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RISK-ORIENTED APPROACH APPLICATION AT PLANNING AND ORGINIZING ANTIEPIDEMIC PROVISION OF MASS EVENTS

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Mass events tend to become more and more dangerous for population health, as they cause various health risks, including infectious pathologies risks. Our research goal was to work out scientifically grounded approaches to assessing and managing epidemiologic risks as well as analyze their application practices implemented during preparation to the Olympics-2014, the Games themselves, as well as other mass events which took place in 2014–2016. We assessed epidemiologic complications risks with the use of diagnostic test-systems and applying a new technique which allowed for mass events peculiarities. The technique is based on infections ranking as per 3 potential danger categories in accordance with created criteria which represented quantitative and qualitative predictive parameters (predictors). Application of risk-oriented approach and multi-factor analysis allowed us to detect exact possible maximum requirements for providing sanitary-epidemiologic welfare in terms of each separate nosologic form. As we enhanced our laboratory base with test-systems to provide specific indication as per accomplished calculations, it enabled us, on one hand, to secure the required preparations, and, on the other hand, to avoid unnecessary expenditures. To facilitate decision-making process during the Olympics-2014 we used an innovative product, namely, a computer program based on geoinformation system (GIS). It helped us to simplify and to accelerate information exchange within the frameworks of intra- and interdepartmental interaction. "Dynamic epidemiologic threshold" was daily calculated for measles, chickenpox, acute enteric infections and acute respiratory viral infections of various etiology. And if it was exceeded or possibility of "epidemiologic spot" for one or several nosologies occurred, an automatic warning appeared in GIS.

Planning prevention activities regarding feral herd infections and zoogenous extremely dangerous infections which were endemic for Sochi was accomplished taking the completed assessment into account.

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The positive experience obtained through risk-oriented organization of certain activities aimed at providing anti-epidemic safety of mass international events on the Russian Federation territory allows us to be optimistic about prospects of wider implementation of the approach described above and other similar approaches based on health risk analysis principles.

Key words: *epidemiologic risks, risk-oriented approach, mass events, infectious diseases, epidemiologic surveillance, risk assessment, risk management, geoinformation system.*

Implementation of risk-oriented models into practical activities performed by surveillance authorities is a modern trend. Application of such models helps to optimize expenditures, and to make well-ground distributions of labor resources choosing most vital tasks [3,9].

This effect has cascade nature as motivation preconditions for improving surveillance subjects' activities are created.First of all, various processes, manufactured products, and provided services become safer and it leads to lower risks related to them; consequently, a number of necessary surveillance activities also goes down.

There are changes in the sphere of providing sanitary-epidemiologic welfare of the population as hygienic standardization concepts are being gradually replaced by health risk analysis concepts which are better in line with contemporary social and economic conditions [3]. We should point out that nowadays issues related to assessing risks caused by impacts of chemical and physical environmental factors are studied more profoundly in comparison with biological factors impacts. To control such factors, one usually uses techniques mostly adapted for sanitary microbiology tasks. It is next to impossible to fully solve tasks on predicting epidemiologic situations in relation to a wide range of infectious diseases with the use of such techniques; so, it is also impossible to create sufficient scientific grounds for risk management.

Expert multi-score risk assessment technique is the most widely spread one in everyday activities of epidemiologic surveillance. In some cases qualitative determination of risks level is accomplished without any clear criteria and is based only on experience a correspondent specialist has and only on the results of studying up-to-date information which is available to this specialist. But still a man even having maximum possible competence in his or her sphere of activity makes only subjective assessments and it can greatly influence data interpretation and, consequently, prediction results. In spite of the fact that qualitative techniques in most cases enabled timely identification of arising dangers, it is necessary to create new technologies of epidemiologic risks assessment which will help to reduce or even eliminate a subjective component.

Mass events involve greater and greater dangers for population health including those caused by infectious pathologies [2, 7, 12, 13]. Here epidemiologic risks level depends on a scale, duration, and season during which a mass event takes place, as well as geographic regions its participants and guests come from [14, 15]. Additional workloads on social infrastructure and increased number of contacts between people create favorable conditions for activation of infectious agents transmissions; such infectious agents can be both endemic and brought from other territories [11]. Sporadic cases and group infective episodes are considered from the point of view of potential danger which they represent for a mass event as a whole or its separate stages. All the above-stated makes it necessary to organize specific activities aimed at danger prevention and reacting in case any unfavorable situations occur. It is advisable to introduce a new concept allowing for all peculiarities which mass events have; this new concept is mass events epidemiology. Key significance here is assigned to population health risk analysis.

Our research goal was to create scientifically grounded approaches to

assessing and managing epidemiologic risks during mass events, and to analyze experience of their practical implementation during preparation to the Olympics-2014 and the Games themselves, as well as during other mass events which took place in Sochi in 2014-2016.

Data and methods. Our work is based on reports issued by "Stavropol Scientific Research Antiplague Institute" of Rospotrebnadzor and Rospotrebnadzor Regional office in Krasnodar Kray; these reports were dedicated to the results of these establishments' activities during mass events which took place in Sochi in 2014-2016 (The Olympics-2014, Formula-1 Gran Prix, Russia - ASEAN summit etc.).

Risk assessment in relation to various infectious diseases was accomplished in order to determine a set of activities needed for risks lowering, and for justifying volumes of providing Rispotrebnadzor specialized anti-epidemic team (SAET) with diagnostic preparations. Experts used a new technique based on ranking nosologies as per three potential danger categories according to developed criteria representing qualitative and quantitative predictive parameters (predictors).

The technique is created allowing for mass events peculiarities and is first of all designed for making short-term forecasts. It involves determining whether there are epidemiologic risks predictors: yes (they exist) means 1 point, no (they are absent) means 0 points. To determine risk parameter for each separate nosologic form we should divide the obtained sum of points by a number of predictors, so that to calculate arithmetic mean for a sum of points. Risks levels were labeled as high (0.68-1.0), average (0.34-0.67), and low (0-0.33) according to a three-level assessment system.

Results and discussion. XXII Olympics and XI Paralympics Winter Games-2014 in Sochi were the greatest and the most significant sport mass event which took place on the territory of the Russian Federation in XXI century. From epidemiologic point of view, their peculiarities were the total duration of the event, which was longer than incubation period of most nosologic forms, as well as a great number of people, sportsmen, team members, maintenance personnel, and fans, being in the limited space; some of those people arrived from regions which were endemic in terms of extremely dangerous infections exotic for Russia.

There was a lot of analytical work accomplished prior to the Olympics; its results enabled determining that feral hers infections and zoogenous infections of bacterial and viral etiology registered in Krasnodar Kray represented a real danger. These infections agents belong to the 2nd pathogenicity group. Such infections occurrence was caused by a number of factors: 1) all land transport routes went through the Kray territory (motorways and railways); 2) airports in Krasnodar, Gelendzhik and Anapa received guests of the event and could be used as reserved ones; 3) a big share of fans and maintenance personnel were permanents residents of Krasnodar Kray, and this maintenance personnel included those who worked on sports objects, volunteers, and other people who had direct contacts with participants and guests of the event in their everyday activity; 4) a significant number of food stuffs suppliers certified by Sochi-2014 Organization Committee was also located on the Kray territory. Therefore, a possible carrying of infections and their agents from Krasnodar Kray was a considerable danger for sanitary-epidemiologic welfare of local population, participants and fans. Risk-oriented model was applied for epidemiologic surveillance over feral herd infections and zoogenous extremely dangerous infections on this territory.

"Internal" risk for epidemic complications occurrence during the Olympics-2014 and other mass events later on organized in Sochi was assessed in relation to hemorrhagic fever with renal syndrome (HFRS), West Nile fever (WNF), Crimean hemorrhagic fever (CHF), tularemia,

brucellosis, and anthrax (table) [8]. To do this, a list of 10 questions was made on the basis of studying retrospect and live data; the questions comprised predictive risk parameters (7 were general and 3 were specific for feral herd infections and zoogenous infections).

Table

Assessment of risk for epidemic complications occurrence in terms of feral herd infections and zoogenous extremely dangerous infections in Krasmodar Kray during a mass event (on the example of the Olympics-2014)

No.	Predictors (questions)	Predictor occurrence (points) (yes is 1; no is 0)					
		HFRS	WNF	CHF	Tularemia	Brucellosis	Anthrax
1	Have any disease cases been registered on Krasnodar Kray territory over the last 5 years?	1	1	0	1	0	1
2	Have any disease cases been registered in Sochi over the last 5 years?	1	0	0	0	0	0
3	Have any disease cases been registered on Krasnodar Kray territory in a season of a mass event over the last 5 years?	1	0	0	0	0	0
4	IV* over the last 5 years is authentically > than IV over the last 20 years (for WNF and anthrax: IV over the last year is authentically > than IV over the last 5 years)	0	0	0	0	0	0
5	IV in a season of a mass event over the last 5 years is authentically > than IV over the last 5 years	0	0	0	0	0	0
6	IV over the last 5 years is authentically ≥ 0,1	1	0	0	0	0	0
7	Are epidemic and epizootic infection onsets characteristic for Krasnodar Kray territory during a season of a mass event?	1	0	0	0	0	0
8	Has an infectious agent been detected (DNA, antigens, or antibodies to it been detected) during examinations of field materials taken on Krasnodar Kray territory over the last 5 years**	1	1	1	1		
	Have epizooties been registered on Krasnodar Kray territory over the last 5 years***					1	1
9	Has a number of infectious agent carriers on Krasnodar Kary territory over the last year been authentically higher than average multi-year number?**	0	0	0	0		
	Were there any adverse territories in terms of infection 1-3 months prior to a mass event in Krasnodar region? (adverse territories and anthrax burials in case of anthrax) ***					1	1
10	Has the infection value for infectious agent carriers on Krasnodar Kray territory over the last year been authentically higher than average multi-year value?**	0	0	0	0		
	Is any reinforced surveillance and limits on a number of food stuffs suppliers absent during a mass event?***					0	0
Total points sum / risk parameter		6/0,6	2/ 0,2	1/ 0,1	2/ 0,2	2/ 0,2	3/ 0,3

Note: * denotes intensive value (IV) over 100,000 people;
** denotes questions only for feral herds infections;
*** denotes questions for extremely dangerous zoogenous infections

Calculated "internal" risk parameter for WNF, CHF, tularemia, brucellosis, and anthrax, was low, but it was average for HFRS.

Overall epidemiologic situation as per feral herd infections and zoogenous infections with agents belonging to II pathogenicity group remained relatively safe. Diseases cases weren't group episodes and were sporadic. 68.2% cases in morbidity structure over 200-2014 belonged to HFRS; epidemic onsets for this disease are characteristic in subtropical areas of Krasnodar Kray throughout a year which is related to climatic peculiarities and natural reservoirs of Hantavirus. In particular,

in Sochi over 200-2015 8 cases (40%) of this infection were registered in autumn; 4 (20%), in winter; 3 (15%), in spring: and 5 (25%), in summer. Additional dangers were determined by the results of epizootologic research of the Kray territory. For example, in 2013 39.0% of samples with HFRS were taken in Adler district of Sochi where most sport and infrastructure objects were located and where participants and guests of mass events lived [8].

Available epidemiologic data and the results of accomplished assessment within population health risk management activities gave the grounds for a decision to take preventive measures against HFRS before the Olympics-2014. Additional activities on territory development and deratization were organized in Adler district in Sochi. Quarterly planned epizootologic examinations were provided at stationary observation points in forest-park zones; such examinations were also accomplished two times a year (in spring and in autumn) in Hantavirus feral herds. Experts worked out recommendations for medical and preventive organizations in Krasnodar Kray on providing better readiness for possible HFRS infection; training workshops for medical personnel devoted to diagnostics and treatment of feral herd infections and extremely dangerous infections were organized [8].

Due to all the implemented activities we managed to avoid serious epidemiologic complications in terms of HFRS. An only case of this disease was registered in Sochi in August 2014.

When greatest mass events takes place, risks increase substantially and workloads also grow dramatically; therefore, additional labor resource are usually brought from other administrative territories and the RF regions [6]. To reinforce laboratory services during the Olympics-2014 a specialized anti-epidemic team (SAET) from Rospotrebnadzor "Stavropol Antiplague Institute" worked in Sochi [5, 10]. SAET indicative laboratory functioned in Sochi during mass events which took place in spring, summer, and autumn in 2014-2016.

One of the tasks which were assigned for the team was to prepare for diagnostics of maximum list of infectious diseases. As per results of world epidemiologic situation analysis a list of agents inducing 82 nosologic infectious forms was drawn. Polymerase chain reaction (PCR) was determined as a basic specific indication technique for most pathogens of bacterial and viral nature. Volume of necessary stock of PCR test-systems required for analysis as per epidemic parameters was calculated with the use of a technique designed for mass events and based on determining epidemic complications risk in relation to each separate nosologic form. Assessment criteria in form of questions (totally 16) were formulated allowing for providing multi-factor analysis principles use.

Specific weight of various factors in the overall questions structure was as follows:

– "internal" epidemiologic risks as per an infection were 0.4375;

– "external" epidemiologic risks as per an infection were 0.125;

– risk for infection spread in the region was 0.125;

– risk for biological terrorism with the use of infectious agent was 0.0625;

– retrospect data on epidemic complications as per an infection during mass events were 0.0625;

– peculiarities of laboratory diagnostics organization during a planned mass event were 0.1875.

So, overall questions structure included not only epidemiologic risks but also algorithms of materials introduction into research; in other words, it enabled determining whether SAET was a main or a support base in diagnostics of a corresponding nosologic form. And a question list was flexible allowing changes in specific weights of various factors depending on a specific event peculiarities.

All infections were divided into three groups with the use of the developed technique according to degree of preparation each infection required: minimum preparation (or basic

one), increased preparation, and maximum preparation. After this division a possible volume of laboratory research during a mass event was set for each infections group and PCR test-systems stocks were accumulated on the basis of research volumes calculations. Stocks accumulation was accomplished as per 1:2-1:4 research ratio in relation to basic one for additional specific indication technique (an immune analysis technique).

As a results, equipping of SAET with diagnostic drugs during preparation to mass events was based on systemic principle. Risk-oriented approach application together with multi-factor analysis enabled precise calculations of possible maximum needs of the team in case of each separate infectious nosologic form. The number of performed research on epidemiologic reasons didn't exceed forecast figures. A stock of diagnostic test-systems was preserved for detection of absolutely all pathogens and it proves that SAET was sufficiently equipped with all necessary materials.

To facilitate managerial decisions in the sphere of sanitary-epidemiologic welfare of population during the Olympics-2014 experts of Rospotrebnadzor "Stavropol Scientific Research Antiplague Institute" created an innovative product, namely, a computer program based on geographical information system (GIS) platform [4]. This instrument made it possible to carry out a live time-spatial situation analysis. GIS-program included several layers: data on infectious diseases among population in the region, sanitary-hygienic situation at epidemiologically significant objects (ESO), information on workloads of laboratory bases, results of laboratory examinations performed on specialized occupational groups (workers who are included into such groups are to have regular medical check-ups; the list is approved by the RF Government) and on hot water supply systems in terms of Legionella occurrence, as well as other essential information. To implement the system into everyday work, an information interaction algorithm was created and later on implemented. Data from Rospotrebnadzor regional operative office in Krasnodar Kray were sent to a SAET on-duty worker: they were then processed and fed into the system. Information was available for specialists who participated in providing sanitary and epidemiologic safety of the event. All the data could be viewed and analyzed through any stationary or mobile device provided it had access to the Internet at a speed not less than 1 Mbit per minute [1, 4, 8].

Within the frameworks of risk-oriented approach application 629 epidemiologically significant objects in Sochi mapped in the GIS were preliminary ranked as per results of surveillance activities; they were divided into having "low", "average", "high", and "too high" risks for population. Disciplinary actions or additional inspections were assigned depending on the objects' potential danger. If certain preventive activities were accomplished then according to sanitary-hygienic situation assessment ESO could be moved into other categories with lower risk. All the necessary information was real-time presented in the GIS.

To control epidemiologic situation in the region, new analysis criteria were first used: "dynamic epidemiologic threshold", or a number of sick people on a certain territory over time; "epidemiologic spot", or spatial location of a diseases cases over an analyzed period of time [1, 4, 8].

"Dynamic epidemiologic threshold" criterion was adapted exactly for short-term and relatively short-term events. It helps to assess situation development as most up-to-date information is used when calculating it. It makes it possible to react most promptly in case epidemiologic situation deteriorates and it is truly essential during a mass event. During the Olympics-2014 "dynamic epidemiologic threshold" was calculated daily for measles, chickenpox, acute enteric infections and acute respiratory viral infections of various etiology. When it was exceeded and a possibility of an epidemiologic spot formation as per one or several nosologies occurred, a warning automatically appeared in the GIS.

During the Olympics-2014 several episodes of epidemiologic spots formation were registered; such epidemiologic spots meant

that diseases cases occurred in close proximity to each other and away from other diseases cases, there was one preliminary diagnosis out within 1-3 days time. For example, due to prompt reaction, specialists managed to prevent spread of measles.

Conclusions. Thus, new scientifically grounded approaches oriented at population health risk analysis concepts were worked out and later implemented during planning, organizing and accomplishing activities within epidemiologic surveillance system during preparation to and mass events themselves in Sochi.

A set of preventive activities in relation to feral herd infections and zoogenous infections endemic for Sochi territory and Krasnodar Kray as a whole, was planned allowing for accomplished assessment of epidemiologic complications risks. For the first time, a technique aimed at determining SAET needs in diagnostic preparations during mass events is introduced. Equipping SAET with test-systems for specific indication on the basis of performed calculations enabled to provide necessary readiness of laboratories, on the one hand, and to avoid excessive expenditure, on the other hand. Application of the GIS in everyday work during the Olympics-2014 made it possible to get a number of advantages, including more simple and faster information exchange in intra- and interdepartmental interaction.

Risk-oriented organization of certain activities in the system of providing anti-epidemic safety during mass international events on the RF territory was quite new experience for us. Its results make us optimistic about future prospects of wider implementation of the described approaches and other similar ones based on health risk analysis, into theory and practice of epidemiological surveillance.

Implementation of the created technique for assessing epidemiologic complications risks seems to be vital exactly during preparation for mass events which have fixed time limits. Its various modifications were applied in developing managerial decisions on preventing feral herd infections and zoogenous extremely dangerous infections as well as in determining volumes of equipping SAET with diagnostic test-systems. An issue of whether it is advisable to develop the technique further by introducing step-up and step-down coefficients for specific questions and danger factors representing their significance in the overall structure, still requires scientific justification.

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CHEMICAL FACTORS OF SOIL POLUTION IN TAGANROG AS POPULATION HEALTH RISK FACTORS

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Our research goal was to perform a hygienic assessment of soil pollution with chemicals on areas aimed for housing and recreation zones in Taganrog, Rostov region. Due to the fact that surface layer of city soils is an open dynamic system which is tightly connected to atmosphere and hydrosphere we treated pollutants content in soils as indicators of territory anthropogenic transformation and technogenic load on population. We used atomic-adsorption spectrophotometry to detect heavy metals and highly efficient liquid chromatography to detect 3,4-benzpyrene content. The results comprise 660 examined soil samples taken from 19 monitoring points; they were examined to detect 7 pollutants content (lead, zinc, copper, nickel, cadmium, chromium, and mercury) over 2008–2015; 144 samples were examined to detect 3,4-benzpyrene content over 2013–2015. We determined that priority pollutants among detected metals were zinc and lead; their content in city soils amounted up to 5.91 and 1.95 maximum permissible concentration. Complex indicator of city soils contamination varied from 1.61 to 2.02, long-term average annual value being 1.83. 3,4-benzpyrene was confirmed to be a substantial risk factor for population health as its concentrations exceeded maximum allowable values in 65.28 % of examined soil samples at average and maximum concentrations (2.45 and 38.05 MPC correspondingly). We recommend to include this chemical into systematic environmental quality monitoring. We detected regional peculiarities of soil pollution with chemicals on city territories aimed for housing, territories of pre-school children facilities, and recreation zones.

Key words: *hygienic assessment, social-hygienic monitoring, risk assessment, risk factors, chemical soils pollution, heavy metals, 3,4-benzpyrene, carcinogenic risk.*

If we want to provide sanitary and epidemiologic welfare and hygienic safety for the population we should improve the national system of social and hygienic monitoring based on using the maximum full objective data on components of "environment - population health" system. It helps to substantially decrease influence exerted by uncertainty factor when working out management decisions in the sphere of

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prevention and health improvement. Implementation of modern highly efficient physical-chemical techniques applied for hygienic assessment of environment components becomes really vital as we need to take immediate action aimed at improving domestic risk assessment and analysis methodology including principles of hygienic standardization based on risk assessment [2, 6, 7, 9, 11, 12, 13].

Urban ecosystems which form in most contemporary cities are characterized with apparent destructive effects in all environment components including soils in areas aimed for housing. Soil is a most essential environment component and it to a great extent determines environment quality and safety parameters, exerts considerable influence on population health and sanitary-hygienic conditions of life activity. Therefore, data obtained via dynamic monitoring over chemical pollution of soils in urbanized territories and changes it undergoes under technogenic load influence attract most attention among other environment parameters which require hygienic characteristics in social-hygienic monitoring system. Such data are also of great importance when danger is identified and exposure is assessed within the procedure of population risk analysis. City soils are an open dynamic system closely connected with atmosphere and hydrosphere; chemical pollution content in their surface horizon is an evidence of intensity and character of their anthropogenic transformation. Thus, dynamic monitoring over geochemical pollution parameters becomes one of the obligatory directions in studying prevalence of ecologically dependent nosologic forms including malignant neoplasms characterized with specific localizations and process types among population of large industrial centers [1, 8, 10, 14, 18].

3,4-benzpyrene being a 1st danger category pollutant holds a special place among priority xenobiotics and super-ecotoxicants with high degree of persistence, potential carcinogens and chemical carcinogenesis modifiers which accumulate in soils of industrial cities; dangerous chemical pollutants also include lead, chromium, cadmium, and nickel. 3,4 benzpyrene is a most widely spread carcinogenic and mutagenic muiltring aromatic hydrocarbon (MAH) in environment. It can be found in emissions of stationary industrial sources and motor transport. As a result of sedimentation and precipitation, 3,4-benzpyrene pollutes soil mantle, penetrates into vegetation easily and becomes a part of nutritional chains through crop production with apparent biological magnification. So, detecting 3,4-benzpyrene in soils becomes greatly vital in ecological analytics system and in social-hygienic monitoring [1, 3, 5, 15, 16, 17, 19]. Thus, when research on ecological assessment of soil and vegetation pollution level was previously accomplished in Rostov region, 3,4-benzpyere was detected in a zone influenced by emissions from Novocherkasskaya state district power station and its concentrations were considerably higher (up to 39.2 times) than maximum permissible concentration (MPC) [4]. We should note that application of 3,4-benzpyrene mass concentration assessment results in social-hygienic monitoring system substantially increases information value of hygienic assessment of environment chemical pollution including soils pollution; this hygienic assessment is then followed by health risk assessment.

Our research goal was to give hygienic characteristics of chemical soils pollution in Taganrog as per data obtained in the course of social-hygienic monitoring allowing for applying highly-sensitive technique of 3,4-benzpyrene detection.

Data and methods. When performing complex assessment of chemical soils pollution in areas aimed for housing and recreation zones in Taganrog, Rostov region, we used the results of examining 660

samples tested as per seven pollutants content including lead, zinc, copper, nickel, cadmium, chromium, and mercury; all the samples were taken over 2008-2015. They were taken at 19 monitoring points, 8 of which were located on the territory of municipal pre-school children facilities, 8 were situated in areas aimed for housing and influenced by motor transport emissions (in close proximity to crossroads with heavy traffic), and 3 were in recreation zones (Pushkinskaya embankment, Primorskiy park and "Solnechniy" beach). Unfavorable situation with Taganrog population morbidity of malignant neoplasms determined the necessity to expand a range of sanitary-chemical examinations and to include a procedure of potential carcinogenic risk assessment. Thus, since 2013 research on 3,4-benzpyrene content in environment objects has been performed according to a new state assignment within social-hygienic monitoring frameworks; soils have been included into this research (144 soils samples were examined over 2013-2015). Metal content in soils was determined via atomic-absorption technique with the use of "Kvant-2A" atomic-absorption spectrometer. We applied a technique aimed at measuring benzpyrene mass concentration in soils, grounds and sewage precipitations via highly efficient liquid chromatography (certificate No. 27-08 dated March 04, 2008). The mentioned measuring technique can be applied to soil and ground and specifies benzpyrene mass concentration detection via highly efficient liquid chromatography with fluorimetric detection; it provides results of benzpyrene mass concentration measuring within 4-80 mkg/kg range. The applied equipment includes "Stayer" stationary liquid chromatograph with fluorimetric detector and a PC with installed software "MultiChrom for Windows XP", version 1.5.

Degree of chemical soil pollution was assessed as per complex soil pollution index (Ksoil). To detect the index, we used a sum of separate pollutants concentrations coefficients (quotients from division of actual substances content in soil by their maximum permissible concentration) according to the methodical guidelines issued by RF Goscomsanepidnadzor on February 26, 1996, No. № 01-19/17-17 "Complex detection of anthropogenic load on water objects, soil, and atmosphere in areas aimed for housing". Complex soil pollution index (Ksoil) was calculated both in the city as a whole, and for separate categories of monitoring points (territories of municipal pre-school children facilities, areas aimed for housing in close proximity to crossroads with heavy traffic and recreation zones). When processing data, we used our own specialized software and professional package of statistic programs «Statistical Package for Social Science» (SPSS) version 13.0.»

Results and discussion. Examination results over 2008-2015 prove that copper, nickel, and mercury content in soils of monitoring points doesn't exceed their maximum permissible concentrations. Average concentrations of these metals amounted to 23.03±1.04 mg/kg, 20.48±0.55 mg/kg and 0.049±0.008 mg/kg, correspondingly. And their share contribution into complex soil pollution index was 4.08 %, 5.99 % and 0.54 %, correspondingly.

The maximum pollution index among all the detected metals belonged to zinc with its average concentration being 166.50±7.51 mg/kg (0.76 MPC) and share contribution into Ksoil being 17.71 %.

Zink content was higher than maximum permissible concentration in 15.76% samples with maximum index being 5.91 MPC.

Lead took the second rank place with its concentration being higher than MPC in 1.67% of examined samples and its average content in soils being equal to 38.36±2.30 mg/kg, maximum index being 1.95 MPC and specific weight in Ksoils equal to 6.90 %.

Table 1

Indices of soil pollution with metals in Taganrog, Rostov region, over 2008-2015

Indices		Taganrog as a whole, over 2008-2015	including:		
			Municipal pres-school children facilities	Housing areas (crossroads)	City recreation zones
Number of examined soil samples	abs.	660	288	288	84
LEAD (MPC is 130 mg/kg)					
Specific weight of samples with content higher than MPC	%	1,67	I 0,69	3,11	0,00
Average actual concentration	MPC	0,295	0,282	0,351	0,145
Minimal actual concentration		0,008	0,008	0,025	0,010
Maximum actual concentration		1,953	1,759	1,953	0,922
ZINC (MPC is 220 mg/kg)					
Specific weight of samples with content higher than MPC	%	15,76	12,80	22,92	1,19
Average actual concentration	MPC	0,757	0,720	0,905	0,367
Minimal actual concentration		0,025	0,025	0,025	0,031
Maximum actual concentration		5,913	1,917	5,913	1,724
COPPER (MPC is 132 mg/kg)					
Specific weight of samples with content higher than MPC	%	0,00	0,00	0,00	0,00
Average actual concentration	MPC	0,174	0,169	0,193	0,128
Minimal actual concentration		0,002	0,002	0,010	0,005
Maximum actual concentration		0,958	0,958	0,890	0,523
NICKEL (MPC is 80 mg/kg)					
Specific weight of samples with content higher than MPC	%	0,00	0,00	0,00	0,00
Average actual concentration	MPC	0,256	0,270	0,250	0,228
Minimal actual concentration		0,005	0,028	0,005	0,015
Maximum actual concentration		0,681	0,681	0,479	0,428
CADMIUM (MPC is 2 mg/kg)					
Specific weight of samples with content higher than MPC	%	0,45	0,35	1,19	0,35
Average actual concentration	MPC	0,174	0,184	0,135	0,175
Minimal actual concentration		0,000	0,030	0,000	0,014
Maximum actual concentration		5,300	1,010	5,300	2,070
CHROMIUM (MPC is 6 mg/kg)					
Specific weight of samples with content higher than MPC	%	0,34	0,00	0,79	0,00
Average actual concentration	MPC	0,146	0,130	0,188	0,060
Minimal actual concentration		0,000	0,010	0,003	0,000
Maximum actual concentration		3,983	0,988	3,983	0,438
MERCURY (MPC is 2.1 mg/kg)					
Specific weight of samples with content higher than MPC	%	0,00	0,00	0,00	0,00
Average actual concentration	MPC	0,023	0,016	0,033	0,014
Minimal actual concentration		0,000	0,000	0,000	0,000
Maximum actual concentration		0,881	0,192	0,881	0,098

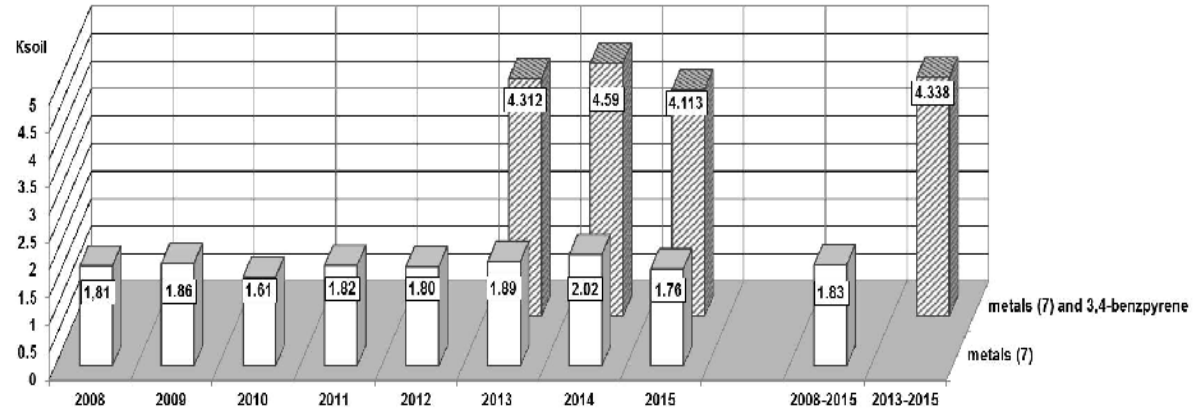

Figure 1. Complex index of chemical soils pollution in Taganrog over 2008-2015

Cadmium content higher than MPC was detected in 3 samples (0.45 %), and chromium content higher than MPC in 2 samples (0.34 %). maximum cadmium content was equal to 5.3 MPC, and chromium, 3.98 MPC.

The accomplished comparative analysis revealed that the highest content indices for such metals as lead, zinc, cadmium, and chromium, were detected in areas aimed for housing influenced by massive emissions of motor transport (crossroads), when their content was higher than MPC in 3.11 %, 22.92 %, 1.19 % and 0.79 % of examined samples. Soil pollution indices were significantly lower on territories of municipal pre-school children facilities where lead content (0.69%), zinc content (12.80%), and cadmium content (0.35%) in examined samples was higher than MPC. The lowest soil pollution indices were detected in recreation zones where only one sample had zinc content which was higher than MPC (table 1).

Complex city soils pollution index (Ksoil) determined by content of seven metals varied within 1.606 to 2.019 during the whole examined period. Average value amounted to 1.825, including municipal pre-school children facilities with 1.956, areas aimed for housing in close proximity to crossroads with heavy traffic with 1.910, and recreation zones with 1.077 (table 1, figure 1).

Results obtained over 2013-2015 prove that city soils are heavily polluted with 3,4-benzpyrene. Thus, 65.28% of 144 examined samples contain this pollutant in concentrations exceeding MPC, its actual average concentration being equal to 0.049±0.013 mg/kg (2.45 MPC). And its maximum registered content amounted to 0.761 mg/kg (38.05 MPC). And it is understandable that 3,4-benzpyrene pollution was considerably higher in areas aimed for housing in close proximity to crossroads with heavy traffic. MPC was exceeded in 71.30% of all examined samples with its average actual concentration being equal to 0.053±0.016 mg/kg (2.65 MPC). Recreation zones were less polluted with 3,4-benzpyrene as its concentrations higher than MPC were detected only in 50.00% of samples and its average and maximum concentration amounted to 1.85 MPC and 7.71 MPC, correspondingly (table 2, figure 2).

With 3,4-benzpyrene content taken into account in hygienic assessment of chemical soils pollution, its complex chemical index value and structure changes greatly. Thus, average value of complex index (Ksoil) over the last three years amounted to 4.338, with 3,4-benzpyrene share contribution being 56.44 % (table 2, figure 1).

Table 2

Indices of soils pollution with 3,4-benzpyrene in Taganrog, Rostov region, over 2013–2015

Indices		Years of monitoring			Taganrog as a whole over 2013-2015	including:	
		2013	2014	2015		Areas for housing (cross roads)	City recreation zones
Number of examined soils samples	abs.	48	48	48	144	108	36
Samples with concentrations higher than MPC (0.02 mg/kg)	abs.	35	34	25	94	77	18
Specific weight of samples with concentrations higher than MPC	%	72,92	70,83	52,08	65,28	71,30	50,00
Average actual concentration	mg/kg	0,0484	0,0514	0,0471	0,0490	0,0529	0,0369
	MPC	2,42	2,57	2,35	2,45	2,65	1,85
Its limiting error (±□, p<0.05)	mg/kg	0,0198	0,0114	0,0321	0,0127	0,0163	0,0128
Specific weight of pollutant in Ksoil	%	56,17	56,00	57,20	56,44	58,92	63,41
Minimum actual concentration	mg/kg	0,0044	0,0077	0,0032	0,0032	0,0044	0,0032
	MPC	0,22	0,39	0,16	0,16	0,22	0,16
Maximum actual concentration	mg/kg	0,3710	0,1542	0,7610	0,7610	0,7610	0,1542
	MPC	18,55	7,71	38,05	38,05	38,05	7,71

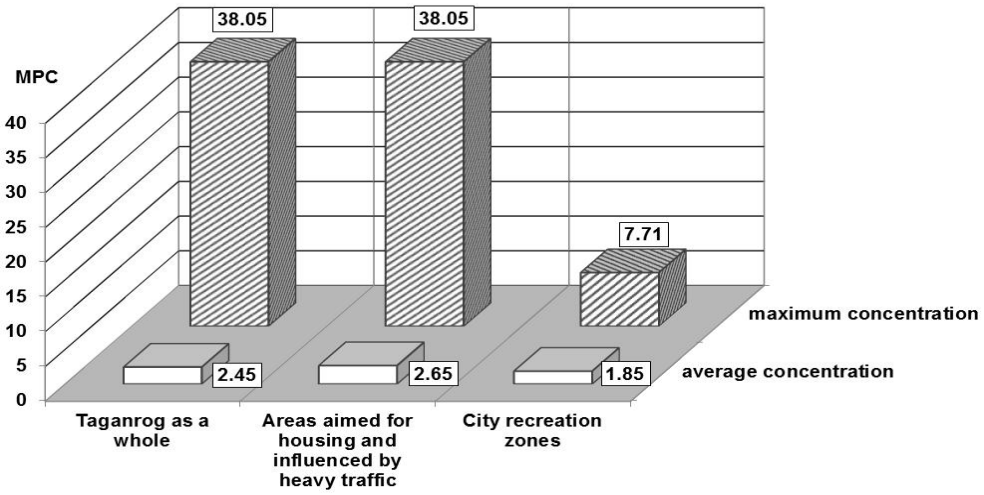

Figure 2. Indices of soils pollution with 3,4-benzpyrene in Taganrog, Rostov region, over 2013–2015

Conclusion. So, in our research we detected high level of soils pollution with 3,4-benzpyrene in Taganrog. This pollutant is highly stable, has great accumulation capacity in natural ecological systems and penetrates nutrition chains quite easily. Its carcinogenic, mutagenic and teratogenic effects on people are proved. It is advisable to examine 3,4-benzpyrene as a priority pollutant. In our opinion, integration of relevant databases into

regional geoinformation systems (GIS) and software providing data transfer into assessment of carcinogenic effects risk caused by chemical soils pollution in Rostov region would be a very promising trend in developing hygienic assessment of chemical soils pollution in social-hygienic monitoring system. Sampling examination of crop production (fruit and vegetables) grown on personal plots in the city in terms of 3,4-benzpyrene content in it is to take place in accordance with State Standard P 51650-2000 "Food stuffs. Techniques for detecting benzpyrene mass concentration". All the results obtained in this work will give grounds for population health risk assessment.

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INFLUENCE EXERTED BY HELICOBACTER PYLORI ON REGULATORY T-CELLS DIFFERENTIATION

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Estimating risks of infections induced by gram-negative Helicobacter pylori, is a vital problem for healthcare due to wide spread of the agent and wide range of induced pathologies which include malignant neoplasms in gastrointestinal tract. The agent is prone to long-term chronic persistence despite its "fragility" and its being greatly demanding to culturing conditions. The persistence issue is of special interest here as it is related to data on Helicobacter pylori capability to change immune response in infected people inducing suppressive regulatory immune reactions which are more favorable for the agent, both in stomach and in a whole body. Our research goal was to estimate Helicobacter pylori capability to induce differentiation of regulatory CD4+CD25+FoxP3+ human T-cells as basic mediators of immune response regulation under direct contact

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between bacteria and T-cells without any participation of most professional antigen-presenting cells. Our re-

search objects were clinical isolates of Helicobacter pylori and T-lymphocytes samples taken from people who didn't have Helicobacter pylori-infection in their case history; isolates and samples were jointly cultivated in vitro. We applied cytofluorometry to estimate changes in regulatory T-cells content. We detected that if T-lymphocytes and Helicobacter pylori were jointly cultivated during 18 hours in ratios from 1:10 to 1:50, regulatory T-cells content in cultures increased 2.12 times on average. This effects doesn't require any dendritic cells in a culture and obviously affects T-lymphocytes which are originally committed to regulatory T-cells in their development. Also, in our opinion, influence exerted on regulatory T-cells differentiation is a specific feature of Helicobacter pylori.

Key words: *Helicobacter pylori, lymphocytes, regulatory T-cells, differentiation, co-stimulation, antibodies, flow cytofluorometry, cell cultures.*

Helicobacter pylori (*H. pylori*) is a gram-negative bent bacillus which selectively forms colonies on mucous coat of human stomach and duodenum. At the moment *H. pylori* is considered to be an etiological agent causing acute and chronic gastritis, as well as etiologic pathogenic factor causing stomach and duodenum ulcer, stomach carcinoma and MALT-lymphoma [1, 10]. To succeed in colonies formation on mucous coat of stomach and duodenum, *H. pylori* has to overcome numerous mechanisms of inborn and adaptive immune system of a host which include acute neutrophilic and lymphocytic infiltration of a damaged area, as well as production of bacteria-specific IgM и IgA [2]. However, in spite of immune response evolvement, *H. pylori* can successfully persist in a stomach for decades [8].

