal to 0.63 in the first group (95% CI 0.56-0.71); 0.46, in the second group (95% CI 0.39-0.55); 0.45, in the third group (95% CI 0.39-0.53).

As we eliminated structural age discrepancies with standardization, it only slightly changed initial values of occupa-

tional risks in the examined groups (Table 1).

We detected AH frequency increase by 16% in the first group; by 15% and 19% in the second and third group correspondingly; but AH risks remained statistically significantly low in all the occupational groups. Thus, RR amounted to 0.71 in the first group (95% CI 0.63-0.79); 0.50, in the second group (95% CI 0.43-0.59); 0.55, in the third group (95% CI 0.48-0.64).

AH prevalence and risks in the occupational groups: initial data standardized as per age and adjusted by "a healthy worker effect"

The examined parameters		Occupational group			
		1 group	2 group	3 group	4 group
A share of people older than 50, %		21,21	11,09	9,76	39,71
Initial AH frequency and risk	Frequency, %	33,82	24,6	24,24	53,29
	RR	0,63	0,46	0,45	–
	95% CI	0,5–0,71	0,39–0,55	0,39–0,53	–
Standardized AH risk and frequency	Frequency, %	37,57	26,71	29,57	–
	RR	0,71	0,50	0,55	–
	95% CI	0,63–0,79	0,43–0,59	0,48–0,64	–
Standardized AH risk and frequency, adjusted by "healthy recruitment effect"	Frequency, %	51,77	48,99	60,96	–
	RR	0,97	0,92	1,14	–
	95% CI	0,88–1,07	0,82–1,03	1,04–1,26	–

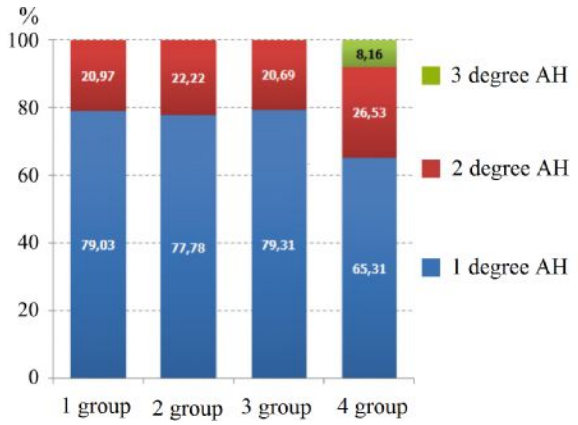

Figure. Prevalence of arterial hypertension as per degrees (%) in occupational groups among people younger than 35

AH frequency in workers younger 35 was equal to 16.83% on average and it was statistically significantly lower than in the reference group where it was equal to 28.65% (p=0.0004). AH prevalence in the age group younger than 35 was as follows: 21.16% in the first group; 16.67%, in the second group; 11.79%, in the third group. We should also note that no miner younger than 35 had 3 degree AH while this parameter was equal to 8.16 in the reference group. meanwhile, frequency of 1degree and 2 degree AH among all the examined people younger than 35 was comparable (Figure).

The obtained data allow us to consider young workers employed at coal-mining enterprises (younger than 35) to be the healthiest population group in comparison with the non-organized sampling of Kemerovo region population of the same age; it confirms that "healthy recruitment effect" really exists.

To eliminate "healthy recruitment effect" influence, we adjusted AH prevalence by a ratio between AH frequency in miners' groups who were younger than 35. As a result, AH frequency grew in all the examined groups, however, statistically significant discrepancies were detected only in the third occupational group: 60.96%

and 53.29%, correspondingly (p=0.005) (Table 1). AH prevalence was equal to 51.77% and 48.99% in the first and second groups correspondingly (p<0.05). As a result of adjusting the obtained data by "healthy recruitment effect" AH risks changed in the third occupational group from statistically significantly low to statistically significantly high, from 0.55 (95% CI 0.48-0.64) to 1.14 (95% CI 1.04-1.26). However, AH probability in two other groups was comparable with the reference group: RR was equal to 0.71 in the first group (95% CI 0.63-0.79) before the adjustment and 0.97 (95% CI 0.88-1.07) after allowing for "healthy recruitment effect"; 0.50 (95% CI 0.43-0.59) and 0.92 (95% CI 0.82-1.03) in the second group, correspondingly. So, AH risks for miners increased by 14% in the first group; by 22%, in the second one; by 31%, in the third one.

According to the obtained data AH probability grew most in the third occupational group among underground miners and drifters. Initially, people with these occupations tended to have quite low values of AG prevalence which could be explained through occupational selection effects which took place during recruitment. However, as workers became older and their working experience grew longer, they faced the same regularities of gradual AH frequency growth as did people from an unorganized population sampling. And here influence exerted by adverse factors which were AH predictors [1, 16] led to additional increase in AH risk. So, when assessing AH prevalence and AH risks in the occupational groups where occupational selection occurrence can't be omitted, it is necessary to perform additional adjustment to eliminate influence exerted by "health recruitment effect".

Conclusion:

Arterial hypertension prevalence among workers employed at coal-mining enterprises is lower in comparison with an unorganized sampling of Kemerovo region population and amounts to 28.46% and 53.29% correspondingly.

Lower arterial hypertension probability among miners is determined by occupational selection.

When "healthy recruitment effect" influence is eliminated, arterial hypertension risks grows considerably among underground miners and drifters in comparison with a general population sampling.

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RISK OF DUST BRONCHOPULMONARY PATHOLOGY DEVELOPMENT IN WORKERS EMPLOYED IN VARIOUS ECONOMIC BRUNCHES UNDER IMPACTS EXERTED BY OCCUPATIONAL RISK FACTORS: CLINICAL AND HYGIENIC ASPECTS

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We performed complex clinical and hygienic research on 234 workers suffering from occupational bronchitis; they were employed in petrochemical industry, mining, civil engineering, as well as in construction. Group of workers with occupational diseases comprised hose suffering from dust bronchitis and toxic-dust bronchitis. Workers employed in the examined branches had to work under exposure to production aerosols with complex structure and they working conditions had 3.2–3.4 hazard degree. We showed that occupational factors exerted negative influence on workers' health as they caused occupational bronchitis development, grave complications, and frequent associated diseases evolvement. The paper dwells on the results of our research on lipid peroxidation products content in workers exposed to production aerosols. We detected increased activity of free radical oxidation caused by impacts exerted by production aerosols; here we revealed that growth in lipid peroxidation products depended on duration of work under hazardous conditions. We set a goal to detect correlation between polymorph gene types of xenobiotics transformation enzymes and occupational bronchitis evolvement via polymerase chain reaction technique; to achieve this, we analyzed polymorphic locuses in a group of sick workers (131 people) and healthy ones (156 people). We determined genetic markers which had protective significance in terms of occupational bronchitis evolvement risk. The research results prove that occupational bronchitis nature and peculiarities of its clinic picture are determined both by occupational impacts and individual features of a worker's body.

Key words: *working conditions, risk factors, production aerosols, workers, occupational bronchitis, health state, health parameters, xenobiotics transformation genes.*

Today occupational diseases of the respiratory tract which occur at industrial enterprises are a great medical and social challenge as they are widely spread and do substantial economic damage due to persistent temporary disability of qualified staff [2, 4].

"Dust" diseases are multi-factor ones as they are caused by complex impacts exerted by environmental and genetic factors [5, 6,

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7, 12, 17, 19].

A lot of research proves that production aerosols are a risk factor causing occupational bronchitis [3, 4, 9]. Production aerosols tend to contain various components and their complex impacts on respiratory organs together with multiple factors of exogenous and endogenous nature existing at different productions lead to a great variety in clinical signs of occupational bronchitis [1, 13, 15, 18].

A human body can possible have an individual response to impacts exerted by occupational environment factors; this response can often be determined by genetic polymorphism of enzymes which participate in biological transformation of xenobiotics, There are scientific papers which prove a contribution made by polymorphic cytochrome P-450 genes and glutathione transferase genes in pathogenetic mechanisms of occupational bronchopulmonary system diseases [8, 14].

Our research goal was to study clinical and hygienic peculiarities of how bronchitis evolved and its clinical course in workers exposed to production aerosols.

Data and methods. We performed a profound examination of 234 patients suffering from occupational bronchitis and treated in the in-patient clinic of Ufimskiy Scientific Research Institute for Occupational Medicine and Human Ecology. All patients were under dynamic observation since they had their diagnosis put; they were workers employed in petrochemical industry, mining, civil engineering, and in construction. We applied sanitary-hygienic techniques, clinical-laboratory techniques, molecular-genetic ones and statistic methods.

Working conditions the examined patients had to function in were assessed as per sanitary-hygienic properties of working conditions provided by Rospotrebnadzor Bashkortostan regional office; the assessment also allowed for results obtained by researchers from Labor Hygiene and Physiology Department of Ufimskiy Scientific Research Institute for Occupational Medicine and Human Ecology. We assessed occupational routes and working period spent under production dust impacts as well as occurrence of such predisposing hazardous factors as air temperature and humidity in a working area and physical loads.

Clinical-laboratory research included a complete blood count, biochemical blood study, microbiological examination of sputum, respiratory organs X-ray study, external respiration (ventilation function) assessment, and cardiac ultrasound. Peripheral blood parameters were assessed via electronic-pulse calculation of blood cells with "Sysmax" hematologic automatic analyzer (Japan). To assess intensity of free radical lipid oxidation, we detected malonic dialdehyde in blood serum via spectrophotometry. We performed a general sputum analysis, as well as analyzed it as per microflora content and its sensitivity to antibiotics. External respiration function was examined via computer flowmetry with "Spirolab II" spirometer.

The examined patients suffering from occupational bronchitis were divided into two groups depending on a production aerosol structure and nature:

Group I was made of patients with toxic-dust bronchitis caused by a production aerosol which contained toxic and/or allergenic compounds dust (140 people). Group II were patients suffering from dust bronchitis caused by weakly fibrogenic dust with low allergenic metals content (94 people). Males vs. females ratio amounted to 68% and 32% in group I, and 75% and 25% in group II correspondingly. Average age at

which occupational bronchitis was detected was 46.76±7.72. Age and working period didn't have any significant discrepancies in both groups. 156 healthy workers employed at an ore mining and processing plant with working period under hazardous conditions equal to 10 years were included into our reference group; they all didn't have respiratory organs pathology in their case history and were considered to be fit for further employment at their working places. Working period under hazardous conditions amounted to 13.28±6.6 years, and average age was 43.37±0.55 years.

All the examined patients from groups I and II were combined and then divided into smokers and non-smokers. Active smokers group comprised 112 people (47.9%), and ex-smokers group was made up of 41 (17.5%). 122 people were non-smokers (52.1%). A smoker's index was calculated for each smoker.

Molecular and genetic research was performed on 131 patients suffering from occupational bronchitis and on 156 healthy workers form the reference group. DNA was extracted as per a conventional technique of phenol-chloroform extraction [16]. We applied polymerase chain reaction of DNA synthesis to analyze polymorphic types of the first xenobiotics biotransformation phase genes (A2455G of CYP1A1 gene, C1053T of CYP2E1 gene, A415G of EPHX1 gene) and the second xenobiotics biotransformation phase genes (GSTM1, GSTT1 and GSTP1 genes). 53 people with dust bronchitis and 78 people with toxic-dust bronchitis were included into an occupational patients group. All the patients were distributed into three groups as per their diseases severity: mild disease (38), average severity (21) and severe disease (72).

We performed mathematical processing with "Stitistica v.6.6" software («StatSoft»), and MS Office Excel 2007 applying Student's t-criterion, $\chi 2$ criterion with Yates correction for fourfold tables, and Fischer's criterion. Dependencies were estimated as per odds ratio, (OR).

Results and discussion. Basing on the performed complex of clinical and hygienic research we detected that toxic-dust bronchitis evolvement was related to long-term exposure of workers employed in petrochemistry, chemical industry, and at welding workshops (average working period 22.65±0.54) to production aerosols containing dust of toxic and/or allergenic compounds in concentrations which were 6-11 times higher than MPC (hazard class 3.3-3.4) together with unfavorable microclimate, in-plant noise, and labor process hardness (hazard class 3.1-3.2).

Dust bronchitis evolved due to exposure to weakly fibrogenic dust (average working period 22.61±0.53) which contained 6-8% of silicone dioxide. Patients suffering from dust bronchitis were mostly workers employed in underground pyrite ore mining and personnel of engineering workshops at civil engineering enterprises. Exposure to dust in concentrations 7-12 times higher than MPC (hazard class 3.3-3.4) when working period was long was frequently combined with negative impacts exerted by vibrations, noise, and unfavorable microclimate, and with physical loads (hazard class 3.1-3.2).

When analyzing complaints we revealed that cough prevailed among them all in each patient: 29.5% had non-productive cough, 45.7% had cough with mucoid sputum, 24.8% had cough with mucopurulent sputum. 25.6% complained on dyspnea during intensive exercise and fast walking, 50.4% had it during moderate exercise, 9%

had it even at rest, and only 14.9% patients didn't have such complaints. 34.2% patients had occasional wheezing and apparent dyspnea. 52.1% patients from group II and 41.4% patients from group I had mucoid sputum ($\chi 2=15.1$; p=0.0007; df=1). Mucopurulent sputum was more frequently detected in patients from group I (30.7%) than from group II (16.0%) ($\chi 2=5.80$; p=0.017; df=1). Clinical and functional deviations grew as the disease progressed and complications occurred. Objective signs corresponded to a stage of the disease. patients groups were comparable in terms of breathing disorders gravity and repeatability of complaints.

As we examined external respiration functions and applied x-ray diagnostics in the examined patients' groups we revealed signs of bronchopulmonary obstruction and lung emphysema in 62% patients and it gave us grounds to diagnose chronic obstructive lung disease. 38% of the examined patients had chronic non-obstructive bronchitis, 37.2% had diffuse pulmonary fibrosis, 24.8% had pulmonary hypertension signs. We detected radiological changes of cellular type which were characteristic for bronchictasia in 26.9% cases. Patients from group I had bronchictasia ($\chi 2=4.19$; p=0.04; df=1) and chronic pulmonary heart (30.0% against 17.02%) authentically more frequently than patients from group II ($\chi 2 =4.410$; p=0.03; df=1).

Patients suffering from occupational bronchitis had increased leucocytes, stab neutrophils, monocytes, and ESR in 38% cases; they had dysproteinemia (hypoalbuminaemia mostly due to increased α2-, β-globulins contents) in 18% cases.

