# MEDICAL-ECOLOGICAL STUDIES IN THE AMUR BASIN (RUSSIA): TO PROBLEM OF ONCOLOGY

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Russia's part of the Amur basin is found to be one of the least ecologically studied territories of Russian Federation so far. The Khabarovsk Territory as a significant part of the region is characterized by rather extreme climatic conditions and evident physical-geographical contrasts determining high heterogeneity of the territory – existence of separate geographical areas [4]. The existence of the vast geochemical provinces with, sometimes, extremely high content levels of many microelements is to appear as particularity of the territory as well [2]. For instance, more than 40 % of the region is referred to the areas with high radon-disaster. A lot of facts point to existence of natural factors array for high cancer risk among human population there. So, the development of research for "cancer ecology and geography" is considered as an actual scientific issue.

Non-obviousness of the natural oncology risk factors obstructs their separation from the general number of external (environmental) blastomogenic factors and, thus, requires a particular methodical approach development to make adequate oncology-epidemiological analysis. Usually, it is difficult to reveal the natural background influence upon cancer risk in big cities due to ambience is basically determined by strong anthropogenic (industrial and urban) impact. Obviously, the methods and principles of studying of natural malignant tumors (MT) factors should be different ones for the subpopulations in settlements without big and middle industrial enterprises. This criterion corresponds to the settlements with the less than 5000 population. The revealed regularities of distribution of main MT forms (cancer of lungs, gullet, belly, large intestine and breast) throughout different climate and geochemical provinces in the Khabarovsk Territory that has appeared as a result of our comprehensive studies before.

The main issues of studies of the Amur inhabitants were defined as follows:

1) development of methodology for epidemiological research for the influence of natural environmental factors upon cancer risk increase;
2) research for levels, structures and onsets of oncology diseases among humans who have been living in small settlements of Khabarovsk Territory in 1982-2006 years;
3) development of methodological approach to the combined geographical and medical clustering the territory;
4) mapping the main MT forms distribution throughout of the Amur region;
5) within the framework of the environmental studies, initiation of ecology-biochemical monitoring in order to make the systemic assessment of the role of microelements concentration in ground and underground water (including radon wa-

ter) as well as climate features in the rising risk of main MT forms and other social significant diseases (SSD).

We realize the interdisciplinary studies for these SSD forms' origin and their territorial distribution whys using the mathematical modeling and new information technologies methodology. There were studied the features of the different diseases spread, including MT, as a result of human activity influences, without taking into account the facilities of ecological-geographical (especially landscape-(hydro)geochemical) taxonomy. In the most general sense, any landscape-(hydro)geochemical clustering is considered as a division of territory by number of areas distinguished by several parameters, which are to render certain influence upon the considered disease risk increase. By geographical method of so-called “zoning” (division into districts or sub-regions, or clustering process), the same territory might be portioned out in different ways on areas that are to be different ones by disease forms [4, 7]. However, territorial position of chosen area itself, aside from the factors, taken into account when zoning a given territory, is put into the analysis and complemented by obtained information about factors, which are determined by their geographical position. The natural, demographic, social and other issues are to be subsumed to such additional information. These factors are entirely to be taken into account in explanation of studied disease spread character in given areas.

In this article, a methodology of ecological-geographical clustering in order to analyze the population epidemiology data is shortly presented. Specified clustering method was applying when studying MT spread among the children within the Khabarovsk Territory. MT spread assessment is considered to be impossible without determination of minimum number of observation units, or taxa. By a lot of reasons, such taxa are to be nor areas, neither administrative territories.

The territory of Russia’s Far East seems very vast and, thereby, lies within several natural zones. Climate features of the largest plain, the marshy Middle-Amur Plain (Sanjiang Plain within China), vary significantly from the North to the South, and, likewise, depend on relief and sea vicinity. Different parts of that territory are very irregularly inhabited ones and characterized by the different economic development level. Administrative districts, though, are more homogeneous according to economic development degree, but, as a rule, are characterized by the non-high number of population. This obstructs to get a reliable picture of spread of such rare phenomena as, for instance, MT among children of the region. Thereby, optimum taxon is presented to be neither vast territory, nor territory with the small population, but area nearing to administrative districts.