There are some mechanisms which favor long persistence of *H. pylori* in a host; increased CD4+CD25+FoxP3+ T-regulatory cells content which can at least be observed at later contamination stages is one of them [9]. T-regulatory cells (T-reg) are a specialized subpopulation of CD4+ T-lymphocytes which is able to suppress activity of other lymphoid cells and either prevent or decrease intensity of inborn and adaptive immune response. T-reg basic physiologic function is to maintain peripheral tolerance [12]; T-reg absence or deficiency lead to evolvement of grave pathologies with autoimmune etiology [11]. At the same time, T-reg excessive activity is known to favor both infection process and tumors growth [13, 16].

Mechanism which helps *H. pylori* to induce increase in T-reg quantity has not been clearly defined yet, although immune-regulatory effects of T-reg induced by helicobacteriosis have been described. Thus, in particular, it is known that experimental autoimmune diseases proceed milder in experimental animals contaminated with *H. pylori*, [5, 15]. An attempt to generate T-regulatory cells via most profoundly described model of immune responses induction (T-lymphocytes activation by dendritic cells stimulated by helicobacter) gave controversial and multidirectional results. It led to induction of both T-reg and T-helpers of the 1st and 17th types which were active immune response stimulators [14]. Moreover, if during an experiment immune response shifts were detected to inhibiting T-reg as well as stimulating T-helpers of the 1st and 17th type, then mixed immune response without prevalence of any part was mentioned in both basic research and contemporary works [7, 8]. In our opinion, the existing data prove there are additional mechanisms which manage T-reg differentiation. They can be either stomach microenvironment conditions or direct effect exerted on lymphocytes by the agent able to contact them in mucous coat. Hypothesis of direct contact is most easily tested and has limited experimental confirmation [3, 4, 6].

Our research goal was to detect whether *H. pylori* exerted any influence on T-reg differentiation under conditions of direct contact between bacteria and T-cells and to assess the degree of such influence, as well as without participation of dendritic cells as most active antigen-presenting cells of immune system.

Data and methods. Our research objects were samples of whole peripheral blood taken from people with gastroenterological diseases (n = 6), who didn't have *H. pylori* in their case history and it was also proved by

objective research data, and also *H. pylori* clinic isolates obtained during diagnostic fibergastroscopy. 8-9 ml of blood were taken only once, into vacuum vials with sodium heparin (Vacuette, Germany). Work with samples started not later than 2 hours after sampling. Mononuclear cells of peripheral blood (MCPB) were extracted from blood samples via centrifuging (45 minutes, 1500 turns per minute) on «Diakoll-1077» density gradient («DiaEm», Russia). The obtained MCPB were divided into adhesive monocytic fraction and non-adhesive lymphocytic one via adhesion on plastic (2 hours). Only lymphocytic fraction was used in further research. *H. pylori* was extracted out of bioptic material obtained during diagnostic fibergastroscopy from antral section and body of stomach performed on patients with positive CLO-test. The obtained material was ground mechanically and sowed on Colombian agar (Becton Dickinson, USA) and 10%-defibrinated donor blood was added to it as well as antibiotics which were needed to suppress growth of extraneous microflora and fungi (10 μg/l of vancomycin, 5 μg/l of Trimethoprimum, 2 μg/l of nystatin, all produced by Teva, Israel). Cultivation was performed under microaerophilic conditions at 37 °C, during 7 days. Helicobacter was identified on the basis of cultural and morphological features. To assess influence exerted by *H. pylori* on lymphocytes differentiation to T-regulatory cells direction, we accomplished joint cultivation of lymphocytes with various bacteria concentrations (we used 1:10, 1:20, and 1:50 lymphocytes to *H. pylori* ratios) for 18 hours under the following conditions: 5 % CO_2, 37 °C, RPMI-1640 medium (Gibco, USA) adding 10% embryonic calf serum and 0.3 g/l L-glutamine ("Paneko", Russia). A part of lymphocytes was jointly cultivated with bacteria with additional stimulators, such as CD3 molecule monoclonal antibodies (1 μg/ml, eBioscience, USA), or CD3 and CD28 antibodies mixture (1 μg/ml, eBioscience, USA and 3 μg/ml, Beckman Coulter, France). Lymphocytes without *H. pylori* supplement were negative control for all cultures. Lymphocytes cultivated with *E. coli* in 1:50 ratio, both with and without antibodies, were additional control. After 18 hours we applied cytofluorometry to assess T-regulatory lymphocytes content in cultures as cells of CD4+CD25+FoxP3+ phenotype. To paint the said markers, we used FITC-tagged CD4 antibodies, APC-tagged CD25 antibodies, PE-tagged FoxP3 antibodies, all produced by eBioscience, USA. Membrane permeabilization necessary for FoxP3 tagging was conducted with the use of «Foxp3 / Transcription Factor Staining Buffer Set» (eBioscience, США) as per manufacturer's instructions. We performed the analysis with the use of FacsCalibur cytofluorimeter (Beckton Dickinson, USA). To statistically process the obtained data, we used Newman-Keuls criterion.

Results and discussion. Figures 1 and 2 present the data on influence exerted by *H. pylori* on lymphocytes differentiation to T-reg direction when dendritic cells were absent in cultures. As we can see, adding *H. pylori* to T-cells culture led to authentic increase in T-regulatory CD4+CD25+FoxP3+ cells after 18 hours of joint cultivating (average T-reg content in cultures without bacterial stimulation amounted to 6.01 ± 0.72 % of all CD4+ cells, but when *H. pylori* was added in 1:10 ratio, T-reg content grew up to 15.04 ± 1.97 %, $p<0.01$).

Cells content in cultures with lymphocytes-bacteria ratio being 1:20 and 1:50 was also authentically higher than control values for non-stimulated lymphocytes (12.7 ± 1.53 % for 1:20 and 10.42 ± 1.97 % for 1:50, discrepancy from control is authentic, $p<0.01$).

At the same time, as we can see, there was a trend of inverse dose relation in a number of ratios. 1:10 ratio had the greatest growth in T-reg quantity which went down as bacteria number in cultures grew. However, this trend remained statistically not authentic. So, the obtained data reveal that *H. pylori* has some influence on responding T-lymphocytes regardless of dendritic cells presence in a culture (as most efficient antigen-presenting cells); in our opinion, this influence was mediated by direct contact between bacteria and responding T-lymphocytes).

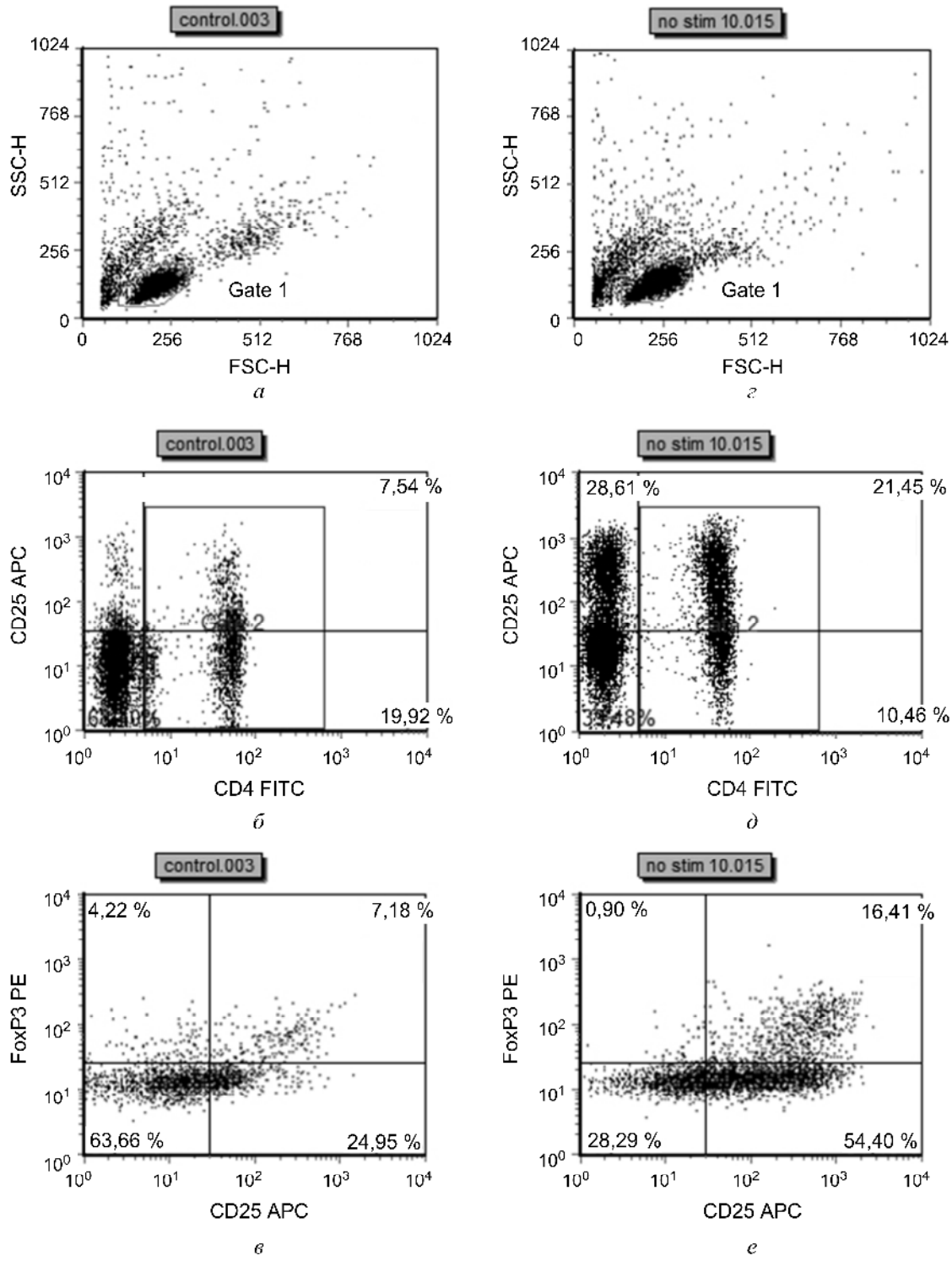

Figure 1. *H. pylori* increases T-regulatory cells content in joint cultivating with lymphocytes: *а – в* are the data obtained in representative experiment, T-regulatory cells content in cultures without *H. pylori* (*а* is cells distribution as per light scattering, *б* is CD4+CD25+ cells extraction, *в* is FoxP3+ T-regulatory cells extraction, the estimated population is in the upper right quadrant); *г – е* the data obtained in representative experiment, T-regulatory cells content in cultures, which grew with *H. pylori* (*г* is cells distribution as per light scattering, *д* is CD4+CD25+ cells extraction, *е* is FoxP3+ T-regulatory cells extraction, the estimated population is in the upper right quadrant). estimated markers and registered parameters are given at axes, cells percentage is given in angles of quadrants

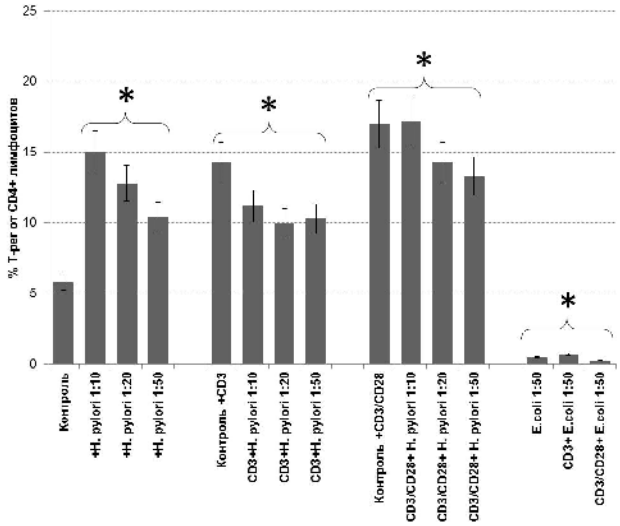

Figure 2. *H. pylory* influence on T-regulatory cells differentiation. Stimulation variants are given below the diagram. Control is lymphocytes without bacteria and antibodies; * discrepancies with control culture are authentic, $p<0.01$

(x-axis: control; y-axis: % of T-reg in CD4+ lymphocytes)

At the same time, there can be some impacts caused by B-lymphocytes present in cultures under these experimental conditions as such cells also have antigen-presenting properties. To exclude their impacts in future, we plan to perform B-cells depletion.

To check co-stimulation significance, we had additional culture types where not only bacteria but also CD3 and CD28 stimulating antibodies were applied; such antibodies gave T-cells a signal similar to antigen-presenting cells stimulation.

Figure 2 presents the results of analyzing cultures with antibodies. As we can see, stimulation with antibodies instantly led to significantly high levels of T-reg content in cultures (14.0 ± 1.29 % of T-reg for cultures where only CD3 without *H. pylori* were added, 16.54 ± 2.13 % for cultures where CD3 and CD28 mixture was added, a model of more comprehensive stimulation, but still without *H. pylori*). *H. pylori* introduction into cultures didn't cause increase in T-reg content (for cultures with CD3 T-reg content amounted to 11.25 ± 1.06 % for 1:10 ratio, 10.04 ± 1.14 for 1:20 ratio, 10.28 ± 1.54 % for 1:50 ratio, there were no authentic discrepancies with culture with CD3 without *H. pylori*; T-reg content amounted to 16.93 ± 3.74 % for cultures with CD3 and CD28 mixture for 1:10 ratio, 13.95 ± 2.13 % for 1:20 ratio, 12..82 ± 1.28 % for 1:50 ratio, there were no authentic discrepancies with culture with CD3+CD28 mixture without *H. pylori*). Just like in case with cultures stimulated by *H. pylori* only, we observed a trend to inverse dose relation between microbe dose in a culture and T-reg content.

All values of T-reg content in cultures with CD3 and CD3+CD28 were authentically different from T-reg content in cultures of lymphocytes without antibodies and *H. pylori* ($p<0.01$) and they had no discrepancies with cultures stimulated by *H. pylori* without antibodies. So, *H. pylori* stimulates lymphocytes differentiation to T-reg at the level of activation by antibodies. Lack of increase in T-reg content in cultures stimulated simultaneously by *H. pylori* and antibodies can probably be explained by polyclonal character of antibodies' activating effect which resulted in differentiation of all CD4+ T-cells initially committed to development into T-reg. To check specificity of *H. pylori* effects, we used lymphocytes cultures stimulated by another microbe which inhabited human gastrointestinal tract, namely *Escherichia coli (E. coli).*

Lymphocytes and *E. coli* cultures which we used grew both with and without CD3 and CD28 antibodies. Lymphocytes and *E. coli* ratio was 1:50. As we can see on Figure 1, E. coli didn't cause T-reg growth in cultures and prevented antibodies' stimulating effects. Thus, the data we obtained show that effects which stimulate T-reg differentiation are caused exactly by *H. pylori* and apparently they are not mediated by pathogens patterns (which are similar in *H. pylori* and *E. coli,* both being active gram-negative microbes).

Conclusions. Assessing whether microbes can modulate immune responses is a vital fundamental and practical task, in particular, if such modulation makes for microbes survival in a host. A better insight

into such mechanisms undoubtedly can help both to predict possible risks caused by a microbe and to raise the efficiency of therapeutic approaches to pathologies caused by such microbes. In our work we showed *H. pylori* ability to exert differentiating effects on T-lymphocytes directing them to T-regulatory cells. If there were no dendritic cells in cultures (immunocytes population), the process as per contemporary data had most apparent ability to manage immune response. Within the examined group, such effects were observed when microbes and T-cells ration in cultures was from 1:10 to 1:50, and they didn't require antigen-presenting cells or stimulating antibodies' presence in cultures. On average, growth in percentage of T-regulatory CD4+CD25+FoxP3+ cells among CD4+ lymphocytes amounted to 2.12 times. Apparently, under this experiment conditions, *H. pylori* influence affected cells initially committed to development into T-reg, as polyclonal stimulation with CD28 antibodies and/or CD3 antibodies "absorbed" the effect from bacteria introduction; cultures stimulated only with antibodies, as well as antibodies together with *H. pylori*, had no statistic discrepancies in T-reg content. Apparently, differentiating effect was a specific feature of *H. pylori*, as lymphocytes stimulation with another microbe able to survive in human gastrointestinal tract for a long time (*E. coli*) didn't lead to increase in T-regulatory cells content. So, we essentially showed that *H. pylori* was able to exert influence on T-regulatory cells differentiation; this effect wasn't mediated by presentation of microbe antigens with dendritic cells, but evidently it depended on direct influence exerted by the microbe on T-cells. Insight into this mechanism' nature may enable determining its active principle which induces T-reg development and hence is potentially a natural tolerogenic factor which can be used as a medication.

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ON DETECTING REFERENCE LEVEL OF ACROLEIN CONTENT IN CHILDREN'S BLOOD

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The article gives the results of complex chemical-analytical and clinical-laboratory research in course of which biological media of children living in Perm region were examined. To study impacts exerted by exogenous acrolein we examined 156 children in 2014–2016, aged 5–10, attending pre-school facilities and schools, and living in Perm region. As we conducted this research we detected average annual acrolein concentration in atmosphere on the examined territory; this concentration was equal to 0.000024 mg/m3, and it was 1.2 times higher than reference acrolein concentration in the air for chronic inhalation exposure. Average group acrolein concentration in children's blood was 1.2 times authentically higher ($p<0.05$) than regional background level of acrolein content in blood of children living on conditionally clean (control) territory of Perm region. Average content of malonic dialdehyde in blood plasma and IgG specific to acrolein was 1.2 and 1.4 times authentically higher than physiological standard for these parameters ($p<0.05$). Average group concentration of delta-aminolevulinic acid in urine was detected at the top limit of physiological standard. Applying odds relation criterion ($OR=e^{a0-a1x}$) we obtained authentic models for correlation between acrolein content in blood and G immunoglobulin specific to acrolein, antioxidant activity of blood plasma, crude bilirubin in blood, and delta-aminolevulinic acid in urine ($F>3.96$, $p\leq0.05$). We used increased content of delta-aminolevulinic acid in urine as a limiting marker for effects occurring at chronic inhalation exposure to acrolein. Basing on the results of the performed examination we recommend concentration equal to 0.10 mgr/dm^3 as a reference level of acrolein content in blood at chronic inhalation exposure

Key words: *acrolein, chronic exposure, response markers, blood, highly efficient liquid chromatography, delta-aminolevulinic acid, bilirubin, reference level.*

Nowadays, protection of population health is among top priorities in state policy. Atmosphere becomes more and more contaminated every year due to increased emissions of technogenic substances, and it requires greater attention and expert solutions to problems of providing safe environment for population.

As per World Health Organization data, up to 500,000 compounds are used in industry, which are potentially capable to contaminate environment. Volatile organic compounds (VOC) are the most widely spread among multi-components structure of air pollutants. Acrolein is a priority pollutant among volatile organic compounds [3].

Acrolein (acrylic aldehyde, ethylene-aldehyde, 2-propionic aldehyde) is an

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elementary unsaturated aldehyde with high reactivity; it is a colorless, tear-inducing liquid with strong smell, very volatile and with low boiling temperature (52.7 °C). It is contained in the air as vapor, vapor pressure being 0.145 MPa at 5 °C [14].

Acrolein is used in production of acrylic acid, methionine, 1,3-propandiol, pyridine, glutaralaldehyde, β-picolin, acrylonitril, medications, herbicides, flavoring agents, plasticizers, etc. [14]. Motor transport emissions, combustion activities, photooxidation of hydrocarbons which are contained in the air (propylene, 1,3-butadiene, pentadiene), households and industrial waste burial, contribute greatly into total air pollution in big cities [1, 2, 12]. In everyday life a substantial contribution is made by tobacco smoke, release out of polymeric materials, heating of butters and fats, both vegetative and animal ones, during cooking (roasting, smoking).

Average daily concentration and maximum single permissible concentration of acrolein in atmosphere amount to 0.01 and 0.03 mg/m3 correspondingly. Reference concentrations of the toxicant in the atmosphere (RfC) are extremely small and amount to 0.0001 mg/m3 for acute inhalation exposures and 0.00002 mg/m3 for chronic exposures [11]. Danger category is 2. Regional background level of acrolein content in blood of children living in Perm region amounts to 0.138 ± 0.035 mg/dm3 [9].

Acrolein enters a human body mostly via inhalation. Under chronic exposure acrolein exerts overall toxic, irritating, and allergenic effects and also has mutagenic properties [12, 16]. Research of chronic effects of acrolein on lungs functioning revealed that it made for inflammation and damage to respiratory organs tissues in adults [17]. But children to a greater extent are prone to toxicants' effects, and acrolein which is contained in tobacco smoke in concentrations equal to 1.6–3.6 μkg/m3 [21], can cause a bronchospasm and increased secretion of mucous coat cells which is characteristic for bronchial asthma. Besides, lung functioning can deteriorate and number of bronchial asthma cases can increase under chronic exposure in childhood [16].

Acrolein induces oxidizing stress in a body. Cells death induced by acrolein and mostly having a form of necrosis, is accompanied by accumulation of active oxygen forms (AOF) in them [20, 22]. Acrolein can directly stimulate mitochondrial oxidizing stress violating the function of electrons' mitochondrial feed system [21].

But at the same time acrolein is a natural metabolite of a human body and can be found in its biological media (blood and urine) [13]. Acrolein is formed endogenously in micro-quantities as lipid peroxidation product in metabolic processes of polyamines (spermine and spermidine) [10, 23].

Our research goal was to define reference level of acrolein content in children's blood under long-term intake with atmospheric air as per results of assessing "acrolein concentration in blood - response markers" correlations.

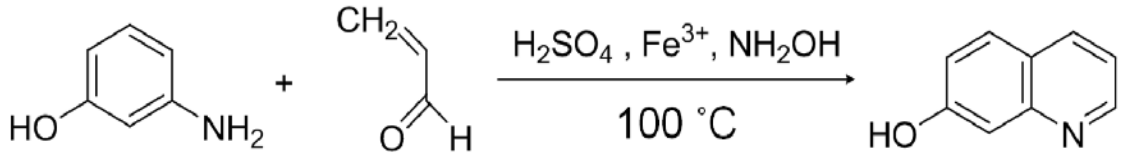
Data and methods. In accordance with the set goals, we examined a group of children (n = 156) in 2014-2016, aged 5-10 years, attending pre-school children facilities and schools and living in Perm region since their birth.

Acrolein in the atmosphere on the examined territory was detected as a derivative with the use of fluorometry in conformity with Methodical Guidelines 4.1.3356-16 "Measuring acrolein mass concentration in the atmosphere via highly efficient liquid chromatography" [8].

Biomedical research was accomplished in conformity with obligatory observation of ethical principles on medical-biological research stated in Helsinki declaration dated 1975 with supplements made in 1983 and RF State Standard 52379-2005. A legal representative of each child included in our sampling gave his or her written informed consent to voluntarily take part in biomedical research carried out by experts of Federal Scientific Center for Medical and Preventive Health Risk Management Technologies.

We determined acrolein content in blood via highly efficient liquid chromatography on

reversed phase C18 with fluorimetric detection in accordance with Methodical Guidelines 4.1.3158-14 [7]. The range of measured acrolein concentrations in blood amounted to 0.1–5.0 mg/dm3. Before the analysis, we performed a reaction of acrolein derivatization with meta-aminophenol in order to transfer the analyte from its free state into bound one and to obtain a derivative 7-hydroxyquinoline, a stable compound capable of fluorescence (figure 1).



Meta-aminophenol Acrolein 7-hydroquinoline

Figure 1. Reaction of acrolein derivatization with 3-aminophenol

We studied several biochemical parameters as response markers at acrolein inhalation intake [1, 4, 18, 19] (crude and conjugated bilirubin in blood serum, delta-aminolevulinic acid content in urine, antioxidant activity, malonic dialdehyde content in blood plasma, creatinine concentration in blood serum) with the use of unified techniques [5]; we also studied immunologic parameters (acrolein-specific IgG content) via allergosorbent testing with enzymatic mark. All the research was performed by experts of biochemical and cytogenetic diagnostics department at Federal Scientific Center for Medical and Preventive Health Risk Management Technologies.

We justified biological response markers as per odds relations calculation (OR) characterizing correlation between acrolein concentration in blood and biochemical response parameters. OR>1 condition was taken a criterion of correlation existence [13].

We detected parameters of odds relation dependence on acrolein concentration in blood via regression model making in a form of exponential function OR=ea0–a1x, where OR was odds relation parameter; x was acrolein concentration in blood, mg/dm3; a0, a1 were model parameters detected with regression analysis technique.

The validity of the obtained model was assessed via single-factor variance analysis as per Fischer criterion (F>3.63). Discrepancies in results were considered to be statistically significant at $p \leq 0.05$ [15].

Reference level was defined on the condition. We took a value corresponding to the upper 95% confidence limit of the obtained model as a reference level [6].

We accomplished processing of all the data obtained in the course of our research and model parameters assessing with the use of Statistica 6.0 applied software and other specialized software.

Results and discussion. Over 2014–2016 average annual acrolein concentration in the atmosphere amounted to 0.000024 mg/m3 on the territory where the examined group lived. It turned out to be lower than average daily concentration and maximum single permissible acrolein concentration in the atmosphere but it was 1.2 times higher than the reference acrolein concentration in the air for chronic inhalation exposure [11].

Acrolein concentrations detected in blood of children from the focus group varied within 0.10–2.34 mg/dm3 range. Average group concentration amounted to 0.16 ± 0.01 mg/dm3, which was authentically 1.2 times higher ($p<0.05$) than regional background level of acrolein content in blood of children living on conditionally clean territory of Perm region [9].

We studied biochemical and immunologic parameters of blood and urine taken from the examined children; the results are given in Table 1 as average group values ($M \pm m$).

Analysis of biochemical and immunologic parameters of children's blood under chronic inhalation exposure to acrolein revealed authentically 1.2 times higher (p<005) average group malonic dialdehyde content in plasma and 1.4 times higher acrolein-specific IgG content in comparison with physiological standard. Average group concentration of delta-aminolevulinic acid in urine was detected at the upper limit of physiological standard and it proves there's a trend of increase in this parameter under chronic exposure to acrolein.

We built relation models showing dependence of biochemical and immunological parameters of children's blood (effect markers) on acrolein concentration in blood (exposure marker) and it helped us to obtain authentic models (F>3.96; $p \leq 0.05$) of correlation between acrolein concentration in blood and increased crude bilirubin content in blood plasma, increased level of delta-aminolevulinic acid in urine, lower antioxidant blood plasma activity, increased acrolein-specific IgG content in blood plasma (Table 2).

Table 1

Results of analyzing biochemical and immunologic parameters of blood and urine taken from children (n = 156), 2014–2016

Parameter, unit of measure	Standard	Focus group, $M \pm m$	Validity of discrepancy, p
Antioxidant plasma activity, %	36,2–38,6	35,8 ± 1,4	>0,05
Crude bilirubin, μmol/dm^3	0–18,8	9,31 ± 1,35	>0,05
Conjugated bilirubin, μmol/dm^3	0–4,3	2,50 ± 0,17	>0,05
Delta-aminolevulinic acid in urine, μmol/dm^3	0,0012–0,013	0,013 ± 0,001	>0,05
Malonic dialdehyde in blood plasma, μmol/dm^3	1,8–2,5	3,02 ± 0,12	<0,05
Creatinine in blood plasma, μmol/dm^3	28–88	57,9 ± 1,4	>0,05
Acrolein-specific IgG, st.un.	0–0,15	0,33 ± 0,11	<0,05

Table 2

Parameters of mathematic models describing "acrolein concentration in blood - odds relation (OR = ea0–a1x) of deviations in laboratory parameter" dependence

Laboratory parameter	Model parameters		Fischer criterion, F	Validity, p	Acrolein concentration in blood, mg/dm^3
	a_0	a_1			
Antioxidant plasma activity, %	–1,27	8,09	113	<0,05	0,15
Crude bilirubin, μmol/dm^3	–5,27	37,72	74,99	<0,05	1,14
Delta-aminolevulinic acid, μmol/dm^3	–0,85	7,29	108,94	<0,05	0,10
Acrolein specific IgG	–2,50	9,04	43,21	<0,05	0,25

Crude bilirubin content in blood of children from the focus group was higher than physiological standard in 3% cases (n = 153). Dependence of odds relation for increase in bilirubin content in blood on growth in acrolein concentration in blood (F = 74.995; p<0.05) is described with the following equation $OR = e^{-5,273-37,772x}$. In the given case 95%-upper confidence limit of reference level of acrolein in blood is equal to 0.14 mg/dm^3.

Antioxidant activity of blood plasma in children from the focus group was lower than physiological standard in 52% cases (n = 121).

Authentic dependence of odd relation for decrease in antioxidant plasma activity on acrolein concentration in blood ($F = 113$; $p = 0.05$) is described with the following equation $OR = e^{-1,267-8,086x}$. In the given case 95%-upper confidence limit of reference level of acrolein in blood is equal to 0.15 mg/dm^3 (Figure 2).

Delta-aminolevulinic acid level in urine characterizing porphyrinic metabolism disorder was on average 1.5 times higher than in 44% of the examined children ($n = 98$). Dependence of odds relation for increase in delta-aminolevulinic acid in urine on acrolein concentration in blood is described with the following equation $OR = e^{-0,851-7,291x}$ ($F = 108.94$; $p = 0.05$), 95%- upper confidence limit of reference level of acrolein in blood is equal to 0.10 mg/d,^{3} (Figure 3).

The obtained results correlate with the data taken from scientific research; according to these data, chronic exposure to acrolein leads to disorders in porphyrinic metabolism, lower antioxidant plasma activity and consequently to Red/Ox cells potential disorders.

Acrolein-specific IgG in children from the examined group was higher than physiological standard in 46% cases ($n = 74$). Dependence of odds relation (OR) for increased acrolein-specific IgG level on acrolein concentration in blood is described with the following equation $OR = e^{-2,503-9,044x}$ ($F = 43.213$; $p = 0.05$), 95%-upper confidence limit of reference level of acrolein in blood is equal 0.25 mg/dm^3 (Figure 4).

Basing on the calculated relation models ($p = 0,05$), we calculated levels of exposure marker content (acrolein concentration in blood, mg/dm^3), which cause immune system suppression and disorders in oxidation-reduction cells potential, porphyrinic metabolism disorders, and disorders in bilirubin metabolism.

Minimal acrolein content in blood (0.10 mg/dm3) was detected in case of increased delta-aminolevulinic acid concentration in blood which was higher than physiological standard. In relation to that, we recommend to use increased delta-aminolevulinic acid content in urine as reference level of acrolein content in blood (concentration equal to 0.10 mg/dm3) and as a limiting effect marker under chronic exposure to acrolein.

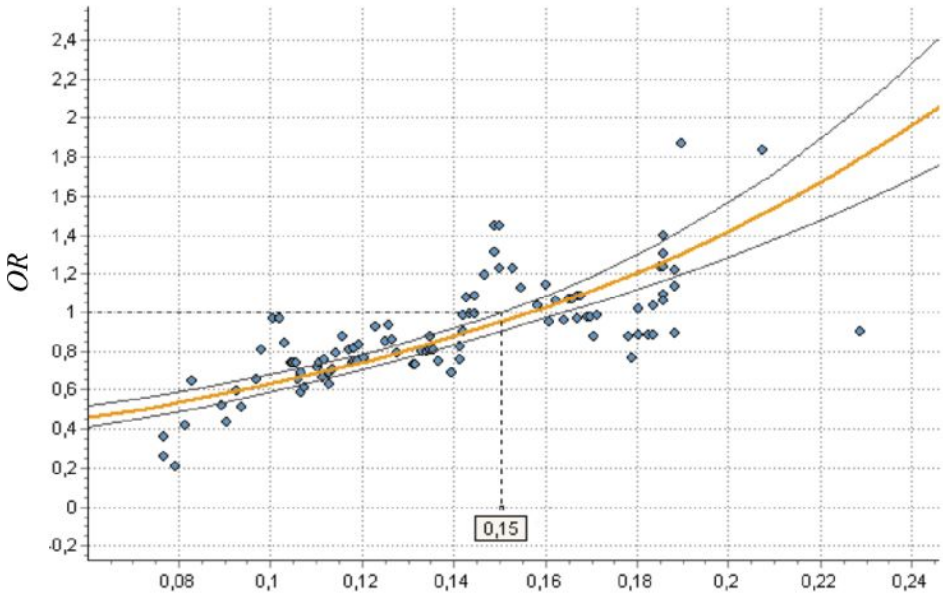


Figure 2. Dependence of odds relation (OR) for lower antioxidant activity of blood plasma on acrolein content in blood

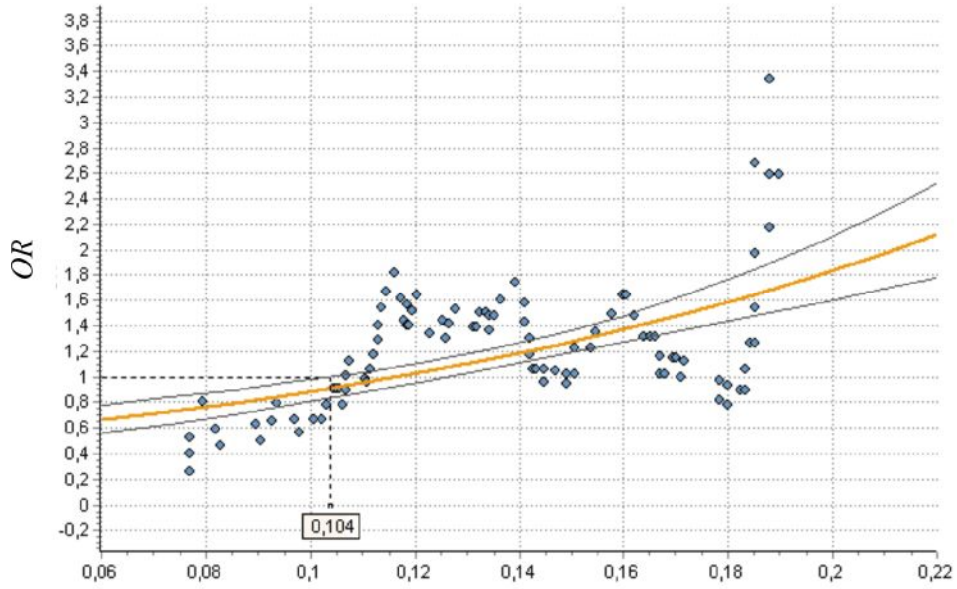


Figure 3. Dependence of odds relation (OR) for increased delta-aminolevulinic content in urine on acrolein concentration in blood concentration in blood

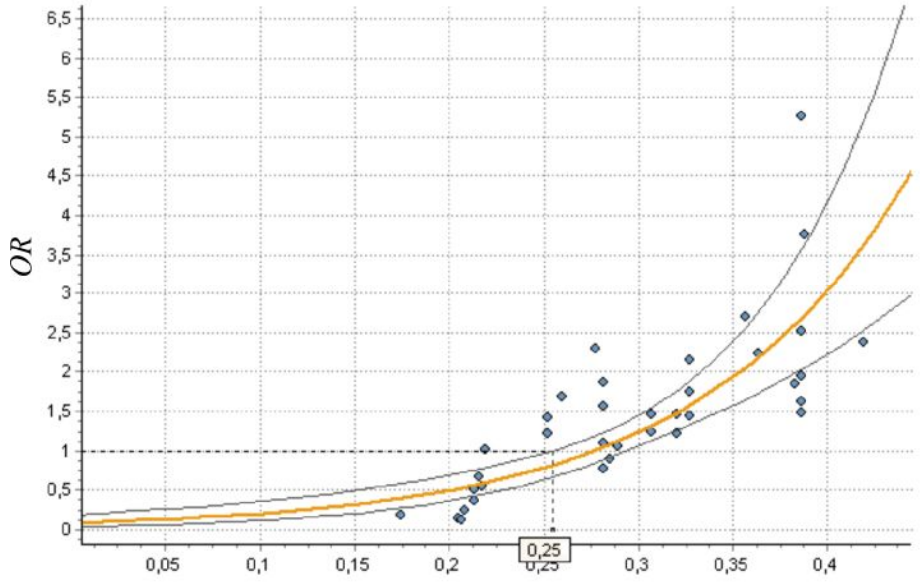


Figure 4. Dependence of odds relation (OR) for increased content of acrolein-specific IgG on acrolein content in blood

Conclusions:

1. We detected authentically higher malonic dialdehyde content in blood plasma and acrolein-specific IgG, both parameters being 1.2 and 1.4 times higher than physiological standard correspondingly ($p<0.05$), average

group concentration of delta-aminolevulinic acid in urine was detected at upper limit of physiological standard.

2. We obtained authentic models of correlation ($F>3.96$; $p\leq0.05$) between acrolein content in blood and disorders in porphyrinic metabolism as per increased delta-aminolevulinic content in urine, oxidizing stress occurrence as per antioxidant activity of blood plasma, suppressed immune response as per acrolein-specific IgG content.

3. We detected acrolein concentrations in children's blood (mg/dm3), which caused immune system suppression, decrease in antioxidant blood plasma activity, disorders in porphyrinic and bilirubin metabolism; these concentrations were equal to 0.25; 0.15; 0.14 and 0.10 mg/dm3 correspondingly.

4. We recommend acrolein concentration equal to 0.10 mg/dm3 as reference level of acrolein content in children's blood; this concentration was detected at studying dependence of odds relation (OR) for increased delta-aminolevulinic acid content in urine on acrolein concentration in blood.

5. The detected reference acrolein concentration in blood can be used as a safety parameter under long-term intake of acrolein with atmospheric air within biological monitoring frameworks, when assessing population health risks, in diagnosing ecologically-dependent changes in health state, when assessing efficiency of medical-preventive activities, as well as evidence base used in sanitary-epidemiologic studies, investigations, and examinations.

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

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NUMERICAL MODELING OF ACIDITY DISTRIBUTION IN ANTRODUODENUM AIMED AT IDENTIFYING ANOMALOUS ZONES AT CONSUMING DRINKS WITH DIFFERENT PH LEVEL

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The article focuses on describing mathematical model of a multi-phase flow in antroduodenum and its application for predicting digestive process features, including pH level detection. The suggested sub-model representing antroduodenal area of gastrointestinal tract is being developed within the frameworks of mathematical multilevel model depicting evolution of damage to critical organs and systems under exposure to risk factors. We introduced damages as per three functions (motor, secretory and absorbing one) to several gastrointestinal tract zones (body of stomach, antrum, and duodenum) and to pancreas and liver, into the sub-model. Mathematical problem statement includes records of mass and impulse conservation equations for mixture of liquid incompressible phases; ratios for mass flow intensity vector due to diffusion processes; ratios for mass sources due to reactions, secretion and components absorption, food dissolution, initial and terminal conditions. We obtained numeric experiment results when drinks with various pH level (2.3; 3.5; 7) were consumed; they revealed that anomalous considerable increase in acidity occurred in pyloric opening zone and duodenal cap zone when a drink with pH level equal to 2.3 was consumed. The results presented in this work make a considerable contribution into mathematical modeling development used to describe multiphase flows in biological channels with variable form. We showed that obtained acidity levels in various antroduodenum zones correspond to experimental data given in the works of other researchers. In future the model can be applied to predict risks of duodenum damages evolvement together with detecting areas of their localization under exposure to negative factors.