Our research on free radical processes activity in patients groups I and II revealed increased intensity of lipid peroxidation which was 2.3 times higher than in the reference group (p<0.001) (Table1).

Table 1

Lipid peroxidation products levels in patients groups I and II, $M \pm m$

Parameter	Group I	Group II	Reference group
Malonic dialdehyde, μmol/l	5,53 ± 0,8*	5,47 ± 0,7*	2,42 ± 0,04

Note: * – validity of discrepancy with the reference group (p<0.001).

Patients suffering from occupational bronchitis tended to have greater lipid peroxidation activity estimated as per malonic dialdehyde contents as they working experience became longer.

As we performed microbiological examination of sputum we revealed that 74.8% patients with occupational bronchitis had mostly bacterial microflora consisting of 2-4 component associations.

Bacteria from Staphylococcus (75.1%) stem and Streptococcus (62.6%) stem prevailed among microorganisms detected in patients. Bacteria from Enterobacteriacea family and gram-negative non-fermentative bacteria were less frequently detected, in 18.7 and 13.8% patients correspondingly.

The greatest number of people with diagnostically significant seeding was detected in patients' group I where such bacteria as Kl. pneumoniae occurred 3.4 times more frequently than in group II; fungi Candida from stem, 2.7 times more frequently, and Br. Catarrhalis, 2.5 times more frequently (Figure 1).

Smoking as an independent factor can make a substantial contribution into chronic bronchitis development in people exposed to production aerosols [10, 11, 20].

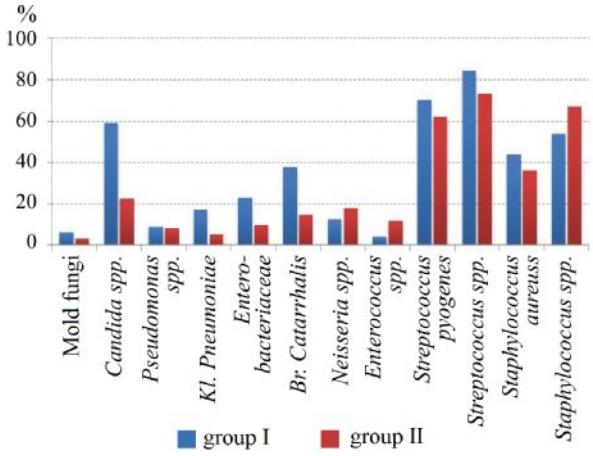

Figure 1. Microflora seeded from sputum of the examined patients from groups I and II, %

We analyzed ventilation disorders in patients depending on their smoker status allowing for an important contribution made by smoking in chronic bronchitis genesis. Non-smokers prevailed among patients suffering from occupational bronchitis with I degree of respiratory failure. Smokers and ex-smokers much more frequently had grave chronic bronchitis with apparent respiratory failure of II-III degree. Respiratory failure became more grave as a smoker index grew.

As most occupational factors are polytropic and workers are under combined exposure to several hazardous factors it determines frequent occurrence of associated diseases in patients suffering from occupational bronchitis.

19.2% examined patients had associated occupational pathology in other organs and systems; 9.4% of them had three occupational diseases, and 1.7% suffered from even four of them. As a rule, such diseases evolved in workers with long-term working experience (more than 20 years) and they tended to develop gradually and become chronic. Sensorimotor system pathology prevailed in the morbidity structure and it was mostly represented by vegetative-sensory polyneuropathy (13.25%), chronic lumbosacral radiculopathy (3.0%), scapulo-humeral periarthrosis (3.8%), and humeral epicondylitis (1.3%). Occupational ENT-organs pathology was detected in 5.0% patients (sensorineural hearing loss and allergic rhinitis).

We performed a retrospective analysis of medical files on 82 patients suffering from occupational bronchitis (852 case histories) with observation period over each patient being longer than 10 years. The analysis revealed authentic deterioration of all the ventilation parameters by the end of the examined period with transformation into obstructive and restrictive-obstructive disorders.

When patients had their first examination in a medical-social examination office we detected significant specific weight of disability (61.5% patients with toxic-dust bronchitis and 40% with dust bronchitis), 19.2% patients from group I and 20.0% patients from group II had the 2nd degree disability; 42.3% and 20.0% correspondingly had the 3rd degree disability. By the end of the examined period (after 10 years) a share of people with confirmed disability grew by 11.6% in group I and by 26.7% in group II. We should note that a number of people with more grave disability (2nd degree) increased by 23.1% in group I and by 6.7% in group II.

We compared patients with occupational bronchitis and healthy workers in order to identify genotypes associated with predisposition to bronchopulmonary system failures. We didn't reveal any substantial discrepancies between the overall sampling of people with occupational bronchitis and the reference group as per polymorphic locuses of CYP2E1, GSTM1 and GSTT1 genes

We detected statistically significant increase up to 23.7% in *2C allele of A2455G polymorphic variant of CYP1A1 gene in healthy workers in comparison with 13.5% in people with occupational bronchitis ($\chi 2=7.05$; $p=0.009$), and it marked their re-

sistance to the disease (OR=0.50; 95%CI 0.30-0.84).

Examination of frequencies distribution for microsomal epoxide hydrolase (EPHX1) gene phenotypes revealed increase up to 20.5% in frequency of fast microsomal epoxide hydrolase phenotype among health workers in comparison with 10.9% among patients with occupational bronchitis ($\chi2$=4.18; p=0.041) which can mean that people with fast epoxide hydrolase phenotype have greater adaptability. So, fast phenotype of T337C polymorphic variant of EPHX1 gene is in this case a resistance factor which reduces risks of occupational bronchitis evolvement (OR=0.47; 95%CI 0.23-0.97).

Analysis of A313G polymorphic variant of GSTP1 gene revealed increase up to 45.5% in *A*G heterozygote genotype in healthy workers in comparison with 31.2% in patients with occupational bronchitis ($\chi2$=5.38; p=0.021). Presumably *A*G genotype is a marker showing resistance to occupational bronchitis evolvement (OR=0.54; 95%CI 0.32-0.92) (Table 2).

Table 2

Frequencies distribution for A313G polymorphic variant of GSTP1 gene in patients with occupational bronchitis and in the reference group

Genotype	Patients with occupational bronchitis		Reference group		χ^2	*p*
	n	%	*n*	%		
**A*A*	75	60,0	79	50,6	2,09	0,149
**A*G*	39	31,2	71	45,5	5,38	0,021
**G*G*	11	8,8	6	3,9	2,19	0,139

We performed comparative analysis of frequencies distribution for genotypes and polymorphic locuses alleles of CYP2E1, EPHX, GSTM1, GSTT1 genes in groups of patients with toxic-dust bronchitis and dust bronchitis and didn't reveal any significant discrepancies. Frequency of *1A*2C genotype of CYP1A1 gene A2455G polymorphic variant was more than 2 times lower among patients with toxic-dust bronchitis (10.4%) in comparison with the reference group (23.7%) ($\chi2$=4.23; p=0.039; df=1), which was a marker showing resistance to toxic-dust bronchitis evolvement (OR=0.37; 95%CI 0.14-0.96).

Comparison of toxic-dust and dust bronchitis based on the analysis of polymorphic variants of microsomal monooxygenase system genes and antioxidation protection genes showed a basic similarity of occupational bronchitis pathogenesis which occurred due to weakly fibrogenic dust inhalation and due to inhalation of a production aerosol with complicated structure including generally toxic substances and sensitizing substances.

Analysis of A2455G polymorphic variant of CYP1A1 gene in groups of patients with various clinical course revealed that *1A*2C heterozygote genotype of A2455G polymorphic variant of CYP1A1 gene was detected in 35.3% patients with mild disease severity, in 22.2% patients with average disease severity, and in 12.5% patients with severe disease and it wasn't at all detected in patients with extremely severe disease ($\chi2$ =13.89; p=0.031; df=6) (Figure 2).

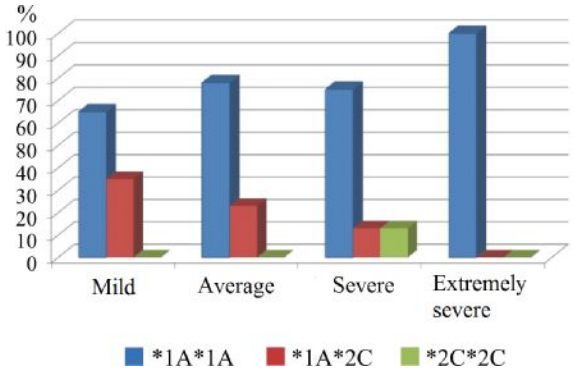

Figure. 2. Frequencies distribution for genotypes of A2455G polymorphic variant of CYP1A1 gene in patients from group II depending on diseases severity

CYP1A1*1A*2C heterozygote genotype can be considered a protective factor in relation to bronchitis evolvement in the group of patients suffering from toxic-dust bronchitis.

So, our research allowed us to detect that a nature of evolving occupational bronchitis and peculiarities in its clinical picture were determined not only by hazardous occupational factors but also by individual peculiarities of a patient. Due to our examining polymorphism of xenobiotics biotransformation enzymes genes we revealed genetic markers associated with workers' resistance to occupational bronchitis.

Conclusions:

1. Workers employed in the examined economic branches had to function in working conditions characterized with prevailing exposure to production aerosols with complicated structure corresponding to 3.2-.4 hazard class. Workers employed at petrochemical and chemical enterprises and at welding workshops mostly suffered from toxic-dust bronchitis caused by exposure to a production aerosol with complicated structure containing generally toxic, sensitizing and irritating dust; workers employed in mining and civil engineering suffered from so called dust bronchitis caused by exposure to weakly fibrogenic dust with low allergenic metals content as opposed to group I.

2. Occupational bronchitis in workers exposed to production aerosols had a number of peculiarities: the diseases tended to progress which led to early disablement due to obstructive-restrictive disorders growth, prompt occurrence of various infections, and grave complications including pulmonary heart.

3. We detected hyperactivation of free radical oxidation processes under long-term exposure to production aerosols; we also detected authentic increase in lipid peroxidation products as working experience under hazardous conditions grew.

4. There are protective markers in relation to occupational bronchitis evolvement. They are *2C allele of A2455G polymorphic variant of CYP1A1 gene, AG genotype of A313G polymorphic variant of GSTP1 gene, and fast phenotype of T337C polymorphic variant of EPHX1 gene. *1A*2C genotype of A2455G polymorphic variant of CYP1A1 gene is associated with milder clinical course of dust bronchitis.

5. We present a set of informative molecular-genetic and biochemical markers which can be used in assessing risks of occupational bronchitis evolvement and in individual forecasts for the disease clinical course.

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OCCUPATIONAL REPORIDUCTIVE SYSTEM DISEASES IN FEMALE WORKERS EMPLOYED AT WORPLACES WITH HARMFUL WORKING CONDITIONS

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The paper outlines the data obtained in the course of long-term research dedicated to studying the extent to which reproductive system pathologies in workers with high-risk occupations are occupationally induced. Their peculiarity is joint impacts of various occupational factors (for example, impacts exerted by chemicals together with physical and biological factors, and labor hardness and intensity as well) on a female body.

Our research goal was to examine the extent to which reproductive system pathologies in workers with high-risk occupations were occupationally induced. To achieve it, we applied statistical estimate of correlation between health disorders and work.

Our occupational group included a number of occupations with harmful or hazardous working conditions in civil engineering, metallurgy, chemical industry, polymer-processing industry, and health care as well. As a rule, working conditions class of workers from the examined groups varied from 3.1 to 3.3; and occupation with permissible working conditions were used as a comparative group.

The research results revealed that there are certain occupations with high risk of reproductive health disorders evolvement and infants development pathologies evolvement. They are:

– model makers and checkers in civil engineering and crane operators at a metallurgic plant;

– analysts at chemical analysis laboratories, chemical engineers in chemical industry (including petrochemical plants, polymer-processing plants, and organic synthesis plants);

– surgeons, obstetrician-gynecologists, midwives, surgical nurses working in in-patient departments.

Estimate of correlation and occupational dependence of reproductive system diseases on working conditions revealed that women with harmful working conditions (3.1–3.3 hazard class) had defective pregnancies or labor pathologies which had strong and average correlation with working conditions. Health disorders in newborns were estimated as per very strong correlation with mother's work. Thus, we can state that a mother occupational risk induction for a child health is fundamentally proved. On the basis of the obtained results we rank female workers with 3 class 2 harm degree working conditions as having an occupation with high risks of reproductive health disorders.

We worked out an algorithm aimed at managing these risks; it should be applied in order to lower occupational risks for reproduction in female workers.

***Key words**: female workers, working conditions class, reproductive health, newborns' health, occupational risk, statistic estimate of correlation.*

Introduction. An issue of estimating damage to workers' health caused by unfavorable production factors has been attracting experts' attention for several decades; however, for the first time such concepts as "occupational risk" and "occupational risks management" appeared in the RF Labor Code only in 2011 (Federal Law No. 238 issued on July 18, 2011 "On making alterations into the Russian Federation Labor Code).

Occupational risk is a probability of

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damage to health resulting from impacts exerted by hazardous and (or) dangerous production factors when a worker fulfils his or her working tasks in conformity with a labor contract or in any other cases; a procedure of its assessment is set forth by a federal executive authority.

Occupational risks management is a set of interrelated activities which are elements of labor safety management system and which include measured aimed at detecting, assessing and lowering occupational risks (Federal Law No. 421 issued on December 28, 2013).

Actually nowadays each employer is to assess occupational risks for employees and implement efficient measures aimed at its elimination or reduction. However, only highly qualified experts in occupational medicine can solve such a task and even they sometimes don't allow for all the aspects related to occupational risks.

Assessment of a risk for the reproductive system is one of such aspects; such assessment is truly vital for the Russian Federation as approximately 49% of all working population are women [11].

Maternityd is the most important mission in a life of any woman. Unfortunately, great occupational risks can prevent female workers from fulfilling their reproductive functions.

Given all the above mentioned, we see an issue of preserving and improving workers' reproductive health as one of top priority tasks as it creates conditions for the country economic development. Actuality of this issue is confirmed by Russian and international documents. In particular, in 2004 the WHO adopted "Reproductive health strategy" and "Resolution on the family and health", and in 2007, "Global plan of action on workers' health" (2008-2017). The ILO issued a number of conventions on the issues: Convention No. 156 on workers with family responsibilities (1981), Convention No. 183 on maternity protection (2000), Convention No. 187 Promotional framework for occupational safety and health (2006), etc.