A lot of natural and anthropogenic factors directly impact upon human population health status. The offered ecological-geographical clustering is to take into account possible influence of natural environment and social-economic conditions upon arising risk of noninfectious lethal diseases among human population of Russia Far East. A specific method of physi-

cal-geographical clustering was applying for assessment of territorial spread of SSD, for instance, MT spread among children [5].

The main feature of children's leucosis distribution throughout the Far East appears to be presence of several areas with high sick rate. These areas with high sick rate among boys are insulated one from another and have different climate-geographical conditions. Standard disease factor equaled to 26.4 occasions per 100,000 male-babies there. Specified frequency of leucosis among boys is estimated in Upper-Zeya and Selemdzha as well as in Zeya-Bureya localities (the northern part of the Amur basin). In contrast with average value of the sick rate level, relative chance (RC) of appearance of leucosis factor in these districts seems really high one (RC = 1.47-2.13; assessment reliability is more than 0.95). Over the most of the Amur region, leucosis widely spreads, but less for girls than boys. At the same time, for some areas high levels sick rate among girls were revealed. Thus, over the North Sikhote-Alin' area, standard sick rate has reached 19.4 occasions per 100,000 of female-baby populations, but in Zeya-Bureya area this factor was 8.9. Specified frequency of leucosis distinguishes some girl populations of the biggest cities of region - Blagoveshchensk and Khabarovsk. Average annual standard factor sick rate in these cities was is 8.6 and 6.0 occasions per 100,000 girls accordingly. Against mean regional level sick rate, RC of leucosis appearance among girls over all territories mentioned was estimated as rather high one (assessment reliability is more than 0.95). Meanwhile, there was marked the territorial distribution unevenness of leucosis both among boys and girls. In different studied areas, standard factors of sick rate and relations of chances differ greatly from average regional value. As far as these differences are observed in some areas in comparison with average regional value due to the geographical clustering method, so, natural environment, probably, renders a certain influence upon children's leucosis territorial spread.

What phenomena to be put under study those are oncological diseases of lungs, gullet, belly, large intestine and breast cancer as well as medical-ecological background status of the Amur region as a whole.

Methods of study of general sick rate and death-rate due to MT of key sites nearing small settlements (with population amount less than 5,000):

- analysis of notices of patients who the first time in life gets diagnosis about cancer or other MT,
- analysis of neglected case protocols,
- analysis of oncological dispensary observation cards,
- analysis of histological studies casebooks,
- analysis of autopsies protocols,
- analysis of medical certificates and acts on deaths,
- and measurements of natural radiation background levels within areas around small settlements with use of aero- and space survey data and GIS.

What is already done to date? What is to be basis for further medical-ecological research [4-7]?

What is done is follows:

1. There analyzed a dataset on microelement contents (lithium, beryllium, vanadium, chromium, cobalt, zinc, honeys, gallium, germanium, strontium, arsenic, rubidium, yttrium, zirconium, molybdenum, silver, tungsten, lead, thorium, uranium) in soil and ground in sites around certain small settlements.
2. In sites around certain small settlements as well, there studied nitrate, nitrite, zinc, cuprum, iron, magnesium, potassium, lead, arsenic, quicksilver concentration in surface water.
3. With use of weather monitoring data by Far-East Regional Department of Russia State Hydrometeorological Service and relevant data catalogues, there were estimated main climatic features within sites around certain small settlements.
4. There was implemented the statistical processing of "rough" intensive and extensive factors, their average error, age sick rates, standard factors by direct and inverse methods, average error of standard factor, cumulative factors, relative risk factors, multifactor correlation and regression analysis, discriminate analysis and information modeling.
5. There were mapped the main forms MT spread on the basis of oncology-epidemiological clustering of the Khabarovsk Territory.

Ideology of information modeling methodology in ecology, medicine, medical informatics and human biology develops some original game-theoretical models (GTM) of human population behavior and its adaptation to extreme conditions, as well as uses the system methodology when analyzing human impact on ecosystems and back impact upon human population in developed areas of Russia Far East. The original hypothesis on features of MT generation among children subpopulation [5] and aborigines of the Amur region was formulated [12]. The interrelations between water contamination factors (such as organic matter, toxic metals and microelements) and inherent reasons for oncogenesis were studied by means of information modeling method with using data on medical-ecological monitoring of the Amur basin [4, 5].