Key words: *mathematic modeling, functional damages evolution, antroduodenum, pH level, neutralization of acid, mucous tunic damages, tract motility, risk factors.*

Technologies and industrial productions are developing rapidly nowadays and it leads to greater volumes and wider spectrum of chemicals' emissions into the environment. Consequently, food stuffs can contain increased toxicants' concentrations, including heavy metals, which can penetrate, for example, vegetables and fruit via contaminated soil, atmospheric air, and water used for irrigation. Besides, manufacturers use new food additives to improve taste or to prolong storage life; however, impacts which are exerted on a body by such additives are not studied enough. Irregular and imbalanced

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nutrition also makes for additional risks for negative responses in terms of health; in particular, we can mention fast-food, fatty food and food rich in calories, beverages with increased acidity. For example, acidic content of gastrointestinal tract (GIT) can cause substantial damage to teeth enamel and dentin due to erosive factors [10, 13]; it can also cause ulcer evolvement in stomach and duodenum [20, 22].

The existing models applied for assessing influence exerted by environment on health as a rule are "black box models" and they don't apparently allow for variable exposure of factors, impact duration and mechanisms, organs and systems physiology [4, 9]. To get more profound insight into processes of damage evolving in organs and systems, a group of researchers, including the authors of this paper, offer to use a mathematic model based on multi-level approach [2]. The upper (or macro) level of the model deals with averaged interaction between organs and systems with the use of ordinary differential equations which describe damage evolution. Damage characterizes functional capabilities of an organ and it can be from 0 to 1 (0 means there are no functional disorders, 1 means that functions fail completely). Damage is assumed to change over time (age) due to natural aging processes and self-recovery processes in organs, non-normative intake of nutrients and chemicals, and medical treatment. Average (or meso) level is focused on physiology of a particular organ or system, damage mechanisms, interaction with other systems of a body. We should point out that at this stage sub-models of respiratory, digestive, and neuro-endocrine system at meso-level are being worked out [6, 8]. Later on it may become necessary to create models which will help to describe damage processes at cellular (or micro) level.

To solve tasks related to penetration of chemicals into a human body with food stuffs and drinking water, we are working out a digestive system model at meso-level [5]. This model is rather complicated and it requires additional sub-models creation to describe digestion and damage accumulation in various digestive organs and gastrointestinal tract sections more profoundly. This paper is dedicated to problems related to creating one of such mathematical sub-models describing physiological processes in antroduodenal section (antroduodenum) of gastrointestinal tract. It is this section where damage to mucous coat and ulcer evolvement occurs most frequently [1, 3], and it results from changes in balance between protection and damage mechanisms [22]. Increased acidity in the tract is one of the basic factors causing accumulation of damage in mucous coat; this increased acidity can be caused by various reasons, including insufficient alkali secretion for acid neutralization, defects in local bloodflow, and many other factors.

Direct measuring of acidity in gastrointestinal tract [11] has a number of disadvantages: it requires substantial time and material costs; measuring can be accomplished only in several points in certain moments, predicting is complicated, and an examined individual can suffer from unpleasant sensations. Besides, penetration of measuring devices into a human body can skew research results. In comparison with an experiment, mathematical approaches enable rapid changes in research design, including / excluding separate factors or conditions.

To consider space-distributed properties in gastrointestinal tract, it seems advisable to describe the examined processes with the use of multi-phase media mechanics techniques applying differential equations in partial derivatives. Mathematical models used for describing food flow in esophagus, [7, 25], stomach [14, 15, 18], and bowels [17, 16, 19], have been actively developed over the last decade. We should note that researchers, when developing models, as a rule consider tract motor function while biochemical reactions, digestive glands secretions, and food components absorption are given less attention. Comparatively few works deal with multi-phase modeling. Here realistic 3D shape of gastrointestinal tract sections and functional disorders occurrence, as well as food

dissolution under hydrochloric acid and enzymes impacts, are not taken into account.

We accomplished conceptual and mathematical tasking, worked out algorithms of 3D shape reconstruction and tract motility as per ultrasound results, obtained some results on food dissolution speed at disorders in antroduodenum secretory function at previous stages of the research within the frameworks of the mathematical model which is described in this paper and deals with multi-phase flow in antroduodenum [26].

Our research goal was to examine acidity in antroduodenal section of gastrointestinal tract applying mathematical modeling in order to identify abnormal zones when consuming drinks with various pH level.

Data and methods. We studied multi-phase flow in antroduodenal section of gastrointestinal tract; in general, the first phase was multi-component liquid (water, pepsin, hydrochloric acid, sodium hydrogen carbonate, carbon dioxide, sodium chloride, dissolved complex proteins, fats, carbohydrates, polypeptides, and chemicals). Components were assumed to be dissolved at molecular level. To describe food, we used several liquid phases with various viscosity. Food particles were thought to have spherical shape in interphase interaction functions, phases differed as per dimensions ranges. Interphase interaction forces were considered to be proportional to differences in speeds of interacting phases.

Mass transfers from food phase into first phase components (water, dissolved proteins, fats, carbohydrates, and chemicals) under exposure to acid. Speed of interphase transfer depends on pH level of a medium, food dissolves only in acidic medium. Model allows for reaction of neutralization between acid and sodium hydrogen carbonate, and enzymatic reaction between pepsin and complex proteins.

We introduced damage to several sections of the tract into the model; these sections included body of a stomach, antrum, and duodenum; we also introduced damage to pancreas and liver which determined intensity of sodium hydrogen carbonate mass source in the area where ducts from these organs are located. Damage was defined as per each function, namely motor, secretory, and absorption one. We assumed that when motor function failed, it caused decrease in peristaltic wave amplitude in antrum and duodenum, and contractive capabilities of pyloric opening became weaker; when disorders in secretory function occurred, intensity of acid or alkali mass flow at the area boundary (tract walls) went down; in case of disorders in absorption function, mass outflow of chemicals became less intense.

The suggested model doesn't apparently allow for acid hypersecretion. Increased acid discharge is thought to be determined by regulatory mechanisms failure, or inadequate response to food stimulation. Only muscle weakness of circular layer in tract walls is considered among mechanisms which cause decrease in motor function; other disorders, for example, changes in contractions periodicity, are not taken into account. Lower toxicants absorption caused by damage to a tract wall can be explained by changes in mucous coat properties due to long-term exposure to a toxicant which is one of tolerance mechanisms. We should note that our model doesn't allow for dynamic changes in phases viscosity and density; nevertheless, phase properties in numeric experiments can be changed and we can analyze results which can correspond to, for example, various digestion stages in a stomach.

Speed of hydrochloric acid secretion is described by a dependence on average near-wall concentration of dissolved proteins, fats, and carbohydrates in a body of a stomach. Intensity of pepsin mass source is defined by dissolved proteins concentration. Physiological motive makes it advisable to use only near-wall concentration as receptors located in tract walls measure control element level and give a signal to control. The described regulation occurs locally as opposed to a signal to change intensity of sodium hydrogen carbonate mass source. Alkali secretion in antrum and duodenum as well as with pancreas and liver fluid depends on acid near-wall concentration

in a body of a stomach and on neuro-endocrine system functionality responsible for giving a signal to control. The above-mentioned dependences are described with correlation with saturation similar to Michhaelis-Menten equation.

So, mathematical tasking includes record of mass conservation and impulse conservation equations for a mixture of liquid incompressible phases, correlations for the intensity vector of mass flow at the expense of diffusion processes, correlations for mass sources at the expense of reactions, secretion, and components absorption, food dissolution, initial and boundary conditions [26]. At a first approximation all the processes are thought to be isothermal, so mathematical tasking doesn't include temperature effects.

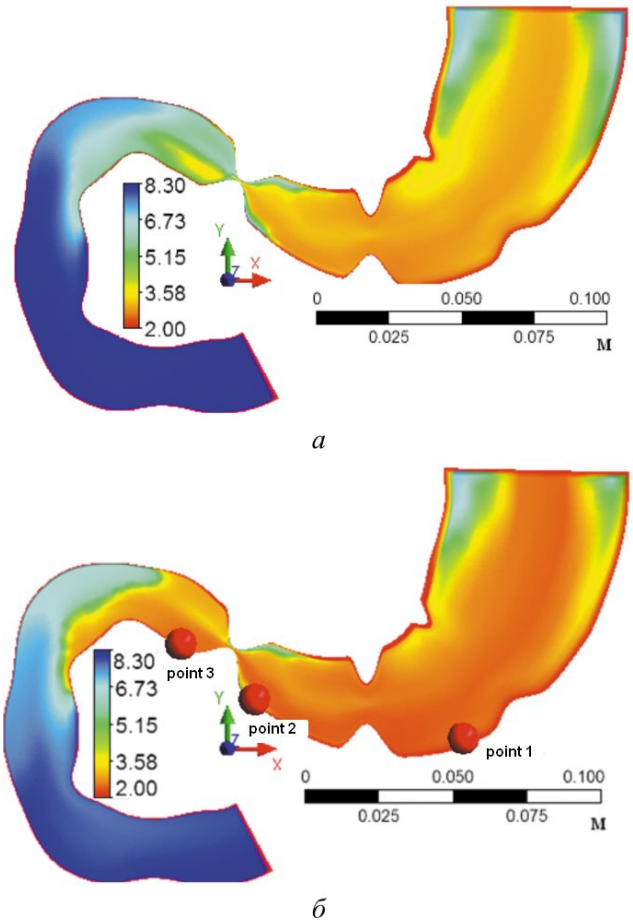
Results and discussion. We examined the effects caused by initially increased acidity (for example due to intake of acidic liquid) on dynamic distribution of acidity in antroduodenum. In this case the model became a bit simplified as we considered one-phase multi-component liquid (water, acid, sodium hydrogen carbonate, sodium chloride, and carbon dioxide).

At the initial moment of time increased acid concentration in stomach was set which corresponded to a beverage with a certain volume and acidity. The first scenario was focused on the case when a beverage with neutral acidity was consumed (pH = &) in a volume equal to 170 ml (for example, water). In the second scenario we analyzed acidity distribution in gastrointestinal tract when a beverage with increased acidity was consumed (pH = 3.5, volume equal to 170 ml), it could be, for example, apple juice, orange juice, any other fruit juice, or a fizzy beverage. In the third scenario we considered the case when a beverage with acidity (pH = 2.3) in a volume equal to 170 ml was consumed. Such acidity level is characteristic for lemon juice, Coca-Cola and other fizzy drinks [24].

There were no functional disorders in antroduodenum in all three scenarios, in particular, intensity of hydrochloric acid secretion and sodium hydrogen carbonate secretion corresponded to the physiological standard observed in a healthy man.

If we analyze the results obtained in the first scenario, we can see that acidity in stomach cavity varies from 2.5 to 3.5 pH (figure 1, *a*). The parameters correspond to physiological standards. A zone with lower acidity (from 5 to 7 pH) occurs in near-wall layers of antrum and duodenum in order to provide protection from negative impacts.

In scenario 3 we can observe increased acidity in antroduodenum cavity (figure 1, *b*). Near-wall pH reaches 3 in the duodenal cap area and it can cause negative impacts on mucous coat of the tract. Three monitoring points are highlighted on figure 1, *b* in near-wall layer of stomach body (point 1), pyloric area (point 2), and duodenal cap (point 3).



a

б

Figure 1. Acidity distribution in the tract:
a – scenario 1, t = 330 s;
б – scenario 3, t = 330 s

In the first scenario we can observe that acidity in near-wall layers of stomach is within the physiological standard (figure 2, *a*). A slight increase in acidity occurs in pyloric area of stomach and duodenal cap area due to acidic content penetrating duodenum from stomach which is determined by increase in acid production intensity in response to stomach stretching.

In the second scenario pH level in near-wall layer of stomach and in pyloric area is close to values obtained in the first scenario when water was consumed (figure 2, *a*, *b*). In this case protection mechanisms of antrum mucous cost and pyloric area neutralize acid attack. pH in duodenum decreases to 4 during 5.5 minutes after a beverage intake due to acidic content penetration into bowels, and it remains substantially higher than the values obtained in scenario 3 (figure 2, *в*).

In the third scenario we can observe substantially increased acidity in pyloric area of stomach and duodenal cap area due to acidic beverage intake (figure 2, b, c). pH level in near-wall layer of stomach pyloric area starts to increase gradually (3 minutes after a beverage was consumed) and slowly due to acid neutralization and acidic beverage transfer into bowels. As a beverage comes into bowels in duodenal cap area, acidity remains substantially higher (2,3 pH).

On the whole we can note that if there are no functional disorders, sodium hydrogen carbonate neutralizes excessive acidity in antroduodenum more efficiently when a drink in a set volume with pH > 3.5 is consumed. Beverages with pH equal to 2.3 have much greater damaging potential for mucous coat of gastrointestinal tract walls as in scenario 3 acidity level in antroduodenum remained critically high during the whole estimated time. But if there is a disorder in alkali secretion, we can expect the area of potential damage to tract walls to be bigger. Acid negative impacts can reveal themselves in suppression of mucous coat cells capability to recover [23].

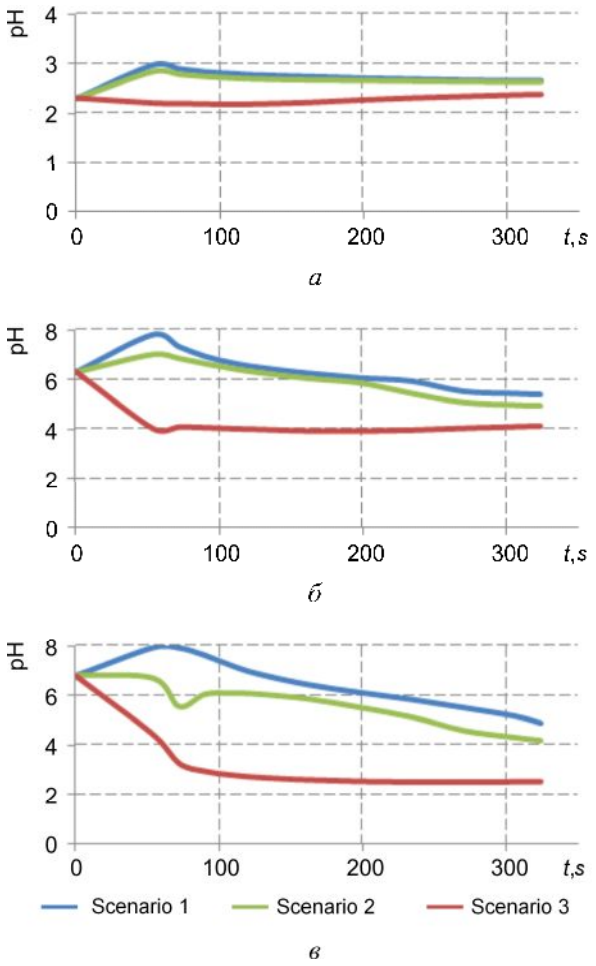


Figure 2. pH level dynamics near tract walls in various sections of it: *a* – body of stomach (point 1); *б* – pyloric area (point 2); *в* – duodenal cap (point 3)

The obtained results on acidity distribution in the tract coincide with the known experimental data: healthy people have pH level equal to 2.7 in body of stomach [12], and when Coca-Cola is consumed, a period of increased acidity in duodenum grows authentically [21].

Conclusions. The suggested mathematical model of multi-phase flow in antroduodenum can be used to highlight areas with abnormal increased acidity in pyloric area of bowels and duodenum depending on volume and pH of a consumed beverage.

Besides, in our further research we are planning to carry out numerical research on influence exerted by phases' viscosity and density, functional disorders occurrence,

individual properties of tract shape and motility on features of multi-phase flow in antroduodenum area of gastrointestinal tract.

The results presented in this paper make a substantial contribution into development of mathematical modeling trend used for describing multi-phase flows in biological channels with complicated shape and moving boundaries, and with mass sources. A very promising trend in model development is identifying parameters of tract areas damage evolution due to acid impacts, self-recovery, and medical treatment. In this case the model can be applied for predicting risks for damage evolvement with detecting areas of its possible localizations. For more efficient practical use, it is advisable to extend range of diseases and disorders described by the model, as well as to add enzymes activity in it to get more detailed description of digestion processes in duodenum.

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MULTIVARIATE ANALYSIS OF STRUCTURE AND CONTRIBUTION PER SHARES MADE BY POTENTIAL RISK FACTORS AT MALIGNANT NEOPLASMS IN TRACHEA, BRONCHIAL TUBES AND LUNG

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The article gives the results of multivariate analysis of structure and contribution per shares made by potential risk factors at malignant neoplasms in trachea, bronchial tubes and lung. The authors used specialized databases comprising personified records on oncologic diseases in Taganrog, Rostov region, over 1986-2015 (30,684 registered cases of malignant neoplasms, including 3,480 cases of trachea cancer, bronchial tubes cancer, and lung cancer). When carrying out analytical research we applied both multivariate statistical techniques (factor analysis and hierarchical cluster correlation analysis) and conventional techniques of epidemiologic analysis including etiologic fraction calculation (EF), as well as an original technique of assessing actual (epidemiologic) risk. Average long-term morbidity with trachea, bronchial tubes and lung cancer over 2011-2015 amounts to 46.64 $^{o}/_{oooo}$. Over the last 15 years a stable decreasing trend has formed, annual average growth being –1.22 %. This localization holds the 3rd rank place in oncologic morbidity structure, its specific weight being 10.02 %. We determined etiological fraction (EF) for smoking as a priority risk factor causing trachea, bronchial tubes and lung cancer; this fraction amounts to 76.19 % for people aged 40 and older, and to 81.99 % for those aged 60 and older. Application of multivariate statistical techniques (factor analysis and cluster correlation analysis) in this research enabled us to make factor structure more simple; namely, to highlight, interpret, give a quantitative estimate of self-descriptiveness and rank four group (latent) potential risk factors causing lung cancer.

Key words: *social and hygienic monitoring, risk assessment, risk factors, malignant neoplasms, carcinogenic risk, factor analysis, hierarchical cluster correlation analysis*

Currently, the priority direction in addressing problems associated with innovative methodological database for hygienic research is to improve national methods for risk assessment and analysis. This is a modern toolkit that significantly expands analytical and prognostic capabilities of researchers, including elements of situational and simulation modeling [6, 8, 9]. The methodology for risk assessment and analysis

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harmoniously complements conventional techniques of epidemiologic analysis, adapted for socio-hygienic monitoring at regional and municipal levels. Thus, in the Rostov region, when studying cause-and-effect relationships in the "environment - population health" system, parallel with the categorized data, presented in formal state and industry statistical reports, the specialized databases are in use. They are formed based on personified records of malignant tumors events, which conditions using the techniques of multivariate statistical analysis [10].

A wide spectrum of heterogeneous carcinogenic risk factors of genetic (hereditary), environmental (carcinogens, chemical carcinogenesis modifiers and others), occupational-production and of individual nature is included in the number of potential causes of cancer development. Currently, active and passive tobacco smoking is considered as a priority risk factor for lung cancer (LC). Its role is assessed as more significant than such an individual spectrum risk factor, as alcohol abuse [2, 4, 14]. Thus, according to epidemiological studies, the etiological fraction (EF) of tobacco smoking in the cause structure of malignant tumors of trachea, bronchial tubes and lung for men varies within the range of 85-95%. For women, this indicator is somewhat lower, and makes 65-80% [2, 16, 17, 19]. It is shown that in men who smoke more than 30 cigarettes a day, the relative risk (RR) of lung cancer is 4.3-4.5 times higher than that of smokers with fewer than 10 cigarettes [15]. At the same time, data obtained in a number of studies show that risk of developing lung cancer depends more on the length of employment than on the intensity of tobacco smoking [4]. The combination of active and passive smoking with the effects of hereditary background that potentiates its effect is considered as an individual oncologic predisposition to lung cancer [1]. According to a number of authors, both overweight, and low physical activity, and lack of fruits and vegetables - the main source of antioxidants, are also referred to significant individual risk factors, along with tobacco smoking and alcohol abuse [13, 14]. Among the risk factors of the population level, an important role is played not only by anthropogenic air pollution with carcinogenic xenobiotics, but also by the effects of ionizing radiation, primarily due to radon. Thus, according to meta-analysis results, about 10% of all lung cancer deaths are caused by radon, more than 30% of deaths are among non-smokers [5, 11, 12, 18, 20].

From our point of view, taking into account the hypothesis on multi-casual nature of malignant neoplasms (MNs), a compulsory component of risk factor analysis within the framework of socio-hygienic monitoring is studying their structure. It is important the quantitative characteristics and qualitative interpretation of the most typical combinations: group (latent, larvate) risk factors, which combine heterogeneous, but closely correlated together, initial parameters [7, 10].

The purpose of the study was to analyze the structure and the contribution of potential factors of carcinogenic risk to priority localizations and forms of malignant neoplasms.

Materials and methods. Analytical studies were carried out following a specialized database of personified records on oncologic pathology in the city of Taganrog, the Rostov region, with a population of about 255,000 people. During the period covered (1986-2015), 30,684 cases of malignant tumors were recorded. We've applied two multidimensional mathematical-statistic methods: factor analysis and cluster hierarchical correlations analysis [7, 10]. Correlation matrices in factor analysis were calculated based upon the information of 107 different potential risk factors and other significant parameters registered in special "Investigation charts on the case of newly diagnosed malignant neoplasm". The group (latent) factors were taken by principal components method. To determine the number of group (latent) factors, we used Kaiser and Cattell criteria. Factor rotation was carried out according to Varimax. The initial data

applicability for factor analysis was evaluated by Kaiser-Meyer-Olkin measure of sampling and Barlett sphericity. Each of the group (latent) factors taken combines the closely correlated together original (recorded in the primary database) risk factors and the relatively high values of factor loads. The significance (contribution per shares) of individual initial potential risk factors within each taken group (latent) factor based on factor analysis, was estimated from the calculated values of their factor loads; which, in turn, quantitatively characterize the level of relationship between the initial and the group (latent) factors. The initial potential risk factors were regarded as highly informative and significant at the values of the corresponding factor loads of 0.500 and more. A qualitative interpretation of the taken group (latent) factors consisted in the semantic identification thereof through initial potential risk factors. Applying the method of cluster hierarchical correlations analysis made it possible to classify initial potential risk factors with their grouping into hierarchically organized clusters and to represent the results graphically in visual dendrograms. The oncologic morbidity analysis was carried out using specialized software package "Turbo oncologist", version 2.01. It ensures databases creation of both the categorical form, upon statistical reports, as well as personified databases. It implements algorithms of epidemiological analysis of intensity (level), structure, dynamics and spatial characteristic, as well as the original method of assessing actual (epidemiological) risk [3]. When carrying out the factor analysis and hierarchical cluster analysis of correlations, a professional software package “Statistical Package for Social Science” (SPSS), version 13.0 was used [7].

Results and discussion. In doing this research, we went on with studying the structure and contribution per shares of potential risk factors for malignant neoplasms of priority forms and process localizations [10]. We used data on the lung cancer incidence, the long-term average annual occurrence of which among the population of Taganrog for the period 2001-2015 made 46.64 ± 3.26 o/oooo. And over the past 15 years, there has been a steady decline in the disease incidence with an average annual growth rate of 1.35%. The long-term morbidity dynamics model, described by the exponential curve with the equation: $\mathbf{P(X) = 45.101 \cdot 0.987^X}$, where **P(X)** is the incidence rate for the year with the ordinal number X, was statistically valid ($p<0.05$). It was used to calculate the mid-term extrapolation prognosis for 2016 and 2017: 36.30 ±3.71o/oooo, and 35.81 ± 3.71o/oooo, respectively (Fig. 1).

In the structure of total cancer incidence, this localization of malignant neoplasms over the past 15 years stably ranks third with a specific weight of 10.02%. The epidemiological risk assessment done, taking into account regional criteria, based on the calculation of the standardized background risk for the population of regional subordination cities over a fifteen-year period (27.72 o/ooo), allows MN of trachea, bronchial tubes and lung to considered as the priority for the population of Taganrog. For these neoplasms, an increased actual risk level was diagnosed with its individual norm-based score (Wi) equal to 1.069 (fourth ranked among the cities of the Rostov region).

According to an estimate of the main potential risk factors prevalence for the period of 1986-2015, the percentage of smokers among 3,480 patients with MN of trachea, bronchus and lungs is 82.18% (with a city-average of 38.14%). According to the data for the last thirty years, the etiological fraction (EF) of smoking in the occurrence of malignant neoplasms of the given localization makes 76.19% for the residents of Taganrog at the age of 40 years and older, 81.99% for the people aged 60 years and over. 36.38% of patients with lung cancer have chronic respiratory diseases, 13.31% - malignant neoplasms of similar localization among blood relatives,
27.97% have specific adverse occupational factors, 23.97% - heterogeneous risk factors in everyday life, including passive smoking.

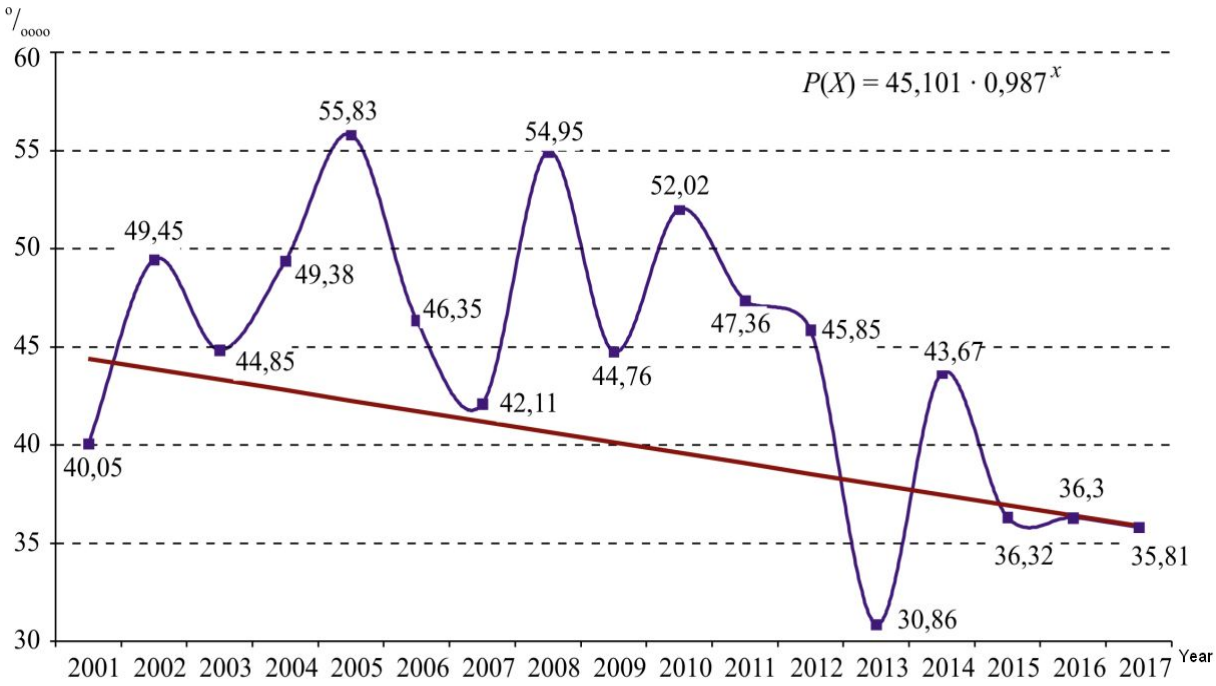

Figure 1. Dynamics of trachea, bronchial tubes and lung MNs incidence in the city of Taganrog over 1986-2015 and medium-term extrapolation prognosis for 2016 and 2017

For eight iterations, we obtained the results of factor analysis fulfilled. It was possible to determine and interpret meaningfully the four group (latent) factors, explaining total variance of 86.525%.

The group factor was ranked first with a variance share of 37.082%, which combines four primary registered potential risk factors. The highest factor load (0.982) in the structure of the first group (latent) factor accounts for active smoking. It should be noted that only cases of habitual and partisan tobacco smoking of 5 years smoking period or longer were taken into account. The second rank place among the initial potential risk

factors belongs to chronic respiratory diseases. The corresponding factor load thereto is 0.885. The factor of alcohol abuse, with a factor load of 0.678 ranks third.

The fourth: predominant strong alcoholic beverages drinking (0.601). Thus, the first group (latent) factor, taking into account the specifics of initial potential risk factors it includes, and interrelations between them, can be meaningfully interpreted as "individual habitual intoxications and concomitant chronic diseases of respiratory system".

A group (latent) factor of the second rank with a variance share of 19.003% combines three initial potential risk factors, which on the whole should be interpreted as "unfavorable parameters of anthropogenic load and industrial-occupational environment." The first two ranks by the values of factorial loads are taken by the initial risk factors: 1) living in residential areas with relatively high levels of anthropogenic impact on atmospheric air due to motor transport emissions (0.777); 2) living in a zone of intensive emissions effect from stationary sources of industrial enterprises (0.647). The third initial potential risk factor is a specific occupational hazard (0.531).

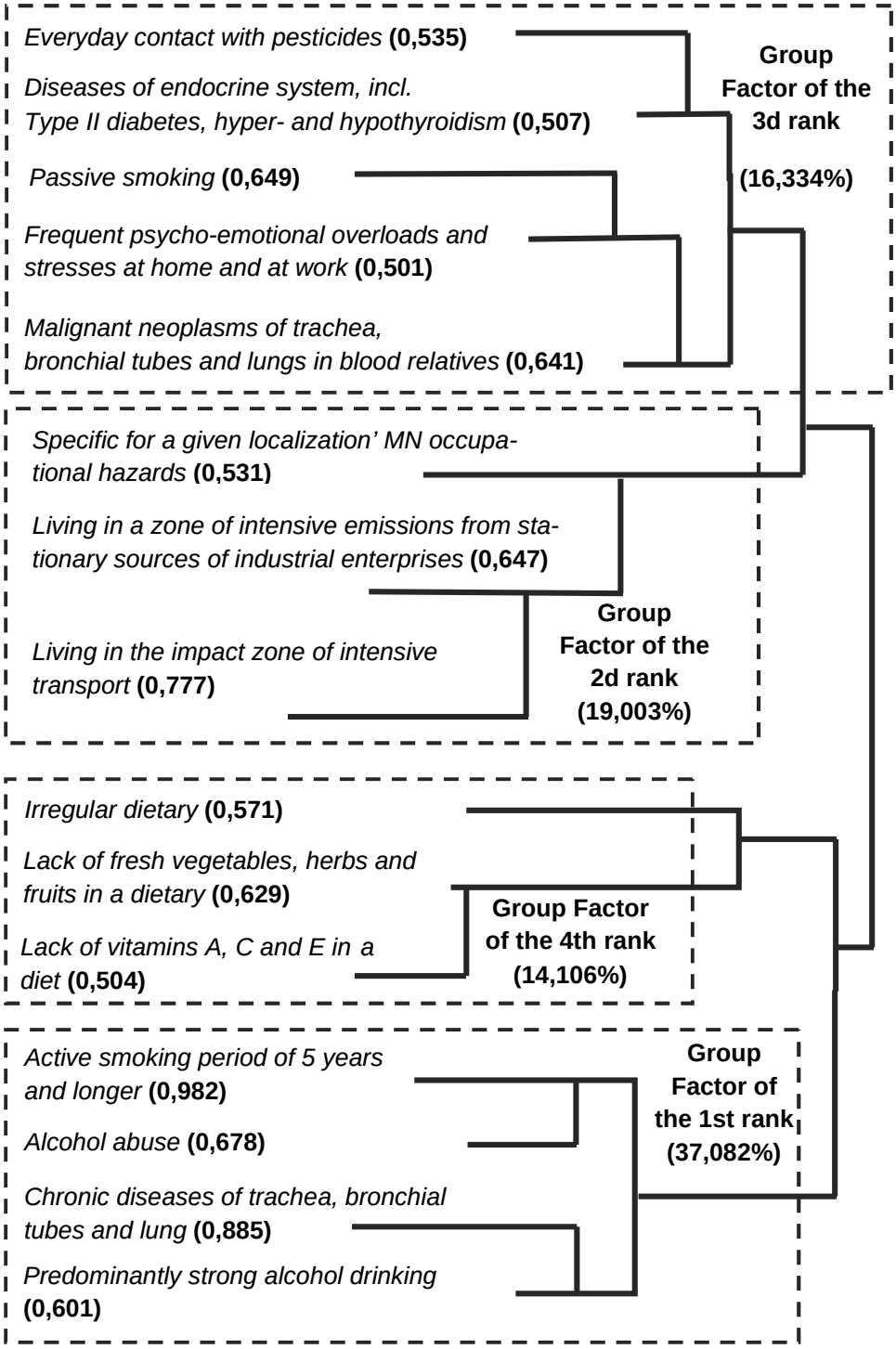

Figure 2. Dendrogram of the factors structure at MN of trachea, bronchus, and lung in the city of Taganrog for the period of 1986-2015.

This refers to the contact mentioned in the patient's history with various occupational hazards specific for a given malignancies localization: chromium, nickel, arsenic and their compounds; silica, soot, asbestos, benzene, toluene, wood dust, ionizing radiation and others.

A group factor of the third rank with a 16.334% variance share is interpreted as "hereditary predisposition and potential risk factors of the individual spectrum". It combines five initial factors: 1) MN of trachea, bronchus and lung in blood relatives (factor load 0.641); 2) frequent psycho-emotional overloads and stresses in family and at work (0.501); 3) passive smoking (0.649); 4) diseases of endocrine system, including type II diabetes, hyperthyroidism, hypothyroidism (0.507); 5) everyday life contact with pesticides (0.535).

A group factor of the fourth rank with a variance share of 14.106% is interpreted as "individual features of food ration and diet". In this group, three initial risk factors for the individual spectrum were identified: 1) lack of fresh vegetables herbs and fruits in a dietary (factor load 0.629); 2) irregular dietary (0.571); 3) a lack of foods high in vitamins A, C and E in a diet (0.504). According to hierarchical cluster analysis of correlations, it's been established that in the structure of the first rank group factor, the most closely pair-wise interact: a) active habitual and partisan smoking of 5 years period and longer, and alcohol abuse; b) chronic diseases of trachea, bronchial tubes, lung, and predominantly strong alcohol drinking (Figure 2).

Within the second rank group factor, the most closely related factors are residence in the areas of relatively high levels of air pollution with automobile transport and in a zone of emissions from stationary sources of industrial enterprises. In the structure of the third rank group factor ("hereditary predisposition and potential risk factors of the individual spectrum"), in the cluster correlations analysis, the relationships in the two groups of the initial factors were found. The first group includes contact with pesticides in everyday life and diseases of endocrine system, the second: passive smoking, frequent psycho-emotional overloads and stress at home and at work, as well as hereditary predisposition – malignant neoplasms of respiratory organs in blood relatives. In the group factor of the fourth rank ("individual features of dietary"), the commonality of the two primary factors is determined: a deficiency in fresh vegetables, herbs and fruits in combination with a deficit of vitamins A, C and E (Figure 2).

Conclusion. Thus, using factor analysis for the purpose of studying an optionally arranged system "population and individual factors of cancer risk - malignant neoplasms of trachea, bronchus and lung" makes it possible to determine and quantify its structural organization. This allows for assessment of practical value for optimizing management decisions and justifying the priority of preventive and health-improving measures being developed. Cluster analysis of correlations adds to the results of factor analysis in detecting the groups of closely related variables (of the primary potential risk factors) and provides their visual representation in the form of informative dendrograms.

Applying these multidimensional statistical techniques in this study made it possible to simplify the factors structure: to isolate, interpret, quantify the informational content (by the contribution share to the total variance). We've managed to range, according to the confidence level, and to study the hierarchical structure of four group (latent) potential risk factors for occurrence of trachea, bronchus and lungs MNs.

Based on the results of factorial and cluster analysis of correlations, the option of further optimization for the monitoring procedure is a significant reduction in the volume of primary information being recorded during transition from scientific research to actual practice. For this purpose, for each identified group (latent) risk factor, among the closely correlated together primarily recorded risk factors, a marker-factor is distinguished – of the highest factor load, which is subject to further registration at socio-hygienic monitoring.

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RISK FACTORS AND PREDICTING HEALTH DISORDERS IN INFANTS BORN FROM MONOCYESIS AFTER IN VITRO FERTILIZATION

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Issues of health state and factors determining it in infants born due to in vitro fertilization (IVF) have been frequently discussed over recent years. The question yet to be answered is whether health disorders are related to burdened pre-morbid state of a mother as per extragenital and obstetric-gynecologic pathology or they are caused by IVF. Selective transfer of only one embryo has tended to increase recently, and, given this trend, specialists all around the world, and in our country as well, face a problem of detecting risk factors which cause health disorders in children born in monocyesis after IVF. Prognostic algorithm for most frequent pathologies is being worked out and it will help to implement targeted and differentiated approach to their prevention. We have completed clinical examination of infants during the first year of their life; all these infants were born in monocyesis after IVF (n=121). We have also questioned and interviewed their parents and analyzed data taken from infants' development records over a year as well. We have applied Wald sequential mathematical analysis to determine risk factors and create prognostic tables comprising most frequent somatic health disorders such as congenital abnormalities, iron-deficiency anemia, atopic dermatitis, absence of perinatal CNS damage compensation. We have detected that factors related to a mother's and newborn's health (extragenital morbidity, obstetric-gynecologic case history, pregnancy course) exert their influence on health disorders evolvement in such children during their first year of life; we have also shown that social factors and factors associated with IVF procedure don't have any statistical significance.

Key words: *risk factors, health disorders prediction, children from monocyesis, IVF, congenital abnormalities, iron-deficiency anemia, atopic dermatitis, perinatal CNS damages.*

There have recently been a lot of discussions on health state and factors determining it in children born due to in-vitro fertilization (IVF) [1, 2, 4, 6, 7, 8, 17, 24, 28, 29]. As per data given by various authors, IVF programs efficiency varies from 20 to 40%, number of born children from this group doesn't exceed 6-25% of all implanted embryos and 56-78% of occurred pregnancies [5, 8, 25]. We should point out that conception, fetus development and maturation due to application of auxiliary reproductive technologies takes place under conditions which differ from physiological standards rather substantially [4, 10, 21]. Embryo sensitivity to environment factors at pre-implantation stage is considerably high and it can cause fetus pathologies evolvement depending on its gestation stage [9, 10, 12, 16].