The RF Government issued an order dated March 08, 2017 which adopted the National strategy on action in the interests of women (2017-2022); it mentions the importance of reproductive health protection development, especially for working women due to the fact that approximately one million women are employed at working places with hazardous and/or dangerous conditions (1,145.1 thousand as per data collected in 2015).

A great number of the reproductive system diseases are proven to be occupationally induced; they cause problems with conception and child-bearing and may even lead to infertility [2, 7, 8, 14]. Experts are especially concerned about occupations with high risks as women having them are under joint effects exerted by various production factors (for example, chemical impacts together with physical and biological factors, labor hardness and intensity etc.) [12,15]. Unfavorable effects can occur in case of chemicals concentrations being equal to or even lower than permissible levels due to the fact that if various factors impacts are unidirectional, either additive or synergy effects can be observed.

Our goal was to examine occupational causality of the reproductive system pathology in workers with risky occupations calculated with the technique of statistic estimation of correlations between health disorders and work which was created by professor E.I. Denisov [1] basing on data taken from literature and our own long-term research.

We made up a group of risky occupations which comprised a number of occupations with hazardous or dangerous working conditions from civil engineering, metallurgy, chemical industry, polymer-processing industry, and public healthcare as well.

Results. We detected that workers employed at metallurgic productions and in public healthcare had the most unfavorable working conditions (3.2-3.3 danger category as per P. 2.2.2006-05 [10]); workers employed at petrochemical production and polymer-processing productions had 3.1 danger category of working conditions.

We analyzed reproductive disorders in workers employed at civil engineering productions as galvanizing workers, patternmakers, and checkers [3]. We detected average and high correlation between reproduction pathology and occupational activity.

Increased occupational risk of inflammatory processes evolvement in internal genital organs was detected in patternmakers (OR=4.67 (95% CI, 1.31−16.59) and checkers (OR=3.45 (95% CI, 1.13−10.55). Moderately high risk of spontaneous miscarriages was detected among checkers and was equal to OR=3.24 (95% CI, 1.06−9.90) (Table1).

Table 1

Occupational risk (OR odds relation) of reproductive disorders in female workers employed at civil engineering productions

Reproductive system diseases	Basic occupations					
	Galvanizing workers		Patternmakers		Checkers	
	OR	95 % *CI*	*OR*	95 % *CI*	*OR*	95 % *CI*
Inflammations in female pelvis organs	0,77	0,18–3,41	**4,67***	**1,31–16,59**	**3,45***	**1,13–10,55**
Genital organs descent	0,61	0,17–2,26	1,43	0,44–4,70	1,34	0,51–3,59
Spontaneous miscarriages	1,78	0,48–6,66	1,11	0,27–4,62	**3,24***	**1,06–9,90**
Gestosis of the second half of pregnancy	2,08	0,49–8,93	3,26	0,79–13,55	1,46	0,40–5,30
Threat of miscarriage	1,27	0,39–4,13	1,03	0,30–3,52	1,62	0,61–4,28

Note: *** –** changes are statistically significant, P <0.05

Such an occupation as a crane driver is the most unfavorable for women in metallurgy (3.3 danger category) as it is characterized with joint effects exerted by labor hardness, local vibrations, and heating microclimate. When we examined occupational causality of reproductive system pathology among such workers, we chose office workers with working conditions belonging to 2 danger category as our control group.

As we analyzed occupational causality of the detected gynecological pathology in female crane drivers, we revealed that an etiological share of production factors in infertility evolvement was equal to more than 50%; it allowed us to consider occupational causality to be high, and female infertility to be occupationally induced pathology.

As we studied health state of pregnant female workers, pregnancy and birth complications, as well as newborns health, we revealed that pregnancy problems were closely related to unfavorable working conditions; the highest occupational causality was observed for threat of miscarriage, gestosis of the first half of

pregnancy, intrauterine hypoxia and a fetus arrested development (Table 2).

Similar data were obtained when health state and reproductive function of female workers employed at chemical productions were analyzed; we assigned oil processing industry, polymers production and processing, and organic synthesis to such productions [4,5,9]. Such chemical production occupations as chemical analysis laboratory workers and chemical engineers were considered to be highly risky as they were characterized with joint effects exerted by chemical factors, labor hardness, and heating microclimate (Table 3).

As per data obtained by A.A. Potapenko и M.R. Alex [6, 13], public healthcare is one of the spheres with the biggest number of problems for female health. Thus,

Table 2

Occupational risk of reproductive health disorders in female crane drivers

Reproductive system diseases	Frequency, *M* ± *m*, %	*OR*	*CI* 95 %	*EF*, %
Inflammations in female pelvis organs	53, ± 2,5	1.44	0,77–2,70	23,08
Menstrual cycle disorders	24,3 ± 3,39	2,16	1,04–4,46	46,67
Hysteromyoma	26,5 ± 3,48	2,02	1,0–4,04	42,86
Mammary gland diseases	7,5 ± 2,08	1,95	0,4–8,6	46,67
Infertility	17,5 ± 3,0	2,44	1,0–4,76	54,29
Threat of miscarriage during the 1st half of pregnancy	84,7 ± 3,95	**15,53***	**8,0–30,14**	68,89
Threat of miscarriage during the 2nd half of pregnancy	66,6 ± 3,89	20,75	9,9–43,18	86,81
Gestosis of the 1st half of pregnancy (toxicosis)	39,04 ± 3,39	**3,84***	**1,8–7,8**	63,41
Gestosis of the 2nd half of pregnancy	26,6 ± 2,92	1,84	0,8–3,9	38,19
Iron deficiency anemia of pregnant	53,3 ± 3,72	2,57	1,39–7,7	42,31
Chronic intrauterine hypoxia	37,1 ± 3,33	**7,09***	**3,12–16,09**	79,29
Intrauterine arrested development of a fetus	20,0 ± 2,61	**7,33***	**2,2–23,6**	83,52

Note: *** –** changes are statistically significant, P <0.05.

Table 3

Occupational risk of reproductive health disorders in female workers employed at petrochemical productions

Reproductive system diseases	Frequency, *M* ± *m*, %	*OR*	*CI* 95 %	*EF*, %
Inflammations	53,9 ± 2,5	**2,1***	1,14–3,79	33,3
Benign neoplasms in uterus and uterine adnexa	29,1 ± 2,3	2,00	1,29–3,12	41,1
Fibrous-cystic mastopathy	24,8 ± 2,2	**2,23***	1,01–4,9	48,0
Menstrual function disorders	9,5 ± 1,5	2,06	0,95–4,47	49,1
Infertility	6,3 ± 1,2	3,10	0,4–24,6	66,7
Spontaneous miscarriages	8,9 ± 1,4	2,22	1,00–5,10	52,3

Note:* – changes are statistically significant, P <0.05

danger category of working conditions of surgeons, dentists, obstetrician-gynecologists, phthisiologists, nurses, and workers employed at clinical-diagnostic and bacteriological laboratories was assessed as 3.3; radiologists, physical therapists, and functional diagnostics experts, as 3.2. We should also highlight joint effects exerted by chemical and biological factors together with labor hardness and intensity which occur in these occupations.

We detected high gynecological morbidity among public healthcare workers especially such ones as menstrual health disorders, inflammations, and genital organs descent.

We revealed occupational causality of reproductive disorders practically for all the examined occupations, especially for obstetrician-gynecologists and surgical nurses (Table 4).

As we analyzed pregnancy and birth pathologies in medical workers we revealed that all the birth complications occurred in them authentically more frequently ($p<0.001$), than in the control group (94.5±0.79 against 59.31±4.08 in the control group).

Table 4

Occupational risk of reproductive disorders in medical workers

Reproductive system diseases (ICD 10)	Obstetrician-gynecologists				Surgical nurses			
	M ± *m*, %	*OR*	*Cl* 95 %	*EF*, %	*M* ± *m*, %	*OR*	*Cl* 95 %	*EF*, %
Menstrual cycle disorders	22,4 ± 3,5	**2,28**	1,21–4,30	63	32,5 ± 3,7	**2,58**	1,47–4,53	61
Inflammations in female pelvis organs	28,8 ± 4,1	**2,23**	1,13–3,65	55	32,5 ± 3,7	**2,10**	1,34–3,29	53
Genital organs descent	12,0 ± 2,9	**2,65**	1,11–6,31	63	32,5 ± 3,7	**2,22**	1,0–4,93	54
Threat of miscarriage	34,5 ± 4,5	**2,82**	1,90–4,19	46,5	32,5 ± 3,7	**2,35**	1,66–3,33	57,6
Gestosis of the 2nd half of pregnancy	20,0 ± 3,8	**2,07**	1,25–3,43	25,0	32,5 ± 3,7	1,87	1,24–2,84	46,8

Note: * – ICD 10 is international classification of diseases, the 10th review

Discussion. As a result of the performed research we detected that occupations with high risks related to reproductive health disorders in workers and pathologies in children during their first year of life were the following:

- patternmakers and checkers in civil engineering and crane drivers in metallurgy;

- chemical analysis laboratory workers and chemical engineers in chemical industry (including petrochemical production, polymer processing, and organic synthesis);

- surgeons, obstetrician-gynecologists, midwives, and surgical nurses employed at in-patient hospitals.

Our assessment of correlations between reproductive system diseases and working conditions and occupational causality of such diseases revealed that women who had to work under hazardous conditions (3.1-3.3 danger category) had pregnancy complications and birth pathologies which were highly and averagely correlated to their working conditions. Health disorders in newborns were assessed as being greatly correlated to a mother's work. So, we can consider a fact of a mother's occu-

pational risk inducing health disorders in a newborn to be fundamentally proven. Basing on the obtained results, we assigned certain occupations into highly risky one as per reproductive health disorders; those were occupations with 3.2 danger category as per hazardous working conditions. Summary data on occupational causality of reproduction disorders and degree of correlation between these disorders and work of females employed in the examined industries are given in Table 5.

To decrease occupational risks for reproduction in female workers, we created an algorithm of actions aimed at managing this risk (Figure). A primary assessment of the risk for all the women of childbearing age is performed at the first stage; it can be a re-assessment in case any changes occur, for example, pregnancy, recent childbirth, or breastfeeding. It is also necessary to give female workers complete information on a potential risk both for their own health and for health of a newborn.

Table 5

Occupational causality of reproductive health disorders in a number of occupations from some industries

Reproductive health parameters	Public healthcare	Metallurgy	Chemical industry	Petrochemical industry	Civil engineering
Menstrual cycle disorders	high		very high	high	
Benign neoplasms	high	average	high	average	
Infertility		high	high	high	
Metroptosis and colpoptosis	very high			average	average
Inflammation in pelvis organs				high	very high
Anemia of pregnant	average	average			
Threat of miscarriage during the 1st half of pregnancy	high	very high	average	high	average
Threat of miscarriage during the 2nd half of pregnancy	high	almost full	average	high	average
Gestosis of the 1st half of pregnancy		high			
Gestosis of the 2nd half of pregnancy	average	average	average	very high	very high
Intrauterine hypoxia of a fetus		very high	very high		
Congenital malformations of a fetus			high		
Intrauterine arrested development of a fetus		almost full			
Stillbirths			average		
Perinatal damage to central nervous system			high		
Preterm delivery			high		
Miscarriages				high	average

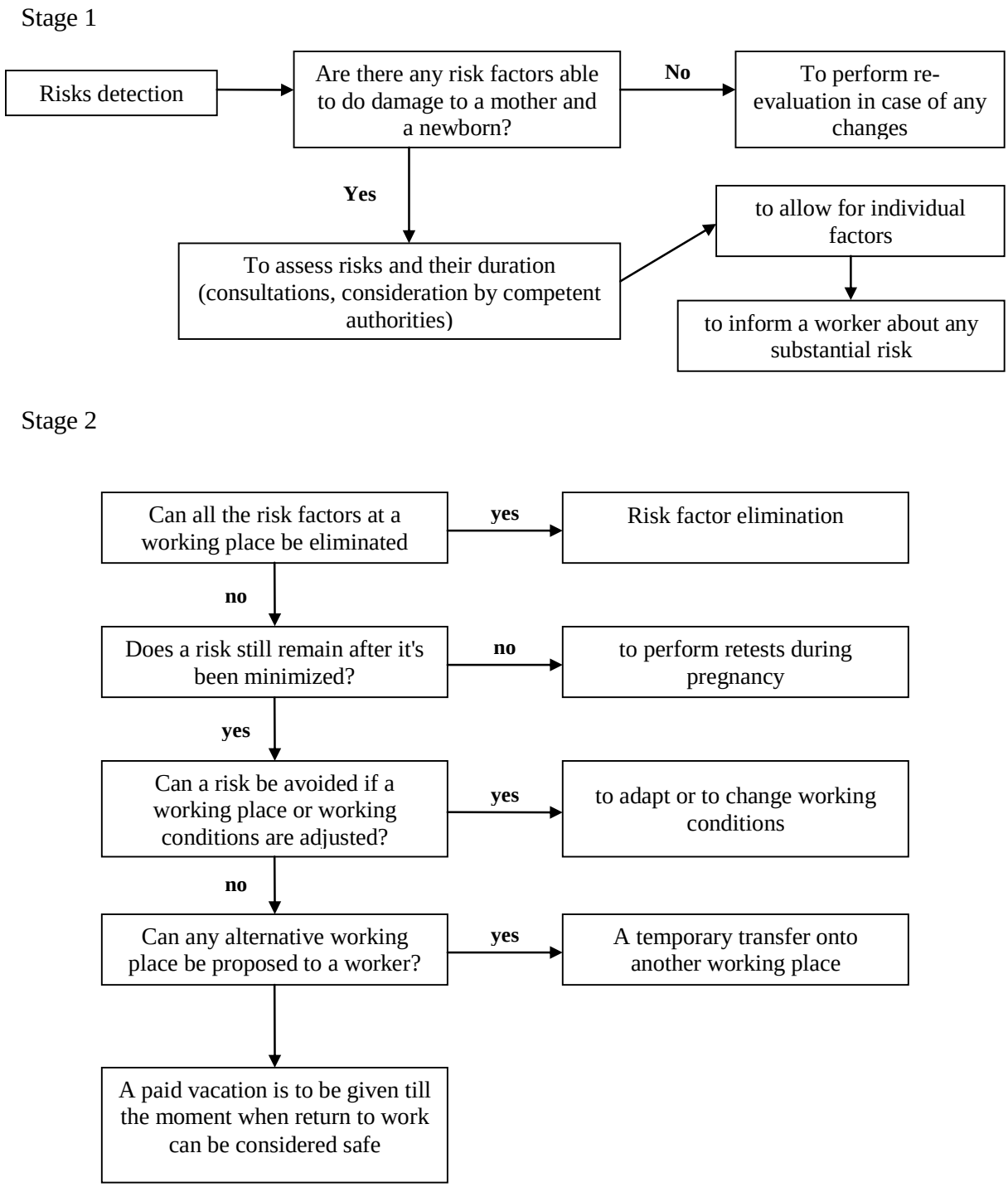

Figure. An algorithm for managing occupational risks for the reproductive system

The second stage in risk management comprises issues of eliminating risk factors at a working place. It is obvious that a situation in which risk factors can be eliminated and permissible working conditions are created is the most preferable.