We designed information models of social-economic issues of public health system management in the Khabarovsk Territory on the example of noninfectious lethal and socially significant forms of non-lethal diseases. There were elaborated the mathematical model of global information-technological processes impact upon social-economic and eco-psychological issues of living in the Amur basin, as well as main socio-dynamical scenarios of this region development and population life quality alteration in Russia Far East with taking into account the losses due to SSD. One of these diseases further studies ways sounds to be comprehensive ecological-geographical studies over the Amur basin. This way seems at this moment to be the most quickly developing direction of epidemiology not only of infectious, but noninfec-

tious pathology as well. Cancer-epidemiology is considered to be important section of noninfectious lethal diseases epidemiology. The preference is given to multifactor basis of MT generation; the impact of pathogenic combination of environment and constitutional-genetic factors upon an individual is to be considered. There is laid large meaning to environment creating SSD levels, particularly if we talk about regional features. Climate-geographical factors, feeding features, air and water pollution issues, as well as contacts with domestic and industrial chemical and physical carcinogens etc are included in these features.

Along with human impact, factors of natural environment and its change play certain role in processes of induction and promotion of many noninfectious diseases. Cancer epidemiology studies regularities of MT distribution over the Amur basin and is conditioned by natural environment. These studies are aimed on the malignancies spread features. This problem is referred to the field of analytical epidemiology, which is to dare for particular methods quite often within the framework of population studies. In number of analytical epidemiology issues there is found research for the factors of small intensity that, nevertheless, are to determine MT spread regularities. One should refer to such factors the environment impact on an organism, among which some ones have low probability to induce tumors in contrast with individual risk factors, spreading over the territory, as well as influence on the whole or on the most of population living on this territory. The research for factors of small intensity by cohort methods or by the method of "event-checking" as a rule appears to be inefficient. Population epidemiological analysis allows overcome contradictions of standard epidemiological studies. It includes study of the whole population, living on the under investigation territory. Herewith factors of frequency sick rate, death rate etc. within administrative regions (settlements) are to be studied, but as mentioned, a number of natural (warm-up conditions, solar radiation, microelements contents in ground etc.), social (joblessness rate, average profit per capita etc.), demographic (birth rate levels, death-rate, migration characteristics etc.) and other factors also might be referred to parameters of small intensity.

Let’s consider hydrobiochemical issues among a lot of ecological problems over the Amur Basin. Drinking water quality of is one of the main factors effecting on a person’s health status. Consumption of spoiled water promotes dysfunctions of all, without excluding, the organs and organism’s systems to lead to a lot of heavy diseases development and significantly reduce one’s life length. Particularly this is correct for children as far as if water content in adult organism is 60-70 %, in infant organism – 80 %, but five-month embryo consists of water by 94 %. In turn, quality of drinking water in the water-supply system depends on three main factors: 1) pollution degree of natural water reservoirs; 2) the methods of water treatment on water-production stations; and 3) state of water-delivery network. At presence, harmful admixtures in the Amur and underground water that feed nearby-Amur settlements, mostly adulterate the drink-water quality. Deterioration of the Amur environment is inseparably connected with atmosphere pollution, soil and water contamination by products of agricultural, industrial and domestic activity. As far as water is produced for drinking only from underground and open water sources, it is necessary to stress that due to natural water cycle,

in combination with high dissolution ability of water, almost total contamination being concentrated in sewages of industrial and agricultural enterprises and in domestic sewages, one way or another, comes in water-supply systems. A lot of contamination, by sewages or via other ways, figuratively goes back to the people, and thus human-altered environment influences directly upon one's health.