As per data taken from the recent

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domestic and foreign literature, there are several factors in a mother causing pathological course of neonatal period in children from IVF group. Such factors include burdened obstetric-gynecological case history, late reproductive age, ovary activity stimulation, pre-term delivery, multiple pregnancy, comcomitant somatic pathology, social status, education, and etiology of infertility [2, 5, 7, 8, 11, 12, 14, 15, 18, 22]. As per results presented by E.V. Vartanyan [2], risk factors are inflammatory diseases of reproductive system, menstrual function disorders, infertility duration, miscarriages and abortions in case history, surgeries performed on abdominal cavity organs and small pelvis organs, and sexual diseases.

In A.N. Plaksina's opinion [20], health of a child born after IVF pregnancy is determined by the following factors in a mother: missed miscarriage (20.3%), miscarriages at various terms (28.6%), multiple pregnancy (11.1%), and threat of miscarriage (48.3%). The author states that women who are older than 30 and have secondary infertility run increased risk for giving birth to a baby with low birth weight and low gestation term.

Some authors say that a method invasiveness is the basic burdening factor which influences infants from IVF group [2, 14]. Other believe that high morbidity and deviations in development of such children are related only to abnormal pregnancy and delivery course [18, 19]. Influence exerted by different superovulation stimulation schemes in IVF programs on health of a future baby is not sufficiently studied and described in contemporary scientific research [8]. At the same time there are data in literature on higher risks for congenital malformations of genitals in boys whose mothers underwent superovulation stimulation procedure and took progestin during pregnancy [12].

Infertility related to endometriosis is known to be hardly curable, and even IVF application in patients suffering from endometriosis has very low efficiency. Influence exerted by this factor on health of a future baby is not studied sufficiently [10].

Some scientists assume that unfavorable perinatal outcomes are related only to multiple pregnancy after IVF [16]. However some latest research prove that risk of giving birth to a sick infant even in case of monocyesis due to IVF is growing. But we couldn't find enough information on the matter [6, 9, 13, 24, 27].

Several reasons determining reproductive technologies application still exist and later they influence pregnancy course, delivery, and health of a future baby [4, 7, 9, 15, 17, 21, 25, 31].

There are practically no scientific works which deal with issues of combined impacts exerted by biological and social factors on somatic health formation in children born due to IVF depending on a number of transferred embryos [13, 22, 26, 27, 30].

Selective transfer of only one embryo has recently tended to increase in many countries, including Russia. And it becomes really essential to study factors causing health disorders risks in order to work out mechanisms of their prediction in children born from monocyesis after IVF. It will allow to apply differentiated and targeted approaches to prevention of most frequent pathologies and reduce risks of their evolvement [23, 30].

Our research goal was to highlight risk factors and work out predictive tables for most frequent health disorders (congenital malformations, iron-deficiency anemia, atopic dermatitis, absence of perinatal central nervous system (CNS) damage compensation) in one-year old children born from monocyesis after in-vitro fertilization.

Data and methods. We examined one-year old children born from monocyesis after IVF ($n = 121$). Their health was assessed in early neonatal period and after their one-year birthday as per clinical examinaiton results. We assessed morbidity as per appealability to a polyclinic and via dynamic observation over infants including functional methods of examination (according to Order No. 1346n dated December 21, 2012). We collected biological and social case history by copying data from patients' individual cards used at applying to auxiliary reproductive technologies

(form No. 111-1/u-03); data from a newborn development history (form No. 097/u) and from a child development history (form No. 112/u, form No. 003/u). Certain factors were clarified during questioning and interviewing parents with the use of a specially designed "Questionnaire on detecting social-biological risk factors".

We processed the obtained results statistically using MS Excel XP and Statistica 6.0 software. Discrepancies in relative indices were studied as per Pierson χ^2-criterion with Yates correction. Discrepancies were considered authentic at $p<0.05$. We detected correlations between studied indices via calculating Spearmen correlation coefficient (R). We calculated odds relations (OR) and relative risk (RR) for various factors in OpenEpi program with defining 95% confidence interval (RR, 95% DI). To detect risk factors for most frequent health disorders and working out a predictive table, we used Wald sequential mathematic analysis [3]. Having proved validity of discrepancy in frequency with which an examined factor occurred in children groups with health disorders and without them ($p<0.05$), we calculated predictive coefficients (PC) for each factor level. Predictive coefficients were calculated as per formula: $PC = 10 \lg (P_1/P_2)$ when a factor occurred, $PC = 10 \lg (1 – P_1/1 – P_2)$ when a factor was absent, where P_1 and P_2 was a frequency of a factor occurrence in compared groups. If an obtained value was positive it was an evidence of a factor negative influence.

Results and discussion. We detected that overall morbidity level in children from the basic group during the first year of their life was 1.3. times higher than in the control group (214.9 and 171.1 per 100 people correspondingly), due to higher occurrence frequency of perinatal central nervous system damage (P CNS D) (66.1 and 39.7 % correspondingly; $\chi^2 = 12.97$, $p = 0.000$), congenital malformations, mostly due to minor heart malformations (MHM) (33.1 and 17.4 % correspondingly; $\chi^2 = 7.91$, $p = 0.005$), iron-deficiency anemia (14.0 and 5.8 % correspondingly; $\chi^2 = 4.13$, $p = 0.042$), atopic dermatitis (8.3 and 2.5 % correspondingly; $\chi^2 = 3.16$, $p = 0.046$), thymus hyperplasia (7.4 and 1.7 % correspondingly; $\chi^2 = 4.67$, $p = 0.031$).

We detected significant factors for evolvement of most frequent health disorders in children basing on the analysis of the following data: biological case history (extragenital morbidity, obstetric-gynecological case history, mothers' reproductive function, a child's health state), and social case history (education, social status, occupational hazards of parents, family wealth, and family relations) of children born from monocyesis after IVF, as well as factors related to IVF procedure (IVF protocol duration, a number of IVF attempts, IVF techniques, and embryo quality).

We detected that risk factors causing:

– *congenital malformations* were: a mother suffering from chronic inflammatory diseases of urinary system (RR 4.4; 95 % CI 2.29–8.37), missed miscarriage in case history (RR 4.4; 95 % CI 2.29–8.37), spontaneous miscarriages in case history (RR 4.0; 95 % CI 2.03–7.88), male infertility (RR 3.3; 95 % CI 1.23–8.79), fetoplacental insufficiency (FPI) (RR 3.3; 95 % CI 1.60–6.96), threat of miscarriage (RR 3.2; 95 % CI 1.59–6.62), colpitis during pregnancy (RR 3.2; 95 % CI 1.59–.,26);

– *iron-deficiency anemia* were*:* birth after gestation period shorter than 37 weeks (RR 5.1; 95 % CI 2.04–12.60); birth after the third and more pregnancy (RR 4.7; 95 % CI 2.05–10.62); anemia of pregnant (RR 4.3; 95 % CI 1.88–9.93); fetoplacental insufficiency (RR 4.0; 95 % CI 1.70–9.41); intraventricular hemorrhages (IVH) (RR 3.2; 95 % CI 1.33–7.78);

– *atopic dermatitis* were*:* burdened allergic case history (RR 8.6; 95 % CI 2.95–25.20), preeclampsia (RR 8.5; 95 % CI 1.70–9.41), birth after gestation period shorter than 37 weeks (RR 7.0; 95 % CI 1.97–25.44), artificial nutrition since the very birth (RR 3.9; 95 % CI 1.19–12.93);

– *absence of perinatal CNS damage compensation by one-year birthday* were*:* birth after gestation period shorter than 37 weeks

(RR 3.3; 95 % CI 1.90–5.84), fetus growth retardation (RR 3.1; 95 % CI 1.94–5.17), gestational arterial hypertension (RR 3.1; 95 % CI 1.95–5.16), chronic adnexa inflammation in case history (RR 2.8; 95 % CI 1.46–5.34), neurocirculatory dystonia (NCD) in a mother (RR 1.9; 95 % CI 1.40–2.70), fetus growth retardation (RR 1.9; 95 % CI 1.34–2.66), intraventricular hemorrhages of the 2nd degree in neonatal period (RR 2.7; 95 % CI 1.57–4.60), iron-deficiency anemia in a child (RR 1.9; 95 % CI 1.09–3.53).

We detected that the greatest influence on evolvement of most frequent health disorders in children born from monocyesis after IVF was exerted by biological factors related to health of a mother and a newborn. Social factors had no statistic significance.

We analyzed factors influencing evolvement of most frequent health disorders in examined children related to IVF procedure (table 1).

We detected that factors determined by the very procedure had no statistically significant influence on evolvement of most frequent health disorders in children born from monocyesis after IVF.

Basing on the highlighted biological risk factors for children born from monocyesis after IVF, we worked out formalized tables for predicting congenital malformations evolvement, iron-deficiency anemia, atopic dermatitis, absence of perinatal central nervous system damage compensation by one-year birthday (table 2).

Table 1

Factors, related to IVF procedure, for most frequent health disorders in children born from monocyesis, abs. (%)

Index	Factor							
	Congenital malformations		Congenital malformations		Congenital malformations		Congenital malformations	
	yes	no	yes	no	yes	no	yes	no
	n = 21	*n* = 84	*n* = 16	*n* = 89	*n* = 10	*n* = 95	*n* = 12	*n* = 93
IVF protocol:								
short	2 (9,5)	13 (15,5)	4 (25,0)	11 (12,4)	1 (10,0)	14 (14,7)	1 (8,3)	14 (15,1)
long	19 (90,5)	71 (84,5)	12 (75,0)	78 (87,6)	9 (90,0)	81 (85,3)	11 (91,7)	79 (84,9)
Number of IVF attempts:								
1st	14 (66,7)	61 (72,6)	11 (68,8)	64 (71,9)	7 (70,0)	68 (71,6)	6 (50,0)	61 (65,6)
More than 2	7 (33,3)	23 (27,4)	5 (31,3)	33 (37,1)	3 (30,0)	35 (36,8)	6 (50,0)	32 (34,4)
IVF techniques:								
IVF	8 (38,1)	31 (36,9)	8 (50,0)	31 (34,8)	2 (20,0)	37 (38,9)	3 (25,0)	36 (38,7)
IVF + ICSI	13 (61,9)	53 (63,1)	8 (50,0)	58 (65,2)	8 (80,0)	58 (61,1)	9 (75,0)	57 (61,3)
Quality of embryos:								
excellent, A type	15 (71,4)	63 (75,0)	10 (62,5)	68 (76,4)	5 (50,0)	73 (76,8)	6 (50,0)	72 (77,4)
good, B type	6 (28,6)	19 (25,0)	6 (37,5)	19 (23,6)	5 (50,0)	20 (23,2)	6 (50,0)	21 (22,6)

Table 2

Predictive table for health disorders in children born from monocyesis after IVF during the first year of their life

Risk factors	Predictive coefficients (PC)			
	Congenital malfor-mations	Congenital malformations	Congenital malfor-mations	Congenital malformations
1	2	3	4	5
Extragenital pathology in a mother				
Chronic inflammatory diseases of urinary system:				
yes	+7,00	–	–	–
no	–0,75	–	–	–
Burdened allergic case history:				
yes	–	–	+4,93	–
no	–	–	–2,61	–
NCD (VNS somatoform disorder):				
yes	–	–	–	+7,24
no	–	–	–	–0,78
Obstetric-gynecological case history				
Chronic adnexa inflammation in case history:				
yes	–	–	–	+2,83
no	–	–	–	–2,13
Endometriosis in case history:				
yes	+2,98	–	–	–
no	–0,99	–	–	–
Spontaneous miscarriages in case history:				
yes	+5,09	–	–	–
no	–1,23	–	–	–
Missed miscarriage in case history:				
yes	+7,00	–	–	–
no	–0,75	–	–	–
Male infertility:				
yes	+3,01	–	–	–
no	–1,63	–	–	–
This pregnancy course				
Fetoplacental insufficiency:				
yes	+4,89	+3,74	–	–
no	–0,68	–1,63	–	–
Fetus growth retardation:				
yes	–	–	–	+5,08
no	–	–	–	–0,54
Preeclampsia:				
yes	–	–	+5,12	–
no	–	–	–1,70	–
Threat of miscarriage:				
yes	+4,21	–	–	–
no	–0,97	–	–	–
Gestational arterial hypertension:				
yes	–	–	–	+6,09
no	–	–	–	–0,39
Anemia of pregnant:				
yes	–	+5,22	–	–
no	–	–0,96	–	–
Colpitis during pregnancy:				
yes	+3,36	–	–	–
no	–1,01	–	–	–

Continuation of table 2

A child's health state				
Birth after gestation period shorted than 34 weeks:				
yes	+4,22	–	–	–
no	–2,44	–	–	–
Birth after gestation period shorted than 37 weeks:				
yes	–	+3,79	+3,93	+2,66
no	–	–2,38	–3,52	–0,86
Birth after the 3rd or more pregnancy:				
yes	–	+5,82	–	–
no	–	–2,39	–	–
Artificial feeding since the very birth:				
yes	–	–	+4,55	–
no	–	–	–5,68	–
Non-traumatic intraventricular hemorrhages of the 2nd degree in case history:				
yes	–	+7,60	–	+6,09
no	–	–1,99	–	–0,39
Iron-deficiency anemia:				
yes	–	–	–	+6,88
no	–	–	–	–0,53

An individual forecast is determined by a sum of predictive coefficients (PC). We used Wald's formula to determine predictive threshold (PT) value which allows to assess validity of health disorders evolvement in children born from monocyesis after IVF during the first year of their life (congenital malformations, iron-deficiency anemia, atopic dermatitis, perinatal central nervous system damage compensation) [17]. We considered not more than a 5% probability of an error in a forecast to be acceptable and determined that predictive threshold (PT) for a possibility of these health disorders evolvement was equal to +13, and their absence, –13.

If the predictive coefficients sum is equal or more than +13, than the forecast is unfavorable, and one can predict evolvement of congenital malformations (as per PC sum in the second column); iron-deficiency anemia during the first year of their life (as per PC sun in the third column); atopic dermatitis (as per PC sum in the fourth column); absence of perinatal CNS damage compensation by one-year birthday (as per PC sum in the fifth column).

If the PC sum is equal or less than –13, the forecast is favorable, and one can predict absence of such health disorder evolvement.

If the PC sum is within +12 to –12 range, than the forecast is uncertain, and we don't have enough data to make a decision on it (attention group).

We recommend pediatricians to include children with unfavorable forecasts into a risk group as per such health disorders evolvement and assign preventive activities which can lower such risks evolvement.

Conclusions. So, in the course of our research we detected biological risk factors for most frequent disorders in somatic health of children born from monocyesis after IVF during the first year of their life; such disorders include congenital malformations, iron-deficiency anemia, atopic dermatitis, consequences of perinatal CNS damage. We detected that somatic health formation in children born from monocyesis after IVF during the first year of their life is greatly influenced by factors related to a mother's health (extragenital morbidity, obstetric-gynecological case history, pregnancy course). and a newborn's health. Here social factors and factors determined by IVF procedure itself don't exert any statistically significant influence.

We worked out predictive tables which can help to predict evolvement of health disorders in a child born from monocyesis

after IVF just after its birth; we hope these tables will be suitable for practical use by neonatologists, district pediatricians, and family doctors.

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RISK-ASSOCIATED HEALTH DISORDERS OCCURING IN JUNIOR SCHOOLCHILDREN WHO ATTEND SCHOOLS WITH HIGHER STRESS AND INTENSITY OF EDUCATIONAL PROCESS

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We performed comparative sanitary-hygienic assessment of regime, stress and intensity of educational process in different educational establishments, a comprehensive secondary school and an innovative educational establishment - lyceum. We detected that studying regime tended to be tight, classes were longer and more intense than in an ordinary school, and educational process involved considerable intellectual, sensory and emotional loads for children; such loads reached "1st category intense" level. Schoolchildren attending lyceums are also busy with additional educational programs and it significantly increases length of total educational load on them. By the end of a school year 20% of lyceum pupils suffer from sympathoadrenal system overstress and it doesn't only determine emotional tonus level in children but also leads to disorders in concentration and decision-making speed, lower reading speed and articulation, slower motor reactions. 15% of lyceum pupils have higher activity of autonomous nervous system and lower adaptation of cardiovascular system to psycho-emotional and physical loads. Lyceum pupils also run 2.5 times higher risk of chronic nervous system diseases evolvement than school children attending ordinary schools. Autonomous nervous system disorders, posture disorders and nutrition disorders are predominant nosologic pathology forms in lyceum pupils as they occur in them 1.6-2.9 times more frequent than in schoolchildren of the same age who attend an ordinary comprehensive school. We detected direct correlation between higher intellectual and emotional components of educational process, and total educational intensity as well, and frequency of autonomous system disorders and musculoskeletal system diseases in pupils.

***Key words**: children, educational process, elementary school, regime, intensity and stress risk-associated health disorders, nosologic pathology forms.*

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Nowadays there is an apparent negative dynamics in children health parameters, and it is most obvious for schoolchildren [3, 8, 9]. Observation results reveal that by the end of school years a share of healthy children decreases by 2.0-5.0 times and amounts to not more than 3.5% of school leavers; besides, a number of children who has the 3rd and 4th health category increases substantially, up to 43% [11, 20]. As per data obtained by Age Physiology Institute of Russian Academy of Education, frequency of eyesight disorders and posture disorders grows by 5 times in children during their school education period; psychoneurological disorders frequency becomes 4.0 times higher, and cardiovascular system pathologies and digestive organs pathologies occur 3.0 times more frequently [7, 11, 19].

Educational process intensification and wide implementation of information technologies in it are among the most significant risk factors causing health deterioration for contemporary schoolchildren [1, 2, 4, 10, 13, 15]. Reforms which school education undergoes, and implementation of new specialized authors' programs, as a rule, involve greater volumes and complexity of learnt subjects, application of a wide range of innovative teaching and learning technologies in educational process, educational process intensification, and growth in total educational load. Physical activity reduces, and structure of students' educational regime deteriorates [6, 10, 12, 13, 15, 17, 18, 21]. It was detected that when interactive equipment was applied in educational process, it exerted negative impacts on students' psychoemotional health, their visual organs, and nervous system, even if all the existing regulations on its operation were strictly observed [5, 7, 14, 16]. Educational load duration is an additional risk factor. Nowadays it takes schoolchildren a long time to do their homework; 50% of them spend such a long time doing it that it exceeds hygienic standards more than twice [7]. High intensity of educational process combined with unfavorable sanitary and hygienic learning conditions and, quite often, with malnutrition, can lead to overexhaustion, hypodynamia, lower working capacity, stress-induced functional disorders in organs and systems, disharmony in physical development, and chronic pathologies evolvement, in schoolchildren [1, 2, 4, 8, 9, 10, 20, 23].

Multi-factor analysis results reveal that educational process organization holds the first rank place as per contribution into students' health in grammar schools and lyceums (up to 25%). The second and third places belong to students' psychophysiological peculiarities (up to 20%) and ecological situation existing in places where educational establishments are located. In traditional schools the leading factors determining schoolchildren health dynamics are social ones (up to 24%), the second place is taken by level of school organization and attendance (23%), and the third place belongs to ecological factors (23 %) [8].

Thus, hygienic research results give evidence that health-preserving educational technologies design for secondary schools, and first of all, for innovative organizations, requires further examinations of influence exerted by various educational loads on students' health. We also should improve regulatory base in the sphere of educational process technologies and organization.

Our research goal was to perform comparative examination of peculiarities which regime, educational process stress, and educational process intensity has in educational establishments of two different type (an ordinary school and a lyceum); we also assessed their influence on students' health.

Data and methods. Our research objects were:

– educational process regimes, as well as educational process intensity and stress parameters for children from the 1st, 2nd, 3rd, and 4th grade in a standard secondary school and an innovative educational establishment, namely lyceum;

– 190 children aged 7–11 from 1–4th grades, attending a secondary school (89 schoolchildren) and innovative educational establishment, lyceum (101 schoolchildren).

Our research subjects were:

– lessons and breaks schedule;

– educational programs, applied in educational process in a secondary school and in a lyceum;

– sociological examination questionnaires collected among parents;

– protocols of neuropsychological testing performed on pupils from 1-4th grades in the examined educational establishments;

– clinical-laboratory parameters of pupils' health;

– protocols of functional and instrumental techniques used for assessing pupils' health.

Medical and biological research was conducted in full conformity with ethical principles stated in Helsinki Declaration (1983) and the RF State Standard "Appropriate Clinical Practices" (ICH E6 GCP). The research program was approved by the ethics committee of Rospotrebnadzor Federal Scientific Center for Medical and Preventive Health Risk Management Technologies (Protocol No. 2, 2016). To perform sociological, clinical-functional, and laboratory research, we made sure that a legal representative of each examined child gave his or her voluntary written consent to take part in them. The research was accomplished within the framework of scientific research work funded by the state according to a plan of such work given to Rospotrebnadzor Federal Scientific Center for Medical and Preventive Health Risk Management Technologies.

Sanitary-hygienic research included comparative assessment of educational process regimes, educational load stress and intensity in 1-4th grade in a secondary school and in a lyceum.

To perform comparative assessment of educational processes regimes we examined classes schedules in 1-4th grade in a school and in a lyceum paying special attention to their conformity with Hygienic Requirements 2.4.2.2821-10 «Sanitary-epidemiologic requirements to conditions and organization in general education establishments».

We examined learning activity stress for pupils in full conformity with federal recommendations on providing medical assistance for learners «Hygienic assessment of learning activity stress for learners» [22]. Our examination involved assessing intellectual, emotional, and sensory loads during a lesson, their monotony, and working regime. To assess stress caused by each of the examined load types objectively, primary education teachers performed this assessment as per scoring system (from 1 to 4), where 1 score corresponded to the 1st stress category; 2 scores, the 2nd category; 3 scores, the 3rd category with 1st stress degree (3.1), and 4 scores were the 3rd category with the 2nd stress degree (3.2). The final assessment of stress caused by each of the examined load types was calculated as a mean value of all the components. This obtained mean value for all factors of a certain load type was compared with standard values fixed in the federal recommendations «Hygienic assessment of learning activity stress for learners»:

– «optimal» (1st category) – 1.0–1.5 scores;

– «allowable» (2nd category) – 1.6–2.5 scores;

– «stressful» (3rd category) – 2.6–4.0 scores:

– «stressful with 1st stress degree» (3.1 category) – 2.6–3.5 scores;

– «stressful with 2nd stress degree» (3.2 category) – 3.6–4.0 scores.

Teachers-psychologists were invited to take part in analyzing results of examining educational process stress.

To assess educational process intensity, we performed a sociological examination. Data were collected through voluntary questioning conducted among pupils' parents; a questionnaire for the research was designed by experts from the laboratory for sociological risks analysis techniques of

Federal Scientific Center for Medical and Preventive Health Risk Management Technologies. The questionnaire included medical, social-economic, and ecological sections, as well as questions devoted to assessment of educational process intensity.

Clinical and functional examination of the children was completed in two stages; the first one was at the beginning of school year (September) and the second, at the end of the third term (March). Research program included assessment of physical development, functional state of cardiovascular and respiratory systems, assessment of children's psychoemotional state and motor functions development. Besides, we examined general somatic morbidity of the children and determined their individual health groups. All research was accomplished as per standard procedures. Clinical examination included outpatient development records analysis; the children were also examined by medical specialists (pediatrician, gastroenterologist, neurologist, and physical training therapist). We carried out electrocardiographic examination on «Schiller AT-2 plus» electrocardiograph; spirography was made on «Schiller PS spirometry» spirometer (SP-260 sensor, Schiller AG, Switzerland); ultrasound scanning of thyroid gland was performed with «Vivid q» scanner (GE Vingmed Ultrasound AS, Norway) with the use of linear matrix sensor 5–15 MHz. We applied computer testing system «Vienna» (VTS, Austria) to assess children's neuropsychological state and their motor functions development.

Laboratory research was performed in certified laboratories as per standard procedures and only certified equipment was applied (AcT5diff AL automatic hematologic analyzer, the USA, France, Backman Coulter Inc; «Konelab 20» biochemical analyzer, ThermoFisher, Finland; «Infinite F50» immune-enzyme analyzer, Austria, Tecan). Our work involved assessing hematologic and biochemical parameters, immunologic state and non-specific resistance, hormonal homeostasis, neuromediators level, and genetic state. Quality control in all performed diagnostic research was provided by conducting laboratory quality control (as per order issued by the RF Public Health Ministry No. 45 dated February 07, 2000), by participation in Federal system of external quality assessment (laboratory certificate No. 10843 for biochemical research, No. 10845 for general clinic research) and in EQAS international system for laboratory research quality assessment (laboratory certificate No. 9473).

We analyzed all the data obtained in the course of sanitary-hygienic, clinical-functional, and laboratory research with the use of Statistica 6.0 statistic analysis software and with specially designed software compatible with MS-Office. Research results were mathematically processed with the use of parametric statistic techniques. Samples features were given as a mean (M) ± standard error of the mean (m). We compared two unlinked groups as per Student's t-criterion value. Any discrepancies corresponding to probability error estimate $p \leq 0,05$ were considered to be statistically significant. Statistical processing of the sociological research results was accomplished via calculating and comparing arithmetical mean values, as well as determining frequency and structural features. We checked validity of discrepancies in sociological parameters as per sex, age, and educational establishment criteria with the use of non-parametric Kruskal-Wallis criterion (for more than two samples; "age" as grouping variable), and Mann-Whitney criterion (for two samples; "sex" and "educational establishment" as grouping variables).

Results and discussion. Comparative hygienic assessment of educational process regimes in secondary school and in lyceum revealed that 1st and 4th grade pupils attended them in the first shift (classes started at 8.30), and 2nd and 3rd grade pupils, in the second shift (classes started at 15.00 in secondary school and at 14.15 in lyceum). Learning week lasted for 5 days for 1-3rd grades (from Monday to Friday), and 4th grade pupils had to study 6 days a week (from

Monday to Saturday). As per classes schedule, a lesson in 1st grade lasted for 40 minutes in school and for 35 minutes in lyceum; lessons in 2-4th grade in school lasted for 45 minutes, and in lyceum for 40 minutes. Breaks had the same length in both shifts in school and they were either short (10 minutes) or long (20 minutes). A long break in the first shift usually took place after 2-3rd lesson, and in the second shift, after 1-2nd lesson. Short breaks in lyceum lasted for 5-10 minutes in the first shift, and a long one was 20 minutes and took place after 4-5th lesson. During the second shift in lyceum short breaks lasted for 5 minutes, and a long one which was after 1-2nd lesson lasted for 15 minutes. A break between shift in school was 50 minutes and in lyceum only 10. So, overall time 1st grade pupils had to spend at school amounted to 3 hours 20 minutes, and it was only 2 hours 40 minutes in lyceum as lessons and breaks there were shorter. This time period amounted to 4 hours 35 minutes for 2-4th grade pupils in school, and to 3 hours 50 minutes or 4 hours, in lyceum.

According to schedule, weekly load in 1st grade of secondary school amounted to 21 hours. in 2-3rd grade, to 22 hours, and in 4th grade, to 23 hours. In lyceum weekly load for 1st grade pupils also mounted to 21 hours, but it reached 23 hours in 2nd grade already. Daily educational load in 1st grade in both educational establishment didn't exceed 4 lessons; however, one day a week there was the fifth lesson (physical training). 2-4th grade pupils usually had 4-5- lessons a day; besides, lyceum schedule for 4th grade included two physical training lessons on Saturday. We examined classes schedule for primary grades in both examined establishments; the examination revealed that the schedule was worked out allowing for school subject difficulty and peculiarities of pupils' daily and weekly mental working capacity. Educational process in 1st grade in both educational establishment didn't include any marks-based assessment of knowledge and homework, and "step-by-step" educational regime was applied during the first two terms. The most difficult subjects (mathematics, Russian, a foreign language) were taught to 1st grade pupils as the 2nd lesson, and to 2-4th grade pupils, as the 2nd-3rd lessons. There were no double lessons on the same subject in junior classes in both educational establishments. When classes schedule was drawn up in school, subjects varying in difficulty interleaved both during a day and a week; thus, basic subjects (mathematics, Russian, a foreign language, natural study, informatics) interleaved with lessons on music, art, technology, and physical training. This hygienic requirement wasn't fulfilled in lyceum. To increase children's physical activity in both educational establishments the schedules included three physical training lessons and it corresponded to maximum allowable weekly school load. Two physical training lessons out of three in school were swimming and rhythmics, while in lyceum pupils had only standard physical training lessons. Pupils' daily load calculation made as 11-score scale by I.G. Sivkov [14], revealed that Wednesday was a day with the highest load in school, and Monday and Friday were the easiest. There were two days with the highest load in lyceum, Wednesday and Thursday, and besides, Monday and Friday also had rather high points for mental load, namely 23-24.

Thus, educational process organization analysis gives evidence that general requirements stated in 2.4.2.2821-10 «Sanitary-epidemiologic requirements to conditions and organization in general education establishments» were met in secondary school. But in lyceum, subjects varying in difficulty didn't interleave, and educational load was not distributed adequately during a week, breaks were shorter, as well as a break between two shifts (Table 1).

Hygienic assessment of learning activity stress for pupils revealed that it was not optimal in either of the examined establishments. Educational process stress reached 1.8-2.2 scores in secondary school (2.05 ± 0.31), and in lyceum, 1.7–2.5 scores

(2.10 ± 0.52), which was not statistically different (p = 0.86) and corresponded to allowable load level (1.6–2.5 scores) (Table 2).

At the same time, intellectual loads in junior school grades don't exceed allowable level (2.3-2.5 scores), but most pupils of 1-4th grades in lyceum (3.03-3.5) have "stressful with 1st stress degree" intellectual loads (2.6-3.5). Sensory loads level (1.5-1.9) for school pupils corresponds to optimal and allowable levels, but they reach 2.8 scores for 4th grade lyceum pupils and are "stressful with 1st stress degree". However, if emotional loads in 1-3rd lyceum grade correspond to optimal and allowable levels (1.5-2.3 scores) and are "stressful with 1st stress degree" only for 4th grade pupils (2.8 scores), then 1st grade school pupils (3.0) and 4th grade school pupils (2.8) undergo stressful emotional loads (1st stress degree) which are optimal only in 3rd grade (1.5 scores). If we generalize the obtained results, we should point out that specific components of educational process in both examined establishments are mostly optimal/allowable for 1-3rd grades, and only intellectual loads for lyceum students reach "stressful with 1st stress degree" level (2.5-3.5 scores). Most substantial discrepancies are observed in 4th grades; all basic components of overall stress in lyceum belong to "stressful with 1st stress degree" (intellectual loads have 3.0 scores; sensory loads, 2.8 scores; emotional loads, 2.8), but in school only emotional loads reach such a level (2.8), while others have scoring varying from 1.6 to 2.5.

Table 1

Educational process organization conformity with 2.4.2.2821-10 «Sanitary-epidemiologic requirements to conditions and organization in general education establishments» in junior classes of secondary school and lyceum

Criterion	conforms (+) /doesn't conform (–)	
	secondary school	lyceum
Educational process organization in 1st grade	+	+
Beginning of classes	+	+
Shifts	+	–
Lessons duration	+	+
Breaks duration	+	–
Daily load	+	+
Weekly load	+	+
Having «difficult» subjects as 2–3rd lessons	+	+
Subjects varying in difficulty interleave	+	–
Double lessons	+	+
Three lessons of physical training	+	+
Distribution of educational load during a week	+	–

Table 2

Results of educational process stress in junior grades of different educational establishments (scores)

Parameter	1st grade		2nd grade		3rd grade		4th grade	
	school	lyceum	school	lyceum	school	lyceum	school	lyceum
Intellectual loads	2,5	3,0	2,8	2,5	2,3	3,5	2,5	3,0
Sensory loads	1,6	1,5	1,9	1,9	1,5	1,8	1,6	2,8
Emotional loads	3,0	1,5	1,5	2,3	1,8	1,5	2,8	2,8
Loads monotony	2,0	1,5	2,0	2,0	2,3	2,3	2,0	2,3
Working regime	2,0	1,0	1,7	2,0	1,3	1,3	2,0	1,6
Overall educational process stress	2,2	1,7	2,0	2,1	1,8	2,1	2,2	2,5

As we examined education intensity as per results of parents' questioning, we detected that all school pupils from 1-4th grades attended classes 5 days a week while only 75% lyceum pupils in the same grades had 5-day-schedule, 18.2% attended lyceum 6 days a week, and another 6.8% had mixed schedule, 5-6- days a week (contingency coefficient 0.3, p = 0.0001, average correlation). Questioning results enabled detecting that only 66.7% of school pupil had 5 lessons a day or more, while in lyceum all pupils had such quantity of lessons a day (contingency coefficient 0.5; p = 0.0001; strong correlation).

Only 25.7% parents of schoolchildren mentioned creative home tasks while 41.6% parents of lyceum pupils told their children had to do such tasks (contingency coefficient 0.2; p = 0.045; weak correlation).

We detected in our research that regardless of educational establishment type 32.9% pupils attending classes in the first shift spent more than two hours a day to do their homework. There were two time more such pupils in the second shift (58.4%) (p = 0.001). In general, 3.8% school pupils and 16.9% lyceum pupils spent less than one hour on their homework (p = 0.003); 47.4 and 38.2 % correspondingly (p = 0.19), from one to two hours; 42.3 and 37.1 % (p = 0.46), from two to three hours; 6.4 and 7.9 % pupils from compared groups (p = 0.68), more than three hours. We didn't detect any statistically authentic discrepancies between "educational establishment type" and "average time spent on doing homework" variables (p≥0.05). The obtained results revealed that each second pupil from junior grades (48.8 % in secondary school and 44.9 % in lyceum; p = 0.003) spent more time on doing his or her homework than it was recommended by 2.4.2.2821-10 «Sanitary-epidemiologic requirements to conditions and organization in general education establishments».

The research results revealed that 85.3% of junior grades pupils in school and 91.1% in lyceum (p = 0.20) attended additional educational establishments; and each third of them attended more than one (26.8 % school pupils and 34.9 % lyceum pupils; p = 0.22). However, schoolchildren attended sports sections less frequently than lyceum pupils (50.0 % against 74.1 %; p = 0.001). Overall, 68.8% school pupils and 82.8% lyceum pupils had regular physical training and did sports (p = 0.02). 32.8% school pupils and 49.3% lyceum pupils from them did it every day/4-5- times a week (p = 0.02); 61.8 and 41.1 % correspondingly (p = 0.004), 2-3- times a week; 5.5 and 9.6 % (p = 0.28), once week. Most primary school pupils, regardless of their educational establishment, spent from 3 to 5 hours a week on doing sports (42.6 % school pupils and 43.1 % lyceum pupils; p = 0.94); a bit more than one third, 6–8 hours a week (35.2 and 33.3 % correspondingly; p = 0.78); about 12 % children spent on doing sports only 1-2- hours a week; about 10 %, 9 and more hours a week.

So, the results we obtained due to sanitary-hygienic assessment of educational process prove that education in innovative establishments (lyceum) involves tighter regime of classes for children; period of their daily learning activity lasts longer than in secondary school during a week; lyceum pupils undergo significant intellectual, sensory, and emotional loads, and educational process during a lesson is rather intense; homework often involves creative tasks. Practically all pupils attending innovative educational establishments have additional classes every day (they go to sport sections, art schools, or visit tutors). Besides, one third of them deal with two different subject spheres during their additional classes, and it leads to substantial increase in total volume of learning activity loads.

We didn't perform any statistically significant discrepancies in 1st grade pupils from two different educational establishment after comparative analysis of somatometric examination results. Their weight-height parameters, chest and head circumference, and carpal dynamometry data were quite similar and didn't have any deviations from physiological age standard (p = 0.45–0.98), and children also had similar values of body

Table 3

Comparative characteristic of physical development parameters in 1st grade pupils attending different educational establishments

Parameter	Boys			Girls		
	Lyceum	School	Validity of discrepancies	Lyceum	School	Validity of discrepancies
Height, cm	130,33 ± 6,08	130,21 ± 5,96	0,98	125,80 ± 4,52	124,75 ± 4,95	0,76
Body weight, cm	26,97 ± 3,99	28,18 ± 6,62	0,76	22,69 ± 1,82	23,74 ± 5,03	0,70
Chest circumference, cm	60,33 ± 4,05	60,64 ± 7,64	0,94	56,30 ± 3,06	56,50 ± 5,53	0,91
Chest excursion, cm	8,25 ± 1,91	7,36 ± 1,39	0,45	7,30 ± 2,26	7,00 ± 0,93	0,81
Head circumference, cm	52,00 ± 1,35	53,64 ± 1,98	0,18	50,60 ± 2,32	52,25 ± 1,39	0,19
Right carpal dynamometry, kg	9,00 ± 2,26	9,29 ± 3,89	0,90	6,40 ± 2,01	6,75 ± 1,67	0,79
Left carpal dynamometry, kg	7,50 ± 1,68	7,79 ± 3,04	0,87	5,80 ± 1,87	5,63 ± 2,58	0,92
Body weight index (st.units)	15,82 ± 1,66	16,49 ± 2,66	0,67	14,33 ± 0,66	15,18 ± 2,09	0,44
Pignet index (st.units)	43,03 ± 5,94	41,40 ± 10,96	0,79	46,81 ± 3,62	44,51 ± 8,41	0,62

Table 4

Comparative characteristic of physical development parameters in 4th grade pupils attending different educational establishments

Parameter	Boys			Girls		
	Lyceum	School	Validity of discrepancies	Lyceum	School	Validity of discrepancies
Height, cm	144,67 ± 8,21	142,93 ± 5,00	0,72	145,71 ± 8,88	147,75 ± 6,99	0,72
Body weight, cm	38,85 ± 3,78	35,69 ± 8,43	0,50	35,29 ± 7,51	37,13 ± 8,52	0,75
Chest circumference, cm	66,44 ± 9,04	66,21 ± 6,36	0,93	65,36 ± 5,99	66,0 ± 7,38	0,89
Chest excursion, cm	8,05 ± 2,34	8,13 ± 2,67	0,96	7,60 ± 2,38	8,31 ± 1,89	0,64
Head circumference, cm	52,39 ± 1,65	53,36 ± 1,50	0,39	53,36 ± 1,95	53,88 ± 1,36	0,87
Right carpal dynamometry, kg	13,06 ± 2,44	12,93 ± 2,06	0,94	11,43 ± 2,28	9,88 ± 2,31	0,34
Left carpal dynamometry, kg	11,39 ± 2,23	12,50 ± 1,95	0,46	10,57 ± 2,28	9,56 ± 1,90	0,50
Body weight index (st.units)	17,97 ± 4,13	17,32 ± 3,14	0,82	16,43 ± 2,04	16,83 ± 2,49	0,91
Pignet index (st.units)	37,30 ± 8,35	38,29 ± 15,25	0,91	42,06 ± 3,64	44,63 ± 10,86	0,66

Table 5

Dynamics in physical development parameters for pupils over 4 learning years in different educational establishments

Parameter	Boys			Girls		
	Lyceum	School	Validity of discrepancies	Lyceum	School	Validity of discrepancies
Height, cm	14,34 ± 2,15	12,72 ± 1,96	0,27	19,91 ± 2,71	23,0 ± 2,97	0,13
Body weight, cm	11,88 ± 2,89	7,51 ± 2,53	**0,03**	12,6 ± 4,67	13,39 ± 4,78	0,81
Chest circumference, cm	6,11 ± 0,55	5,57 ± 0,11	0,06	9,06 ± 2,53	9,50 ± 2,46	0,82
Chest excursion, cm	0	0,77 ± 0,03	0,06	0,30 ± 0,02	0,31 ± 0,14	0,93
Head circumference, cm	0,39 ± 0,15	0,28 ± 0,14	0,29	2,72 ± 0,14	1,63 ± 0,38	**0,001**
Right carpal dynamometry, kg	4,06 ± 2,35	3,64 ± 2,98	0,83	5,03 ± 2,39	3,13 ± 1,99	0,22
Left carpal dynamometry, kg	3,89 ± 1,96	4,71 ± 2,5	0,61	4,77 ± 2,08	3,93 ± 2,24	0,58
Body weight index (st.units)	2,15 ± 0,9	0,83 ± 0,9	**0,05**	2,10 ± 0,35	1,65 ± 0,29	**0,05**

weight index and Pignet index, as well as chest excursion (p = 0.18–0.92) (Table 3). Results of physical development examination for 4th grade pupils were also quite similar in both comparison groups (p = 0.39–0.94) (Table 4). At the same time, comparative analysis of 4-year dynamics in somatometric parameters allowed to detect authentically higher body weight index values in girls, as well as higher growth rate in body weight index in all lyceum pupils (p = 0.05) (Table 5).