But if a risk still remains after its minimization it is necessary to take further steps aimed at a working place adjustment (for example, to apply up-to-date engineering and design solutions, improved equipment and technological processes), and working conditions improvement.

If even a minimal risk for a female worker's reproductive health still exists, it is necessary to offer a temporary transfer to an alternative working place, or in case there isn't any, to grant a paid vacation till the moment when return to work is considered to be completely safe.

This created algorithm can be applied in any sphere of activity where women are employed.

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A PRIORI ASSESSMENT OF OCCUPATIONAL HEALTH RISK FOR VEGETABLES GREENHOUSE WORKERS

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We performed comprehensive hygienic examination of working conditions in greenhouses at a greenhouse complex in Saratov region. Our research goal was to a priori assess occupational health risk for greenhouse workers on the basis of working conditions classification as per deviations of environment parameters and working process from the existing hygienic standards. We examined microclimate parameters in cold and warm seasons, contamination or working area air with hazardous chemicals and aerosols; we also performed occupational and time studies of work activities when basic working tasks were accomplished during an annual vegetables growing cycle in greenhouses. We detected that greenhouse workers during their working activity were exposed to a set of hazardous factors; the prevailing ones were heating microclimate, occurrence of hazardous chemicals and dust in increased concentrations in working area air, hardness of labor process which involved excessive physical exercise, long-term work in an inconvenient posture, frequent body bendings, and necessity to spend a lot of time standing. Overall hygienic assessment of greenhouse working conditions corresponded to 3 degree category of hazardous conditions (3.3 danger class) allowing for impacts exerted by a set of hazardous working environment factors and working process itself during annual working cycle. Hazardous working conditions caused occupational health risk for greenhouse workers which, in conformity with R 2.21766-03, corresponded to high (intolerable) risk when urgent activities aimed at its reduction were to be accomplished. Our research result prove that it is vital to perform further research on greenhouse workers health as per data on periodical medical examinations, more profound study of morbidity with temporary disablement, and other socially significant health parameters.

Key words: *greenhouse workers, working conditions, hazardous production factors, occupational health risk, a priori assessment.*

Nowadays new technologies are being implemented in the sphere of greenhouses cultures growing; they involve replacement of soil mixtures with hydroponic substrates (coir fiber, silicate cotton, etc.), automation and mechanization of all technological processes, introduction of fertilizers solution to each plant through a drop watering system. But all these innovations unfortunately haven't resulted in elimination of all the working process factors which can be hazardous for greenhouse workers' health. Occupational activities of greenhouse workers still involve functioning under unfavorable microclimate determined by specific technological processes and increased leak resistance of cultivating facilities, contacts with pesticides, agricultural chemicals

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and products of their destruction, biological protection agents and disinfecting agents, as well as by labor process hardness and intensity [2,4,7,8,11]. Our analysis of scientific literature proves that hazardous working conditions exert negative impacts on female greenhouse workers [1,3,5]. Unfavorable working conditions are risk factors causing general and occupational diseases evolvement in greenhouse workers; such diseases may lead to temporary and, in some cases, to persistent lost of working capacities [12,13,14,15].

Given all the above-stated, examination and hygienic assessment of working conditions which exist in the sphere of greenhouse plants cultivating and creation of preventive activities aimed at eliminating occupational diseases risk for greenhouse workers' health can be considered vital.

Our research goal was to perform a priori assessment of occupational risks for vegetables greenhouse workers' health on the basis of working conditions classification as per degree of deviations in working environment parameters and labor process form the existing hygienic standards.

Data and methods. We accomplished our research on one of large greenhouse complexes in Saratov region specializing in year-round growing of tomatoes and cucumbers on hydroponic substrate. We carried out complex hygienic examinations of working conditions which a basic occupational group - vegetable growers - had to work under. We examined microclimate parameters, working area air contamination with hazardous chemicals and sprays; we performed occupational and time studies of working activities when basic working tasks were performed during an annual working cycle; all our examination were performed with the use of conventional techniques applied in occupational hygiene and medicine.

Working factors and labor process factors were hygienically assessed as per deviations in their actual parameters from the existing hygienic standards according to P 2.2.2006-05 [10]. Occupational risk was assessed in conformity with a technique fixed in P 2.2.1766-03 [9].

All the obtained data were statistically processed with the use of Microsoft Office-2007 (MS Excel-07, MS Word-07) software, and Statistica 10.0 software.

Results and discussion. A greenhouse complex which was chose as our research object is a complicated engineering construction equipped with all the necessary tools to grow vegetables in conformity with the adopted technology. Vegetables are grown in blocks of greenhouses with glass covers; greenhouses are combined in 4 blocks, each block containing 4 greenhouses (the overall greenhouses square amounts to 24 hectares, each greenhouse square is equal to 1.5 hectares). The complex also has amenity rooms and auxiliary rooms.

Greenhouses are also equipped with stationary technological systems of water heating, ventilations, cover shading, feeding with carbon dioxide, additional lighting, automated regulating and managing the equipment in order to maintain fixed temperature and humidity regime (air temperature for growing cucumbers is to be 19-28°C and air humidity, 70-90 %; air temperature for growing tomatoes is to be 18-26°C, and air humidity 60-70%).

Lighting in the greenhouses is natural due to glass covers; there is also additional lighting (luminous lamps). Ventilation is also natural (fanlights). Water supply and sewerage are centralized. Water taken from this centralized water supply system is also used for drinking. Heating comes from the

own boilers which function due to natural gas. Technological processes related to watering and fertilizers introduction, as well as transportation and cargo handling are performed by machines.

Certain stages in the process of vegetables growing in greenhouses require application of agricultural chemicals serving as root-feeding and top-feeding. Top-feeding is a basic way to provide plants with microelements; it is usually done through spraying plants with agricultural chemicals solutions. Root-feeding is done via introducing fertilizers solutions to each plant through a drop watering system. ready solutions are directly fed in these drop watering systems. Vegetable growers don't have any direct contacts with agricultural chemicals. Air feeding of plants is done with carbon dioxide during the whole vegetation period from 7 a.m. to 19 a.m.; preset concentrations are maintained by an automatic regulation system.

To fight plant pests and diseases, pesticides (insecticides and fungicides) are widely used at the complex. Treatment with pesticides is usually performed in the evening by a specialized group of workers who are responsible for plants protection; after it greenhouses usually remain closed for a long period, from 12 to 24 hours. But sometimes vegetable growers enter greenhouses on the next day in the morning thus violating the rules on safety working procedures after chemical treatment with pesticides; it proves that they are exposed to effects exerted by pesticides residues. The examined complex usually applies the 3th generation pesticides which are mostly represented by synthetic pyrethroids and hormonal preparations. Their basic peculiarities are abilities providing faster self-destruction in the environment. Such biological agents as antibiotics, vitamins, and snouted mites which eliminate plant pests, are also used in the complex activities.

Agricultural technology at the examined complex consists of a number of successive stages which differ in their duration and which are characterized with a complicated structure involving a lot of operations and high labor input required for production processes. These are the main stages which vegetable growers have to perform during their annual working cycle: sowing seeds and taking care of seedlings; seedlings planting; plants formation; harvesting and taking care of plants; plants mass disposal; greenhouses cleaning and disinfecting; getting greenhouses ready for the next working cycle; various maintenance and repair works (painting of equipment, mounts tightening, support columns adjustment, etc.).

Such works as seedlings growing, plants formation, harvesting, and taking care of plants, are the longest stages in the working cycle. During them a specific, artificially created temperature and humidity regime is supported in the greenhouses; this regime involves relatively constant increased air temperature and humidity levels. Works related to plant mass disposal and greenhouses disinfection took place twice a year and lasted from 5-10days up to 1 month a year; they were usually performed with all the doors remaining open and all the climatic systems being switched off.

Our research revealed that unfavorable microclimate was the basic peculiarity of vegetable growers' working conditions at all the production cycle stages (Table 1). Thus, during a warm period (when outdoors temperature was +20-24°C) indoors air temperature exceeded permissible levels. It was the highest (by 4-8°C than the permissible one) during such works as taking care of plants and harvesting. Envi-

ronmental heat load index (EHL-index) which reflected combined effects exerted by air temperature, its motion speed, and its humidity, on a human heat exchange with the environment, exceeded permissible values by 2,3°C - 3,0°C during this period.

When the same operations were performed during a cold time of a the year, air temperature was on average 7,8°C higher than the permissible one, and the EHL-index was 2,1°C higher. Relative air humidity exceeded its permissible levels by 2-5% practically during all the production cycle stages. Air mobility in the greenhouses was limited and didn't exceed 0.1 m/sec while its permissible values vary from 0.2 to 0.5 m/sec.

Therefore, vegetable growers were exposed to heating microclimate during the whole production cycle in the greenhouses. Hygienic assessment of working conditions as per microclimate parameters corresponded to 3.1 hazard category during seedlings growing and planting, and during plants formation; it corresponded to 3.3 hazard category during taking care of plants, harvesting, and plants mass disposal.

Heating microclimate (increased air temperature, high humidity, and limited air mobility) during a working shift together with intensive physical activity exerted negative impacts on heating state of female workers. When we performed an integral assessment of heating microclimate in conformity with the Methodical Guidelines 4.3.2755-10 [6], we revealed that risk of females' bodies overheating ranged from moderate to very high during a warm period of the year, and heat accumulation in the body ranged from 2.66 to 4.56 kJ/kg. Risk of overheating ranged from weak to moderate during a cold period of the year.

Air environment in the greenhouses was contaminated with hazardous chemicals at all the production cycle stages. Working area air was constantly contaminated with carbon dioxide which was fed to plants during the periods of plants formation and harvesting. Carbon dioxide concentrations didn't exceed MPC (650 ppm). However, carbon dioxide is known to exert negative influence on human

Table 1

Hygienic assessment of microclimate parameters during various works performed by greenhouse vegetable growers

Works (number of research)	Works category as per hardness	Warm period								Working conditions category	Cold period								Working conditions category
		Air temperature, °C		EHL-index, °C		Relative air humidity, %		Air speed, m/sec			Air temperature, °C		EHL-index, °C		Relative air humidity, %		Air speed, m/sec		
		permissible	actual	permissible	actual	permissible	actual	permissible	actual		permissible	actual	permissible	actual	permissible	actual	permissible	actual	
Growing and planting seedlings (n=136)	III	15,0–26,0	25,7 ± 1,5	18,0–21,8	22,8 ± 1,2	15–75	66 ± 4	0,3–0,5	0,43 ± 0,24	3.1	17,0–23,0	27,6 ± 0,4	20,5–25,1	25,5 ± 0,2	15–75	66 ± 4	0,1–0,3	0,17 ± 0,24	3.1
Plants formation (n=136)	IIa	18,0–27,0	28,1 ± 1,0	20,5–25,1	25,2 ± 1,4	15–75	66 ± 4	0,2–0,4	0,2 ± 0,1	3.1	17,0–23,0	22,8 ± 0,4	20,5–25,1	–	15–75	66 ± 2	0,1–0,3	0,15 ± 0,04	2
Harvesting (n=320)	III	15,0–26,0	29,4 ± 3,5	18,0–21,8	26,3 ± 3,4	15–75	71 ± 10	0,3–0,5	0,17 ± 0,14	3.3	13,0–21,0	25,7 ± 0,6	18,0–21,8	22,4 ± 0,7	15–75	77 ± 6	0,2–0,4	0,13 ± 0,04	3.1
Taking care of plants (n=292)	IIb	16,0–27,0	30,4 ± 3,6	19,5–23,9	27,3 ± 3,2	15–75	71 ± 12	0,2–0,5	0,15 ± 0,06	3.3	15,0–22,0	26,0 ± 0,6	19,5–23,9	22,6 ± 0,2	15–75	74 ± 7	0,2–0,4	0,12 ± 0,03	3.1
Plants mass disposal (n=165)	IIb	16,0–27,0	33,6 ± 0,9	19,5–23,9	29,0 ± 1,2	15–75	54 ± 11	0,2–0,5	0,3 ± 0,09	3.3	15,0–22,0	17,2 ± 2,7	19,5–23,9	–	15–75	70 ± 10	0,2–0,4	0,16 ± 0,04	2

health under regular and long-term exposure to it.

Greenhouses plants were treated with pesticides during the stage of taking care of plants; the task was performed in the evening by a special group of experts on plants protection. But terms of safe entrance to the greenhouses after such treatment were often violated at the complex, and vegetable growers were exposed to pesticides in concentrations which were 1.1-2 times higher than MPC during the whole year (3.1 hazard category).

When workers performed tasks related to plants mass cutting and getting plants residues ready for disposal, we detected formaldehyde in concentrations 1.4 times higher than MPC and phytogenic dust in concentrations 1.17 times higher than MPC in working area air. Working conditions were assigned into 3.1 hazard category as per working area air contamination with dust and hazardous substances.

Basic working tasks in the process of performing all the technological operations were handled manually and involved substantial physical dynamic loads on arms, body, and legs muscles, as well as static loads appearing when cargoes weighing 10 and more kg were lifted and moved and when a body was frequently bent over by more than 30 degrees. Vegetable growers had to work in a standing position during 85-90% of a working shift performing all types of working tasks and they had to constantly move around an area they were responsible for. Labor process hardness for vegetable growers corresponded to 3.2 and 3.3 hazard category when they performed working tasks at all the production cycle stages (Table 2).

Overall assessment of working conditions which greenhouse vegetable growers had to work under allowing for influence exerted by a set of hazardous working environment factors corresponded to 3.2 and 3.3 hazard category when various working tasks were performed by them during all the production cycle stages (Table 3).