Depending on danger degree, array of heavy metals is split into several classes. The first, the most dangerous class includes arsenic, cadmium, quicksilver, selenium, lead, zinc. The second class contains cobalt, nickel, copper, molybdenum, stibium, chromium; and vanadium, tungsten, manganese, strontium are united into the third one. The higher class of heavy metal danger, the less concentration of poison chemicals and mineral fertilizers widely-used in the agriculture, in atmosphere, soil, food and water, so, the smaller its dosage are to make toxic, mutagenic or carcinogenic effect. At present, more than 1,000 names of poison chemical matters are known over the world. Many of them do not be dissolved, but accumulated in organisms for many years. Natural water is deteriorated by such toxic admixtures as pesticides – toxic chemicals that are applied for planting and wood protection from vermin. Pesticides are easy dissolved in water and so easy fall on the ground, infiltrate and go into streams and lakes, for example, with rainstorms. The pesticides' impact on one's organism could be specific and nonspecific one. Specific action is show as an effect of that toxic material, which stipulates an action of pesticides. So, pesticides, contained quicksilver, are to generate specific diseases, like Minamata disease. Nonspecific effect of pesticides means their abilities of chronically small doses to reduce immune system state, to cause mutation genetic code, as well as different tumors. Besides, in natural water reservoirs there are to be present the herbicides – organic compounds, used in the agriculture for the struggle against weeds, and, also, nitrates – anions of nitric acid used as fertilizers. Excess of nitrate-ions concentration level over more then 50 mg/l makes water dangerous for health. In one's organism nitrates are able to form the components of food nitrosamines that induce MT. In the digestive tract, up to 65 % of nitrate-ions become nitrite-ions, which fall into the blood and tissue of organism. Children of breast age are particularly sensitive to nitrites – by 100 times more than adults. That is conditioned by insufficiently developed children's ferment system as well as greater their hemoglobin's liability to oxidation by nitrites [6, 7]. Specific effect of nitrite-ions is considered to create methemoglobin, which is not capable to carry oxygen to organs and tissues. This generates a figural breach in shelter of organism's transport functions and oppresses its ferment system, which adjusts the cells' breath. First, the organs of digestion and nervous systems are to fail. At nitrites concentrations in water as 1.2 – 2.0 g/l (that corresponds to 45 % level of total hemoglobin cytophylaxis) develop lethal cases.

The list of all synthetic organic materials, which are to be present in natural water bodies, numbers more than thousand names. A lot of these materials are known to possess carcinogenic and mutagenic nature. The best-investigated poly-aromatic hydrocarbon is considered to be 3.4-benz(a)piren. This compound is created as a result of organic fuel combustion. So, its concentration around fuel-energy enterprises, heat supply plants, as well as in places of

motor transport concourse or traffic, is particularly high. This matter is referred to the first class of danger and induces oncological diseases. *Regulations for surface water protection from sewages contamination* assumed in Russia, determines general and special standards of quality factors and water objects. Part of non-soluble contamination accumulated on special paper filters, is to be identified as weighted matter. Content of the most dangerous soluble organic compounds is often estimated just by the value of biochemical oxygen demand ($BOD_5$). General regulations are that total water mineralization is to not exceed 1000 mg/l, soluble oxygen content in water in winter is to be not less than 4 mg/l, in summer – not less than 6 mg/l. Acid capacity of water ($BOD_5$) is to be not more than 2 mg/l. Concentration of lignin must not exceed 2 mg/l. Organoleptic regulations include the upper limits of iron, methylmercaptane and phyrphulole content. Water bodies used for fish-breeding are controlled according to their special requirements regarding oil, some oil products and phenols content. Sanitary-toxicological regulations establish the limits of such compounds as nitrate-ions, trivalent chromium, manganese, lead, quicksilver, fluorine, potassium, calcium, magnesium, sodium, sulfates, chlorides, phosphates, rhodanides and formaldehyde. Toxicological requirements limit content of ions ammonium, cuprum, zinc, 6-valent chromium, cadmium, arsenic, tin, aluminum. In water cyanides and pesticides are to be absent. Quality features for surface water are established practically throughout the whole nomenclature of requirements to water quality. Acidity, oxygen content, $BOD_5$, total mineralization, concentration of chlorides, sulfates, nitrates, nitrites, phosphates, oil products, cuprum, chromium, zinc, lead, nickel, iron as well as bacterial contamination are to be included in the number of water quality characteristics to be estimated. Set of episodic contaminants includes such harmful compounds as pesticides, cadmium, cobalt, fluorine, arsenic, strontium, quicksilver, aluminum. Benz(a)piren, tethraplumbum dioxins, quicksilver, tellurium, beryllium, boron, lithium, molybdenum behavior as well as pathogenic enteroviruses are studied poorly to date. Majority of these matters are exceedingly dangerous [5, 6]. According to categorization of natural water bodies by contamination degree, water is to be considered:

1) clean one if $BOD_5$ < 1-3 mg/l and suspended matter content < 1-10 mg/l,
2) polluted one if 3-6 and 10-50 accordingly;
3) dirty one if 6-15 and 50-100 accordingly;
4) very dirty one if $BOD_5$ > 15 and suspended matter content > 100.