So, in spite of tighter classes regime, as well as intense and stressful learning activity, physical development of children attending innovative educational establishments is quite similar to parameters which children of their age attending traditional secondary schools have.

However, growth rates for body weight and body weight index in pupils attending innovative educational establishment are higher. The detected peculiarity can be related to, notably, social and economic conditions of child-rearing. Questionnaire data analysis revealed that a family of each third lyceum pupil had more than 30,000 rubles income per each family member, and 37.7% had 15,000 rubles income per each family member, while in ordinary school not more than 12.7-14.9% of families correspondingly had such incomes (p = 0.0001–0.003). Besides, as we examined pupils nutrition regimes we detected that 44.6% of lyceum pupils and only 30.7% of school pupils ate regularly (4-5- times a day) (p = 0.04), 51.8% of lyceum pupils and 64% of school pupils had 3 meals a day (p = 0.08), 3.6 and 5.3% of children correspondingly had 1-2-meals a day (p = 0.56). We also detected that 71.6% of lyceum pupils had 1-2 additional mid-afternoon snacks (only 52.2 % of school pupils; p = 0.005), and 28.3 % «had 3-5 snacks» (47.8 % of school children, p = 0.005).

Results of assessing cardiovascular system functional state revealed that at the beginning of school year almost half of the examined 1st grade students in both educational establishments had deviations from physiological standards in specific electrocardiogram parameters (43.1 % of

lyceum pupils and 43.6 % of school pupils; p = 0.96). Heart rhythm disorder as per respiratory sinus arrhythmia was the most frequent (23.5 % of lyceum pupils and 35.9 % of school pupils; p = 0.20), which was typical of children from this age group. A number of children with normal electrocardiogram went down to 52% in 4th grades in lyceum by the end of school year, but this number in school increased to 61.3% (p = 0.68), and heart rhythm disorders were detected 48.0% more frequently in lyceum pupils (p = 0.69), and 38.7% less frequently in school pupils (p = 0.68). We should highlight that sinus bradycardia which was the evidence of vegetative nervous system being more active and of children being poorly adapted increased from 7.8 to 14.6% among junior grades lyceum pupils (p = 0.16) and was authentically higher than the same parameter in school pupils (1.2 %; p = 0.01) (Table 6). The detected opposite trends in dynamics of cardiovascular system functional state in the examined children prove that apparently children attending an ordinary school become gradually adapted to growing educational loads.

As we examined respiratory system functional state we detected that each tenth 1st grade pupil, regardless of his or her educational establishment, had disorders in lungs ventilatory capacity, mostly as per restrictive type, which disappeared in most children by the end of primary school (p = 0.06–0.69).

As per data obtained via ultrasound scanning of thyroid gland not more than 32.5-36.1% of the examined pupils from both educational establishments had physiological structure of the organ (p = 0.60); lyceum pupils had changes in thyroid gland tissue structure 1.6 times more frequently than school pupils (47.5 against 30.6 %, p = 0.02) (Table 7). Cystic-enlarged follicles occurrence was the most frequent reason for changes in the organ structure. We should note that this pathological morphology was 2.1 times more frequent in lyceum pupils than in school pupils (40.0 against 19.4 %, p = 0.002). According to contemporary scientific research, cystic-follicle transformation of thyroid gland evolves not only due to iodine deficiency, exposure to chemicals, traumas, etc., but also due to chronic stress and psychophysical overstrain [24].

Table 6

Dynamics in electrocardiogram parameters in junior grades pupils attending different educational establishments over 4 school years (%)

Electrocardiogram data	1st grade			4th grade		
	Lyceum	School	Validity of dis-crepan-cies	Lyceum	School	Validi-ty of discrep crep-ancies
Standard	56,9	56,4	0,96	52,0	61,3	0,41
Electrocardiogram deviations from standard:	43,1	43,6	0,96	48,0	38,7	0,41
Sinus tachycardia (moderate and apparent)	2	2,6	0,50	5,4	7,5	0,32
Sinus bradycardia (moderate and apparent)	7,8	0	0,10	14,6	1,2	**0,01**
Sinus arrhythmia (moderate and apparent)	23,5	35,9	0,20	28,0	30,0	0,85
Supraventricular extrasystole	9,8	5,1	0,23	0	0	–

Table 7

Results of thyroid gland ultrasound scanning performed on junior grades pupils attending different educational establishments, %

Data of thyroid gland ultrasound scanning	Lyceum	School	Validity of discrepancy
Ultrasound standard	32,5	36,1	0,60
Ultrasound pathology signs	67,5	63,9	0,60
Standard volume of thyroid gland	65,0	55,5	0,18
Changes in thyroid gland volumes	35,0	44,4	0,19
Increased thyroid gland volume	5,0	5,5	0,76
Decreased thyroid gland volume	30,0	38,9	0,20
Standard thyroid gland structure	52,5	69,4	**0,02**
Changed thyroid gland structure	47,5	30,6	**0,02**
Diffuse structural changes	0,0	2,78	0,08
Microfocal neoplasms occurrence	15,0	11,1	0,43
Cystic-enlarged follicles occurrence	40,0	19,4	**0,002**
Ultrasound signs f congenital hypothyroidism	0,0	2,78	0,08

Neuropsychological testing results showed that by the end of school year average response time and movement speed at visual-acoustic stimuli tended to reduce in school pupils ($p = 0.13–0.50$), while they increased in lyceum pupils, and prolongation in time of motor response to a stimulus reached statistic significance ($p = 0.0001$) (Tables 8 and 9).

Overall, motor response time and motor response dissipation were authentically higher in lyceum pupils (595.261 ± 17.228 and 93.011 ± 5.255 msec correspondingly) than in school pupils (526.854 ± 25.234 and 86.366 ± 7.078 msec; $p = 0.001–0.05$). We should note that reading speed and articulation speed authentically decreased by the end of school year in lyceum pupils under exposure to interfering information (literal and colored) ($p = 0.03–0.05$). There were no substantial changes in these parameters in school children during school year ($p = 0.23–0.98$), and response time median for reading even decreased ($p = 0.03$) (Table 10).

All the obtained data prove that by the end of school year pupils attending innovative educational establishment had authentically lower attention function and associative-integrative processes of their intellectual activity became apparently slower than in pupils attending ordinary school.

Comparative analysis of stress hormones content in blood revealed that at the beginning of school year levels of dopamine (36.83 ± 8.85 picogram/cm3 in lyceum pupils and 34.83 ± 2.06 picogram/cm3 in school pupils), noradrenalin (126.76 ± 15.30 and $138.46 \pm\pm 10.90$ picogram/cm3 correspondingly) and adrenalin ($42.80 \pm 12,23$ and 54.10 ± 16.52 picogram/cm3 correspondingly) in pupils from both educational establishments corresponded to physiological standard and didn't have any significant discrepancies ($p = 0.0.34–0.79$).

Table 8

Neuropsychological testing results for junior grade pupils attending secondary school

Test features	Beginning of school year	End of school year	Validity of discrepancy
RT-test			
Average response time (msec)	599,736 ± 27,742	526,854 ± 25,234	0,13
Average motor time (msec)	239,138 ± 16,567	227,854 ± 21,880	0,50
Response time dissipation (msec)	106,057 ± 9,151	86,366 ± 7,078	0,11
Motor time dissipation (msec)	42,276 ± 6,109	35,512 ± 4,876	0,42
Responded correctly (st.units)	15,826 ± 0,094	15,927 ± 0,083	0,27
Didn't respond (st.units)	0,184 ± 0,120	0,073 ± 0,083	0,44
Didn't fully respond (st.units)	0,023 ± 0,032	0,000 ± 0,000	0,32
Responded incorrectly (st.units)	0,561 ± 0,409	0,293 ± 0,592	0,96
STROOP- test			
Interference susceptibility when reading (sec)	0,348 ± 0,052	0,368 ± 0,064	0,98
Interference susceptibility when articulating (sec)	0,259 ± 0,047	0,247 ± 0,049	0,23
Detailed results – baseline for reading response time median (sec)	1,002 ± 0,039	0,914 ± 0,060	**0,03**
Detailed results – baseline for articulation response time median (sec)	0,936 ± 0,031	0,890 ± 0,054	0,50
Incorrect reading results 1 (st.units)	4,287 ± 0,820	2,125 ± 0,714	**0,04**
Incorrect articulation results 1 (st.units)	4,034 ± 1,188	1,850 ± 0,658	0,07
Detailed results-interference conditions for response time median, reading (sec)	1,350 ± 0,068	1,282 ± 0,113	0,10
Detailed results-interference conditions for response time median, articulation (sec)	1,195 ± 0,060	1,137 ± 0,088	0,25
Incorrect reading results 2 (st.units)	9,046 ± 2,523	7,225 ± 2,833	0,93
Incorrect articulation results 2 (st.units)	5,080 ± 1,653	3,625 ± 1,147	0,46

Table 9

Neuropsychological testing results for junior grade pupils attending secondary school

Test features	Beginning of school year	End of school year	Validity of discrepancy
RT-test			
Average response time (msec)	546,731 ± 16,870	595,261 ± 17,228	**0,0001**
Average motor time (msec)	227,164 ± 16,046	240,250 ± 13,460	0,22
Response time dissipation (msec)	94,463 ± 5,773	93,011 ± 5,255	0,71
Motor time dissipation (msec)	37,463 ± 4,033	37,625 ± 3,066	0,95
Responded correctly (st.units)	15,833 ± 0,110	15,943 ± 0,049	0,07
Didn't respond (st.units)	0,194 ± 0,149	0,057 ± 0,049	0,08
Didn't fully respond (st.units)	0,030 ± 0,042	0,000 ± 0,000	0,16
Responded incorrectly (st.units)	0,629 ± 0,527	0,125 ± 0,077	0,06
STROOP- test			
Interference susceptibility when reading (sec)	0,357 ± 0,056	0,437 ± 0,049	**0,03**
Interference susceptibility when articulating (sec)	0,251 ± 0,042	0,303 ± 0,041	**0,05**
Detailed results – baseline for reading response time median (sec)	0,979 ± 0,040	0,954 ± 0,029	0,33
Detailed results – baseline for articulation response time median (sec)	0,908 ± 0,029	0,921 ± 0,026	0,51

Continuation of table 9

Incorrect reading results 1 (st.units)	4,433 ± 0,958	2,080 ± 0,491	**0,0001**
Incorrect articulation results 1 (st.units)	3,791 ± 1,080	2,227 ± 0,523	**0,01**
Detailed results-interference conditions for response time median, reading (sec)	1,336 ± 0,077	1,406 ± 0,071	0,18
Detailed results-interference conditions for response time median, articulation (sec)	1,159 ± 0,058	1,224 ± 0,059	0,12
Incorrect reading results 2 (st.units)	7,910 ± 1,663	5,420 ± 0,863	**0,009**
Incorrect articulation results 2 (st.units)	4,463 ± 1,169	2,864 ± 1,016	**0,04**

Table 10

Neuropsychological testing results for junior grade pupils attending different educational establishments at the end of school year

	School	Lyceum	Validity of discrepancy
RT- test			
Average response time (msec)	526,854 ± 25,234	595,261 ± 17,228	**0,001**
Average motor time (msec)	227,854 ± 21,880	240,250 ± 13,460	0,33
Response time dissipation (msec)	86,366 ± 7,078	93,011 ± 5,255	**0,048**
Motor time dissipation (msec)	35,512 ± 4,876	37,625 ± 3,066	0,16
Responded correctly (st.units)	15,927 ± 0,083	15,943 ± 0,049	0,99
Didn't respond (st.units)	0,073 ± 0,083	0,057 ± 0,049	0,73
Didn't fully respond (st.units)	0,000 ± 0,000	0,000 ± 0,000	1,0
Responded incorrectly (st.units)	0,293 ± 0,592	0,125 ± 0,077	0,57
STROOP- test			
Interference susceptibility when reading (sec)	0,368 ± 0,064	0,437 ± 0,049	**0,05**
Interference susceptibility when articulating (sec)	0,247 ± 0,049	0,303 ± 0,041	**0,05**
Detailed results – baseline for reading response time median (sec)	0,914 ± 0,060	0,954 ± 0,029	0,23
Detailed results – baseline for articulation response time median (sec)	0,890 ± 0,054	0,921 ± 0,026	0,29
Incorrect reading results 1 (st.units)	2,125 ± 0,714	2,080 ± 0,491	0,92
Incorrect articulation results 1 (st.units)	1,850 ± 0,658	2,227 ± 0,523	0,37
Detailed results-interference conditions for response time median, reading (sec)	1,282 ± 0,113	1,406 ± 0,071	**0,05**
Detailed results-interference conditions for response time median, articulation (sec)	1,137 ± 0,088	1,224 ± 0,059	0,1
Incorrect reading results 2 (st.units)	7,225 ± 2,833	5,420 ± 0,863	0,22
Incorrect articulation results 2 (st.units)	3,625 ± 1,147	2,864 ± 1,016	0,31

By the end of school year noradrenalin content in lyceum pupils increased to 232.37 ± 95.69 picogram/cm3 (p = 0.001) (in school pupils, to 229.11 ± 49.00 picogram/cm3; p = 0.001), and adrenalin content (28.25 ± 12.36 against 20.37 ±± 6.53 picogram/cm3 in school pupils; p = 0.48) tended to decrease (p = 0.001–0.07). We should note that dopamine content was authentically lower in lyceum pupils than in school pupils (13.03 ± 8.12 against 26.21 ± 5.75 picogram/cm3, p = 0.01). Hydrocortisone content in lyceum pupils was authentically higher than in school pupils of the same age (408,.37 ± 44.54 against 296.29 ± 51.07 nmol/cm3; p = 0.03), and its level was higher than physiological standard in only 18,0 % of lyceum pupils (only 7,9 % among school pupils; p = 0.03). Simultaneously, serotonin content in lyceum pupils was authentically lower than the same parameter in school pupils (192.69 ± 16.27 against 256.17 ± ± 17.77 ng/cm3, p = 0.02). Thyrothrophin and crude T4 content didn't have any significant

discrepancies in both groups (2.03 ± 0.31 μME/cm3 and 106.38 ± 5.75 nmol/dm3 correspondingly against 2.33 ± 0.23 μME/cm3 and 105.63 ± 4.41 nmol/dm3, p = 0.68–0.87).

We detected in our research that by the end of school year content of cGMP initiating anabolic processes and muscle relaxation reactions was authentically higher in lyceum pupils (4.42 ± 0.94 pmol/cm3), than in school children (3.32 ± 0.51 pmol/cm3; p = 0.04), and its level was higher than physiological standard in 27.3 % of lyceum pupils and reached 7.12 ± 1.91 pmol/cm3 (p = 0.02). There were not more than 6,2 % of children with such levels among school pupils, p = 0.02, and cGMP level in them didn't exceed 5.95 ± 0.64 pmol/cm3 (p = 0.04). Besides, lowered apolpoprotein A1 content and increased "apolipoprotein B100/ apolipoprotein A as per A1" coefficient were detected 1.7 times more frequently among lyceum pupils (24.2% of children); (a number of school pupils with the same levels didn't exceed 14.0-13.8% correspondingly; OR = 1.8; p = 0.03). A number of lyceum pupils with elevated crude cholesterol level (6.06 ± 0.04 mmol/dm3) was 1.6 times higher (12.1 against 7.5 %; OR = 1.4; p = 0.04).

Genetic examination results revealed that 7% of lyceum pupils and 16% of school pupils (p = 0.04) had variant homozygote of glutamate receptor gene (AMPA gene). Its occurrence exerts negative impacts on associative-integrative processes of intellectual activity, speed and volume of memorized information, which ultimately leads to lower efficiency of children teachability. Rarer AMPA gene homozygote occurrence in lyceum pupils is most likely related to stricter requirements set forth for preliminary choice of pupils who can attend innovative educational establishments.

So, laboratory examination results prove that most junior grades pupils, regardless of their educational establishment, adapt to educational processes conditions. However, this process development involves sympathoadrenal system overstrain in pupils attending innovative educational establishments. Lower dopamine and serotonin levels detected in lyceum pupils by the end of school year not only determine lower emotional state of children but also cause slower decision-taking speed, especially under exposure to interfering information. Low dopamine level combined with elevated cGMP content (27.2% of lyceum pupils) has negative influence on pupils' reading speed, articulation speed and motor response time. Low apolipoprotein A1 levels and increase in "apolipoprotein B100/apolipoprotein A as per A1" coefficient detected in each forth lyceum pupil combined with elevated cGMP content are predictors of probable lipoprotein metabolism disorders and cardiovascular pathology evolvement in older age groups.

Analysis of the results obtained in the course of clinical-functional and laboratory examination performed on children attending different educational establishments revealed that a number of absolutely healthy children in both educational establishments didn't exceed 4.0–4.5 % (Table 11).

Table 11

Frequency of basic nosologies detection (ICD-10) in junior grade children attending different educational establishments (%)

Nosology category	Lyceum	School	Validity of discrepancies between groups
Digestive organs diseases (K00-K99)	44,5	56,1	0,11
Nervous system diseases (G00-G99)	57,3	40,4	**0,02**
Respiratory organs diseases (J00-J99)	14,9	20,2	0,34
Musculoskeletal system diseases (M00-M99)	59,3	43,7	**0,03**
Endocrine system diseases (E00-E99)	47,4	31,4	**0,03**
Skin and subcutaneous tissue diseases (L00-L99)	7,9	9,0	0,79
Healthy	4,0	4,5	0,86

Table 12

Chronic somatic pathology structure in junior grade pupils attending different educational establishments (%)

Nosologic form	Lyceum	School	Validity of discrepancies
Digestive system diseases			
Biliary dysfunction syndrome (K83.8)	24,7	33,7	0,17
Functional dyspepsia (K30)	17,8	20,2	0,67
Caries (K02.9)	2,97	4,49	0,96
Chronic gastroduodenitis	1,98	2,2	0,98
Respiratory organs diseases			
Bronchial asthma (J45.0)	0,99	2,2	0,98
Recurrent bronchitis, tracheitis (J39.8, J44.8)	0,99	0,0	0,97
Allergic rhinitis (J30.0, J30.1, J30.3)	5,94	7,86	0,59
Chronic tonsillitis (J35.0)	0.99	0	0,98
Adenoid hypertrophy (J35.2, J35.3)	5,94	10,1	0,31
Nervous system diseases			
Vegetative nervous system disorders (G90.8)	25,7	8,98	0,03
Asthenoneurotic syndrome (G93.8)	31,6	31,4	0,99
Musculoskeletal system diseases			
Posture disorders (M43.8, M43.9)	51,4	32,5	0,01
Platypodia (M21.4, M21.0)	7,92	11,2	0,45
Endocrine system diseases			
Excessive height (E34.4)	9,9	8,98	0,82
Insufficient height (E34.3)	1,98	0	0,98
Malnutrition (E44.1, E46, E67.8)	30,6	16,8	0,03
Obesity (E66.0)	4,95	5,61	0,76
Skin diseases			
Atopic dermatitis (L20.8, L27.9)	7,9	9,0	0,81

Table 13

Dynamics of children distribution as per health groups over primary school learning period in different educational establishments, %

Health group	Lyceum			School			p3	p4
	1st grade	4th grade	p1	1st grade	4th grade	p1		
I	4,5	0,0	**0,03**	0,0	3,6	0,07	**0,02**	**0,05**
II	86,5	92,0	0,19	100,0	85,7	**0,001**	**0,001**	0,15
III	9,0	8,0	**0,04**	0,0	10,7	**0,001**	**0,001**	0,51

Note:
p1 is validity of discrepancy between 1st and 4th lyceum grades;
p2 is validity of discrepancy between 1st and 4th school grades;
p3 is validity of discrepancy between 1st grades of different educational establishments;
p4 is validity of discrepancy between 4th grades of different educational establishments.

Analysis of chronic somatic pathology structure in children of this age group proves that most widely spread nosologies among pupils from both educational establishments are digestive organs diseases (K00-K99), nervous system diseases (G00-G99), musculoskeletal system diseases (M00-M99), and endocrine system diseases (E00-E99).

Our research results revealed that levels of nervous system morbidity among lyceum pupils (57.3 against 40.4 % in school pupils), musculoskeletal system morbidity (59.3 against 43.7 % correspondingly) and endocrine system morbidity (47.4 against 31.4 %) were authentically 1.4–1.5 times higher than among school pupils (p = 0.02–0.03) (Table 12).

Comparative analysis enabled detecting that certain nosologies belonging to various nosologic groups were authentically more frequently detected in junior grade pupils attending lyceum than in school children, i.e. vegetative nervous system disorders among nervous system diseases (G90.8) (2.7 against 8.98 % in schoolpupils, p = 0.03; OR = 2.5; DI = 1.4–3.2; p = 0.02); posture disorders among musculoskeletal system diseases (M43.8, M43.9) (51.4 against 32.5 % correspondingly, p = 0.01; OR = 1.6; DI = 1.2–1.9; p = 0.03), and malnutrition among endocrine system diseases (E44.1, E46, E67.8) (30.6 against 16.8 % correspondingly, p = 0.03; OR = 1.8; DI = 1.5–2.2; p = 0.02) (Table 12).We detected direct correlation between greater intellectual and sensory components of educational process and frequency of vegetative nervous system disorders in pupils (G90.8) (F = 114.31–286.77; R2 = 0.34–0.41; p = 0.02–0.03), as well as between increased intellectual load and general learning activity stress and frequency of musculoskeletal system diseases (F = 73.29–193.83; R2 = 0.29–0.37; p = 0.02).

We examined dynamics of children distribution as per health groups over primary school learning period in different educational establishments; the examination revealed that all 1st grade pupils had the 2nd health group when they started school while only 86.5% of those entering lyceum had the same health group (p = 0.001); however, 4.5 % belonged to the 1st health group (p = 0.02), but 9,0 % had only the 3rd one (p = 0.001). By the end of the 4th school year 3.6 % of school pupils had the 1st health group (0 % among lyceum pupils, p = 0.05), 85.7 % belonged to the 2nd group (92.0 % among lyceum pupils, p = 0.15), however, each tenth child (10.7 %) belonged to the 3rd group (8.0 % among lyceum pupils, p = 0.51) (Table 13).

Conclusions: 1. Innovative educational establishments tend to have tighter organizational regime, longer duration and greater intensity of classes, and educational process involves considerable intellectual, sensory, and emotional loads. Pupils attending innovative educational establishments also have greater loads as they attend additional education establishments so overall educational loads grow significantly.

2. Most pupils attending innovative educational establishments are adapted to educational process conditions, however, by the end of school year 20% lyceum pupils have signs of sympathoadrenal system overstrain. It doesn't only determine children's emotional state but also causes attention function disorders and slower decision-taking, slower reading and articulation speed, longer motor responses time.

3. 15% 4th grade pupils attending innovative educational establishment tend to have elevated vegetative nervous system activity and their cardiovascular system is poorly adapted to psychoemotional and physical loads.

4. 25 % junior grades pupils whose educational process is stressful and intense tend to have low apolipoprotein A1 levels and increased "apolipoprotein B100/apolipoprotein A as per A1" coefficient; when it is combined with high cGMP content, we can treat it as a predictor of lipoprotein metabolism disorders and cardiovascular pathology evolvement in older age groups.

5. Lyceum pupils run 2.5 times higher risk for chronic nervous system diseases, musculoskeletal system diseases and endocrine system diseases, than pupils attending ordinary schools. Vegetative nervous system diseases, posture disorder and malnutrition are prevailing nosologic forms as they are 1.6-2.9 times more frequently detected in lyceum pupils than in school pupils.

6. We detected direct correlation between greater intellectual and sensory components of educational process, as well as overall educational process stress, and frequency of vegetative nervous system disorders and musculoskeletal system diseases occurrence in pupils.

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ASSESSMENT OF BASIC BEHAVIOURAL RISKS CONCERNING HEALTH OF STUDENTS ATTENDING MEDICAL UNIVERSITY

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We chose students from all the six years attending Medical and Prevention Faculty of Perm State Medical University named after academician E.A. Vagner as our research object. Our research goal was to examine and to assess basic behavioral risks which could cause health risks for students attending medical higher educational establishment. We applied a set of techniques in our work: information-bibliographic one (15 literature sources were studied, both periodicals and monographs), sociological one (467 students of Medical and Prevention Faculty were included into a one-time questioning, them all being an entire assembly), statistic one (we calculated relative values and mean values, as well as correlation coefficients). The research was performed in two steps; the first one was based on analyzing subjective evidence, namely, sociologic questioning results; in our second step we focused on examining pathologic damages as per medical examinations data as well as data on morbidity obtained from register of visits to a students' polyclinic.

Students' health is a significant parameter of a society intellectual potential; specific weight of students, both males and females, who take care of their health amounts to 60.0 % and 96.5 % correspondingly. 100 % questioned girls and 58.3 % boys consider their health to be "good". There are gender-based discrepancies in estimating one's health state in all sub-groups and as per all reasons for its preservation. 45 % boys and 40 % girls with quite different self-estimation of their health combine work and study. Students tend to have bad habits as they constantly drink alcohol and smoke. Despite availability of considerable volumes of information on diseases prevention students don't try to use this information and preserve their health. Medical students' lifestyle has such peculiarities as non-rational nutrition, insufficient physical, social and medical activity.

Key words: *self-estimation of one's health, students, risk factors, nutrition, combining work and study, lifestyle, medical activity, medical aid organization, prevention, healthcare program, management.*

In 2014 5.2 million students attended HEEs in Russia; 2.0 million of them received budgetary funding and didn't pay for their study. 4.0 million attended state and municipal educational establishments [8].

A higher educational establishment as a social institute is to educate a competent professional with good physical and mental health. Students are not only members of youth population group, but also they are intellectual potential of the whole society.

The higher is the significance of high professional education, the more often and more acute are its problems. Such problems include job placement for graduates (that's why a new position of a vice-chancellor responsible for graduates' job placement has been introduced in HEEs), family creation, and health of future professionals. Students' health can predict life quality for labor population in this or that region.

All factors significant for students' health can be divided into three groups: 1) social-hygienic ones, 2) medical-biological ones, 3) psychological ones.

To justify any management decisions, for example creation of health-preserving programs in a HEE, we need to study basic

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parameters of students' health, namely morbidity (as per medical health appealability and medical examinations data), disability, medical-demographic indices, and physical development [15].

Self-assessment of one's health is a significant parameter of a person's health. It is very important to promote self-preserving behavior among students attending medical HEEs where a lot of attention in the educational process is paid to prevention issues among population (patients).

Students, just like the whole RF population, don't' think their health to be a basic value. Health self-assessment is an analysis of physical and mental health; it determines a person's behavior. I.V. Zhuravleva et al. [5, 6] state that self-assessment can be used as a health parameter. Researchers believe there is a high correlation between self-assessment and actual data taken from medical documents.

Academic load for students attending medical HEEs is on average 2 times higher than for students of other HEEs. Duration and educational specificity make high demands to their health state.

Health self-assessment can depend on the following factors: sex, age, educational status, territory of living, occupation, social and economic conditions in a region [9, 10]

D.I. Kicha and M.I. Panachina divide all social and hygienic studies of students' problems in our country into four stages:

I stage. 20–30-ties of the XX century. Creation of organizational and methodical grounds for research of students;

II stage. 40–50-ties. Study and determination of standards for youth physical development;

III stage. 60–80-ties. Scientists started to examine students' lifestyle, nutrition and morbidity;

IV stage. Since the beginning of 90-ties a lot of research has been dedicated to studying health and, in particular, physical development [7].

Nowadays all research focuses not only on examining risk factors but also on giving grounds for students' health preservation programs.

Studying data on HEE students health helped us to determine certain regularities:

– when entering a HEE, applicants already have one or several chronic diseases;

– students mostly pursue passive self-preserving behavior patterns, they underestimate influence exerted on a body by drugs, smoking, and alcohol [3, 12, 14];

– rational adaptation to student life is one of the most significant factors facilitating health preservation;

– first rank places in morbidity structure as per appealability to medical organizations (MO) belong to catarrhal diseases, nervous system diseases, sense organs diseases, and urogenital system diseases [4, 11];

– most researchers think that students' health is not studied enough (there is lack of authentic statistics in MO, and research takes place on regional and local level) [2];

– nowadays (under social and economic instability) asocial behavior grows, namely drug-taking and alcohol drinking; there is also increase in sexual diseases cases [1];

– a significant part of diseases is determined by life style, and positive features of self-preservation behavior (giving up bad habits) are a barrier to successful socialization among students [5];

– there are several reasons for students not attending lectures due to a disease: 1) catarrhal diseases (69.3%); 2) traumas (7.7%), 3) digestive organs diseases (3.6%); besides, a number of students who belong to s special medical group in terms of physical activities grows annually [4];

– a specific weight of students attending HEEs and being disabled from their childhood also goes up;

– programs aimed at prevention of students' morbidity are created in HEEs, and health-preserving technologies are used in educational process [13].

Even a quick analysis of works dedicated to studying students' health reveals that the subject of our research is vital.

Data and methods. On January 01, 2017 there were 3,568 students attending FSBEE Perm State Medical University named after Academician E.A. Vagner.

467 students of medical-prevention faculty were our research object; their number amounted to 13.08% of the total number of students (the sample was authentic). We made up a research program in the form of a questionnaire. The main part of the questions was aimed at studying students' self-assessment of their health, as well as at determining characteristics of behavioral risks in its formation.

We accomplished pilot research and questioned 77 third-year students of medical-prevention faculty, or 93.9% of all third-year students. We collected and processed 77 questionnaires in Biostat program. The sample amounted to 16.48% of total number of students at the faculty, and it proved the sample was representative. 20 male students and 57 female students took part in questioning. Ratio as per sex was equal to 1:2.85. Such ratio was characteristic for all years at this faculty. Average number of students as per years amounted to 77 and it also provided representativeness of our sample.

All the questioned students were divided into 2 groups: 1) those taking care of their health; 2) those who neglected their health. Each of these groups consisted of 4 sub-groups depending on self-assessment of their health:

– with "good health",
– with "satisfactory health",
– with "bad health",
– with "difficult to say" answer.

Results and discussion. To interpret the obtained results, we analyzed students' attitude towards their health allowing for discrepancies between groups and sub-groups. Specific weight of respondents, both males and females, who took care of their health amounted to 60.0 and 96.5% correspondingly. Specific weight of males taking care of their health was 1.6 times lower than females. Males assessed their health as "good" in 58.3% cases, as "satisfactory", in 16.7% cases, as "bad" in 0% cases. Each forth student had difficulty in assessing his health. All female respondents took care of their health.

Assessment from the group of those *not taking care of their health* among males was as follows: "good health", 0%; "satisfactory", 75%; "bad", 25.0%.

Structure of female respondents *taking care* of their health, was as follows: 47.3 % respondents assessed their health as "good" and "satisfactory", 5.5 % had difficulty in answering the question, and there were no "bad" assessments. Table 1 represents the whole data.

Table 1

Distribution of third year students of medical-prevention faculty as per attitude towards their health, self-assessment of their health, and sex (%)

Health self-assessment	Sex	Taking care of their health	Not taking care of their health
«Good»	Males	58,3	0
	Females	47,3	0
«Satisfactory»	Males	16,7	75,0
	Females	47,3	0
«Bad»	Males	0	25,0
	Females	0	0
«Difficult to say»	Males	25,0	0
	Females	5,4	0

The obtained data reveal there are gender discrepancies in health self-assessment. It proves that men traditionally tend to over-estimate themselves. The results obtained by us coincide with the data obtained by other researchers [5].

The first and the main reason why all the students took care of their health was their wish to be physically stronger (41.7% males, 43.7% females). The second reason mentioned by females was health deterioration (27.3%), and impact exerted by medical information was the third one.

Male respondents who didn't take care of their health outlined several reasons:

– unwillingness to set any limits for themselves (25.0 %);
– being sure no care guaranteed good health (25.0 %);
– absence of time (25.0 %);

– other reasons (25.0 %).

We should point out that all the questioned students already had some ideas on influence exerted by environmental factors on their health (from the common hygiene course). Thus, a lot of male students thought that environmental factors and their own efforts had greater influence on their health. Bad habits were only mentioned by few students.

Female respondents' answers revealed that in their opinion health was formed under living conditions influence (38.6%) and heredity (19.3%), and each fifth mentioned bad habits.

The questioning revealed that 45% male students and 40% female students of the third year with quite different health self-assessment combined work and studies; 44.4% male respondents and 29.2% female respondents said their work had elements with mental and physical nature. Those were students who was included into groups with "good" and "satisfactory" health self-assessment.

Males with "good" health self-assessment were nervous and tired at their work in 22.2% cases; males with "satisfactory" health self-assessment mentioned the same in 33.3% cases. Female students suffered from much greater stress at work. Thus, females with "good" health self-assessment mentioned exhaustion in 50.0% cases, and with "satisfactory" health self-assessment, in 16%.

We detected a certain correlation in respondents between health self-assessment and having bad habits. 20% male students and 9% female students smoked. A number of smoking males grew as their health self-assessment deteriorated (from 5% among having "good" health to 10% of having "satisfactory" health). As for females, we observed decrease from 5.2% ("good" health) to 3.5% ("satisfactory" health).

None of our respondents didn't take drugs at the moment of research. A part of the respondents were theoretically in drug danger as they were acquainted with drug-addicted people or they had previously taken psychoactive substances. We should pay attention to the fact that students often consumed alcohol (wine, beer, and strong spirits); it was mentioned by 90.0% males and 78.9% females.

We should also mention positive factors influencing respondents' health. Thus, 90.0% males and 93.0% females had physical training:

– daily, 10.0 % males and 12.3 % females;

– often, 35.0 and 22.8 % correspondingly;

– sometimes, 45.0 and 57.9 % correspondingly;

– never, 10.0 and 7.0 % correspondingly.

All the third year students after annual medical examination at the physical culture department were divided into three groups depending on their health; 53.9% males and 58.3% females attended the first (basic) group; 23.1% and 20.0% attended the second one; 23.1% and 21.0% attended the third group. Students' distribution in these groups coincided with their health self-assessment.

Studies in a HEE, especially a medical one, always involves great mental, physical, and emotional load. The questioning revealed that males and females had negative emotions:

– daily, 25.0 % males and 8.8 % females;

– often, 15.0 and 19.3 % correspondingly;

– sometimes, 60.0 and 64.9 % correspondingly;

– never, 0.0 and 7.0 % correspondingly.

Suffering from negative emotions leads to stress and it influences health. Male students daily suffered from stress, 3 times more frequently, than female students.

To be successful in life, most students said they first of all needed such values as wealth, strong character, ability, and talent; the second place belonged to luck and education, health took the third place.

Females thought strong character was the most important, the second place belonged to support by close friends and relatives, and health occupied the third place.

Both males and females thought strong character to be the most important. This factor was very significant for students attending a medical HEE. It is impossible to be a successful student without string character and substantial efforts. And unsuccessful students can't count on free-of-

charge education funded by state budget. Health as a value occupied only the third place in students' minds.

The questioning also revealed that students would like to receive authentic information which could help to preserve and to improve their health (table 2).

There are some common features in demands for knowledge in males and females. For example, all students considered it important to organize rational nutrition depending on their age, sex, and energy costs. This information can be obtained in lectures on "Nutrition hygiene", the fifth and sixth year. But in spite of total computerization students obviously were too lazy to look for such information on their own; nor had they time or willingness to apply for help and for an individual consultation to a medical prevention center. Thus we can state medical activity of the respondents was too low.

Table 2

Interest in information on health improvement shown by students as per information types and sex in rank order

Information type	Males	Females
Eutrophy	1	1
Communication psychology and stress prevention	2	3
Healthy lifestyle	3	2
Protection from adverse factors	4	5
Prevention of circulatory system diseases	5	6
Risk factors for your health	6	4

Respondents, regardless of their health state, were in the same manner interested in communication psychology and stress prevention. It can be explained by significant academic load and continuing adaptation of third year students. All respondents, regardless of their sex and health self-assessment, needed information on issues of healthy lifestyle creation and preservation, on circulatory system disease prevention, and organization of protection from adverse ecological factors.

The questioning revealed that need in knowledge on health preservation had many aspects and was formed consciously. Students took certain measures on diseases prevention on their own (table 3).

Table 3

Preventive measures structure, used by students to improve their health, depending on sex (%)

Diseases prevention activities	Males	Females
Appealing to doctors in a polyclinic in order to have preventive examination, consultation, or prophylactic medical examination	25,0	25,0
Taking vitamins in winter and spring	40,0	70,0
Preventive measures against flu (vaccination, taking vitamins, wearing masks, intensive airing)	50,0	50,0
Preventing acute conditions of chronic diseases	35,0	28,0

Conclusions. Studying literature on the subject of our research and our own pilot questioning of third year students of medical-prevention faculty show that:

– students' health is a significant index of state which society intellectual potential has;

– specific weight of students, males and females, taking care of their health amounts to 60.0% and 96.5% correspondingly;

– health self-assessment being "good" is stated by 58.3% males and 100.0% females;

– there are gender discrepancies in assessing one's health in all sub-groups and motives of its preservation;

– 45.0 % males and 40.0 % females with varying health self-assessment combine studies and work;

– students tend to have bad habits, namely constant alcohol drinking and smoking;

– although information on diseases prevention is quite available in significant volumes, students don't try to use it in due time and to preserve their health;

– irrational nutrition, insufficient physical and medical activity are the main problems of medical students' lifestyle.