Table 2

Assessment of labor process hardness for greenhouses vegetable growers during basic working tasks performance

Working tasks	Labor process hardness parameters						Overall labor hardness assessment
	Physical dynamic load (kg•m)	Static load (kg•sec)	Weight of a cargo being lifted and moved (kg)	Working posture		Body bendings, times per shift	
				standing, % of a shift	Posture characteristics, (% of a shift)		
Seedlings growing and planting	6840, 2 category	97172, 3.1 category	9, 3.1 category	92	53% inconvenient, 10% forced	582, 3.2 category	3.3 category
				3.2 category			
Plants formation	1500, 2 category	25467, 2 category	3, 2 category	75	30% inconvenient	210, 3.1 category	3.2 category
				3.1 category			
Harvesting and taking care of plants	4560, 2 category	39125, 2 category	10, 3.1 category	93	63% inconvenient, 15% forced	297, 3.1 category	3.2 category
				3.2 category			
Plants mass disposal	26560, 2 category	41180, 2 category	7, 2 category	90	30% inconvenient, 10% forced	220, 3.1 category	3.2 category
				3.2 category			

Table 3

Hygienic assessment of vegetable growers' working conditions when they performed basic working tasks

Working tasks	Working environment factors				Overall working conditions assessment as per P 2.2.2006-05
	Chemical	Microclimate	Fibrogenic aerosols (phytogenic dust)	Labor hardness	
Seedlings growing and planting	2	3.1	–	3.3	3.3
Plants formation	2	3.1	–	3.2	3.2
Harvesting and taking care of plants	3.2	3.3	2	3.2	3.3
Plants mass disposal	3.1	3.3	3.1	3.2	3.3

Table 4

Parameters and criteria of vegetable growers' occupational risk assessment when they performed basic working tasks

Working tasks	A priori risk parameters (as per P 2.2.1766-03)		
	Working conditions category (as per P 2.2.2006-05)	Occupational risk category	Urgency of activities aimed at risk lowering
Seedlings growing and planting	3.3	High (intolerable)	Urgent activities are required
Plants formation	3.2	Average (significant)	Actions are to be taken in due time
Harvesting and taking care of plants	3.3	High (intolerable)	Urgent activities are required
Plants mass disposal	3.3	High (intolerable)	Urgent activities are required

A priori assessment of occupational risk which was performed in accordance with the techniques stated in the Guide P 2.2.1766-03, allowed us to reveal that risk for vegetable growers' health varied from insignificant (moderate) to very high (intolerable) during the whole annual production cycle depending on working tasks performed by them (Table 4).

Therefore, in spite of new technologies implementation, greenhouse vegetable growers are exposed to impacts exerted by a set of hazardous factors during their working activities; these factors include heating microclimate, working are air contamination with hazardous chemicals, and labor process hardness.

Conclusions.

1. Integral assessment of working conditions which greenhouse vegetable growers had to work under was performed in conformity with the Guide P 2.2.2.2006-05 as per aggregation of all the working environment factors exerting their influence on workers' health during the whole production cycle. the assessment revealed that working conditions belonged to 3.3 hazard category.

2. We detected "high intolerable" occupational risk for vegetable growers' health and it proves that further research on health of workers from this occupational group is required. This research can be based on data obtained during periodical

medical check-ups, more profound examination of their morbidity causing temporary disability, and other socially significant health parameters.

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EXAMINATION OF SOCIAL AND PSYCHOLOGICAL FACTORS CASUING OCCUPATIONAL STRESS IN LABOR MIGRANTS

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We examined significance which social and psychological factors had in occupational stress evolvement in labor migrants who came to Moscow and Moscow region from Central Asia republics. A separate issue was sexual harassment occurrence which female migrants and Moscow region females faced. Psychological tension, i.e. occupational stress, is a contemporary danger in non-conventional working process (labor migration) and it attracts attention of occupational medicine experts. We determined that there were some social and psychological reasons for occupational stress, such as dissatisfaction with work, low level of integration in working teams, poor living conditions. As per questioning results we revealed single harassment cases (3-5%) and their number was the same both for female migrants and for females from Moscow region. Neuro-emotional labor intensity category amounted to 3.3-3.2 for millwrights, subways builders, steelmen, and road construction workers; it amounted to 3.1 for other workers; as for female migrants employed in social sphere, their work category was 3.2. The following physiological and psychological peculiarities characterize people with low working adaptation as per criteria of great occupational stress evolvement probability: low attention level, slow visual signals perception, prevalence of high systolic and diastolic blood pressure as a sign of arterial hypertension evolvement. Functional state of labor migrants mostly corresponds to "working strain of 1st and 2nd degree" and "overstrain". Staging in occupational stress evolvement in labor migrants is determined by level of labor neuro-emotional intensity.

It seems vital to provide social and psychological support for labor migrants which can include improvements in occupational training, informing workers on health risks occurring at their working places, training on safe working practices, development of occupational selection culture, organization of rational work and rest regime, providing social support for workers.

Key words: *labor migrants, social and psychological factors, occupational stress, neuro-emotional labor intensity.*

There are data in literature proving that psychosocial factors can cause stress at a workplace, deteriorate workers' health and lead to lower occupational activities efficiency [3,9]. Today such issues related to occupational stress as its reasons, peculiarities of its evolvement and its manifestations in various occupational activities are considered vital and worth studying [6,7,8].

Social and economic changes in post-Soviet states which have been taking place over the last decades have resulted in a complicated and unstable economic situation and it has influenced people's lives considerably as their living standards have dropped dramatically. A lot of them had to leave their homes and start looking for a job outside their countries. This trend can be traced in everyday life worldwide and it is also apparent in Central Asia republics. Employable citizens from former USSR

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republics come to many RF regions to find a job. Migrants face various stressors, psycho-emotional, psychosocial, and climatic-ecological factors in their working activities; these factors lead to decrease in body adaptation responses and increase in morbidity and mortality risks. Research performed on labor migrants working in various RF regions revealed that more than 30% of employable population lived under constant social and psycho-emotional stress [13,14,15].

As per data given by US National Center for Health Statistics, recently about 25% of men and women have mentioned apparent emotional stress at their workplace. Literature analysis revealed that certain consequences of strict demands at workplaces, poor work control, and insufficient support provided for workers became apparent in high health risks. Grave neuro-emotional load leads to body functional strain and overstrain which causes 3 times higher risks of primary hypertension evolvement [7]. Most potential stressors at a workplace are identified and described; they are divided into two basic groups, physical and psychological ones [2]. Physical factors which cause stress at a workplace include hazardous and dangerous working conditions: intense noise, high or low temperature, toxic gases or vapors impacts; all such factors are usually accompanied with work areas being overcrowded and isolated.

Economic globalization has resulted in growing competition among RF enterprises and it in its turn leads to stress factor growth among labor migrants who are employed at various enterprises and productions. Number of people suffering from occupational stress is growing most dramatically exactly among labor migrants. Basing on psychophysiological and epidemiological research on stress at a workplace, we detected a correlation between working environment, labor organization, and work nature with pathological physiological changes in adaptation processes evolving in migrants' bodies; these changes can cause risks of various occupational diseases [3,4,5,10,11].

Over the last years a lot of efforts have been made to reveal significance of certain psychosocial features such as labor motivation, labor satisfaction, and sexual harassment among female migrants; scientists have also been trying to find optimal solutions concerning working processes organization, rational workplace organization, and interpersonal relations harmonization. However there are no enough data on studying correlation between social and psychological parameters and labor intensity and physiological features of adaptation processes evolving in migrants' bodies; this very issue is our research subject.

Our research goal was to study significance and peculiarities of psychosocial factors in occupational stress evolvement in labor migrants who had different neuro-emotional loads at their workplaces.

Methods. Social and psychological research is usually based on questioning. Questioning is a technique involving use of questionnaires which were developed by WHO experts on the basis of "Country profile" and adapted by us to fit in with our tasks.

Our research included labor intensity characteristics based on job analysis; we took workers with certain hazard category and labor intensity and analyzed their jobs in conformity with P 2.2.2006-05 Guidelines allowing for their working activities structure giving scores to each type of loads [12]. Psychophysiological research was performed with the use of relevant specialized tests including health, activity, and mood assessment; stress; anxiety; rate of visual and auditory information reception via chronological reflexometry; atten-

tion concentration as per Bourdon test with Landolt rings with the consequent calculation of perceived information volume; short-term memory state as per "numbers-specific memory"; personality structure determination as per MMPI tests and Spielberg test. We applied Leary techniques to determine types of interpersonal relations in teams; these techniques were aimed at workers' psychological compatibility assessment.

We performed physiological assessment of cardiovascular system state as per heart rate, systolic blood pressure, diastolic blood pressure, functional changes index as per Baevskiy, and heart rate variability.

Research results. We performed our research on six professional groups which were selected allowing for neuro-emotional, psychosocial, and psychoemotional loads. We assessed significance of psychoemotional and psychosocial factors including labor satisfaction, and cooperation between supervisors and workers. Our examined groups 1 and 2 were made up of labor migrants employed by large construction enterprises in Moscow and Moscow region and working as builders erectors and steelmen; 3 group included subway builders; 4 group was made up of road builders; group 5 was workers employed at a vegetable warehouse; group 6 was made up of workers employed at a vegetable market. A separate group included female migrants employed in social sphere as nurses, child-minders, and housemaids. As we analyzed the structure of the examined groups we detected that basically they were 20.58±2.74 years old with working experience equal to 2.25±0.53 years. Overall, we examined 219 people. We processed our research results with the use of «Statistika for Windows» applied software and assessed our results validity as per Student's criterion.

Hygienic research results revealed that hazardous substances concentrations in working area air didn't exceed fixed standards for both groups of builders. Assessment of noise at workplaces helped to determine that noise level was 1.5-2 times higher than permissible one only for builders-erectors and builders-steelmen, and subway builders.

We performed functional research of workers' bodies in relatively favorable conditions (August - early September) when temperature, air relative humidity and speed were within optimal and permissible range.

Job analysis allowed us to assign labor of migrants employed by large construction enterprises and Mosmetrostroy (subway construction) to 3.3 labor danger category as per labor intensity related to apparent emotional loads and unfavorable work regime. Builders' labor is an injury-prone activity with high risk for one's life especially when work is performed at a height. Responsibility for other people's safety is determined by necessity to work in a team and to coordinate one's actions with other workers' actions and these workers can in some cases be rather low qualified. Labor intensity for road builders has 3.2 danger category as it involves working under time deficiency (it is necessary to form asphalt before it hardens) and it influences working activities. Neuro-emotional labor intensity is also increased due to constant control related to supervisors' attempts to lower wages. As road carpet compaction is performed manually with the use of a hand vibration tool, it exerts local vibration impacts on workers. Labor intensity of vegetable warehouse workers is caused by this work being highly injury-prone; by workers' ignorance about safe work practices; by necessity to work under time deficiency. All this allows to assign it to 3.2 danger category. Working activities of migrants

employed at a vegetable market involve substantial interpersonal communication, language barrier overcoming, possibility to meet negative attitudes which local population may have towards migrants. The obtained results prove that labor is intense and has 3.1 danger category. Labor intensity for female migrants employed in social sphere is caused by their working activities peculiarities especially when they have to attend to seriously ill patients, elderly people, or disabled. They often have to work longer hours, without any days off. In some cases emotional strain evolves, or unfavorable interpersonal relations occur. All these job peculiarities which are detected in social sphere activities allow us to assign such work to 3.2 danger category.

Our questioning results were necessary for assessing frequency of psychosocial factors causing stress at a workplace. We separately studied prevalence and reasons of such phenomenon as sexual harassment among labor migrants. Harassment as behavior which violates personal privacy of a worker is rather new for our country; it has been taken from the Anglo-Saxon countries legislation. Such behavior can include jokes, hints, obtrusive molesting, threats, etc. The US legislative system has certain peculiarities due to which a company and not a supervisor (worker) who committed illegal actions acts as a defendant in court cases related to complaints about harassment. Companies usually wish to avoid publicity and reputation losses so they prefer to pay compensations to a victim rather then lose their clients' respect. According to several authors, a concept of harassment and its difference from just simple courtship is determined by social and psychological perceptions which differ from country to country [1]. Questioning results revealed quite rare cases (3-5%) of harassment, and their quantity was equal both for female migrants and local people in Moscow region. About 77% women never faced harassment.

Prevalence of stress work factors related to apparent neuro-emotional loads turned out not to depend on danger category determined as per labor intensity parameters (Figure 1). Such work requirements as high work speed, and absence of freedom (control over work techniques and quality, its speed, order of operations needed to perform a task) were equal to 20.0±10.39% of cases for subway builders (3.3 danger category); 35.0±8.37% for vegetable warehouse workers (3.1 danger category); 36.67±7.97%, for social sphere workers (3.2 category).

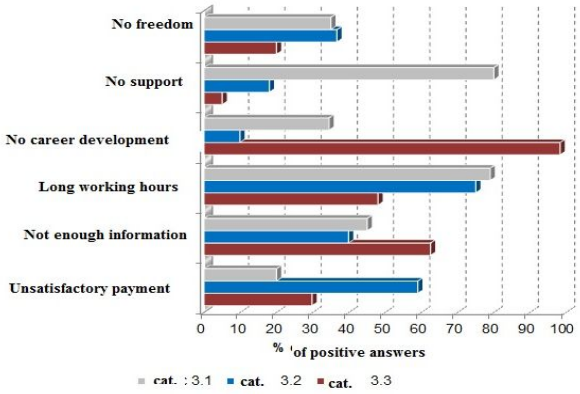

Figure 1. Prevalence of stress factors at a workplace: grew columns show data for vegetable market workers (3.1 category); blue coulmns, social spohere workers (3.2 category); red clumns, builders and subway builders (3.3 category)

Influence exerted by adverse factors of work process and working environment is typical for workers employed by large construction enterprises as 50% of them suffer from it in comparison with 26.6% of people employed in social sphere. Long working hours as a typical feature of their working life were mentioned by workers from all the occupational groups and it resulted in their poor satisfaction with their labor. Limited social support, bad attitudes of supervisors towards their subordinates who

was employed with labor contracts, and absence of cooperation, were also mentioned practically by all workers employed by construction enterprises and we can consider it a significant drawback of work process organization in these teams. Poor career possibilities are most apparent in case of builders: 98.3±3.05%; they were also mentioned by 34.50±8.98% of vegetable market workers; by 9.9±2.035% of social sphere workers. Discrepancies between groups were statistically significant.

Workers employed by large construction organizations and in subway construction often complained on having very little information on their personal contribution into work results, on their supervisors' plans, on their successes and difficulties, and on other corporate news. Workers employed in social sphere often mentioned they didn't have any material stimuli to work better and that they were unsatisfied with their labor; such results were obtained from 58.49± 8.55% of workers employed in social sphere, and only from 20.88±9.05% of vegetable market workers. Discrepancy in frequency of this psychosocial factor occurrence among workers from the examined occupational groups can be caused by differences in their workloads, namely unsatisfactory working regime with long working hours, night shifts, and absence of any days off which were mentioned by female migrants employed in social sphere.