Amur is located between 2 and 3 gradations (by [3, 6]).

Sanitary status of Amur nearby water-supply pump stations of Khabarovsk-city is assessed to be non-satisfied, and the increased degree of potential epidemiological danger was assigned to Amur. Part of water tests is found to exceed hygienic microbiological standards by 23.4 %, and in every third water test there are discovered viruses [12]. In Annual Reports by State Committee of Ecology, in 1991-2001, a lot of tests in water-treatment plant demonstrate microbiological contamination of the Amur water, meanwhile amount of normal samples reduced from 56.8 % down to 15.1 %. Similar results are received in popular bathing places in Amur nearby the city [6]. Water quality nearby Khabarovsk water-supply pump stations in 1999-2001 is recorded to become worse one. According to results of laboratory

analyses, percentage of polluted samples taken from of water-supply sources has risen from 11.1 % up to 23.9 % [7].

In 1970-80, due to specific medicine (chemical) scent detected in several winter fish samples, a question about the Amur phenol contamination has arisen. “Phenol problem” has got a new breath at February 1996, when in the Amur water samples nearby the Tunguska River mouth extremely high concentration of phenols (904 mg/l) has been allegedly registered. Every autumn and winter in 1998-2004, chemical scent was being detected again in autumn salmon [1]. However, as a result of studies conducted by IWEP in the June-November 1999, there was established that chemical scent of fish did not connect directly with the increased phenols content in the Amur water. Scenting matter are studied to-date to have human-made nature as a result of sewage by oil treatment plants and chemical industry and its dynamics is controlled by water temperature conditions through chemical and biochemical oxidation rate. A lot of flourishing shallow lakes within and nearby the Amur floodplain in summer are studied to be sources of certain amount of natural phenols due to algae’s activity, that is why concentration of phenol reaches up to 10 mg/l there [3]. Meanwhile, the total lake inflow in Amur, when low water stage period occurs, is valued as 10-20 % (once in a while up to 30 %) of the Amur flux [11]. So, there is considered to be comparatively low phenols content in the Amur water and be distinctive by its seasonal distribution [1, 3]. At winter period the ice cover does not allow to intake oxygen, required for oxidations of dissolved organic matter (DOM) and hydrobionts’ breath, in the water [9]. Dissolved oxygen consumption is to reduce concentration of DOM and to worsen water quality due to accumulation of highly toxic products of incomplete disintegration of organic materials. Simultaneously, water flux diminishing, at the average by order in contrast with warm period, conditions the corresponding increase of loading rate of wastes upon quality of the Amur water. Because of the low temperature, the winter rate of DOM mineralization is lower than summer one by several times [9]. Joint action of these factors, at long-term low-water period in the Amur basin particularly, brings to that river is unable to treat all the pollution itself, and toxic compounds are to be accumulated in the Amur ecosystem. Herewith these circumstances, a lot of organic compounds are to be destructed in anaerobic conditions with formation of intermediate fugitive products, which tincture non-natural scents to water and fish [1]. This can have crucial effect upon sanitary-ecological status of the river water [8].

Transition of certain pollutions from ice in spring into water is shown as particularity of formation of the river water chemical composition [10]. Certain metal compounds such as tin, lead, chromium and silver ones as well as some oil products accumulate in the snow and ice cover from human-made aerosols [6]. Ammonium nitrogen appeared to be one of toxic matters, which deteriorate the river water. In the Amur water, ammonium nitrogen comes with water influx from a lot of rivers, lakes and swamps, atmospheric precipitation, industrial and domestic sewages, and sewers from agricultural fields and farms as well. Usually atmospheric precipitation contain small amount of ammonium ions, however their concentration increases significantly in the snow cover on the territory subjected by wildfires, and reaches up to 6.28

mlg/l, while the highest concentration of ammonium ions is recorded in swamp water in the July-August, when decomposition of organic matter in water goes intensively [14].