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RISK FACTORS CAUSING EVOLVEMENT OF ALIMENTARY-DEPENDENT DISEASES IN SPECIFIC GROUPS OF WORKERS EMPLOYED AT METALLURGY PRODUCTION AND PREVENTION MEAUSRES DEVELOPMENT

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The article gives the results of hygienic and epidemiologic research of morbidity, nutrition structure, food stuffs safety, working conditions, and actual nutrition of workers employed at metallurgy productions. The research was carried out at "Magnitogorskiy metallurgy plant" PLC. 1208 steel workers and founders made up the main group. Average age of research participants amounted to 40.0 ± 0.75. The sampling was representative. We studied actual nutrition over 2010–2015 via analyzing food consumption frequency and applying extended base of food stuffs chemical structure and analyzing menus with lists of dishes offered for an organized group nutrition. We assessed both qualitative and quantitative parameters, including consumption of basic nutrients, energy, irreplaceable amino acids, lipids, vitamins, dietary fiber, essential and conditionally essential microbiological elements (60 nutrients totally, allowing for losses on a product peeling, edible contents, and other losses occurring at various treatments during cooking). We also assessed nutrition regime and other nutrition features. We detected that ratio between proteins, fats and carbohydrates was the evidence of mostly fat nutrition type. Workers were found to consume insufficient quantity of certain vitamins (A, D, and folic acid) and biological elements (calcium), but they instead consumed excessive quantities of saturated fats and common salt. It is shown that actual nutrition of specific workers' groups at metallurgy production is not rational, imbalanced, and doesn't satisfy body needs causing risks of nutrition state shifts and alimentary-dependent diseases evolvement. Alimentary-dependent diseases on average amounted to 21.6 % in the total morbidity structure in 2010–2015. 10.0 % of all diseases with temporary working disability are diseases determined by mostly nutrition factor. Epidemiologic analysis of morbidity comprising diseases related to non-rational nutrition enabled us to determine priority nosologies, risk groups and risk factors.

We have the grounds for hygienic recommendations aimed at correcting nutrition structure depending on detected deviations.

***Key words**: actual nutrition, working conditions, nutrition state, metallurgy production, risk factors, prevention, nutrition hygiene, alimentary-dependent diseases, preventive nutrition.*

Development of labor potential in our country, professional health preservation and prolonging working period of active population is a significant function of state authority and a base of social policy in the Russian Federation.

Prevention of health losses among working population is a very important task of prevention medicine and it is especially vital nowadays as there are negative forecasts in relation to labor resources dynamics in our country in medium-term period.

Working population today is to be treated

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as a risk group as it constantly undergoes exposure to a whole set of production and non-production factors. And primarily lifestyle factors belong to the latter ones [3].

It is very important not only preserve workers' health in working environment but also to improve it as work at industrial enterprises requires a lot of efforts. Such pathogenic factor as irrational nutrition exerts negative impact on population together with other environment factors (of chemical, physic, biological, and social nature) causing morbidity and mortality [11].

Various scenarios can occur due to this exposure; among other phenomena, potentiation of negative effects on health can underlie them.

Working conditions at a large metallurgic enterprise include physic factors, namely increased air temperature in a working area, increased noise and vibrations, impacts of various radiation, such as heat, ionizing, electromagnetic, and laser one, dustiness and gas pollution, unfavorable illumination environment.

Besides that, plenty of inhalable agents are generated during production processes; among them there are gases, vapor, dust, and aerosols. These agents represent certain toxicological dangers as theн exert irritating, fibrogenic, allergenic, carcinogenic, and mutagenic impacts on a human body [1, 3, 10].

Metallurgic production is characterized with a combination of impacts exerted by negative physic and chemical environmental factors and high physical and neuro-psychic overloads. Therefore, complex impacts of these factors are fundamental in risk assessment.

Working process, in its turn, is characterized with high load on musculoskeletal system and functional systems of a body, as well as on central nervous system [13, 14].

Nutrition is an unique environment factor which influences a human body; it is both an internal and an external factor. It's also a social factor if we consider nutrition structure and nutrition habits; it is also a biological factor as it is related to essential nutrients intake. Finally, this factor can become pathogenic but it can also raise protective functions of body physiological barriers as it lowers risks of exotoxins penetration and facilitates processes of binding poisons and products of their metabolism. It is these nutrition effects which a concept of medical-preventive nutrition is based on [1, 3, 10, 16]. A number of works, both by Russian and foreign researchers, is dedicated to scientific grounds and practical implementation of such approaches [2, 3, 4, 6, 8, 9, 15].

Functional deviations and chronic pathologies growth is one of the factors among certain occupational groups of workers employed at industrial enterprises; such pathology can be alimentary-dependent and it makes it necessary to find ways of improving prevention activities on the basis of up-to-date labor medicine data [5, 12, 17].

First of all, we think it is advisable to perform a complex assessment of influence which occupational risk factor and lifestyle factors have on workers' health. In some authors' opinion, occupational risk concept which has been developing quite intensely over the recent years is a truly innovative and up-to-date approach used to define prevention priorities [7, 11].

We constantly face resources deficiency, so scientific grounds of prevention work priorities are very important for leading risk factors elimination. In relation to that, implementation of activities aimed at nutrition system reorganization is a vital task for the state as nutrition is a vital factor determining workers' health.

All contemporary activities aimed at workers' health protection don't allow for a possibility of production-induced diseases formation, especially under joint impacts exerted by working conditions and lifestyle factors. Here health preservation depends not only on working conditions improvement but also on a set of social, hygienic, medical, and educational activities. At the same time, such important prevention activities as production control and periodical medical examinations are accomplished without taking production-induced morbidity into account and it has negative influence on their efficiency.

An attempt to estimate actual nutrition as a risk factor which can cause chronic pathology evolvement together with unfavorable working conditions and working process factors determined the importance of the chosen

research issue for creating efficient preventive activities.

Our research goal was to accomplish hygienic assessment of actual nutrition of workers with several occupations employed at metallurgic production in terms of its contribution into production-induced morbidity.

Data and methods. Our research was performed at "Magnitogorskiy metallurgic plant" PLC (MMP). 1,208 steel workers and founders were our basic group. Average age of research participants was equal to 40.0 ± 0.75. Our sampling was representative.

We studied actual nutrition of certain workers' groups employed at the enterprise over 2010-2015; when doing it, we analyzed food consumption frequency using extended database on foodstuffs chemical structure and analysis of menus with lists of dishes offered for organized groups nutrition.

When analyzing whether ration was balanced, we assessed qualitative and quantitative indices. Then we compared the obtained consumption values for basic nutrients, energy, essential amino acids, lipids, vitamins, dietary fiber, essential and conditionally essential macro- and microbiological elements (60 nutrients totally, allowing for losses on a product peeling, eatable content, and other losses occurring at various treatments during cooking) with "Standards of physiological needs in nutrients and energy for various population groups in the RF".

We assessed nutrition regime as well as its other features. We calculated consumption values and provision with nutrients with the help of an original computer program based on Visual Basic module to Excel-2000. This program included database on chemical structure of foodstuffs and dishes based on "Foodstuffs chemical structure" tables (2012) and data obtained via laboratory research of foodstuffs.

Analysis was performed with the use of Statistica 6.0 software and MS Excel-2003. We checked normalcy of signs distribution with the use of Shapiro-Wilk criterion. We took p equal to 0.05 as a critical significance in all statistic analysis procedures. To check statistic hypotheses, we applied distribution-free techniques. To compare quantitative data from two independent groups, we used Mann-Whitney U-criterion.

Results and discussion. As we assessed whether ration was balanced, we detected that proteins, lipids and hydrocarbons ration amounted to 1:1.6:5.1 with recommended level being 1:1.1:4.8, and it proves that nutrition type was mainly a fat one.

Daily average values for separate foodstuffs which were consumed by workers employed at metallurgic production are given in table 1.

Table 1

Average daily consumption of various food stuffs by workers employed at metallurgic production (allowing for losses caused by peeling a product and other losses occurring due to treatment when cooking; 2010–2015)

Food stuffs category	P16*	P50	P84	*M*	*SE*
Chicken eggs	6,1	16,8	36,4	27,6	4,59
Bakery	86,1	213,7	298,7	233,6	20,02
Cereals, macaroni	61,1	136,4	332,0	220,0	38,08
Vegetables	261,4	497,4	911,6	590,2	46,56
Fruit	76,1	243,8	443,5	322,4	40,39
Confectionary	7,8	22,0	67,8	36,4	4,16
Butter, fat	10,5	24,7	49,8	30,6	2,75
Meat and meat products	129,4	222,5	362,0	247,3	15,85
Fish and seafood	7,6	20,2	60,6	30,7	3,37
Milk and dairy products	107,7	253,9	644,6	392,8	46,06
Beverages	453,0	777,9	1373,6	907,9	57,07

N o t e: P16, P50, P84 are the 16th, 50th (median) and 84th percentile of variational series correspondingly, *M* is a simple average, *SE* (or *m*) is a standard error of the mean.

Qualitative assessment revealed that specific weight of individuals with excessive energy consumption amounted to 41.6% (excess being equal to 43.7%) whereas only 7.8% respondents had ration with lowered energy value. Also, 26.0% workers didn't consume enough carbohydrates, while 19.5% consumed them in excessive quantity. Protein consumption was average, quite sufficient, and corresponded to physiological standards (109.2 %).

We should note that specific weight of people who consumed food cholesterol in

excessive quantity amounted to 75.3% (excess value being 139.5%); the same figure for triglycerides was 98.3% (excess value being 200.4%)/ When we analyzed omega-6-fatty acids contents we found out that specific weight of people who consumed them in excessive quantity was equal to 61.0% with excess value being 190.9%, and omega-6/omega-3-fatty acids (FA) content deviated from the recommended level rather substantially (table 2).

Table 2

Qualitative assessment of average daily lipids consumption by workers employed at metallurgic production (2010–2015)

Index	Specific weight of individuals with insufficient consumption, %	Specific weight of individuals with excessive consumption, %	Excess value, %
Fats	6,5 ± 0,7	74,0 ± 1,3	60,9
Cholesterol	5,2 ± 0,6	75,3 ± 1,2	139,5
Saturated fatty acids	10,4 ± 0,9	44,2 ± 1,4	64,7
Mono unsaturated fatty acids	5,2 ± 0,6	72,7 ± 1,3	73,3
Poly unsaturated fatty acids, mg	36,4 ± 1,4	2,6 ± 0,5	106,8
Triglycerides, mg	0,0 ± 0,1	98,7 ± 0,3	200,4
Phospholipids, mg	15,6 ± 1,0	43,0 ± 1,4	52,3
Linoleic acid (w-6), mg	2,6 ± 0,5	61,0 ± 1,4	190,9
Linolenic acid (w-3), mg	10,4 ± 0,9	19,5 ± 1,1	170,9
Arachidonic acid (w-6), mg	35,1 ± 1,4	9,1 ± 0,8	200,4
w-6 / w-3 ratio	11,7 ± 0,9	64,9 ± 1,4	111,9

Vitamin consumption in the examined group was higher than on average for population of the Urals and Siberia [11]. It was due to the necessity to compensate for considerable energy consumption caused by high physical activity. However, we should point out that specific weight of people who didn't consume enough A vitamin amounted to 64.9%; folic acid, 80.5% (deficiency value being 58.0%); D vitamin, more than 90.0%/

If we take essential macro- and microelements, then special attention should be paid to insufficient calcium consumption (33.8% respondents) and Ca/P recommended ratio violation related to that (practically 1:1.4).

Research of food status in separate MMP workers' groups revealed that clinical symptoms of vitamin deficiency occurred quite rarely and it corresponded to the data obtained via actual nutrition assessment.

The figure below represents food status assessment for workers employed at metallurgic production as per body mass index.

Such data coincide with the results of workers' actual nutrition assessment. We performed epidemiologic analysis of morbidity and a set of its outcomes (morbidity with temporary incapacity, disability, untimely deaths); the results

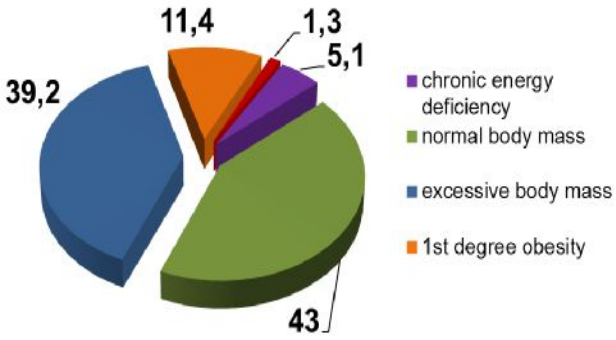

Figure. Food status assessment for workers employed at metallurgic production as per body mass index (%).

correlated with the data obtained via hygienic assessment of nutrition which workers employed at metallurgic production received.

Diseases with etiology wholly dependent on nutrition factor were characterized with apparent and statistically significant growth trend in overall morbidity dynamics for MMP workers (T_{pr} was equal to +6.6; p<0.001). Alimentary -dependent diseases were on average equal to 21.6% in overall morbidity structure in 2010-2015.

We worked out several model menus for the metallurgic plant canteens and recommended to adopt them in full conformity with sanitary regulations. We allowed for seasonality, necessary quantities of basic nutrients, and required caloric value of daily ration. Menus included foodstuffs which could help to prevent diseases caused by micro-nutrients deficiency. We also grounded our recommendations on reduction in consumption of animal saturated fats and growth in orega-3-fatty acids consumption.

All this helped to make range of meat and vegetable dishes in the metallurgic plant canteens wider, increase number of workers who ate 2 or 3 times, to introduce hot breakfast and lunch, and to organize dietetic nutrition.

Conclusions. Hygienic assessment of nutrition revealed that actual nutrition which certain workers' groups employed at metallurgic production received was irrational, imbalanced, and it didn't satisfy physiological needs. So, a risk of deviations in food status and alimentary-dependent diseases evolvement occurred.

Clinically significant symptoms of skin damage related to insufficient provision with micro-nutrients didn't occur frequently. More than a half of the examined workers had excessive body mass (12.7% suffered from obesity with the 1st and 2nd degree).

On average, alimentary-dependent diseases amounted to 21.6% in the structure of overall morbidity in 2010-2015. Diseases caused mostly by nutrition factor amounted to 10.0% of all diseases with temporary incapacity. Epidemiologic analysis of morbidity caused by diseases related to irrational nutrition allowed us to determine priority nosologies, risk groups, as well as risk factors. This information was essential for creating a set of preventive activities for workers employed at metallurgic production.

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ASSESSING OCCUPATIONAL CARCINOGENIC RISKS FOR HEALTH OF WORKERS EMPLOYED AT BLISTER COPPER PRODUCTION ENTERPRISE

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In order to develop ideological grounds for complex assessment of industrial carcinogenic danger, we performed hygienic assessment of contribution made by working environment factors into carcinogenic risks formation for workers employed at blister copper production. The assessment included predictive values of occupational risks. We determined tumor markers levels for occupations with unacceptable levels of carcinogenic risks. We examined mortality caused by malignant neoplasms. It is shown that non-organic arsenic compounds applied in blister copper production are the main factor causing carcinogenic risks. As we calculated individual carcinogenic risks for 25-year working period we found out that total carcinogenic risks for all basic and supplementary occupations in copper-smelting workshops were within the 4th range (more than 1.0 x 10^{-3}). Unacceptable predictive values of carcinogenic risks for 100 % examined occupations appeared already after 5 years of work. We detected excess levels of tumor markers in 73 % of examined workers with occupations characterized with unacceptable values of carcinogenic risks; 19 % of such workers had excess levels of two tumor markers at once. 9 % of examined workers had excess levels of Cyfra 21.1 tumor marker, 14,5 % of workers had high levels of CEA tumor marker, and 59 % of workers had high levels of NSE tumor marker. Intensive mortality indices for male workers employed at copper-smelting workshops as per all localizations amounted to 153.14, whereas they amounted to only 127.25 per 100,000 people for other population groups. Workers employed at blister copper production had higher intensive mortality indices than other people in terms of such nosologies as malignant neoplasms in respiratory organs and chest (86.78 and 47.72 correspondingly), including lung cancer (71.47 and 43.48 correspondingly. The obtained results will help to work out a system for managing carcinogenic risks which will include regulating and controlling activities, managerial activities, technical and technological measures, financial and economic activities, medical and prevention activities plus rehabilitation activities, as well as information and educational activities.

***Key words**: blister copper production, occupational individual carcinogenic risk, mortality caused by malignant neoplasms, tumor markers, carcinogenic risk management, arsenic, nickel, lead, cadmium.*

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Nowadays practically one third of workers in Russia have to work in hazardous and dangerous working environment. As per International Labor Organization assessment, more than 76,000 death cases in Russia are caused by occupational diseases. This situation calls for changes in priorities when planning strategies aimed at population health improvement; namely. the focus needs to be shifted from clinical approach to prevention programs implementation. Therefore, managing occupational risks becomes a most vital task and it means working out a set of activities for preventing adverse impacts exerted by working conditions on health; these activities are to be based on assigning top priority to primary prevention and lowering risk factors influence [16].

P.V. Serebryakov (2007), A.V. Meltser (2008), and some other authors dedicated their research to development of carcinogenic risk assessment methodology. In particular, P.V. Serebryakov was the first to work out an algorithm for calculating individual occupational carcinogenic risks; this algorithm was tested at enterprises which specialized in extracting and processing copper-nickel ores [14]. Issues of occupational exposure to carcinogens, risk assessments and biological monitoring (on the example of arsenic compounds) are also profoundly discussed in foreign scientific literature [17, 18, 20].

Since 2011 Rospotrebnadzor offices and establishments in Sverdlovsk region, together with FBSE "Yekaterinburg medical scientific center for prevention and protection of workers employed at industrial enterprises", have been developing ideological grounds for complex assessment of enterprises' carcinogenic danger [9]. As per results of assessing exposure to carcinogenic factors and working population characteristics, predictive values of individual occupational carcinogenic risk (CR) are calculated; these values are then compared with risks related to non-production impacts. These CR assessments enable researchers to form a risk group of workers who then undergo additional research on early detection of neoplasms signs during preventive examinations; when it is necessary, such workers have additional examinations in a hospital with further regular medical check-ups. In order to give grounds for production factors contribution into malignant neoplasms (MN) evolvement, research on workers' oncologic mortality is conducted. All the above-stated allows us to justify activities aimed at managing carcinogenic risks.

However, there is a number of methodological problems related to calculation of predictive CR values as its aspects, values and criteria are not confirmed in accordance with the established procedure; there is also an issue of assessing proof of relation between an occupation and cancer evolvement as well as determining tumor formation predictors [7,15].

Our research goal was to examine working conditions and assess occupational carcinogenic risks for workers employed at enterprises dealing with blister copper production.

Data and methods. We chose a major enterprise in the Urals specializing in blister copper production as our research object; production in copper-smelting workshop at this enterprise combined such technological processes as mix materials drying, smelting in Vanyukov's furnace (PV-1500), and copper converting.

At the first stage of our research we identified the enterprise carcinogenic danger basing on the initial data taken from its sanitary-hygienic certificate. We determined priority carcinogenic factors of production components (raw materials, products, emissions into atmosphere, sewage discharge, air composition in working area etc.) and formed a data bank (on concentrations) for further assessment of occupational carcinogenic health risk. We based our CR calculations on approaches stated in P 2.1.10.1920-04. "Guidelines on assessment of population health risk under exposure to chemicals which pollute environment" [8] and research conducted by A.V. Meltser and P.V. Serebryakov [5, 14]. CR was calculated for 17 occupations of copper-smelting workshop (drying section, smelting section, and converting section); 420 people were employed at this workshop, namely: drying

operators (6 people), carrier operators (15 people), mix materials handlers (2 people), mix materials loaders (39 people), smelters (70 people), casters (30 people), blowers (37 people), crane drivers (31 people), cleaners (52 people), fireproof materials handlers (3 people), foremen (12 people), powder-gas catching devices operators (44 people), pumping units operators (10 people), electro-gas welders (15 people), maintenance fitters (42 people), electricians (25 people), supervisory instruments and automatic devices fitters (5 people), allowing for actual exposure to arsenic, cadmium, lead, beryllium, and benzpyrene (250 working shifts, 8 hours long each).

At the second stage, we determined tumor markers in blood serum of workers who had these occupations; tumor markers included cancer embryonic antigen (CEA) which was a marker of tumors in trachea, bronchial tubes and lungs, gastrointestinal tract, especially large intestine, pancreas, liver, as well as mammary gland, uterine neck and prostate; Cyfra 21.1 which was a marker of lung cancer (mostly epidermoid one, and less frequently adenocarcinoma and other histological types) and urinary bladder; neuron-specific enolase (NSE) which was a marker of lung tumors, leukemia and tumors of neuroectodermal origin [19].

At the third stage we performed retrospective epidemiologic research on mortality caused by malignant neoplasms among workers employed at copper-smelting workshops and having the same occupations for which CR was assessed [6]. Population living in close proximity to the enterprise was our control group. The research period was 30 years (1976-2005). We calculated intensive mortality indices per 100,000 people of population and workers (distributed as per age and total ones). In addition to the observed mortality in the examined cohorts, we calculated so called expected mortality which was control population mortality standardized as per age. We took age distribution in copper-smelting workshop as a standard. Multiplicity of excess in observed parameters of mortality caused by malignant neoplasms determined the degree of additional risk related to work at the examined production.

Results and discussion. Production aerosols are the primary occupational-hygienic hazard factor among all production factors. As ore raw materials are multi-component ones it makes determining dust chemical structure more complicated. Beside main metal, such materials contain a number of carcinogenic substances such as arsenic, nickel, cadmium, hexavalent chromium, and beryllium [1,4,10]. When concentrate is dried and smelted it involves benzpyrene emissions into working area air [2,3]. Dust of mix materials in smelting section contains 0.25-0.6% of arsenic, 0.05-0.09% of lead and cadmium. As for dust in converting section, it contains 0.03-0.09% of arsenic, 0.04-4.38% of lead and less than 0.1% of beryllium.

We detected increased concentrations of lead and arsenic (up to 0.1 and 0.015 mg/m3, correspondingly) for some occupations in the course of our research. Cadmium, beryllium and benzpyrene content didn't exceed maximum permissible concentration (MPC). Therefore, working conditions in copper-smelting workshop can be classified as having 2.0-3.1 hazard category.

Individual CR calculation for 25-years long working period revealed that total CR was within the 4th range (more than 1.0 x 10-3) for all the examined main and auxiliary occupations of copper-smelting workshop (Table 1). This range is considered to be unacceptable for occupational groups [8], and it fits in with all the previous research as well as supplements them [1,13].

The greatest CR value was detected at workplaces where dust emissions were the biggest (mix materials handler, mix materials loader, carrier operator, powder-gas catching device operator) and also for some repair occupations (electrician, maintenance fitter, supervisory instruments and automation devices fitter). The analysis of the obtained results showed that maximum contribution into CR values at all workplaces was caused by exposure to non-organic arsenic compounds (from 84 to 99%).

Table 1

Individual carcinogenic risks for workers employed at copper-smelting workshop

Workplace	Carcinogenic risk at 25-year long working period					
	Carcinogenic substances					Total carcinogenic risk
	As	Cd	Pb	Benzpyrene	Be	
Drying operator	$3{,}2\times10^{-3}$	$4{,}4\times10^{-5}$	$4{,}6\times10^{-5}$	–	–	$3{,}3\times10^{-3}$
Carrier operator	$4{,}2\times10^{-3}$	$4{,}4\times10^{-5}$	$7{,}5\times10^{-4}$	–	–	$5{,}0\times10^{-3}$
Mix materials handler	$5{,}2\times10^{-2}$	–	$4{,}4\times10^{-5}$	–	–	$5{,}3\times10^{-2}$
Mix material loader	$7{,}9\times10^{-3}$	$2{,}2\times10^{-5}$	$1{,}2\times10^{-4}$	–	–	$8{,}0\times10^{-3}$
Smelter	$4{,}2\times10^{-3}$	$1{,}1\times10^{-4}$	$9{,}4\times10^{-5}$	$1{,}7\times10^{-6}$	–	$4{,}4\times10^{-3}$
Caster	$3{,}7\times10^{-3}$	$4{,}4\times10^{-5}$	$7{,}8\times10^{-5}$	–	$5{,}9\times10^{-5}$	$3{,}9\times10^{-3}$
Blower	$3{,}7\times10^{-3}$	$4{,}4\times10^{-5}$	$7{,}9\times10^{-5}$	–	$5{,}9\times10^{-5}$	$3{,}9\times10^{-3}$
Crane driver	$3{,}2\times10^{-3}$	$4{,}4\times10^{-5}$	$7{,}6\times10^{-5}$	$5{,}9\times10^{-5}$	–	$3{,}4\times10^{-3}$
Cleaner	$4{,}2\times10^{-3}$	$1{,}5\times10^{-4}$	$9{,}4\times10^{-5}$	–	–	$4{,}4\times10^{-3}$
Fireproof materials handler	$3{,}4\times10^{-3}$	–	$7{,}6\times10^{-5}$	$1{,}7\times10^{-6}$	–	$3{,}5\times10^{-3}$
Foreman	$2{,}6\times10^{-3}$	–	$5{,}4\times10^{-5}$	–	–	$2{,}6\times10^{-3}$
Powder-gas catching device operator	$4{,}7\times10^{-3}$	$1{,}5\times10^{-4}$	$1{,}5\times10^{-4}$	–	–	$5{,}0\times10^{-3}$
Pumping unit operator	$3{,}7\times10^{-3}$	$4{,}4\times10^{-5}$	$7{,}3\times10^{-5}$	–	–	$3{,}8\times10^{-3}$
Electro-gas welder	$3{,}7\times10^{-3}$	–	$6{,}3\times10^{-5}$	–	–	$3{,}8\times10^{-3}$
Maintenance fitter	$5{,}1\times10^{-3}$	–	$7{,}5\times10^{-4}$	$1{,}7\times10^{-6}$	$5{,}9\times10^{-5}$	$5{,}9\times10^{-3}$
Electrician	$5{,}2\times10^{-2}$	–	$7{,}3\times10^{-5}$	$1{,}7\times10^{-6}$	$5{,}9\times10^{-5}$	$5{,}3\times10^{-2}$
Supervisory instruments and automation devices fitter	$4{,}7\times10^{-3}$	–	$7{,}5\times10^{-5}$	$1{,}7\times10^{-6}$	$5{,}9\times10^{-5}$	$4{,}8\times10^{-3}$

Benzpyrene, beryllium, cadmium and lead content didn't exert any substantial influence on total CR values. Allowing for the obtained CR values, we calculated the acceptable work period length at which the upper limit of acceptable occupational risk (10-3) was reached. As a result, average acceptable working period for workers employed at copper-smelting workshop amounted to 5 years.

Research on assessment of multi-environment population carcinogenic risks which were caused by exposure to carcinogenic substances from various sources such as atmosphere, drinking water and food stuffs, showed that individual CR for population in a city where the examined enterprise was located amounted to 2.3 x 10-3 (the 4th risk range) [12]. The main contribution into multi-environment carcinogenic risk was made by arsenic, as it was in the case of occupational carcinogenic risk [11].

We determined Cyfra 21.1, CEA and NSE tumor markers in blood serum in the course of periodical medical examination (PME) of workers. Our research revealed that 73% examined workers had excess levels of tumor markers; 19% workers had excess levels of two tumor markers at once. 9% workers had increased Cyfra 21.1. tumor marker; 14.5%, increased CEA tumor marker; 59%, increased NSE tumor marker.

The obtained data on carcinogenic danger of copper-smelting production were also confirmed by the results of epidemiologic study on mortality caused by malignant neoplasms among workers employed at

copper-smelting workshop. Intensive mortality indices for male workers employed at smelting and converting sections of copper-smelting workshop amounted to 153.14 as per all localizations (totally). This parameter amounted to only 127.25 per 100,000 among ordinary male population. Intensive mortality indices for workers employed at blister copper production which were higher than the same indices for population were detected for malignant neoplasms of respiratory organs and chest (86.78 and 47.72 correspondingly), including lung cancer (71.47 and 43.48 correspondingly). The greatest difference in levels of lung cancer mortality among workers employed at copper-smelting workshop and control population was detected in 50-59 age group (425.53 and 159.57 correspondingly) ($p<0.05$).

As we can see from Table 2, statistically significant multiplicity of observed mortality excess over expected mortality was detected among men employed at copper-smelting

Table 2

Ratio of observed mortality caused by malignant neoplasms to expected mortality among men employed at copper-smelting workshop (per 100,000 people)

No.	Neoplasms localization	Observed	«Expected»	Observed indices and expected indices ratio
1	Oral cavity and pharynx	–	3,70 ± 0,88	–
2	Respiratory organs and chest, including:	86,78 ± 21,04	40,70 ± 2,94	2,13*
	- trachea, bronchial tubes, lungs	71,47 ± 19,09	37,40 ± 2,82	1,91
	- nasal cavity and larynx	15,31 ± 8,84	2,52 ± 0,73	6,07
	- pleuroperitoneum and mediastinum	–	0,78 ± 0,41	–
3	Digestive organs and peritoneum organs, including:	25,52 ± 11,41	43,92 ± 3,05	0,58
	- esophagus	–	2,04 ± 0,66	–
	- stomach	15,31 ± 8,84	24,57 ± 2,28	0,62
	- bowels	10,21 ± 7,22	6,49 ± 1,17	1,57
	- liver	–	3,48 ± 0,86	–
	- pancreas	–	5,88 ± 1,12	–
	- others	–	1,46 ± 0,55	–
4	Musculoskeletal system, connective tissue, skin, including:	–	4,32 ± 0,96	–
	- skin	–	1,12 ± 0,49	–
	- bones and connective tissue	–	3,20 ± 0,82	–
5	Urogenital organs, including:	15,31 ± 8,84	8,90 ± 1,37	1,72
	- genital organs	10,21 ± 7,22	2,19 ± 0,68	4,66
	- urinary organs	5,10 ± 5,11	6,71 ± 1,19	0,76
6	Lymphatic organs and hematopoietic system	5,11 ± 5,11	5,63 ± 1,09	0,91
7	Others	20,42 ± 10,21	5,34 ± 1,06	3,82
8	All localizations taken together	153,14 ± 27,94	112,51 ± 4,88	1,36

Note: * - discrepancies are statistically authentic ($p<0.05$).

workshop as per malignant neoplasms in respiratory organs and chest (2.13 times), including tumors in trachea, bronchial tubes and lungs (1.91 times), and nasal cavity and larynx (6.07 times). Besides, observed mortality exceeded expected mortality as per malignant neoplasms in urogenital organs (1.72 times), including genital organs (4.66 times), intestine tumors (1.57 times) and other localizations (3.82 times).

The obtained results will help to work out a system of CR managing which will include

regulation and surveillance activities, organization and management activities, technical and technological activities, financial and economic activities, medical and prevention activities, rehabilitation, as well as information and educational activities. Providing hygienic safety and opportunity of technical achievement of goals set forth in risk managing are to become top criteria here; they should allow for economic efficiency of management decision-making. In future we should use technologies of insuring civil liability in relation to unforeseen damage to health and voluntary medical insurance of working population.

Conclusions:

1. In blister copper production, carcinogenic risk caused by exposure to arsenic, cadmium, lead, nickel, beryllium, and benzpyrene, lies within unacceptable range and is determined mostly by arsenic as other basic carcinogens content doesn't exceed MPC.

2. The biggest carcinogenic risk values are detected for occupations with workplaces where dust emissions are the greatest, as well as for workers occupied with repair and auxiliary work.

3. Most workers who have occupations with unacceptable CR level also have increased levels of tumor markers.

4. Discrepancy between intensive mortality indices as per malignant neoplasms of different localization among workers employed at copper-smelting workshop and ordinary population proves there is an authentic correlation between neoplasms and impacts exerted by carcinogenic risks of production environment.

5. The obtained results will help to give grounds for a set of measures aimed at managing carcinogenic risks caused by shopfloor activity.

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RISKS OF CARDIOVASCULAR DISEASES EVOLVEMENT AND OCCUPATIONAL STRESS

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Our aim was to study how significant psychosocial factors are in occupational stress and cardiovascular diseases evolvement in workers employed at petrochemical production; we also intended to work out a set of preventive measures. Our hygienic and social-psychological research enabled us to detect factors causing stress evolvement in workers employed at petrochemical production. These factors included chemical impact, noise, unfavorable microclimate, labor hardness and labor intensity. High level of risk for their own lives and responsibility for safety of others, as well as work under time deficiency conditions with increased responsibility for the final results, were the most significant psychosocial factors for workers. In the course of questioning we detected that 74 % machine operators, 63 % tool men working with controllers and automatic devices, and 57 % repairmen mentioned having stress at work. Here 38 % workers gave a subjective estimation of their professional activity as having apparent "stress nature". The questioning revealed that 48 % workers with various occupations had increased parameters as per anxiety scale (HADS); 23 % workers had increased parameters as per depressions scale (HADS). Primary hypertension was the most widely spread nosologic form among chronic non-infectious diseases; it was found in 46.1 % operators and in 45.2 % repairmen dealing with processing stations repair. 30.1 % tool men working with controllers and automatic devices had average occupational causation of primary hypertension by production factors. We detected direct relation between hyperlipidemia and age and working period.

We created foundation for preventive measures and worked out a program aimed at increasing resistance to stress at corporate and individual level. It will provide significant social effect and later on economic one. To overcome social stress we need to create safe working conditions at workplaces and to increase labor motivation based on career development possibilities.

Key words: *workers employed at petrochemical production, machine operators, occupational stress, cardiovascular diseases, risk factors, resistance to stress, prevention.*

Occupational stress evolvement or growth in its significance is a distinctive feature of contemporary society [13, 17, 21].

There was research conducted in 27 European Union countries in course of which psychological welfare and psychological distress of 12,594 workers was assessed. One third of all respondents claimed financial difficulties and absence of stability to be primary reasons for stress at a working place

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[24].

This problem is even more vital in Russia. It is due to contemporary social and economic situation which has such peculiarities as instability, decrease in production, low average income per capita of the population, increased labor intensity, absence of effective labor motivation, and, in a number of cases. unemployment [3, 12].

High neuro-emotional and information loads cause stress and overstress in workers' bodies; it results in exhaustion evolvement, and if resources are not recovered sufficiently, then apparent overstrain occurs, occupational stress and health disorders evolve [13, 14, 23].

Efficient labor motivation loss by population, low wages, uncertainty in future, and fear to lose a job are among basic reasons for "social stress" evolvement [3, 20, 28]. A number of authors state that more than 10% of working population live under constant social and occupational stress conditions [5, 8, 18].

Psychoemotional factors cause so called "stress diseases"; such diseases include various psychosomatic disorders, for example, neurotic disorders, circulatory systems diseases, pancreatic diabetes, ulcer is stomach and duodenum, and certain malignant neoplasms. The most frequent consequences of high neuro-emotional loads are primary hypertension and ischemic heart disease [9, 22, 25, 27].

As per INTERHEART research data (2005) a contribution made by psychosocial factors into myocardial infarction risk amounted to 32,5 % [19]. As per results of prospective stage included into Russian component of KORDINATA research, it was determined that depressive symptomatology deteriorated prognosis for patients with arterial hypertension and ischemic heart diseases, led to disability and increased public health care expenses [5, 6]. Contemporary scientific literature contains objective data which characterize occupational stress evolvement in social workers, in law enforcement officers, and in operators [1, 2, 4, 17, 26]. Still we couldn't find any data on psychological state of workers employed at petrochemical production; such workers had to work under adverse influence exerted by unfavorable factors of working environment and labor process, and it makes our research truly vital.

Petrochemical enterprises belong to hazardous industrial objects due to application of hazardous substances having 1-3 danger category, including explosion hazard and fire hazard; such industries often function under high temperature regimes, and it increases risks for incidents occurrence [7, 10, 11]. A lot of technogenic incidents which have occurred both in Russia and abroad in recent years prove it. These incidents had grave consequences, including deaths (China, 2005, 2007; Tobolsk, 2007; Buddyonovsk, 2008; Zabaykalye, 2010; Khabarovsk, 2011; Venezuela, 2012; Kirishi, 2012; Achinsk, 2014; Ufa, 2016).

Analysis of accident rate and incidents in petrochemical productions revealed that more than 70% of all incidents were caused by human factor. Primary reasons for incidents are of organizational character and happen due to safety standards violation, unsatisfactory labor organization, and insufficient attention paid to workers' training in safety standards sphere. Incorrect actions of even one worker can lead to a production incident, and in some cases it can endanger the existence of a whole enterprise. Therefore, issues of workers' reliability in providing safety at a petrochemical production are especially vital [7, 11].

Our research goal was to study how significant psychoemotional factors were for occupational stress and cardiovascular diseases evolvement in workers employed at petrochemical production as well as to work out a set of preventive activities.

Data and methods. To assess occupational factors significance, we performed hygienic and social-psychological research which included anonymous questioning with the use of specially designed questionnaires and psychological testing (test method) with the use of Hospital Anxiety and Depression Scale – HADS (1983). When interpreting results, we allowed for total

anxiety and depression parameter with determining 3 value ranges, namely 1) 0–7 was normal (absence of authentically apparent anxiety and depression symptoms); 2) 8–10 meant subclinically apparent anxiety/depression; 3) 11 and higher were clinically apparent anxiety/depression.

Workers' health state was assessed as per data obtained during in-depth medical examinations with participation of a cardiologist and with the use of functional research techniques, including electrocardiography.

To assess lipid metabolism, we accomplished biochemical research which included determining crude cholesterol contents, high-density lipoproteins cholesterol contents, triglycerides contents, low-density lipoproteins cholesterol content, and atherogenicity index. To assess occupational risk, we determined relative risk (RR) and etiological fraction (EF) of working environment factors in cardiovascular diseases evolvement and degree of their causation [15].

1800 male workers with various occupations underwent in-depth medical examination; their age varied from 18 to 59, average age was equal to 40.2, overall working period on average was equal to 16.8 years. 430 workers took part in questioning.

Three groups comparable as per age and working period were formed depending on working conditions. The first basic group included machine operators (п = 936), the second group were repairmen (п = 384), the third group (control group) included tool men working with controllers and automatic devices (C&AD) (п = 480).

Results and discussion. On a whole, working conditions of workers with basic occupations at petrochemical productions (machine operators and repairmen) as per P 2.2.2006-05 are mostly considered to be hazardous and correspond to 3.1-3.3 danger classes of working conditions; C&AD tool men work under allowable working conditions.

Workers employed at contemporary petrochemical production are influenced by stress factors with various nature and intensity during their labor activities; such factors include working environment factors and labor process ones:

– adverse chemicals (labor conditions class 2.0–3.1);

– in-plant noise (labor conditions class 3.1–3.3);

– vibration (labor conditions class 2.0);

– unfavorable microclimate (labor conditions class 2.0–3.1);

– absence of scheduled breaks;

– labor intensity factors: intellectual, sensory and emotional loads.