When being questioned, workers from all occupational groups with labor involving great neuro-emotional loads mentioned necessity of focusing their attention; for example, workers employed by construction enterprises and in subway construction mentioned it in 32.09% and 39.45% number of cases correspondingly; necessity to perceive information rapidly and precisely was mentioned by 25.0 % and 20.5% correspondingly; necessity to memorize a great volume of information by listening to, by 12.5% and 23.1%, and by looking, by 12.5% and 20.5%; necessity to multitask, by 28,2% and 43.7%. Work under interferences (25.0% positive answers) was most frequently mentioned by vegetable warehouses and markets workers.

As per research results, as labor intensity grew, a share of people complaining on work stress also went up. Stress situations occurred weakly, several times a week in 27.9% of cases among vegetable market workers; in 38.9%, among social sphere workers; in 54.7%, among builders employed by large construction enterprises and subway builders (Figure 2). In other words, stress situations occurred most frequently at workplaces where labor intensity and danger category was the highest.

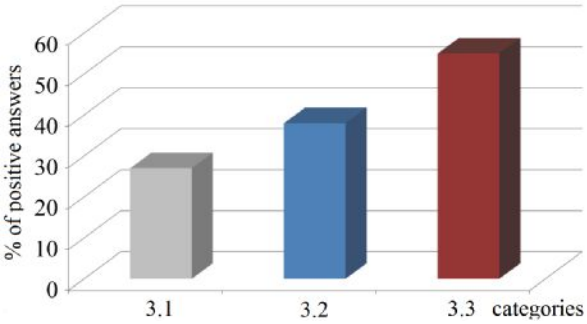

Figure 2. Prevalence of stress factors at a workplace: grew columns show data for vegetable market workers (3.1 category); blue coulmns, social spohere workers (3.2 category); red clumns, builders and subway builders (3.3 category)

When work involves substantial neuro-emotional loads, it leads to poor labor satisfaction. We detected practically the same values before work start in labor migrants employed at construction sites as erectors and steelmen.

Overall, the performed comparative analysis of psychoemotional factors in workers from various occupational groups with different nature, type, and specificity

of labor, revealed that low labor satisfaction occurred in all teams and it was determined by labor intensity.

We observed changes in labor satisfaction during a shift depending on labor intensity. We detected a fall in labor satisfaction over a shift in subway builders (3.3 category) by 9.1% after 8 hours of work and by 10.6% ($p \leq 0.05$) after 12 hours of work; in workers employed by large construction enterprises (3.3 category) by 13.2% ($p \leq 0.05$) after 12 hours of work. At the same time, we didn't detect any drop in labor satisfaction in workers employed at vegetable market (3.1 category as per labor intensity).

Overall, the performed comparative analysis of psychoemotional factors in workers from various occupational groups with different nature, type, and specificity of labor, revealed that low labor satisfaction occurred in all teams and it was determined by labor intensity. The most apparent decrease in labor satisfaction was detected in labor migrants employed by large construction enterprises and subway builders (3.3 category); smaller decrease was detected in vegetable warehouse workers (3.2 category) and vegetable market workers (3.1 category) in conformity with hazard degree determined as per labor intensity. To confirm this statement: calculated correlation coefficients for correlation between labor satisfaction and labor intensity for the first and second group of workers are equal to $r=-0.85$; $p \leq 0.05$; for the third group of workers, $r=-0.64$; $p \leq 0.05$.

Social and psychological factors of group activities efficiency include psychological compatibility of workers and their growing interdependence. Team members' abilities to act together were studied as per Leary tests results. In some cases (15.0+1.2%) we observed negative interpersonal relations which caused low interdependence of workers and made activities costs higher. It is especially typical for migrants employed at construction sites, subway builders, and female migrants employed in social sphere. Insignificant positive interdependence was detected in workers' teams employed at vegetable warehouses.

Basing on Leary test aimed at interpersonal relations detection we revealed that absence of compatibility or low compatibility of workers played a significant part among factors which determined low labor satisfaction in teams. It is possible to use this test at construction enterprises, subway construction organizations, or in road construction, when a team is being formed. We also detected that labor satisfaction was low in teams where supervisors tended to violate labor contracts, paid wages out of time and not in full volume, and didn't provide working conditions in full conformity with hygienic standards. Labor migrants complained on low social support from their supervisors. At the same time female migrants employed in social sphere mentioned friendly attitudes which their authoritative supervisors had towards them.

The results of changes in psychophysiological parameters and work stress levels in migrants under various emotional labor intensity are given in Table 1.

The obtained parameters values revealed the greatest work stress (0.69 arbitrary units) in male migrants employed as erectors by large construction enterprises and as subway builders (3.3 labor intensity category), and it indicated there was increase in amplitude of psychophysiological parameters fluctuations in dynamics during performance of work tasks. Increase in fluctuation range of the examined parameters is caused by strain in regulatory mechanisms which make for body adaptation to new situational conditions. It is determined by 4.0 decrease in attention focus in comparison with 3.1 labor intensity category and by work stress accumulation. We observed lower levels of

Integral parameter of work strain in male migrants depending on labor intensity category

Physiological parameters	Groups of examined workers and labor intensity category				
	Erector and steelmen 3.3	Subway builders 3.3	Road builders 3.2	Vegetable warehouse workers 3.2	Vegetable marker workers 3.1
Latent period of simple visual motor response	Change,%				
	20,1	22,0	17,4	7,5	5,5
Attention focusing as per volume of perceived information	17,3	18,1	15,5	9,1	3,8
Index of functional changes in circulatory system	18,0	16,8	13,5	6,0	2,3
Maximum muscular capacity	26,7	25,4	26,8	13,7	5,1
Integral work strain parameter, arbitrary units					
	0,69	0,69	0,58	0,34	0,18

work strain in workers employed as road network repairmen (3.2 category) as well as in vegetable warehouse workers (3.2 labor intensity category) and vegetable market workers (3.1 labor intensity category), 0.58, 0.34, and 0.18 arbitrary units correspondingly.

Increase in fluctuation range of the examined parameters is caused by strain in regulatory mechanisms which make for body adaptation to new situational conditions. It is determined by 4.0 decrease in attention focus in comparison with 3.1 labor intensity category and by work stress accumulation. We observed lower levels of work stress in workers employed as road network repairmen (3.2 category) as well as in vegetable warehouse workers (3.2 labor intensity category) and vegetable market workers (3.1 labor intensity category), 0.58, 0.34, and 0.18 arbitrary units correspondingly.

Work strain accumulation is accompanied with increase in quantitative values of this strain and leads to evolvement of the second category of it which we observed in case of labor intensity category being 3.2-3.3. And here work strain of the second degree becomes more apparent in prevailing activation processes of vegetative functions. Thus diastolic blood pressure of road network workers grew from 87.3±1.15 to 93.80±1.66 mmHg during their working shift ($p \leq 0.05$). Besides, we revealed a lot of people with borderline arterial hypertension among workers employed by large construction enterprises and among subway builders as their systolic and diastolic blood pressure was within "danger zone" (140/90 – 159/94 mmHg) even among relatively young people aged 30-39 and 40-49. All the above stated proves there is decrease in working capacity and unsatisfactory adaptation of migrants who arrived from Central Asia republics to Moscow region conditions.

Primary psychological reasons for occupational stress evolvement are low qualification, workers having insufficient information on hazards and danger (when working at heights), illusions about safety rules violations having no dangerous consequences. Psychological testing revealed that 50-75% people among labor migrants had increased level of personal anxiety. At the same time situational anxiety wasn't high at the beginning of a work shift and was equal to 20-25 points; by the end of a shift it grew

to 45-55 points which were the evidence that anxiety was already high. We didn't detect any gender discrepancies in migrants' psychological state parameters.

In other words, as per psychological testing, we revealed a significant number of people with increased anxiety caused by labor intensity degree and influence exerted by adverse social and psychological factors. Low occupational selection culture is also a very important factor which causes high social risks. This factor is aggravated by poor vocational training of workers.

Conclusions:

1. Mental stress is a contemporary danger in unconventional labor organization (labor migration); i.e. occupational stress is a problem which attracts a lot of attention of experts in occupational medicine.

2. There are such social and psychological reasons which lead to occupational stress as per specialized analysis data as labor dissatisfaction, harassment, low integration in work teams, and poor living conditions. As per questioning results we revealed quite rare cases (3-5%) of harassment, and their quantity was equal both for female migrants and local people in Moscow region. About 77% women never faced harassment.

3. As per job analysis results we determined labor neuro-emotional intensity categories which were 3.2-3.3 for erectors, steelmen, road network workers, and subway builders; other workers had 3.1 category; labor intensity category for female migrants employed in social sphere was 3.2

4. People with poor labor adaptation as per great possibility of occupational stress evolvement have the following physiological and psychological peculiarities: low attention, low rate of visual signals perception, and prevalence of high systolic and diastolic blood pressure, which proves borderline arterial hypertension is starting to evolve.

5. As per physiological research results we detected stages in functional state formation: work strain of I and II category, and overstrain. Stages in occupational stress evolvement in labor migrants are determined by neuro-emotional labor intensity.

6. Social and psychological support for labor migrants includes better vocational training for workers; personnel being better informed about hazards and danger (when working at heights) of occupational factors; training on safety work practices; openness and visualization of consequences (disability etc) which certain diseases can have; information on what causes diseases; occupational selection improvement; organization of rational work and rest regime with fixed working hours; better interaction and psychological compatibility within work teams; provision of workers' social support.

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EXPERIMENTAL MODELS AND INSTRUMENTAL SURVEYS FOR RISK ASSESSMENT IN HYGIENE AND EPIDEMIOLOGY

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PECULIARITIES OF TOXIC EFFECTS EXERTED BY HEXYL ETHER OF 5-AMINOLEVULINIC ACID AND GROUNDS FOR WORKING OUR REGULATIONS OF ITS SAFE PRODUCTION AND APPLICATION

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Our research object was hexyl ether of 5-aminolevulinic acid applied as plants growth regulator which was synthesized with an original technology by Bioorganic Chemistry Institute of Belarus National Academy of science. Our research goal was to determine peculiarities of toxic effects exerted by this new plants protector on experimental models in vivo/in vitro and to give grounds for hygienic standards of its contents in various media which were to provide its safe production and application. We conducted our research with the use of toxicological, physiological, hematological, biochemical, immunologic, cytogenetic, cytological, and statistical methods. We were the first to perform toxicological assessment of this new plants growth regulator under different regimes, doses and ways of introduction into laboratory animals' bodies and it helped us to detect its toxicometric parameters and peculiarities of its biological effects which became apparent through skin-resorptive and cumulative properties, irritating impacts on mucous tunics, moderate reproductive toxicity without substantial signs of gonadotropic, mutagenic, and allergenic impacts on a body. We detected that toxic impacts exerted by the examined substance on a body was combined with membrane-tropic and cytotoxic effects. We determined criteria and limiting parameters of hazardous effects exerted by hexyl ether of 5-aminolevulinic acid in the course of a chronic experiment, and it gave us grounds for fixing allowable daily dose for a man and for working out a number of regulations on the substance contents in environmental objects (working area air, water, and soil), in food raw materials, and in food products (grain, rape, rape and linen oil). The obtained results were used as a basis for fixing 9 hygienic standards and were used for the state registration of this plant growth regulator; it will provide its safe production and application in agriculture.

Key words: *hexyl ether of 5-aminolevulinic acid, plants growth regulators, toxicity, danger, biological effects, laboratory animals, cells cultures, hygienic standards.*

Application of plants growth regulators is a very promising trend in agricultural production development as such regulators complement application of fertilizers and pesticides. Growth regulators are usually physiologically active substances, either natural or synthetic ones, which make for increase in crop production efficiency via influencing intensity and directivity of plants morphogenesis processes.

In order to achieve new developments in the sphere, experts of Bioorganic Chemistry Institute of Belarus National Academy of Science created a new plant growth regulator on the basis of hexyl ether of 5-aminulevulinic acid (HE-ALA) [8] which efficiently stimulates growth and development of certain agricultures as well as increases plants resistance to unfavorable cultivating conditions [3,11,12].

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To provide safe experimental-industrial synthesis and application of this new substance, it was necessary to accomplish its complete toxicological assessment together with justifying required standards for its contents in human environment objects. All the above stated proves that complex toxicological research aimed at assessing HE-ALA toxicity and danger was really vital; it was also necessary to detect its toxic dynamics and probable ways in which it could exert hazardous impacts on a body and to justify limiting hazard parameters.

Our research goal was to detect peculiarities of toxic effects exerted by HE-ALA on experimental models in vivo/in vitro and to give grounds for a set of hygienic standards providing its safe production and application.

Research objects and methods. Experimental research was performed on 200 non-linear white mice (17–23 g), 325 randomly bred white rats (180–210 g), and 3 white rabbits (4.2–4.5 kg), in full conformity with methodical guidelines [5,13,14].

When performing toxicological research we modeled acute, sub-acute and chronic intoxications. During acute experiments HE-ALA toxic parameters were determined at intragastric, epicutaneous, and inhalation introduction into a body with consequent calculation of lethal doses via probit analysis and determination of values showing potential acute intoxication danger. Ability to cumulate in sub-acute experiments at intragastric introduction and peculiarities of skin-resorptive effects were determined on white rats in repeatable 30-day experiments. Chronic experiment was conducted on white rats during which HE-ALA was intragastrically introduced into animals during 6 months in doses equal to 110, 30 and 11 mg/kg.

We studied sensitizing activity and irritating effects exerted by HE-ALA on eyes mucous tunics and intact cutaneous coverings in conformity with the Instruction No. 1.1.11–12–35–2004 [14].

HE-ALA influence on white rats' reproductive function was examined as per A.A. Dinerman technique [4]. We applied Ames test [17] and cytogenetic chromosome aberrations technique on lymphocytes from human peripheral blood to assess mutagenic activity [18]. HE-ALA cytotoxic properties were studied with transplantable cultures of human embryonic fibroblasts (HEF) and human lung adenocarcinoma A-549 cultivated as per L. Hayflick and P. S. Moorhead technique [19].

To assess the state of toxicity eliminating mono-oxygenase system, we applied microsomal function of white rats' liver [20], in which we determined P450 and P420 cytochromes content, P450-reductase activity, and kinetic parameters (Km, Vmax) of 7-Ethoxycoumarin и 7-Ethoxyresorufin oxidation reactions.