At the meantime, in Khabarovsk city the permanent water quality control in water-supply system where coagulants of new generation like aluminum oxide are used, led to quite perfect quality of drinking water by majority of parameters, and by microbiological factors first of all. If in 1991 amount of samples with unsatisfactory microbiological factors was 8.2 %, but in 2001 it was only 1.7 %. Percentage of tests with bad quality of water from departmental water-supply network for a specified period also reduced markedly: by chemical factors, it became 72.5 % compared with 60 % before; by microbiological it was revealed as 21 % against 5 % before. Meanwhile, however, quality of water from departmental water-supply network stays worse in contrast with municipal one, especially during flood period. The further improvement of water quality in water-supply network, under existing water-treatment technology and quality of pipelines, looks to be impossible [4, 6]. Water quality deterioration in the Khabarovsk Territory is studied to be caused by unsatisfactory sanitary-technical state of water-delivery networks, which damaged by more than 60 % [4, 5]. There is registered the fact that in 1995 year, for instance, number of damage occasions in water-supply pipelines of the Khabarovsk Territory has been registered to be 998. About 70,000 people (11.6 % of Khabarovsk population) use non-standard water, including water characterized by excess of State Sanitarian Standards regarding Fe content (33,000 people), manganese content (8,000 people) and chlorine content (70,000 people) [13].

Because of enormous amount of water quality factors, this comprehensive problem is to be considered in three main aspects. First of all, within ecological-medical aspect, the Amur basin natural water status, including water quantity, the current recommendations on protection and conservation of water resources and also on water use, are to be valued. This aspect has state sound, but quite often inter-state one, as well. Thereby, the comprehensive program aimed to the nature protection and rational (sustainable) land use in those countries, whose territories includes the Amur basin, are to cover three groups of parameters of land use management: 1) level of possible influence on the natural ecosystems; 2) preventing the deterioration of natural environment; 3) investment of nature protection and use of water ecosystems resources. Certainly, the nature protection and rational land use planning over given territory is to include such issue as water resources protection against contamination threatening people's health. According to complexity and interdisciplinarity of the Amur contamination problem, its resolving is considered to be possible just within the framework of certain Amur basin Development Program. Undoubtedly, such Program is to be based upon methodology of agreement between different regional and departmental development strategies, and also on the theory of management in conflict and uncertainty conditions facilitated by GIS, databases (DB), knowledge bases (KB) and remote management networks (RMN), could be applied.

GIS, DB, KB and RMN are applicable to the considered area and correspond to needs of ensuring of system parameters control adequacy to methods and models of manage-decision

concerning the functioning and development of active complex systems – nature-society systems, as well as technology development of hetero-hierarchical electronic and computing neuron-networks as remote control structures. Thereby, there is stipulated the development of technology of decision making in man-machine managerial systems that include bases and principles of building the planning systems of decision making (DMS), architecture of DMS and presentation of knowledge in the system.

In order to resolve such class of problems there was designed global and local models of situations {S} and decisions {R}, allowing to describe different aspects of presentation of situations ensemble, and to form the classes of players, situations, decisions – so, functional conditions of person making the decisions (PDM) and etc. There were designed the algorithms corresponding to categorizations, recognitions and forecasting as a component both situations, and decisions. Creating of game-theoretical models (GTM) for the description of PDM behavior in conditions of given limited or global conflicts are described in [15] regarding the alive systems. Herewith, the "players" appear not just as policy-makers and managers (managers make decisions in the process of operative management, monitoring and control of the ecosystem behavior), but as other engaged persons on different management levels as well. Received on GTM building in the field of water-ecological issues, certain regularities are possible to be spread upon other kinds of land use as well. In [4, 12] there were elaborated the principles of software, information facilities and ergonomics to realize GTM mentioned above within the framework of information-recognition systems on the example of self-organizations processes of open thermodynamic system, which objects of alive nature are considered as.

Along the realization of separate positions of shortly formed problem, in practice (active area of management), high professionals in different areas of knowledge: modeling, planning, designing, making the managerial systems, construction, service etc. are to be attracted, regardless of their citizenships. Finally, how will change Amur itself and the Amur River basin functions in current century with climate change, population change, technological development and urbanization of this region, depends on the whole set of actions, first, in the international scale.

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