Noise and labor intensity are prevailing factors for machine operators, noise and labor hardness together with chemicals prevail for repairmen.

We paid special attention to labor intensity assessment for workers belonging to different occupational groups.

Labor conditions class for machine operators dealing with processing stations corresponds to hazard class 3.1 as per labor intensity as they have to deal with explosion-hazardous and fire-hazardous production, they constantly face risk for their own life, they bear full responsibility for other people's safety and for final results, their errors matter a lot, and they have to work in three shifts, one shit being a night one. Labor conditions for repairmen and tool men dealing with C&AD belong to allowable class (table).

We questioned workers with various occupations, and our questioning results revealed that 74% machine operators, 63% tool men dealing with C&AD, and 57% repairmen claimed to have stress at work. Here 38% workers gave a subjective assessment of their everyday occupational activity as having apparent "stress nature". 69.9% respondents considered their work to be hazardous and dangerous, 62% mentioned intense in-plant noise,

25.7% spoke about fire hazard or explosion hazard, 18.0% complained on too high or too low temperature, 13.4% weren't happy to have to work in three shifts.

Table

Parameters of labor intensity at working places at petrochemical productions

Intensity parameter	Machine operator dealing with processing stations	Tool man dealing with C&AD; repairman
Work content	Solving complicated tasks	Solving easy tasks as per instructions
Labor conditions class	3.1	2
Perception of signals (information) and their assessment	Perceptions of signals with following comparison between actual parameters values and their nominal values. Final assessment of actual parameters values	Perception of signals with the following correction of actions and operations
Labor conditions class	3.1	2
Degree of responsibility for the results of their activities. Significance of errors	Bears full responsibility for functional quality of an end product, work, and task. Errors cause damage to equipment, technological processes failure and may endanger lives of other people	Bears responsibility for functional quality of auxiliary work (tasks). Errors cause additional efforts of supervisors (teem managers and foremen)
Labor conditions class	3.2	2
Degree of risks for own life	Probable	Probable
Labor conditions class	3.2	3.2
Degree of responsibility for others' safety	Possible	Possible
Labor conditions class	3.2	3.2
Shift work	Work in three shifts (one shift is a night one)	Work in two shifts (without a night one)
Labor conditions class	3.1	2
Overall labor intensity assessment	**3.1**	**2**

54% respondents were concerned over gas contamination.As for other dangerous production factors, they were mentioned by respondents in smaller number of cases. Only 12.1% respondents thought their working conditions were safe.

68% respondents were satisfied with labor organization at their production; 64%, with labor conditions; 92% thought they were fully provided with all the necessary protective clothing. We should note that less than two thirds of all respondents were satisfied with their wages and moral motivation and 55% workers complained they had no possibilities of their career development. And also more than a half workers didn't think everybody had equal possibilities of career development. 74% respondents were satisfied with moral and psychological climate in their team and with interpersonal relations with their colleagues. 68% respondents mentioned their supervisor helping them in professional issues and they had quite normal interpersonal relations with him. As per our questioning results, 18% workers told they had conflicts with their colleagues. The most frequent reasons for conflicts included unsatisfactory labor and production organization, distribution of bonuses and extra pay, labor discipline. But despite such conflicts, only 9% workers told they wanted to change their team.

The performed questioning enabled us to reveal ranking in production issues which caused anxiety in workers employed at petrochemical production over 6 months: work under time deficiency conditions with increased responsibility for the final result (23.2%), and substantial changes in work processes (19.4%). Only 27.8% respondents didn't feel anxiety in their working conditions.

We should note that some workers could react with so called distress to stress occurrence at their working place and to lack of support from their relatives; this distress often involved excessive alcohol intake. As per questioning results, workers who didn't have emotional support from their relatives, often drank alcohol (more than 28.2% respondents). Only 9.1% workers had favorable psychological climate in their family. 16.0% drank beer, 12.3% chose wine and 6.9% admitted drinking strong spirits. We think that respondents due to quite understandable reasons were not always sincere when answering such questions, and therefore we assess the obtained data as being somewhat understated.

The results of testing as per HADS scale revealed that subclinical anxiety among machine operators occurred 2.4 times more frequently than among tool men dealing with C&AD (32.3 and 13.4 % correspondingly), subclinical depression occurred 3 times more frequently (17.5 and 5.8 % correspondingly). We should note that subclinical anxiety among repairmen was detected 1.9 times more frequently than among tool men dealing with C&AD (25.1 and 13.4 % correspondingly), and subclinical depression was detected 2.1 times more frequently (12.4 and 5.8 % correspondingly).

Clinical anxiety was diagnosed among machine operators in 7.9% cases; among repairmen, in 4.3% cases; among tool men dealing with C&AD, in 1.3%. Clinical depression was revealed only in the 1st and the 2nd group (1.7% and 0.9& cases correspondingly). There were no detected cases of clinical depression in the control group (figure).

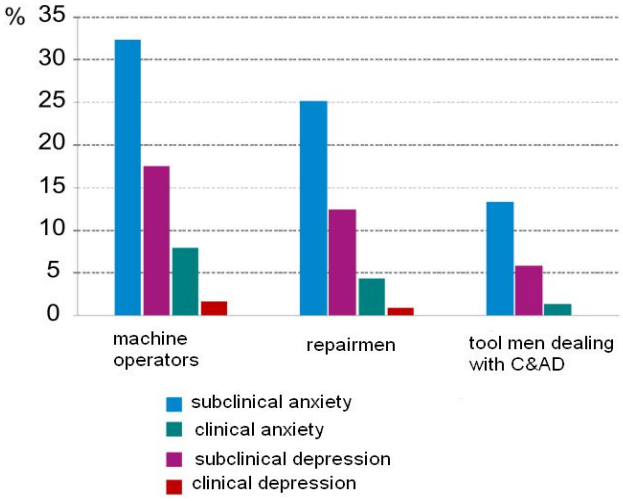

Figure. Frequency of psychosocial factors among workers from various occupational groups.

Circulatory system diseases mostly represented by primary hypertension, cerebrovascular diseases, and ischemic heart disease, prevailed in the structure of revealed chronic non-infectious diseases of workers employed at petrochemical productions.

The most widely spread nosologic form among cardiovascular diseases was primary hypertension which was detected in 46.1% machine operators, in 45.2% repairmen, and in 30.1% tool men dealing with C&AD. As we determined relative risk of etiologic fracture which working environment factors had in primary hypertension evolvement, we revealed average occupational causation of this disease among machine operators (*RR* = 1.53 and *EF* = 35 %) and repairmen (*RR* = 1.5 and *EF* = 33 %).

Authentic increase in primary hypertension frequency and cerebrovascular diseases frequency was detected among machine operators and repairmen after 6-10 years of work and 11-15 years of work in comparison with the same parameters among tool men dealing with C&AD ($p<0.05$).

We should note that arterial hypertension syndrome among workers with working period less than 10 years was mostly caused by vegetative-vascular dysfunction. Increased blood pressure in workers with longer working

period was caused by primary hypertension and atherosclerotic vessels damage.

Ischemic heart diseases was revealed in 4.3% workers; post-infarction cardiosclerosis was diagnosed only among people older than 50 with their working period being longer than 15 years. ECG-symptoms among workers employed at petrochemical productions occurred in 22.1% of examined people and were mostly represented by myocardial hypertrophy in left ventricle, and excitability disorders as per supraventricular and ventricular extrasystoles types.

We detected direct moderate correlation between low-density lipoproteins cholesterol level ($r = 0.58$), crude cholesterol level ($r = 0.56$), atherogenicity coefficient ($r = 0.34$) and triglycerides level ($r = 0.3$) and working period among machine operators.

So, results of hygienic examinations on labor conditions assessment revealed that increased neuro-emotional loads caused by great responsibility for the results of professional activities and significance of errors, as well as high risk for own life and others' safety, were characteristic for all occupational groups also influenced by chemical and physical factors of their working environment. Machine operators had the most intensive labor with hazard class 3.1, repairmen's labor was considered allowable. Psychosocial factors of production and non-production nature cause occupational stress evolvement mostly in machine operators.

The conducted research makes it advisable to work out a set of prevention activities aimed at optimization of working conditions for workers employed at petrochemical productions and at lowering stress factors. All prevention activities can be divided into three groups, namely primary, secondary, and tertiary ones. Here primary prevention focuses on preventing occupational stress at working place by eliminating or reducing influence exerted by initial causes and by increasing workers' psychological adaptation. Rational labor organization, production automation, creation of favorable psychological climate in a team, increase in workers' labor motivation and change in its orientation, expansion of workers' possibilities to take part in decision making should become the primary trends in labor optimization and increase in resistance to stress for occupations with apparent emotional loads.

Secondary prevention is aimed at helping workers already having signs of psychological stress. It includes activities which can reduce influence of stress development in workers and which can either eliminate or decrease strain: relaxation skills training, positive thinking skills, informing workers on their exhaustion level and on possible consequences of stress, time management and conflict management structure. Increased physical activity and giving up bad habits are very important aspects of secondary prevention.

Tertiary prevention is rehabilitation and it is for workers whose health suffered from chronic occupational stress. Tertiary prevention goal is to prevent development of psychic and psychosomatic diseases in order to escape disability and untimely death. Tertiary prevention envisages providing workers with confidential consultations of a medical psychologist and psychotherapy.

Conclusions:

1. Basic risk factors for occupational stress evolvement in workers employed at petrochemical productions are adverse chemicals impacts, in-plant noise, unfavorable microclimate and psychoemotional and physical loads. Labor conditions of workers from basic occupational groups were hazardous and corresponded to labor condition classes 3.1-3.3 according to P2.2.2006-05.

2. Most respondents were satisfied with labor organization and relations in a team. But still workers mentioned low labor motivation related to absence of career development possibilities and low wages.

3. Work under time deficiency with increased responsibility for the final results and social instability were the most significant psychosocial factors for workers employed at petrochemical productions.

4. Machine operators and repairmen had average occupational causation of primary hypertension by production factors. We

detected direct dependence of hyperlipidaemia on age and working period length.

5. The obtained results enabled us to give grounds for a set of prevention activities and to work out a program aimed at increasing resistance to stress in workers at corporate and individual level which will secure significant social and later on economic effect.

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IN-PLANT NOISE AS OCCUPATIONAL RISK FACTOR AT PETROCHEMICAL PLANTS

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The article summarizes the data obtained in long-term research on working conditions estimates and studying damages to hearing organs in workers employed at petrochemical plants. We chose workers employed at five basic organic synthesis productions as an object of our study; these productions include ethylene-propylene, ethylbenzene-styrene, organic alcohols production (butanol and 2-ethylhexanol), phthalic anhydride.

We detected that heating furnaces, compressors, and pumps were the main noise sources at the examined productions. Our research revealed that noise levels at the examined productions varied from 60 to 99 decibel, and calculated equivalent noise levels reached the 3 hazard class with 1st and 2nd hazard degree.

Audiometric research showed that signs of impacts exerted by noise on hearing organs of workers belonging to basic occupational groups (processing machine operators and pumps and compressor operators) occurred authentically more frequently than in case of control equipment mechanics and automatic equipment operators (comparison group) (<0,001). The highest risk of occupational hearing loss was detected for drivers while the same pathology evolved 1.5–2.0 times less frequently in processing machines operators. Frequency of hearing organs damage in all basic occupational groups authentically increased as working period grew. Signs of such damage increased dramatically in processing machines operators' group after 10 years of work but still the overall level was slightly lower than in drivers' group.

It is shown that the most efficient measures of collective protection aimed at noise reduction are application of low-noise technological equipment, acoustic protection (sound insulation and sound absorption, etc), remote control, as well as rational labor and leisure regime. Medical care and vocational rehabilitation of people with occupational hearing loss also contribute significantly into sensory deafness prevention.

Key words: *in-plant noise, working conditions, occupational risk, petrochemical productions, signs of impacts exerted by noise on hearing organs, organic synthesis, вредные и hazardous factors, occupational pathology.*

Occupational disease of a hearing organ is a vital problem all over the world [19,21,24]. As per World Health Organization data, sensory hearing loss of noise etiology has been constantly leading among other occupational diseases in economically developed countries. However, it has recently tended to go down as national programs aimed at protection from noise have been implemented [17,23].

In Russia in-plant noise is also one of the

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leading adverse factors at working places in most industries. Nowadays occupational hearing loss becomes more significant, socially and economically [1,4,6,16]. As per Rospotrebnadzor data, one third of workers undergo in-plant noise impacts these days. It determines a growth in occupational hearing loss levels, especially in the structure of diseases related to physical factors impacts [10].

Sensory hearing loss is one of the prevailing diseases in overall occupational morbidity structure. Its specific weight has doubled over the last decade (from 13.5% to 27.2%). Its specific weight is even higher among diseases caused by impacts which physical factors of working environment exert on workers (59%) [10,13,15].

It is well known that if noise impact on a human body is long-term, it leads to auditory analyzer fatigue which can result in persistent hearing loss if there is no sufficient rest [3, 20]. Auditory analyzer examining with the use of pure tone audiometry is an important diagnostic technique aimed at detecting signs of specific impacts exerted by in-plant noise on a hearing organ [2,14].

Petrochemical industry belongs to such branches where in-plant noise is one of adverse working environment factors, together with air pollution in working areas and unfavorable microclimate [7, 8, 18, 22, 25].

More and more powerful equipment has been applied in petrochemical industry recently, and it has resulted in more intense in-plant noise at working places [5, 8, 20].

Our research goal was to assess probability of occupational hearing organs disorders in workers employed at contemporary petrochemical production basing on dose assessment of in-plant noise.

Data and methods. We chose five petrochemical productions as our research object; they were ethylene-propylene production, ethylbenzene-styrene production (old one with small capacity and modern one with large capacity), organic alcohols production (butanol and 2-ethylhexanol), phthalic anhydride production.

All hygienic research at the examined productions was accomplished in accordance with the current standard-methodological documents, namely: State Standard 12.1.005-88, Hygienic Standard 2.2.5.1313-03, Sanitary Standard 2.2.4/2.1.8.562-96, Sanitary Rules and Standards 2.2.548-96, P.2.2.2006-05.

We assessed hearing organs state in 1,597 workers whose occupations were processing equipment operators, pumps and compressors operators, supervisory instruments and automatic equipment (SI and AE) mechanics.

In order to determine qualitative and quantitative features of hearing function we performed pure tone threshold audiometry in 125-8000 Hz frequency range as per air and bone sound conduction and sound perception according to conventional technique with the use of Interacoustics AD229e audiometer [9,12].

Results and discussion. Technological processes at organic synthesis production are continuous and are controlled remotely. Most technological equipment such as reactors, rectifying columns, tanks, reservoirs, industrial pipelines, separators, heat exchange units, furnaces etc., is placed outside workshops on outdoor grounds. The only exception is pumps and compressors which are placed inside workshops.

Most intense noise at the examined productions occurs due to heating furnaces, compressors, pumps, air cooling condensers as well as compressed air moving in the systems of secondary supervisory instruments and automation equipment.

In-plant noise existing at the examined productions is constant, broadband, with sound level prevalence for certain equipment both at high and low frequencies. Sound volumes depend on equipment type, power, capacity, its functioning regime, on a way in which it is erected on its base and on its connection to pipelines.

Comparative characteristics of in-plant noise intensity at the examined productions didn't reveal any specific discrepancies between them. Rank distribution of the equipment as per level of noise it generates revealed that heating

furnaces were the noisiest, compressors and pumps followed (Table 1).

Table 1

Average data on in-plant noise at organic synthesis productions

Place of measuring	Sound volume, dBA	Higher than MPV, dBA
Heating furnaces	95–99	Ha 15–19
Compressor houses	92–96	Ha 12–16
Pump chambers	85–94	Ha 5–14
Outdoor plants	80–85	Ha 5
Soundproofing cabins	60–63	–
Operator rooms	58–60	–

N o t e: MPV is maximum permissible volume; dBA is corrected sound power volume

Sound volumes produced by heating furnaces reached up to 95-99 dBA which was 15-19 dBA higher than maximum permissible volume (MPV) with maximum sound energy being at 25-500 Hz frequencies.

Noise in compressor houses was 12-16 dBA higher than MPV, mostly at lower frequencies. Noise in pump chambers was constant, broadband and with high frequency. Its volumes fluctuated within wide range from 85 to 94 dBA depending on a pump type, its capacity and functioning regime.

Noise volumes at outdoor plants amounted to 80-85 dBA and it was 5 dBA higher than MPV. Noise volumes in soundproofing cabins and in closed compressor houses were within 60-63 dBA. Noise volumes in operator rooms also didn't exceed MPV and were equal to 58-60 dBA.

Organic synthesis production involves shift work; each shift crew usually consists of processing equipment operators, pumps and compressors operators, and SI and AE mechanics. Technological process at the examined production was a continuous one and therefore working regime included three 8-hour shifts, one shift being a night one.

Processing equipment operators as per their job description had to manage technological process parameters which were shown either on computer screens or control panels in operator rooms. Besides, processing equipment operators controlled the state of the equipment and communications located both on outdoor plants and inside workshops. According to timing research a processing equipment operator spent approximately a half of his work shift in an operator room. Our research results revealed that noise volumes in operator rooms were considerably lower than MPV. Processing equipment operators had to perform maintenance inspection of technological equipment so they periodically left operator rooms up to 6 times a shift (20% of total shift time) and went directly to the equipment which was located both in workshops and on outdoor grounds. As per accomplished timing research processing equipment operators worked under intense noise conditions up to 50% of total shift time.

Technological process in up-to-date ethylbenzene-styrene production is continuous, its control is fully automated, and all technological operations are automatically managed so manual labor is totally excluded. Time period which workers have to spend in close proximity to technological equipment has decreased considerably due to complex mechanization and automation and it makes workers' exposure to adverse production factors less probable.

Workers at the examined production sometimes had to be near outdoor plants when a visual inspection or minor repair was required. Processing equipment operators left operator rooms to perform a maintenance inspection of the equipment and it happened 2 or 3 times a shift and took about 10% of total shift time. Calculated equivalent noise volume allowing for the time spent directly at "noise-making" equipment at the up-to-date production didn't exceed MPV and amounted to 75-78 dBA.

Calculated equivalent noise volumes for processing equipment operators employed at ethylene-propylene production amounted to 85-88 dBA and corresponded to the 3rd class with the 2nd hazard and danger category; they amounted to 83-85 dBA at ethylbenzene-styrene production with small capacity which corresponded to 3.1 hazard and danger class. Equivalent noise volumes at phthalic anhydride production didn't exceed any hygienic standards

and corresponded to the acceptable class 2 (table 2).

A group of pumps and compressors operators was the second in number (about 20% of all workers). Their job responsibilities included maintenance inspections and control over technological pumps and compressors functioning. As per timing data pumps and compressors operators spent up to 70-80% of their total shift time near technological equipment. They also could perform minor and routine repair. Pumps and compressors operators employed at up-to-date ethylbenzene-styrene production spent from 30 to 50% of their total shift time inside pumping and compressor units. They also spent about 10-20% of their total shift time in operator rooms and soundproofing cabins where they made records in logs, spoke on the phone and discussed various production issues.

Pumps and compressors operators were under noise exposure during 70% of their total shift time and as a rule that noise volumes were 12-16 dBA higher than MPV. Allowing for the exposure time we can determine equivalent noise volumes at working places of pumps and compressors operators as having adverse working conditions of 3.2 hazard and danger class.

We should note that in spite of high in-plant noise volumes registered at production with large capacity, calculated equivalent noise volume for pumps and compressors operators allowing for the time spent directly at "noise-making equipment" was 5 dBA higher than MPV which corresponded to 3.1. hazard and danger class (table 2).

The next occupational group in petrochemical production was SI and AE mechanics. They were responsible for maintenance of both "primary" devices (thermometers, flowmeters, pressure gauges) placed directly at equipment and "secondary" ones with their readings displayed on control panels.

SI and AE mechanics spent about 12.3-15.5% of their total shift time on "primary" devices maintenance and about 70-75%, on "secondary" ones. Supervisory instruments in contemporary computerized manufacturing have rather complicated design, therefore mechanics are to be highly qualified. They performed maintenance inspections, routine repair and devices taring, filled up ink into recorders, replaced diagrams etc., in operator rooms. As for outdoor plants, there mechanics replaced pads in devices and columns in chromatographs which registered quality of products in flows. SI and AE mechanics underwent production factors impacts at levels which were considerably lower than permissible levels during 85% of their work shift. Calculated equivalent noise volume was considerable lower than permissible one.

Table 2

Working conditions assessment in terms of intensity of noise impacts exerted on workers employed at organic synthesis production

Production	Working conditions class in terms of noise impacts intensity	
	Processing equipment operators	Pumps and compressors operators
Ethylene-propylene	3.2	3.2
Ethylbenzene-styrene (small capacity)	3.1	3.2
Ethylbenzene-styrene (small capacity)large	2	3.1
Alcohols (butanol and 2-ethylhexanol)	3.1	3.2
Phthalic anhydride	2	3.2

High levels of noise impact make hearing loss evolvement in workers quite probable. Occupational hearing loss parameter is equal to 3,2 ‰ per 10,000 workers.

As we examined hearing organs of workers employed at petrochemical production we thought it advisable to highlight a group with so called pre-clinic form of occupational damage which we called "people with signs of noise impact on hearing organs" [2,11].

313 people employed at petrochemical production (19.6±1.0% of total number of

workers exposed to in-plant noise) had signs of noise impact on hearing organs.

Signs of noise impacts on hearing organs were most frequently detected in pumps and compressors operators in comparison with other basic occupational groups (24.7±1.6%); processing equipment operators followed (15.7±1.4%).

We detected statistically significant discrepancies in frequency with which noise impacts on hearing organs occurred in basic occupational groups in comparison with SI and AE mechanics. However, the most apparent discrepancies were detected in pumps and compressors operators as the analyzed parameter in them had authentic discrepancies even when their working period was less than 10 years ($p<0.001$), and they became more and more persistent as their working period grew.

Statistically authentic discrepancies in processing equipment operators groups were detected only after 10 years of work ($p<0.001$). And as their working period under noise exposure grew, discrepancies became statistically more and more significant.

Dynamics related to working period and describing frequency with which signs of noise impacts on hearing organs occurred is given in Table 3.

As we can see from the given data, generally there are common trends in all the groups. However, it is obvious that noise impacts prevalence among pumps and compressors operators even with rather short working period is substantially higher than in other groups and this trend remains during the whole analyzed working period.

More drastic growth in signs frequency among processing equipment operators is observed after 10 years of work although the total parameter level remains a bit lower than in pumps and compressors operators.

Such dynamics (signs growth) is almost completely absent in SI and AE mechanics occupational group (taken as a control one).

Table 4 gives values of relative risks causing occurrence of signs showing noise impacts on hearing organs in occupational groups. The given data show that relative risk is considerably higher than 5, and it means that the examined effect is almost completely caused by impacts exerted by intense in-plant noise with etiological fraction (EF) varying from 81 to 100%.

Table 3

Prevalence of signs showing noise impacts on hearing organs in workers employed at petrochemical production

Working period, years	Number of people with detected signs of noise impacts, %		
	Pumps and compressors operators	Processing equipment operators	SI and AE mechanics (control)
<10	*19,7 ± 2,6	2,9 ± 1,3	0,8 ± 0,8
10-19	*22,3 ± 3,0	*14,4 ± 2,6	2,3 ± 1,3
20 and more	*29,4 ± 2,6	*23,6 ± 2,4	1,4 ± 0,7
Totally	*24,7 ± 1,6	*15,7 ± 1,4	1,5 ± 0,5

Note: Discrepancies are statistically authentic: *$p<0.001$

Table 4

Relative risk (RR) causing occurrence of signs showing noise impacts on hearing organs in occupational groups

Working period, years	Relative risk (RR) causing occurrence of signs showing noise impacts on hearing organs in occupational groups	
	Pumps and compressors operators	Processing equipment operators
<10	24,6	3,6
10-19	9,7	6,3
20 and more	21,0	16,9
Totally	16,5	10,5

So, clinical-hygienic research revealed that increased levels of in-plant noise impacts at the examined productions caused risk of occupational diseases evolvement in hearing organs.

The conducted research gave ground for implementation of a set of activities aimed at noise reduction; these activities included noise reduction means at sources of its occurrence and means of protection from it on the way it spreads.

We can name such most efficient collective protectors against noise as application of low-noise technological equipment, acoustic means application (sound insulation, sound absorption etc.), remote control, as well as rational labor and rest regime.

But bearing in mind that collective protectors can't always reduce noise volume at working places, we think it's necessary to apply individual protectors of hearing organs (ear phones, ear plugs etc.).

Medical care and occupational rehabilitation of people with occupational hearing loss also play a very important role in sensory hearing loss prevention. Qualitative and regular medical supervision allowing for noise volume and working period at petrochemical production will help to 1) increase a time period during which signs showing noise impact exerted on hearing organs transfer into actual hearing loss; 2) reduce occupational losses among workers under noise volumes which are higher than maximum permissible one and to prolong productive working period.

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PERSONNEL POLICY IN HEALTHCARE: RISKS AND SOLUTIONS

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We studied the dynamics of Perm region population provision with medical personnel over 2006-2015 basing on the official statistics data; the parameter was compared with the average level in the Russian Federation. We detected that provision of Perm region population with physicians and paramedics was higher than average Russian level in the stated period; however, a negative dynamics in parameters occurred and there is still personnel deficiency. A doctors-paramedics ratio improved a bit but it was still lower than in the RF on average and lower than the recommended level. Staffing of physicians' jobs with people decreased a bit in the examined period while staffing of paramedics' jobs, on the contrary, grew up. Also there was a decrease in a number of physicians and paramedics' who combined jobs. Specific weight of certified medical staff was higher in Perm region than in the country on average. Changes which occurred in medical staff distribution as per categories prove that the share of senior age groups increased both among physicians and paramedics. There is a disproportion in provision with physicians and paramedics in terms of various territories in Perm region, and it requires systemic targeted activities of all concerned structures. A system of admission to medical HEEs and colleges needs to be reformed so that applicants could avoid making a mistake in their career choice; it is also necessary to work out a set of measures aimed at raising prestige of a physician' and paramedic's job as well as pay greater attention to social security of medical staff.

Key words: *availability and quality of medical aid, personnel policy, provision with doctors, provision with nurses, staffing, combining jobs, trend, disproportion in distribution, prestige of a physician' and paramedic's job, social security.*

Nowadays public health care in Russia faces a most serious task as it has to increase availability and quality of medical aid. And sufficient quantity of well-qualified medical personnel is the basic condition which can help to solve it [1–7, 9, 10, 14, 15].

There is deficiency in Russian public health care in terms of doctors and nurses [3, 5, 8, 14]. As per data given by the RF Public Health Ministry, 148,200 doctors are required in Russia, and only 52,000 graduate from medical HEEs annually. Also every year 22,000 doctors retire, and 10% doctors are close to the age of retirement or are already of that age [6]. Personnel deficiency is primarily caused by insufficient inflow of young specialists in the field. It is medical HEE graduates who are one of the most vulnerable categories. If we consider losses of medical personnel in the field we can see that 22% of medical students plan to go abroad to get further education, and 11% don't have any intention to work in a medical establishment after graduation. Only 21% of doctors who are younger than 35, and 17% of medical HEE graduates consider it possible to work in rural areas and remote regions [14]. More than 800,000 nurses are required in the country. Annually almost 90,000 paramedics quit public health care (and deficiency in them being 280,000), and only 15,000 of that number actually retire; every year only 50,000 young specialists finish their education and enter the field [6].

Ratio between doctors and paramedics

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quantities in our country is significantly lower than in most developed countries in the world and it leads to imbalance in medical aid system and restricts possibilities to develop aftercare services, nursing, and rehabilitation [2, 8, 9, 14]. In Russia there are 1.8 nurses per 1 doctor on average [13], but the required minimum is 3-4, and therefore doctors have to perform additional functions [2, 6].

There is also a significant disproportion in medical personnel distribution, as per urban and rural areas, in-patient hospitals and out-patient one and polyclinics, as well as in terms of various medical specialties [2, 3, 6, 7, 9, 14]. In relation to that a number of authors assume it would be advisable to return to a system of planned graduates distribution [2, 13].

Average salary of doctors in Russia is 22% lower than average salary in the country. While in so called "new" EU countries doctors get 1.5-2.5 times higher salary than on average [2]. More than 55% doctors say they are dissatisfied with their salary [7]; 80 % quit public health because of low salary [6]. The President of the RF set a task to increase doctors' salary up to 200% of average salary in a region in 2018 [13]. However, we don't have clear understanding of how many staff jobs one doctor will have to take to get such salary.

In the course of our research we detected that 47% nurses had workload higher than standard due to internal jobs combining; 19% combined jobs externally; 35% had more duties than set forth in standards. And at that 59% nurses had constant lack of sleep. 12% questioned nurses said they slept less than 6 hours a night. And low salary was one of the major reasons for increased and excessive workload [11].

More than 30% of population don't think a doctor's occupation is prestigious. And only 20% of doctors themselves think their social status is high [7]. A medical worker status, doctors included, is gradually losing its former popularity [14].

As a problem of medical personnel staffing in state and municipal public health care is a truly burning one, the RF Public Health Ministry issued the Order No.210, dated July, 03, 2002 which adopted "The Personnel Policy Concept in the RF Public Health Care". The concept determined basic issues in human resources management in the field and set forth major tasks aimed at its implementation.

Our research goal was to examine and assess dynamics of population provision with medical personnel in Perm region over 2006-2015 and then work out propositions on increasing efficiency of personnel policy in public health care.

Data and methods. We examined the dynamics of population provision with medical personnel in Perm region over 2006-2015 in comparison with average country indices basing on the official statistic data. We calculated average chronological values of dynamics rows and their errors, as well as increase rates. To determine trends, we accomplished rows equalization as per moving average.

Results and discussion. Our research revealed that from 2006 to 2015 provision with doctors in Perm region was a bit higher than in the RF as a whole. Indices varied from 39.1 to 49.0 per 10,000 people correspondingly. Average chronological value in Perm region amounted to 45.9 ± 3.1 against 42.6 ± 2.4 in Russia.

We also detected significant discrepancies in indices dynamics. In the RF there was a slight but constant growth in the index up to 2009 (by 0.9 - 0.7%), and only starting from 2011, a decrease appeared (2012 and 2015 were exceptions with the growth by 1.8 and 0.3% correspondingly). But in Perm region a decrease in provision with doctors was practically constant (2009 and 2011 were exceptions, with 1.0 and 1.7% growth correspondingly).

2014 was a distinctive one, when provision with doctors dropped greatly, both in Perm region and in the RF (by 14.4 and 16.1% correspondingly). The index in the RF grew by 0.3%, but it remained steady in Perm region (figures 1 and 2). We detected a disproportion in provision with doctors in Perm region territories. For example, in 2015 indices varied from 40.2 (in Perm) to 18.1 (in Alexandrovsk); as for rural areas, from 30.5 (in Chstinskiy dis-

trict) to 10.1 (in Cherdyinskiy district). Loss of doctors occurred in 21 territories out of 47 only over 1 year (in 2014 it occurred only in 13 territories).

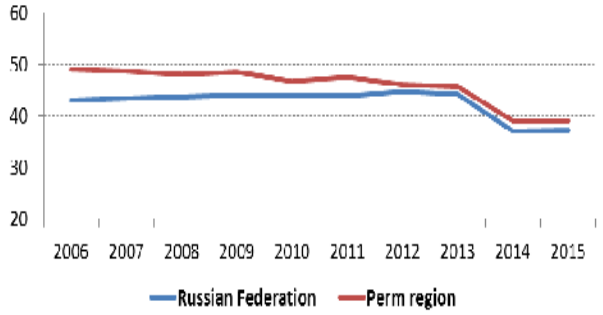

Figure 1. Provision with doctors (per 10,000 people)

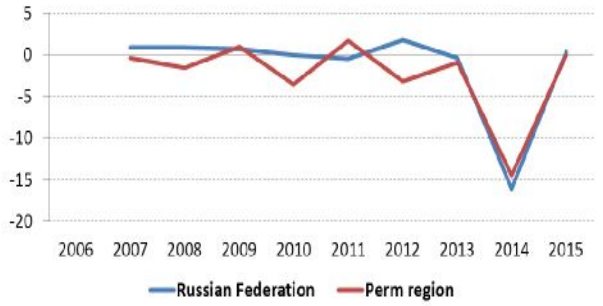

Figure 2. Increase rate in provision with doctors (%)

Moving average calculation showed that there was a persistent trend of decrease in provision with doctors in Perm region in the examined period as opposed to the RF as a whole (Figure 3).

So, in 2015, in comparison with 2006, provision with doctors in Perm region declined by 20.2%, but in the RF it dropped by 13.5% only. The indices amounted to 39.1 and 37.2 per 10,000 people correspondingly, and it was lower than the planned values (42.4 and 40.2 per 10,000 people).

Provision with paramedics over the examined period was also higher in Perm region (from 86.7 to 104.3 per 10,000 people), than in the RF (from 89.6 to 95.0). And only in 2015 the index in Perm region became lower than in the RF as a whole (86.7 against 89.6 per 10,000 people). Average chronological value in the examined period in Perm region amounted to 95.9 ± 5.7 per 10,000 people against 92.7 ± 1.7.

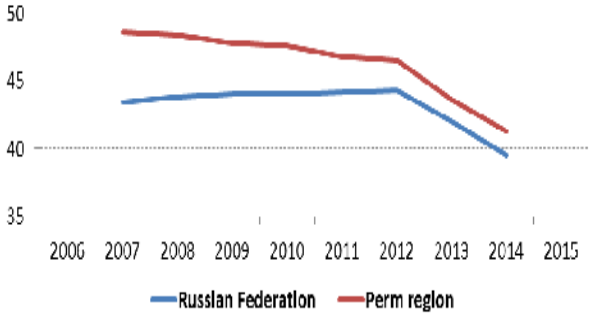

Figure 3. Moving average of provision with doctors (per 10,000 people)

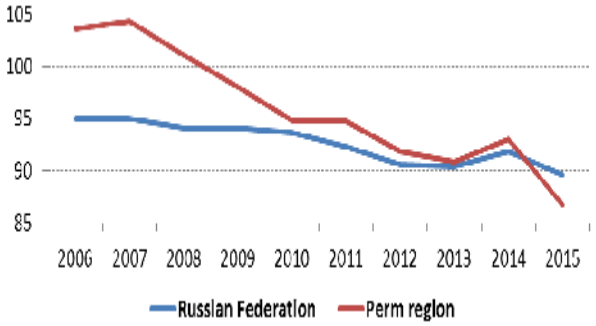

Figure 4. Provision with paramedics (per 10,000 people)

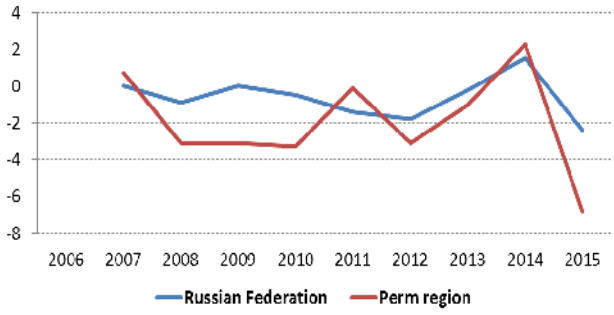

Figure 5. Increase rate in provision with paramedics (%)

2014 was a bit different when the biggest growth in the index occurred both in Perm region and in the RF(by 2.3 and 1.5% correspondingly). In 2015, on the contrary, the greatest decrease in provision with paramedics

occurred (by 6.8 and 2.4% correspondingly) (figures 4 and 5).

We detected a considerable disproportion in provision with paramedics in Perm region: thus, in 2015 it varied in urban areas from 110.1 (in Chaikovskiy) to 60.2 (in Perm); in rural areas, from 118.6 (in Uinskiy district) to 48.1 (in Kungurskiy district). Loss of paramedics over one year occurred in 33 territories.

Moving average calculation revealed that there was a quite persistent trend of decrease in provision with paramedics not only in Perm region but also in the RF as a whole, as opposed to provision with doctors. However, the decrease was more rapid in Perm region (figure 6).

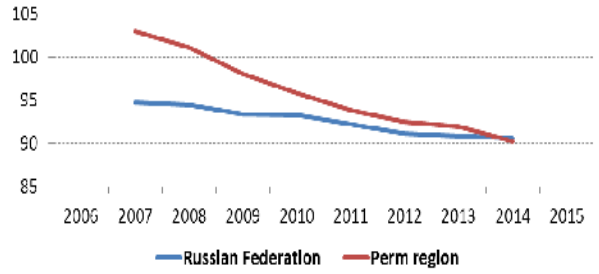

Figure 6. Moving average of provision with paramedics (per 10,000 people)

So, provision with paramedics in Perm region decreased by 16.3% in 2015 in comparison with 2006; it decreased only by 5.7% in the RF (table).

Ratio between doctors and paramedics in Perm region improved a bit over the examined period (from 1:2.1 in 2006 to 1:2.2 in 2015). And still it was lower than in the RF (1: 2.2 in 2006 ; 1:2.4 in 2015) and lower than recommended level (1:3; 1:4) [2,6].

Staffing of doctor jobs with individuals decreased a bit over the examined period, from 62.5 % in 2006 to 61.6 % in 2015. Staffing of paramedics jobs on the contrary increased from 70.0 to 70.1% correspondingly. Coefficient showing jobs combining over the examined period decreased both for doctors and paramedics (from 1.52 to 1.44 % and from 1.38 to 1.31 % correspondingly).

Specific weight of certified medical personnel in Perm region is higher than on average in the RF. Over the examined period specific weight of certified doctors decreased by 0.8% (from 61.9 to 61.4 %), but specific weight of certified paramedics, on the contrary, grew by 5.6% (from 69.5 to 73.4 %). And these indices in 2015 were higher than the same ones in the RF (48.4 and 55.4 % correspondingly). It is interesting to note that specific weight of doctors and paramedics having the highest qualification degree grew in both occupational groups whereas specific weight of personnel with the first and second category went down. It indirectly implies that the share of medical personnel belonging to senior age group grows. Specific weight of certified doctors grew by 57.3% from 2006 to 2015 (from 63.0 to 99.1%), and specific weight of certified paramedics also went up by 50.3% (from 65.6 to 98.6%), and it was higher than in the RF in 2015 (98.3 and 93.4 %).

We conducted sociological research among 5th year students of Pediatric Faculty, Perm State Medical University; its results revealed that only 86% respondents wanted to pursue a doctor's career after graduation. As for the remaining share, only 68% of them had clear vision of their future professional activities [12]. As per data given by Yu. Komarov [6], almost 30 % graduates quit medicine.

Only 40% respondents had at least some idea of activities implemented at federal and regional levels and aimed at solving personnel problems in public health care. 80% respondents gave their own ideas on how to solve them; the first place belonged to increase in doctors' salaries (44%), better working conditions took the second place (20%) and respondents included providing hospitals with up-to-date equipment into this idea; housing provision occupied the third place (11%); 3% respondents offered to return to graduates distribution after they finished studying at HEEs [12].