We examined membranes structural and functional properties with the use of pyrene fluorescent probe introduced into blood shadows suspension of white rats' erythrocytes under exposure to HE-ALA in in vivo and in vitro experiments [2].

All the research results were processed with conventional techniques. Discrepancies between focus groups and control groups were considered to be statistically significant at $p<0.05$.

Results of toxicological and hygienic assessment of this new compound can in future be used for setting safety parameters as per permissible risk criteria.

Results and discussion. We determined basic quantitative toxicity parameters (DL16, DL50, DL84) and danger parameters (S, R) under a single intragastric

introduction of HE-ALA into white mice and rats, both male and female; these parameters didn't have any specific discrepancies (specific sensitivity coefficient is equal to 2.6) and sex discrepancies and allowed to consider the examined substance to be moderately dangerous (Table) [10].

Table

Toxicity and potential danger parameters of acute HE-ALA intoxication

Species	Lethal doses, mg/kg			Potential danger parameters of acute intoxication	
	DL_{16}	DL_{50}	DL_{84}	S	R
Male mice	2540	3000 (2630÷3420)	3540	1,18 (0,99÷1,4)	1,39
Female mice	2470	3170 (2710÷3710)	3900	1,26 (1,13÷1,41)	1,58
Male rats	6350	8800 (6560÷11800)	12500	1,41 (0,97÷2,0)	1,97
Female rats	4800	7800 (5740÷10600)	12600	1,62 (1,12÷2,35)	2,63

Note:

1. DL16, DL50, DL84 are doses leading to 16%, 50%, 84% of deaths.

2. S is a function of "dose - effect" straight line tilt angle.

3. R is lethal doses span.

When we modeled acute inhalation intoxication under maximum achievable HE-ALA concentration we deleted no signs of intoxication and didn't register any deaths; the same situation was under a single introduction of 50% solution on white rats skin in a dose equal to 800 mg/kg. The obtained results prove there is no acute intoxication danger under the above-mentioned exposure ways.

When 50 μl of 50% HE-ALA solution were instilled into a posterior conjunctival fornix of a rabbit's right eye, we observed abundant lacrimation, moderate reddening of conjunctiva vessels, eyelids edema, and blepharospasm, and it allowed us to consider HE-ALA to possess apparent irritating effects. We didn't detect any signs of the substance irritating effects when it had a single contact with intact cutaneous coverings of white rats.

We didn't reveal any sensitizing properties of HE-ALA when studying it in experiments on white mice via modeling reproduction of delayed-type hypersensitivity.

When HE-ALA was intragastrically introduced into male white rats, occurrence of lethal cases at the level equal to 1/5 DL50 allowed us to calculate cumulation coefficient which was equal to 1.6 and characterized the substance as a highly cumulative one. We registered the most apparent changes at intragastric HE-ALA introduction into white rats during 30 days in a dose equal to 880 mg/kg (1/10 DL50); these changes were statistically significant shifts in behavioral activity, increase in summational-threshold parameters (STP) by 78% and in relative mass coefficients (RMC) of internal organs, namely liver, heart, lungs, spleen, kidneys, and adrenals. As for hematologic parameters, we revealed decrease in hemoglobin concentration by 13% and oxihemaglobin by 14%; quantity of erythrocytes, by 15% hematorcit, by 12%, in comparison with the control groups. There were other signs of disorders in acid-base blood balance: authentic decrease in partial oxygen pressure by 24%, increase in partial carbon dioxide pressure by 14%, and increase in bicarbonate blood capacity by 13% against the control. We detected the following changes in white rats' blood serum: 1.5 times increased activity of gamma-glutamyltranspeptidase (GGT) ($p<0.05$), 2.3 times more active alanine aminotransferase (ALT) ($p<0.05$), 2.0 times increase in crude bilirubin content ($p<0.05$), 1.5 times increased C3 complement component and increase in immunoglobulin G by 28 % ($p<0.05$) in comparison with the control group. Hyperenzymemias occurrence with

such pathophysiological grounds as damage to hepatocytes membranes indicates the substance can damage membranes.

Under subchronic intragastric HE-ALA introduction in a dose equal to 440 mg/kg (1/20 DL50) we observed changes in motor activity of experimental rats and increase in STP by 60% ($p<0.05$). When experiments were over, we registered increase in RMCs of experimental rats' heart, kidneys, and adrenals ($p<0.05$), decrease in hemoglobin concentration in peripheral blood by 9%, and 1.6 times increase in crude bilirubin level in comparison with the control group ($p<0.05$). When an introduced HE-ALA dose was reduced to 110 mg/kg (1/80 DL50) we detected only 1.3 times increase in crude bilirubin in white rats' blood serum against the control group ($p<0.05$).

As we studied skin-resorptive HE-ALA properties with the substance being introduced as 50% solution (864 mg/kg) in 30 consequent applications on white rats skin on their backs we didn't reveal any outer signs of intoxication and didn't detect any deaths. However we observed a 21.6% increase in ALT enzymatic activity ($p<0.05$) and 22% increase in urea content ($p<0.05$) in blood plasma while pH of urine decreased to 6.0 ($p<0.05$) in comparison with the control group. Epicutaneous impact exerted by 25% HE-ALA solution in a dose equal to 341 mg/kg led to a 29.6% increase in ALT activity in blood serum of white rats ($p<0.05$). When HE-ALA impact went down to 75 mg/kg (5% solution), we didn't reveal any changes in biochemical parameters.

Standardization of this new plants growth regulator requires determination of its influence on reproductive function and examination of its possible mutagenic impacts [5].

A single intragastric introduction of the substance into female white rats in a dose equal to 1/2 DL50 (3,900 mg/kg) during periods of intensive organogenesis caused clinical signs of intoxication; however we didn't detect any embryos deaths or any signs of teratogenic impacts. Pre-implantation mortality in experimental rats was insignificant. Post-implantation mortality was completely absent both in focus and control groups. Impacts exerted by the substance on the 9th day of pregnancy turned out to be the most crucial for post-natal development; we detected such signs of it as physical retardation of infant rats (development slowed down by 13% as per body weight and by 5% as per body length) ($p<0.05$). The obtained data reveal that HE-ALA has moderate reproductive toxicity. Even when exerting multiple impacts during the whole pregnancy in a dose equal to 1/40 DL50 (195 mg/kg), the examined substance didn't have any embryo-trophic or teratogenic effects and didn't exert any negative influence on postnatal development of offspring.

When HE-ALA was sub-chronically introduced intragastrically into male white rats in a dose equal to 440 mg/kg (1/20 DL50), it had weak gonad-toxic effects as per morphofunctional parameters of gonads which became apparent through testicles RMC growing by 12% ($p<0.05$) and 1.6 times decrease of spermatozoons motion period ($p<0.05$) in comparison to control. When an introduced dose was reduced to 110 mg/kg, we didn't detect the above-mentioned changes.

So, embryo-trophic and gonad-trophic effects were registered only when massive doses of the substance were introduced; such doses led to intoxication of parents' bodies and it gave us grounds to consider such changes in reproductive system parameters as signs of general toxic impacts exerted by HE-ALA [9].

We didn't detect any potential mutagenic activity of HE-ALA in concentrations equal to 1 and 10 μg/ml in Ames test performed on S. typhimurium TA 100 strain with metabolic activation and without it; the same was in a cytogenetic test performed on human peripheral lymphocytes in vitro under exposure equal to 0.05, 0.1 and 0.25 mg/ml [1].

To reveal mechanisms of HE-ALA toxic effects we studied a state of detoxification mono-oxygenase system of white rats liver under chronic intragastric introduction in a dose equal to 440 mg/kg. We detected authentic 1.4 times increase in specific content of P450 cytochrome and 1.5 times increase in specific activity of P450-reductase but maximum speed Vmax and Michaelis-Menten constant Km of 7-Ethoxycoumarin and 7-Ethoxyresorufinoxidative reactions didn't have any discrepancies with the control group. We should point out there was a 3.0 times increase in specific content of P420 cytochrome in experimental animals in comparison with the control groups ($p<0.05$), which can possibly indicate that the examined substance is able to destabilize endoplasmatic reticulum membranes.

The results of experiments performed in vitro on HEF and A-549 cultures revealed that HE-ALA in concentrations equal to 2×10-3 mol×l-1 caused a monolayer degeneration when cells separated from glass. When concentration was equal to 2×10-4 mol×l-1 the substance suppressed HEF cells proliferation 2.8 times, and A-549 cells, 6.3 times, in comparison with the control. We didn't observe any significant influence of the substance on the examined cultures proliferative activity in experiment with exposure to HE-ALA being equal to 2×10-5 mol×l-1: a number of HEF cells increased 16 times during this experiment, and a-549 cells, 26 times in comparison with the initial level before the substance was introduced and it corresponded to normal growth of these culture under in vitro conditions. The calculated value of average efficient concentration of CL50 cytotoxic effects amounted to 1.14×10-4 (1.08×10-4÷1.21×10-4) mol×l-1 for HEF cells culture and to 0.5×10-4 (0.48×10-4÷0.54×10-4) mol×l-1 for A-549 cells culture.

We studied influence exerted by the substance on structural and functional properties of lipid bilayer state within the range of its cytotoxic effects. This influence was examined in vitro via introduction of pyrene fluorescent probe into blood shadows suspension of intact rats erythrocytes. When HE-ALA was added in concentrations equal to 2×10-5, 2×10-4, 2×10-3 mol×l-1 it caused pyrene fluorescence suppression without any changes in excimerization coefficient: ratio between excimers Fe at □em 475 nanometers and Fm at □em 373 nanometers; it proved lipid bilayer degradation occurred.

Our examination of structural and functional parameters which erythrocytes membranes had in subchronic experiment in vivo on white rats revealed there was a decrease in lipid bilayer microviscosity and annular (protein) lipid viscosity which depended on impacts exerted by HE-ALA in a dose equal to 440 mg/kg; it was proven by excimerization coefficients growth but their polarity parameters remained within control values range. We examined intensity of radiationless transfer of electronic excitation energy from tryptophan remains on pyrene and revealed an authentic 38% decrease in this parameter ($p<0.05$), which was the evidence that protein molecules were less submerged into lipid bilayer.

Chronic intragastric HE-ALA introduction into white rats in doses equal to 110, 30 and 11 mg/kg during 6 months didn't cause any clinical signs of intoxication and death. We observed some changes in experimental

animals' nervous system when a dose was 100 mg/kg, namely a 34% decrease in motor activity and summational -threshold parameter in comparison with control groups ($p<0.05$). Impacts exerted by HE-ALA didn't cause any changes in biochemical parameters of blood serum, including crude bilirubin levels which was a marker parameter of subchronic impacts. Urinary system disorders were proven by an authentic decrease in urine hydrogen ions quantity (pH 6.2), 4.3 times lower daily urine output, and 2.6 times lower creatinine clearance against control groups.

Chronic intragastric HE-ALA introduction into white rats in a dose equal to 30 mg/kg led only to an authentic 35% decrease in summational-threshold parameter and it allowed us to determine this impact as being a threshold of a chronic effect (Limchr). Therefore, a functional state of nervous system as per changes in summational-threshold parameter can be considered a limiting parameter of HE-ALA chronic general toxic effects.

Sings of the substance toxic effect didn't occur when a dose was 11 mg/kg (maximum non-effective one) and it allowed us to use this value to calculate HE-ALA permissible daily dose (PDD). Allowing for the substance having considerable cumulative properties, we decreased maximum non-effective dose 100 times (assurance coefficient) and it made PDD being equal to 0.11 mg/kg. Permissible daily introduction (PDI) into a human allowing for PDD and average body weight being 50 kg should not exceed 5.5 mg/day (a sum of all the substance introductions out of various media).

We calculated predictive values of tentatively safe impact exerted by HE-ALA content in working area air as per formulas applied for all the pesticide groups [16]. As we analyzed the obtained values we detected that the lowest calculated hygienic standard value was 0.8 mg/m3.

Tentatively safe HE-ALA content in the atmosphere was set at 0.01 mg/m3 as per calculations [7] allowing for molecular weight, basic toxicity parameters and tentatively safe content in working area air. When tentatively safe content is equal to this value, 0.2 mg of HE-ALA can penetrate a human body with atmospheric air and it is equal to 3.6% of permissible daily introduction (PDI).

To predict tentatively permissible content in water, we applied equations which described correlations between this value, fixed toxicological parameters (DL50), standard contents in other environmental objects (working area air), and physical constants [6]. Minimal calculated tentatively permissible HE-ALA content value was equal to 0.1 mg/dm3. Results of organoleptic examinations of water which contained HE-ALA at a minimum calculated level revealed that there was no smell at 20 °C and 60 °C.

Tentatively permissible HE-ALA concentration in soil was calculated as per permissible daily dose value [15] and was equal to 0.3 mg/kg. Agrotechnical application of the substance in pre-sowing treatment of barley, rape, and fiber flax seeds in conformity with the recommended expenditure rates up to 3 g/g (up to 150 ml/hectare) is unlikely to cause the substance contents in oil being higher than the fixed tentatively permissible concentration.

As the substance is to be applied in cultivaiton of sping barley, winter rape, and fiber flax, we performed caclulations to give grounds for maximum permissible quantities of HE-ALA residues in cereals grain, rape (grains and oil), and fiber flax (oil).

Up to 70% of the plants protector residues can enter a human body with food

products; these residues occur in all media. In this case calculated safe HE-ALA introduction with food products amounts to 3.85 mg/human/daily.

When determining maximum permissible HE-ALA residues level in cereals grain (0.1 mg/kg) and rape (0.6 mg/kg), flax and rape oil (0.6 mg/kg) we allowed for average daily standards of food products consumption.

Consequently, probable daily HE-ALA introduction into a human body allowing for all the standards set for various media amounts to 0.11 mg (2 % of PDI) with food products; 0.3 mg (5.5 % of PDI), with water; 0.2 mg (3.6 % of PDI), with air; totally 11.1 % of permissible daily introduction (PDI).

So, as per toxicological assessment results, we managed to give grounds for a number of technical regulations for HE-ALA content in the environment: tentatively safe HE-ALA content in working area air is equal to 0.8 mg/m3; in the atmosphere, 0.01 mg/m3; tentatively permissible concentration in water reservoirs is 0.1 mg/dm3; in soil, 0.3 mg/kg; permissible daily dose is 0.1 mg/kg; maximum permissible concentration in cereals grain is 0.1 mg/kg; in rape (grain and oil), and fiber flax (oil), 0.6 mg/kg.

Conclusion. We performed complex toxicological and hygienic examination of HE-ALA, a new plants growth regulator under various regimes, doses and ways of introduction into experimental animals bodies. The examination results allowed us to detect parameters of its toxicity and biological impacts peculiarities which became apparent through skin-resorptive properties, cumulative ones, and properties causing mucous tunics irritation, moderate reproductive toxicity without any substantial signs of gonad-trophic, mutagenic and allergenic impacts on a body. We determined that HE-ALA toxic effects on a body were membrane-trophic and cytotoxic. We determined limiting parameters of HE-ALA hazardous effects in a chronic experiment; basing on these parameters, we calculated a permissible daily dose for a human and created a number of regulations for the substance content in environmental objects (working area air, the atmosphere, water, and soil), food raw materials, and food products (cereals grain, rape grain, rape and flax oil).

The obtained data can be used as initial ones in setting reference safety levels as per allowable health risk criteria.

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EXPERIMENTAL MODELING OF AEROSOLS PRODUCED BY MICROORGANISMS IN WORKING AREA AIR AS RISK FACTOR EXERTING HAZARDOUS IMPACTS ON HEALTH OF WORKERS EMPLOYED AT BIOTECHNOLOGICAL PRODUCTION

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Scientific foundation and practices in the sphere of hygienic and ecological standardization concerning biological factors of the environment have a number of peculiarities and are methodically less developed than chemical factors standardization. Efficient industrial control over maximum permissible concentrations of standardized microorganisms-producers in working area air is based on validated instrumental techniques of quantitative assessment. Our goal was to create experimental models for microorganisms-producers' aerosols of a multi-component microbe specimen in working area air as a risk factor causing impacts on health of workers employed at biotechnological production; another task was to work out a procedure for measuring Pseudomonas aurantiaca B-162/255.17concentration and cells and spores of Bacillus sp. BB58-3 strain in working area air. We gave grounds for a technology aimed at quantitative determination of microorganisms-producers in working area air in a modeling experiment; it was based on conventional stages and techniques accepted in microbiological practices, namely air samples taking via aspiration technique allowing for a volume taken; cultivation under conditions which are optimal for examined microorganisms-producers in a nutrient medium with reduced composition; calculation of evolved colonies with specific morphological features; morphologic identification of microorganisms and colonies; calculation of microorganisms' quantity on dishes with recalculation per 1 m^3 of air. Basing on the detected regular concentration dependences of microbe contamination dynamics in air we worked out a procedure for quantitative determination of microorganisms-producers; we also performed metrological estimate of operational properties for assessing microorganisms-producers of a multi-component microbe specimen as a risk factor causing hazardous impacts on health of workers employed at biotechnological production. We validated our measuring procedure in conformity with the requirements set forth by ISO.

***Key words**: biological factor, modeling experiment, microorganisms-producers, multi-components microbe specimens, working area air, hygienic standards, biotechnological production.*

Development of biotechnological industry which belongs to high-tech V and VI social and economic structure is in line with national interests and long-term goals of sustainable social and economic improvements in Belarus [4]. Basic trends in industrial and medical biotechnology are based on application of various stems, species, strains, and serotypes of natural or mutagenic microorganisms including those obtained via genetic engineering as probiotic food preparations, protein producers, biologically active substances and enzymes (amylolytic, proteolytic, pectolytic, cellulo-

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lytic, various antibiotics, amino acids, vitamins, and others), and microbiological specimens for biological protection and increase in cropping power of crops etc [15–19]. However, industrial environment and atmosphere contamination with microorganisms-producers and microbe specimens made on their base is quite possible in the process of their application; they can also penetrate working area air and atmosphere and exert adverse influence on workers' and population's health [2, 3, 6, 9, 12, 13, 14]. Microorganisms-producers occurrence in working area air and direct contact with microbe aerosols in the process of their application in industrial conditions can be health risk factors for workers employed at biotechnological productions as industrial strains of microorganisms-producers are low-pathogenic but they still have great or apparent sensitizing abilities (1-2-degree of allergenic danger) [13, 14].

Therefore, examination of microorganisms properties seems to be vital and practically significant; it is also essential to assess dangers and possibilities of consequences which biotechnological production can have and which can be dangerous for human health. Biotechnological products can contain viable cells and their structural elements; so it is necessary to work out efficient medical prevention activities aimed at elimination of their adverse impacts via hygienic standardization and control over their contents in objects of living environment. Scientific foundation and practices of hygienic and ecological standardization of biological factors in living environment have a number of peculiarities and they are methodically less developed than those related to chemical factors. Development of methodology and techniques for hygienic regulation and standardization of microorganisms-producers and microbe specimens as biological factors of living environment is one of the leading scientific trends pursued now by Scientific and Practical Center for Hygiene of Belarus Public Health Ministry; here a scientific school has been created within the frameworks of this promising trend in preventive medicine. As a result of performed complex toxicological-hygienic research hygienic standardization of more than 100 microbe specimens has been accomplished; maximum permissible concentrations (MPC) in working area air were fixed for 12 new one- and multi-component microbe specimens [1, 3, 5–8, 10, 11].

Efficient industrial control over MPC of standardized microorganisms-producers and microbe specimens in working area air is based on application of validated instrumental techniques of quantitative assessment.

Creation of standardized and validated measuring techniques for microorganisms-producers and microbe specimens concentrations in working area air is a quite complicated analytical task as experimental modeling of microbe aerosols includes optimization of all instrumental technique parameters (air sampling conditions under various microbe loads, microorganisms-producers cultivating and identification etc), determination of analytical properties related to specificity and selectivity, concentration dependences and sensitivity limits of a created technique. Methodical techniques and calculation algorithms for operational characteristics are worked out for such matrixes as water media or food products, but there aren't any such techniques for assessing metrological parameters of measuring biological factors in air medium[6,7].

Our goal was to create experimental models of microorganisms-producers aerosols of a multi-component microbe specimen as a health risk factor for workers em-

ployed at biotechnological production; another goal was to work out a technique for measuring concentrations of Pseudomonas aurantiaca B-162/255.17, and cells and spores of Bacillus sp. BB58-3 strain in working area air.

Data and methods Our research object was «Profibactтм-Phyto», a new microbe specimen based on Pseudomonas aurantiaca B-162/255.17 cells, and cells and spores of Bacillus sp. BB58-3 strain, created by the Institute for Genetics and Cytology of Belarus National Academy of Science.

We applied a system for liquid aerosols creation in inoculation chambers with volume equal to 250 liter (Spectrolab, RF); SAS SUPER100 aspirator (PBI International, Italy), as well as standard microbiological laboratory equipment. Measuring devices and basic equipment were properly verified and gauged.

Nutrition media. We applied selective medium with the following composition: 10.0 grams of tryptone; 1.0 gram of yeastrel; 0.02 grams of water-free calcium chloride; 15 grams of microbiological agar. To create working microbe specimen dilutions, we applied phosphate buffer solution with 0.1% peptone, pH 7,0. We confirmed microbe cells contents in a working culture via seeding a reduced composition on a selective agar medium. To optimize sampling parameters and to determine operating characteristics of a detector (contact Petri dishes with a relevant nutrition medium) we applied working dilution of a specimen, namely 106 CFU/ml.

At the following stages in our experimental modeling of microbe aerosol in an inoculation chamber we took air samples within 10-50 liters volume range. Air samples were taken via aspiration technique on the surface of an agar selective medium with the said structure in two replications; they were then incubated for (48±2) hours at (30±0,5) °C; after that grown typical microorganisms-producers colonies were calculated. We assessed cultural and morphological peculiarities of evolved colonies and calculated quantity of typical ones.

Microorganisms-producers concentration X, CFU/m3, was calculated as per formula:

$$X = (N \cdot 1000) / V, \quad (1)$$

where:

X is concentration of microbe cells and spores in working area air;

N is quantity of microorganisms-producers colonies on a dish;

1000 is a coefficient of recalculation per 1 m3 of air;

V is a volume of a taken air sample, dm3.

Results and discussion MP of Bacillus and Pseudomonas stems are used to biologically stimulate agriculture crops growth and development; they can also be used as a biological protector (Table 1).

Hygienic standards of microbe specimen MPC in working area air are fixed at the level of 5,000 CFU (microbe cells) per 1 m3 for Pseudomonas aurantiaca B-162/255.17 and Bacillus sp. BB58-3, IV danger category [8].

The created technology of MP quantitative assessment in working area air in our model experiment is based on conventional stages and techniques of microbiological practices: air sampling via aspiration technique allowing for the volumes taken; cultivating on a nutrition medium with reduced composition under conditions which are optimal for the examined microorganisms-producers; calculation of evolved colonies with specific morphological features; morphological identification of microorganisms and colonies; calculation of microorganisms quantities on dishes with recalculation as per 1 m3 of air.

Table 1

Profibact TM-Phyto MP Properties

Sources of strains-producers	Morphological, cultural and biochemical features of strains
Bacillus sp. BB58-3 is obtained via induced mutagenesis of a natural strain, antagonist to plant-pathogenic fungi, is not plant-toxic, stimulates plants growth	Bacillus sp. BB58-3. Immovable gram-positive spores-producing straight bacilli with rounded ends, 0.6 x 3-4 μm size. Colonies are small (1.0-3.0 mm) and rounded, flat-convex, with even blade ends, cream colored, non-transparent, with heterogeneous internal structure. Catalase-positive, thermal-stable, obligate aerobe with proteolytic and amylolytic activity.
Pseudomonas aurantiaca B- 162/255.17 is obtained via multi-stage mutagenesis of a natural strain	P. aurantiaca B-162/255.17. Mobile, gram-negative, stright bacilli with rounded ends, 0.6 x 2-3 μm sized, with 2-4 monopolar flagella. Colonies are smooth, flat, with even ends, 2-3 mm in size, yellow-orange, with homogenous internal structure. Obligate aerobe; synthesizes phenazine antibiotics. As nitrogen, it utilizes ammonium salts, urea, and nitrates.

We created a model of spraying in inoculation chambers with 250 liters volume to obtain inhalation modeling of liquid sprays; it allowed us to test regimes of MP concentrations range creation in a closed space with the use of various types of sprayers; with various rates of feeding onto ejectors and air flow sprayers; under various exposures to MS spraying. We optimized parameters of air sampling via aspiration (time and volume) under different microbe loads; we also did it for media compositions and cultivating regimes for microorganisms-producers with their consequent identification. The obtained experimental database allowed us to reveal nature and peculiarities of microorganisms-producers growth depending on microbe specimen concentration in a fixed volume of an inoculation chamber (Figure).

The nature of dependence between a number of colonies on a dish and taken air volume was linear and could be given with an equation given on Figure. Coefficients of R^2 determination were within 0.93-0.96 range and it proved that the obtained results of quantitative assessment of MP concentrations in working area air were really authentic.

Operational characteristics for metrological attestation of the quantitative assessment technique were estimated in con formity with the requirements set forth by the International Standardization Organization (ISO): precision parameters (repeatability and intermediate precision with "operator" changing factor) were determined; extended uncertainty was applied as well as other operational characteristics; such parameters as specificity, sensitivity, frequency of false-positive and false-negative results which are inherent in biological factors assessment were taken into account [8, 11].

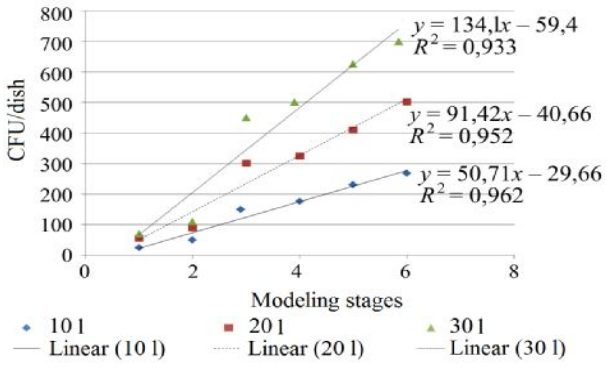

Figure. Dynamics of Pseudomonas *aurantiaca B-162/255.17 and Bacillus sp. BB58-3* strain producers growth in a modeling experiment

Basing on the database obtained in the course of the modeling experiment we assessed operational characteristics of the techniques, carried out the metrological attestation and fixed quantitative assessment techniques for calculating MP concentrations in working area air [5]. Table 2 contains metrological characteristics and specificity and selectivity parameters of the created techniques.

Table 2

Metrological characteristics and specificity and selectivity parameters of the created techniques

Metrological characteristics Specificity and selectivity parameters	Assessment type	Value	
		Pseudomonas aurantiaca B-162/255.1	*Bacillus sp. BB58-3*
Weighted aggregate relative standard deviation in calculation	A	0.052	
Standard repeatability deviation Sr	A	0.012 log10 CFU/m3	
Repeatability limit r	A	0.034 log10 CFU/m3	
Standard intermediate precision (intra-laboratory reproducibility) deviation отклонение промежуточной Sl(O))	A	0.147 log10 CFU/m3	
Intermediate precision limit rl(O)	A	0.41 log10 CFU/m3	
Extended uncertainty (k=2) U	A	0.30 log10 CFU/m3	
Sensitivity	A	1.0	0.96
Specificity	A	0.8	0.6
False-positive results frequency	A	0.038	0.074
False-negative results frequency	A	0	0.25
Selectivity	A	1.415	1.431
efficiency	A	0.97	0.93
Upper limit of linearity	A	Not more than 150 typical colonies per dish with total number of colonies being not more than 300	Not more than 150 typical colonies per dish with total number of colonies being not more than 300

Conclusion. As a result of our experiment on modeling multi-component microbe specimen aerosols in working area air we obtained dependences of microorganisms-producers contents in sequential experiment stages and created a quantitative assessment technique to calculate them.

We assessed operational characteristics of the technique aimed at determining Pseudomonas aurantiaca B-162/255.17 and Bacillus sp. BB58-3 strains in air; we also created quantitative assessment techniques for calculating microbe specimen concentrations in working are air and this technique was certified by Belarus State Metrology Institute.

Application of this quantitative assessment technique in the sphere of microbiological laboratories certification provides objective sanitary and industrial control over these microbe specimen contents in working environment as per their conformity to MPC. Scientifically grounded unified approaches to creation of quantitative assessment techniques aimed for calculating multi-component microbe specimen concentrations in working area air are formalized in a form of application instructions and allow to create similar quantitative assessment tech-

niques for new biological specimens when these specimens are to be assessed as health risk factors which can possibly exert negative impacts on health of workers employed at biotechnological productions.

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