Conclusions:

1. Although provision of Perm region population with doctors and paramedics was higher than on average in the RF in 2006-2015, indices dynamics was unfavorable and there is still personnel deficiency.

The results of personnel policy implementation in Perm region in 2015 in comparison with 2006

Index	Doctors			Paramedics		
	2006	2015	Increase / decrease rate, %	2006	2015	Increase / decrease rate, %
Provision, per 10,000 population	49,0	39,1	–20,2	103,6	86,7	–16,3
Staffing with individuals, %	62,5	61,6	–1,44	70,0	70,1	0,1
Coefficient of jobs combining	1,52	1,44	–5,3	1,38	1,31	–5,1
Specific weight of certified personnel, %	61,9	61,4	–0,8	69,5	73,4	5,6
Specific weight of personnel with certificates, %	63,0	99,1	57,3	65,6	98,6	50,3

2. The ratio between doctors and paramedics over the examined period improved a bit, but still it remained lower than in the RF as a whole, and lower than recommended.

3. Staffing of doctors' jobs with individuals decreased slightly over the examined period, but staffing of paramedics' jobs on the contrary increased. And also coefficient showing jobs combining went down in both occupational groups.

4. Specific weight of certified medical personnel and personnel with certificates is a bit higher than in the RF as a whole. Changes which occurred in distribution of medical personnel as per categories reveal that a share of medical personnel from senior age groups grew, both among doctors and paramedics.

5. There is a disproportion in provision with doctors and paramedics in various territories of Perm region, and it requires systemic and targeted efforts of all concerned structures.

6. To solve personnel problems in public health care, we need to reform system of admission to medical HEEs and colleges so that applicants could avoid making mistakes when choosing a career; we also need to work out a set of activities aimed at making doctors' and paramedics' occupations more prestigious as well as at raising their social security.

7. Issues of personnel policy, labor motivation, ratio between number and structure of doctors and paramedics require permanent monitoring and profound analysis both at federal and regional level.

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DISORDERS IN MELANOPSIN EFFECT OF PUPIL CONSTRICTION AS A RISK FACTOR CAUSING EYE DISEASES

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Risks of eye damage and eyesight deterioration to a great extent depend on how efficient a biomechanical eye system is under energy-saving lighting conditions. The system's efficiency is determined by its adequacy in managing pupils and ciliary muscle.

We analyzed mathematical models describing changes in pupil's diameter which were determined by light-technical parameters of illumination environment (luminance level and brightness). We highlighted the importance of ganglionic cells and the role they play in managing pupil's diameter (miosis) when they are exposed to blue light within 480 nm spectrum. Basing on the assessment of a pupil's constriction under exposure to various light stimuli (blue, red, and green ones) we worked out a melanopsin effect concept of a pupil's retention at miosis and showed that it could be a diagnostic sign of some diseases (age-related direct retinopathy, pancreatic diabetes) under exposure to a blue light impulse with a certain wave length. Under exposure to blue light within 480 nm spectrum ganglionic cells form a managing signal for a sphincter muscle of a pupil and ciliary muscle which provides accommodation (as per Helmholtz) and regulates aqueous humor flow in ciliary channel.

All modern energy-saving light sources have a low energy level at wave length equal to 480 nm due to gap in their spectrum in comparison with sunlight spectrum with the same light temperature and luminance level. Inadequate management of pupil's diameter under artificial lighting conditions leads to melanopsin effect disorders and causes disharmony in managing aqueous humor outflow. All the above-stated factors under long-term visual load cause eye diseases risks in modern illumination environment.

We detected that contemporary mathematic models describing pupil's diameter fluctuations needed to be refined allowing for new knowledge on functional peculiarities of retina cells and energy-saving light sources spectrum.

***Key words**: biomechanical eye system, LED illumination, blue light, pupil constriction, ganglionic cells, melanopsin effect, myopia evolvement risk*

Issues of contemporary illumination environment hygiene and growing risks for eyes diseases caused by light from artificial sources are intertwined. Light impacts on eyes depend on a pupil diameter size and light spectrum quality which programs managing functional structures of a visual analyzer. Inadequate program management of a human eyesight biomechanical system increases eyes diseases risks.

Nowadays people's illumination environment is determined by energy-saving light sources and information displaying devices.

Ophthalmologists and hygienists have assessed the results of mass implementing compact luminous lamps and LEDs in South Korea, Japan, and China; the assessment

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revealed that there was a similar trend existing in all these countries, namely constant and stable growth in myopia cases number. This issue significance is also highlighted by recent research conducted in South Korea (where people use compact luminous lamps and LEDs everywhere); the research results were almost surreal as practically 96.5% of all 19-year-old (military age) men had myopia [41]. Historically human eyesight biomechanical system developed in sunlight environment and in unlimited visual space. "One can't get an insight into what the eye is without knowing the Sun. That's why the eye is solar, as a poet says", Sergey Ivanovich Vavilov told closing his wonderful book "Eye and Sun". Sunlight gets to retina through pupil and manages its size via relevant ganglionic cells and brain sections.

A man usually reacts negatively at bright-blue light flashes. " Pupillary reflex is in blue zone of a spectrum. Blue light sends the strongest signal to muscles in iris in order to close a pupil" doctor David H. Sliney told, an expert of US army on physiological effects exerted by LEDs, laser and other sources of bright light, who worked at US Army Center on health improvement and prevention medicine. In his work "Ensuring safety in LED lighting" [29] he pointed out that ganglionic cells were very important for an eye protection as such cells could keep a pupil small. Rods and cones can cause only short-term pupil constriction and it then again dilates within approximately 10 seconds. David H. Sliney also told that pupil size was approximately equal to 2 mm outside and was backed by photo-sensitive ganglionic cells, and upper eyelid protected a retina part which was below it [43].

A key moment for an eye pupil in classic light technique is its response at a value which is proportionate to quantity of white light which gets to retina. A human pupil diameter can vary from 1.1 to 8.0 mm.

Designers of optical devices with various functions were the first who paid certain attention to studying regularities in pupil diameter changes depending on luminance. When such devices are used human sight is maximum limited in visual space. Without an insight into these regularities it is hardly possible to design a qualitative optical device. Researchers in their works were guided by an assumption that pupillary reflex could be caused by various reasons, but first of all, by changes in background brightness. As background brightness grows, pupil diameter goes down. In general, this dependence is expressed with a formula by V.V. Mashkov [11]:

$$Dp = 5 - 3th\,(0{,}4lg\,L), \qquad (1)$$

where Dp is pupil diameter, mm; L is background brightness, cd/m2; th is hyperbolic tangent.

Dependence of pupil diameter on brightness calculated as per formula (1), is given on Figure 1 (curve 1).

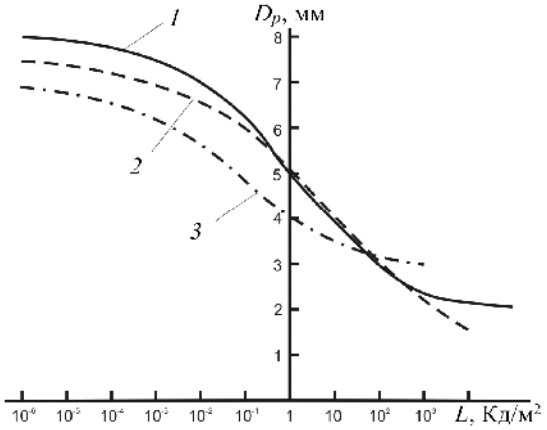


Figure 1. Dependence of eye pupil on background brightness. Broken line shows dependences obtained by R.Reeves (curve 2) and N.I. Pinegin (curve 3) [20]

N.I. Pinegin detected in his research that decrease in field angular size at constant brightness leads to pupil dilatation [13, 20]. T.N. Khatsevich examined dependence of pupil diameter in the process of watching images on electro-optical image convertor display (EOC) in night viewers [20]. Adaptation field (EOC display) peculiarities related to luminophor radiation, brightness fluctuation on a display, and scintillation occurrence, cause certain changes in pupillary response, namely, pupil size growth. And here

dependence of pupil diameter on EOC display brightness is given by the next formula:

$$Dp = 5{,}5 – 1{,}5th[0{,}5lg\,(0{,}06L)]. \quad (2)$$

The formula is true at 10–4 cd/m < L < 102 cd/m., that is, at actual EOC display brightness which, as a rule, gleams with green light [22].

The given data analysis reveals that when retina is exposed to luminous light, all formulas for calculating eye pupil diameter are to be changed towards its growth [20].

Pupil diameter growth is caused not only by all the mentioned factors but also by eyes diseases occurrence (Figure 2).

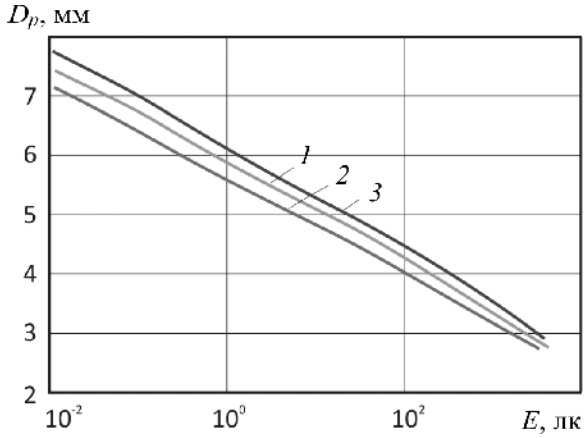


Figure 2. Dependence of eye pupil diameter on luminance on pupil: 1 is emmetropic eye; 2 is hypermetropic eye; 3 is myopic eye

When myopia occurs, eye pupil diameter is bigger than in case of normal eyesight. Diameter also depends on accommodation state and convergence state; when they are enhanced pupils contract, but when they get weaker, pupils dilate. Such changes can also occur when only accommodation or only convergence change [20].

As technologies developed, experts in the laser technique field responsible for photo-biological safety joined specialists on telescopes, light technicians, and specialized optical devices designers. Mathematical models for changes in human pupil diameter were of great interest for domestic light technicians when they solved applied tasks. Photo-biological safety issues have got their attention only nowadays after mass implementation of LED lighting. Foreign research on laser safety underlies regulatory documents on light sources photo-biological safety; such research often applies mathematical models of pupil diameter dependence on luminance, brightness, and photon flow. John Marshall, professor of ophthalmology at University college in London, dealt with eyesight problems since 1965, when he received a grant from Royal Air Forces and examined devastating impacts exerted on retina by lasers. He claimed that at that time they needed a much better insight into a way light interacted with retina, and what mechanisms could potentially cause eye damage. He, together with German and American scientists, created a database which gave grounds for international codes of practices aimed at people protection from possible devastating impacts exerted by lasers. Researchers extended the obtained results on potentially devastating effects caused by incoherent light. Their achievements were included into codes of practices used by large international organizations, such as World Health Organization (WHO), UN ecological programs and International Red Cross [31].

First works on laser safety enabled visual alignment charts creation to compare various light sources and safety areas (as per doctor David H. Sliney). Pupil diameter is in the center of these alignment charts as it fully determines an object projection on eye retina. Also "blue danger" areas are given in the presented alignment chart. But as time passes, new discoveries are made and new standards for photo-biological safety are created. For example, in accordance with State Standard IEC/TR 60825-9-2013 on laser devices safety a new concept, maximum permissible exposure (MPE), was introduced; under normal conditions, the concept doesn't contradict the results of biological effects occurrence. MPE value depends on radiation wave length, exposure duration, tissue state and exposure area size. A source angular size determines an image size on retina for visible and near infrared radiation within a range from 380 to 1,400 nanometers; the image here greatly depends on eye pupil diameter. This state standard determines "blue danger" with maximum permissible exposure on an eye assessed within wave length range from

380 to 1,400 nanometers and based on standard eye pupil size equal to 7 mm for duration shorter than 0.5 sec and equal to 3 mm for duration longer than 0.5 sec. Depending on brightness of observed light field pupil diameter varies from values smaller than 2 mm and greater than 7 mm depending on individual peculiarities of a person, an object of observation, and age. Formula (3) can be applied to calculate pupil diameter dзр (mm) depending on brightness value L (cd/m) of an observed object.

$$d_{çð} = 1,29\,ì\,ì + \frac{6,62\,ì\,ì}{1+\left(\frac{L}{8,24\,êä/ì^{2}}\right)^{0,32}} \qquad (3)$$

This formula is difficult for calculations. A clearer dependence of pupil diameter on brightness is given in State Standard IEC/TR 60825-9-2013 [4] (Figure 3).

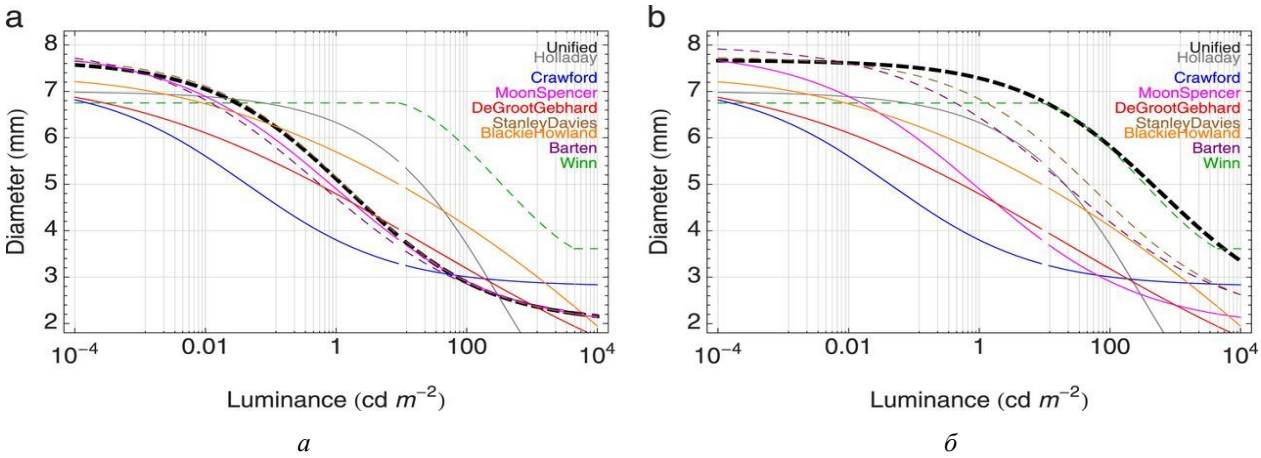
MPE values correction within wave length range from 380 to 1,400 nanometers for duration <0.5 sec in case pupil diameter is of standard size is performed in proportional dependence on its square. When a light source is used under different lighting conditions (for example at daytime and at night), calculating safety at pupil diameter being equal to 7 mm is the most correct variant [4].

Figure 3. Pupil diameter dependence on an observed object brightness according to State Standard IEC/TR 60825-9-2013 [4]

A newly created State Standard P MEK 62471-2013 «Lamps and lamp systems. Light-biological safety» [5] doesn't contain such comments. And we should point out that such regulatory document as State Standard IEC/TR 60825-9-2013 applied a mathematical model showing pupil diameter dependence on an observed field brightness in accordance with P. Reeves, JOSA 4, 35–43 (1920), and these are pupil diameter models which were created before 1920. To achieve their goals, A.B. Watson and J.I. Yellott, experts of NASA Research Center and Cognitive Sciences Department at California University, generalized existing mathematical models for pupil diameter dependence on brightness [46]. They created a new united formula which comprised brightness effects, adapting field size, and an observer's age. These researchers examined the following models: Holladay (1926); Crawford (1936); Moon and Spencer (1944); De Groot and Gebhard (1952); Winn, Whitaker, Elliott, and Phillips (1994); Stanley and Davies (1995); Barten (1999) and Blackie and Howland (1999). Summarized results are given on Figure 4.

Such a variety of mathematical models for pupil diameter dependence on brightness and other factors implies that these models are created under great uncertainty and lack of knowledge on how biomechanical system of eye pupil managing functions in modern lighting environment.

This uncertainty decreases as new discoveries in the sphere of eye cells functioning and their fitting together into a united biomechanical system for pupil diameter managing are made. This system operates according to functional systems laws by P.K. Anokhin. According to him, "...looking for a system as higher and more common functioning principle for many phenomena can give much better results than just only analytical techniques in studying particular processes".



а *б*

Figure 4. Pupil diameter as per several formulas: *а* is field diameter 60°, binocular sight; *б* is field diameter 10°, monocular sight. Broken lines show formulas, which depend on adaptation field size, an observer's age or binocularity. Volunteers' age for both figures is 30

In 1964 N. Viner, founder of cybernetics, stated that "Main issues of biology... are related systems and their organization in time and space". These concepts became a methodical ground for our analysis of visual analyzer functioning in modern lighting environment which differs from sunlight in terms of its spectrum form at a fixed luminance level.

Scientists for more than 150 years thought that a human eye contained only photoreceptor cells, rods and cones, which interacted and enabled accumulating visual experience by a person via brain visual cortex. It was thought that only those cells which transformed light spectrum into code messages of managing signals provided information for an eye biomechanical system to support sight quality in lighting environment.

Peculiar light-sensitive ganglionic cells of ipRGC type (intrinsically photosensitive retinal ganglion cells), or mRGC type (melanopsin-containing retinal ganglion cells) were discovered [3].

Such cells, as opposed to previously discovered ganglionic cells, contain light-sensitive pigment melanopsin which is different from other photosensitive eye pigments, rhodopsin of rods and iodopsin of cones which are unable to response directly to blue light in 480 nanometers range. These light-sensitive ganglionic cells are a new, third type of eye retina photoreceptors. As opposed to rods and cones known for 200 years, they are directly excited under exposure to light even when "classic" eye photoreceptors are blocked [34].

Due to research accomplished in various medical centers and universities in the USA and England it was determined that melanopsins have different subtypes with individual light sensitivity. Photo-ganglionic cells of M type are being examined most intensely. Melanopsin is a light-sensitive substance of these cells; it responses within wide range of colors, from 480 to 460 nanometers. M1 subtype melanopsin has two peaks of maximum sensitivity to blue light, namely:

– M1 Brn3b- at 460 nanometers;

– M1 Brn3b+ at 480 nanometers.

As new information is accumulated, a general form of curves showing M1type melanopsin spectral sensitivity is adjusted. It is detected that efficiency of managing eye pupil diameter at closing with M1 Brn3b+ melanopsin is determined by a curve for a person able to see and for a blind one [34]. A research on changes in pupil diameter depending on melanopsin excitement degree was also accomplished [26].

Only high irradiance by light of 480 nanometers (more > 11 log photons cm-2 c-1) caused significantly more stable response in the form of pupil constriction over time in people able to see [34].

Nowadays large-scale research is being conducted in world centers; it focuses on assessing influence exerted by human and animal visual analyzer on light stimuli (blue, green, and red light) [23, 24]. A standard response is taken to analyze this reaction (Figure 5).

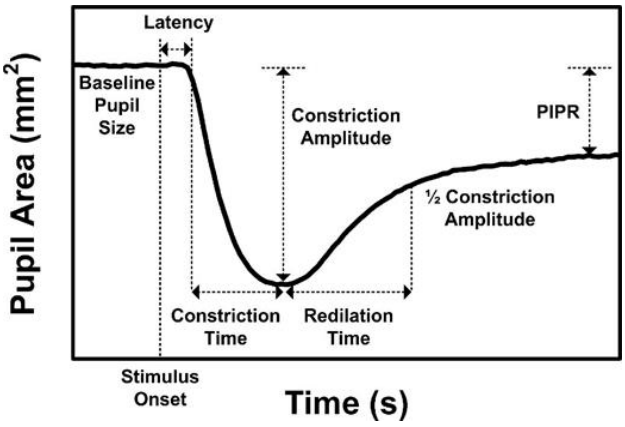


Figure 5. Pupil response dependence on contracting light impulse [23]

Standard response is characterized with baseline pupil size (without a light stimulus), maximum pupil constriction amplitude (under exposure to a light stimulus), and post-illumination pupil response), PIPR. It is PIPR parameter that provides information on efficiency of managing pupil constrictions.

To perform mass examination of ganglionic cells contribution into managing pupil size at different light stimuli, mice's pupils are usually taken as research objects. Research conducted on mice revealed that a pupil contracted significantly greater under 480 nanometers blue light than under red light [24].

Analogous research was conducted on two volunteers groups. Volunteers in one group had good eyesight, but volunteers in the second group were blind [34].

Pupil diameter was proved to be equal to 4.19 mm under luminous lighting of 4,000 K, luminance on cornea being 135 lumen 1.14·1014 (photons/cm^2/s) and calculated irradiance of eye retina by light stimuli being 0,54 mw/cm^2. It is the evidence that lighting by a luminous lamp at a dip in 480 nanometers area of a spectrum exerts complex influence. Soomin Lee et al. in their work describe light stimuli impacts exerted by two color lights (blue, 470 nanometers, and green, 532 nanometers) and by blue light separately on volunteers' eyes [28]. The resulting PIPR responses are given in Figure 6.

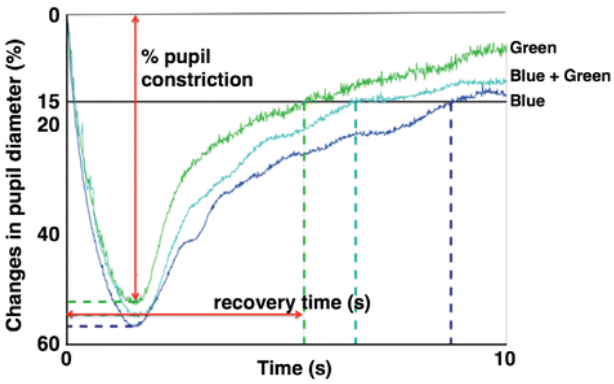


Figure 6. Changes in Japanese volunteers' pupil diameter at separate and simultaneous exposure to impulses of blue (470 nanometers) and green (532 nanometers) light (light source was a matrix with separate LEDs with a dip in 480 nanometers area)

The given dependence clearly shows why pupil diameter grows in EOC photooptic devices, and formula (2) allow for this growth.

Nowadays research on assessing PIPR value employs sources of blue and red light with various wave length, allowing for drug stimulation of an eye. Thus, to assess PIPR value, D.H. McDougal and P.D.R. Gamlin applied sources of red light with 613 nanometers length and blue light with 493 nanometers length in their work (Figure 7).

The third type are circular muscle fibers (Muller's muscle). They consist of separate fiber bundles which don't form compact muscle mass and have circular direction. They are located in anterointernal section of ciliary body, at interior edge. These fibers are considered to be a part of radial muscle. When radial and circular sections of ciliary muscle contract, a lumen of a rim formed by ciliary muscle decreases, and thus a place of Zinn ligament fixation gets closer to lens equator, resulting in lens curvature growth.

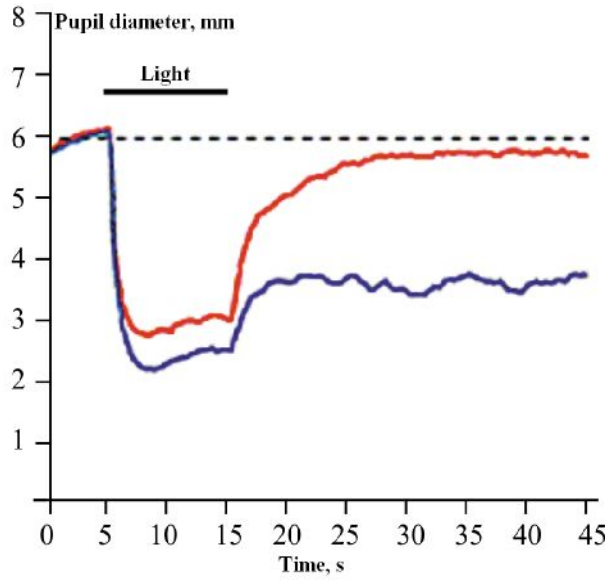


Figure 7. Pupil constriction induced by a light stimulus lasting for 10 sec with 493 nanometers wave length at 14.0 log quanta cm-2 s-1 irradiance (blue curve) and 613 nanometers wave length at 14.0 log quanta cm-2 s-1 irradiance (red curve)

The fourth type are iridal muscle fibers (Calasans' muscle) located at the junction of iris root and ciliary muscle. They are a thin bundle of muscle fibers going to iris root. Obviously, they regulate a gap between iris and lens providing minimal dynamic resistance for aqueous humor outflow from posterior chamber into anterior one.

Joint functioning of all above-mentioned fibers provides for accommodation. When ciliary muscle is strained, ligaments relax thus reducing lens capsule strain. Here lens form becomes round, and lens itself moves along optical axis towards iris. General scheme of such movements is given in works byI.N. Koshitsa, an expert in biomechanics. But movement models are well studied in adults, not in children. Ciliary body is rich with nerve endings, however, it is not developed enough in newborns, therefore a lot of diseases evolve without any pain. Only by 7-10 years of age all functions of ciliary body are completely developed [2, 12, 21]. Given this fact, it is very important that artificial lighting environment has a spectrum which is relevant to sunlight.

Examining an object at close distance in any age is accompanied with accommodation, convergence, and pupil constriction. With the help of these three physiological mechanisms better perception and better vision of an examined object becomes possible. Essentially all three phenomena are part of just one act, namely setting eyes at close distance. Previously there was a lot of argument whether pupil constriction during examining an object at close distance was related to accommodation or convergence. But it turned out to be related to both processes. Pupils constriction when eyes are set at close distance occurs only when an object is 40 cm away from eyes or closer. Pupil constriction is most clearly visible when an object is 15-20 cm away from eyes. Figure 8 presents a dependence for pupil diameter changes on accommodation level.

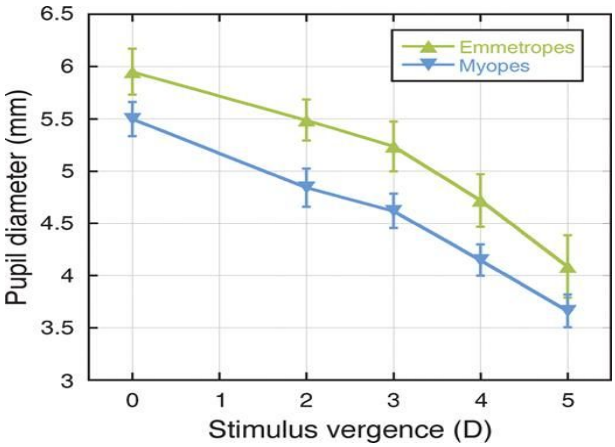


Figure 8. Dependence for pupil diameter changes on accommodation level [44]

The most recognized accommodation theory is Hermholz's theory; he proved that when accommodation strain is at maximum, anteroposterior lens size increases from 3.6 to 4.0 mm, curvature radius of lens anterior surface drops from 10 mm to 6 mm, and posterior surface, from 6.0 to 5.6 mm [19]. The higher is accommodation level, the smaller is anterior radius of lens which has certain physical and age limits [37].

Decrease in lens curvature and its moving towards iris leads to additional strain in Calasans' muscle for providing an adequate gap between iris and lens, that is equal inflow and outflow of aqueous humor. In 2010 Janice Tarrant et al. examined correlation between lens curvature, image clearness, wavefront aberrations, and accommodation processes [44]. They applied wavefront analyzer in their works to measure eye aberration in 13 volunteers with good eyesight (emmetropes) and 17 volunteers with myopia needed for examining 4 objects at various distances. When an examined object was moved closer, pupil constriction at first was rather slight, but then they contracted quite rapidly. An additional pupil constriction occurs when accommodation and convergence enhance synergizingly. Pupil constriction range at setting eyes at close distance varies a lot [16, 37, 39]. It implies that ciliary muscle is strained greater in case of myopia than in case of emmetropia. In this situation lens is more convex, and initial violation of balance between aqueous humor inflow and outflow occurs.

Pupil constriction and retention mechanism at accommodation and convergence is interesting for researchers when they solve applied tasks [25, 27]. Researchers in their experiments applied LCD-displays, OLED-microdisplays, and a white sheet of paper with letters lit by an incandescent lamp, to create visual images. Influence exerted by 480 nm blue light on managing pupil diameter when luminance came from a light source which differed from sunlight, was of particular interest for scientists. Some authors used letter on LCD-display and OLED-miscrodisplay (eMagin, США) as a visual stimulus [25]. Luminance level was about 15 cd/m^2. Two situations were examined: far (LCD-display), 2.75 m away; close (OLED-miscrodisplay), 30 cm away. Examinations involved volunteers' participation; they were young people aged 27.8 ± 2.4.

Other researchers use LCD-display for watching movies as a visual stimulus, and their volunteers were children (a very relevant focus group nowadays) aged from 6 to 16 [27]: 76 were regularly developed children and 41 children had Down's syndrome (DS). Research allowed to obtain dependence of changes in pupil diameter on accommodation level (Figure 9).

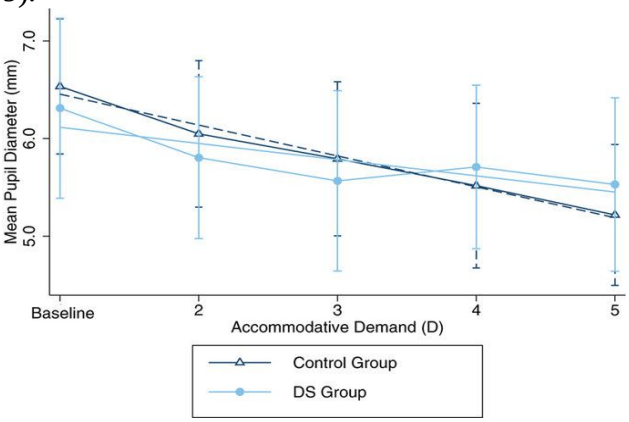


Figure 9. Dependence of changes in pupil diameter on accommodation level

S.Plainis in his work used the letter "E" printed on white paper lit by an incandescent lamp as an observation object [40]. Background brightness was equal to 5 cd/m2. Nevertheless, eye retina illumination was not constant for each object and level placement due to discrepancies in pupil sizes. All measurements were performed on natural pupils without introducing any drugs (mydriatic or cycloplegic). Seven volunteers aged from 23 to 33 (average age was 28) took part in this research. Four volunteers had normal eyesight (emmetropes), and three had bad eyesight (myopes) (ranged from –2.00 to –2.50 D), adjusted with glasses [40]. The greater adaptation response was, the bigger was miosis degree, and the correlation was linear. Each accommodation diopter induces 0.18 mm pupil constriction. Linear character of the dependence correlates well with the dependence given in Figure 9.

With mutual bracing of lens, iris, ciliary muscle and high sensitivity of pupil diameter managing system in mind, we can draw up a mathematical model (formula 4) for actual pupil diameter value at its closing under lighting environment when certain visual functions are performed.

$$D_{ac} = D_{in}(E, \lambda) - \Delta D(A) - \Delta D(K), \quad (4)$$

where D_{in} (E, λ) is initial pupil diameter at environment illumination and light spectrum;

ΔD(A) is a change in pupil diameter at accommodation induced by ciliary muscle strain degree (Bruecke's muscle, Ivanov's muscle, Muller's muscle, and Calasans' muscle);

ΔD(K) is changes in pupil diameter at convergence.

From methodical point of view it is very important to understand what figure a current pupil diameter value goes to when visual functioning take place.

Visual perception quality depends on retina resolution ability, light diffraction in pupil area, and peculiarities of eyes optical media. One of peculiarities a human eye has is occurrence of focal area depth, and there can't be any changes in image quality within its boundaries. Hence, there is an optimal sufficient pupil diameter value which provides such focal adjustment.

Visual perception is regulated not only by physiological optics but also by cortical structures of central nervous system. Improving eye optics via decrease in aberration, one can increase visual resolution from an ordinary level to higher one.

Aberration can be chromatic, diffractive, and spherical.

Chromatic aberration is an image distortion related to a situation when visible light rays with different wave length fall on lens in a parallel bundle, refract, and then don't focus in one point. Short-wave rays (blue-green) focus further from retina than long-wave (red) ones. This phenomenon is called longitudinal chromatic aberration. As a result an image is blurred and its edges are painted. If a blue rays focus is superposed with retina, a point image is surrounded with red aureole, and vice versa. Perceived objects shapes can be painted red in case of hypermetropia, and blue, in case of myopia. Under lighting with white light a man doesn't discern color edges around observed objects. It is explained by color aureoles overlapping each other and small angular sized of color edges. Chromatic aberrations don't exert any significant influence on central vision.

Diffractive aberration is related to disorder in linearity, light wave deviation during its spread by sharp edges of opaque or translucent structures which form holes. A pupil is an example of such structure in an eye. Due to light diffraction at a pupil edge where a clear transition from shadow to light should take place according to geometric optics laws, a number of light and dark diffraction rims occur and they are projected on retina. As a pupil diameter decreases, a diameter of light scattering diffraction rim increases. But spherical aberration also decreases.

Spherical aberration is a state, when there are discrepancies in a light ray refraction between a center of spherical optical surface and its periphery. Lens and cornea curvature underlies spherical aberration. Influence which spherical aberration has on image quality depends on pupil size. When pupil size is small (from 2 mm to 4 mm), spherical aberration is minimal, but it grows drastically as a pupil dilates. To maintain image quality at maximum level simultaneously providing minimal levels of diffractive and spherical aberration, we need to provide optimal sufficient pupil diameter value (D_{os}) not only for securing minimal aberration level but also for securing accommodation process (5) [1].

(5)

$$D_{os} = D_{in} (E, \lambda) – \Delta D (A) – \Delta D (K) = const.$$

Din (E, λ) forms environment illumination and light spectrum

All modern energy-saving light sources have low energy level at wave length equal to 480 nm due to a dip in this area as opposed to sunlight spectrum with the same color temperature and luminance. Inadequate functioning of pupil diameter management channel under artificial lighting leads to disorders in melanopsin effect of pupil retention at its constriction. And this, in its turn, results in additional efforts of ciliary muscle required for maintaining qualitative vision. All this together causes eye diseases risks under long-term visual load in modern lighting environment.

When there is residual strain in ciliary muscle or it suffers from grave overstrain, aqueous humor inflow and outflow balance is violated. I.N. Koshits et al. described contribution such violation makes into myopia evolvement in great details [17, 18]. Due to their research results and description of mechanisms regulating uveal scleral outflow path it became possible to get better understanding of a role which radial and circular parts of ciliary muscle (Ivanov's muscle and Muller's muscle) play in active regulation of uveal scleral outflow path in an eye.

Average speed at which aqueous humor is produced in a human eye equals to about 2 mm3/min as per physiological standard, changes range as per physiological standard amounts to 1.5–4.5 mm3/min. A period of aqueous humor renewal in an eye amounts to 90 min, that is, approximately 3 ml (3 cm3) of aqueous humor flows through an eye anterior section daily with average eye volume being less than 7.5 mm3. Slight variations in intraocular fluid production or outflow will have significant influence on intraocular pressure [14].

To provide efficiency and precise functioning of muscles which manage flows it is necessary: 1) that signals coming to Edinger-Westphal nucleus entrance were formed under sunlight impacts on retina cells; 2) that sunlight spectrum adapted visual analyzer structure to adequate algorithms of functional elements work to provide vision quality together with minimizing diseases risks. Sunlight spectrum, with hygienic limitations taken into accounts, manages Brueecke's muscle, Muller's muscle, and Ivanov's muscle state quite adequately; it also does so in case of aqueous humor outflow valves which are described in works by I.N. Koshits et al. [17]. We also considered Calasans' muscle state as this muscle manages a size of a gap between iris and lens at accommodation. "Iris - lens" valve role and functioning wasn't given enough attention in above-mentioned models for managing aqueous humor flow [17]. Although a role this gap plays in glaucoma evolvement is vividly discussed in works which describe models for this disease evolvement, Calasans' muscle state (its degeneration) is neglected in them. Notably, experts from Biomedical Engineering Department and Chemical and Materials Technology Faculty at Minnesota University performed mathematical modeling of accommodation microfluctuations processes and iris shape [30]. Research is going on now but their models don't allow for Calasans' muscle functioning.

Drug models for various tonic states of ciliary muscle were used to detect that accommodation apparatus functioning is directly related to an eye hydrodynamics; flow direction and volumes of liquid depend on accommodation fluctuations amplitude. Light spectrum which is not adequate to sunlight spectrum leads to disharmonizing in the way functional elements of visual analyzer operate. It becomes visible through:

– a dilated pupil when 480 nm light is absent in a spectrum which is characteristic for energy-saving lighting and displays lighting;

– disorder in rhodopsin synthesis out of vitamin A, a dip in 380 and 480 nm spectrum;

– dried eyes syndrome when working at displays which proves there is a disorder in aqueous humor management;

– an ascending trend in intraocular pressure after long-term (5 hours) staying under LED-lighting [8]. Thus, intraocular pressure measured via non-contact tonometry (Tn) amounted to 17.35 ± 1.1 mm Hg before the research and to 17.67 ± 1.1 mm Hg after it was over (5 days) at luminance being 400 meter-candela and correlated light temperature being 4,000-4,500 K [30].

As for apparent intraocular pressure, low standard zone for it (9-12 mm Hg), average standard zone (13-16 mm Hg) and

high standards zone (17-22 mm Hg) depend both on anatomic peculiarities of venous sinus position and on peculiarities of ciliary muscle fixing to scleral spur. It all shows that under artificial lighting aqueous humor management is disharmonized due to additional compensation for inefficient pupil constriction management which ciliary body muscles have to perform when an object is observed at a close distance. Accumulated strain in muscles managing aqueous humor flows leads to greater risks for increased uncertainty in managing state of trabecular and uveal scleral ways valves. Here disorder in "inflow" and "outflow" equality results in forming its excessive quantities thus creating conditions for accelerated stretching of en eye optical axis.

Average length of a human eye from cornea to retina center amounts to 23.5 mm. Each 1 mm increase in its length adds 3.0 diopter of myopia.

Persistent disorders in aqueous humor outflow can cause glaucoma, choroidal neovascularization, and macular degeneration [8, 28, 33]. As for cataract, there is various research on its relation to high degree myopia [36].

When disorders occur in melanopsin effect of pupil retention at its constriction, systematic destructive changes in eye functional elements take place. Persistent inadequate pupil diameter management becomes a systematic stimulus under contemporary lighting conditions and in information displaying devices; it creates an additional load on accommodation and convergence mechanism.

Conclusions:

1. Modern mathematic models for pupil diameter fluctuations require adjustment allowing for new knowledge on functional peculiarities of retina cells and spectra of energy-saving light sources.

2. We formulated conditions for melanopsin effect of pupil retention at its constriction in lighting environment; these conditions envisage an obligatory dose of 480 nm blue light in a spectrum of any artificial light source.

3. Inadequate pupil diameter management under artificial lighting conditions leads to disorders in melanopsin effect of pupil retention at its constriction and additional work of ciliary muscle needed for maintaining qualitative eyesight and keeping balance in aqueous humor inflow and outflow. All this together with long-term visual load leads to greater risks for eye diseases evolvement in modern lighting environment.

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