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The Establishment of the Cause-Effect Relationship of the Formation of Somatic Diseases in the Population of Pre-Aral under the Influence of Ecological Factors

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Abstract

BACKGROUND: The largest ecological disaster of anthropogenic origin is the drying out region of the Aral Sea.

AIM: The study aimed to establish the cause-and-effect relationship of formation of diseases among the adult population under the influence of environmental-hygienic factors in the region of Aral Sea.

METHODS: The article identifies the relationship of somatic diseases in the surveyed population and identifies the leading type of aberrations under influence of ecological factors in this region.

RESULTS: The article presents the results of multidimensional statistical analysis (correlation, linear and non-linear regression, and logistic) with the gradual establishment of the presence of the influence of the environmental factor on the development of a particular nosology and determining the significance of this influence, and also the prediction of the incidence growth with an increase in the level of the environmental factor was assessed.

CONCLUSION: This article provides the leading nosologies from the main classes of diseases throughout the Aral Sea region.

Introduction

One of the ecologically unfavorable regions is the drying out region of the Aral Sea – the largest ecological disaster of anthropogenic origin [1]. At the present time, there is no reason to deny the existence of environmentally caused diseases, the origins of which are associated with the harmful effects of the habitat. Special attention of scientists and health workers is attracted by the problems of the quality of public health in ecologically unfavorable regions of Kazakhstan [2], [3]. However, the question of what kind of diseases can be considered environmentally conditioned and even the terminology, which denotes diseases related to the state of the environment, is controversial.

Konstantinov *et al.* suggested that the group of eco-dependent diseases includes most of the common diseases – cardiovascular, gastrointestinal, oncological, respiratory, endocrine, and others. In conditions of environmental pollution, these common diseases appear at an earlier age, their prevalence increases, they are more often transformed into a chronic form and are difficult to treat [4]. Moreover, Varaksin *et al.* [5] concluded that most of the diseases that are investigated in sociohygienic monitoring are ecologically dependent diseases, their connection with environmental factors exists, but it is not that strong to be obvious. It can be said that environmentally dependent diseases are those diseases for which state of the environment contributes to their prevalence, especially their course, but is not the only nor the main reason for their occurrence.

At present, chronic diseases of those organs and systems of the body that are performing barrier functions at the interface between the two environments, external and internal, are becoming increasingly widespread, and thus maintain and preserve the purity of the internal environment of the body: The respiratory, digestive, immune, lymphatic, and excretory systems as well as liver and skin [6], [7]. The pathogenetic role of environmental

pollution in the development of diseases can manifest itself in the form of various effects. It can be the change in the structure of morbidity, prolonged and chronic course of diseases in all age groups, the course of diseases in atypical forms and manifestations, the increase in morbidity and inhibition of immunological reactivity of the organism, the growth of oncological morbidity, the chronization of pathologies of all organs, and systems [6]. Moreover, Sabirov *et al.* demonstrated the effect of chemical pollution to the chromosomal mutagenesis in the region of the Aral Sea [8]. Also, a correlation is found that people from the pre-Aral region have the highest frequency of digestive system diseases in Kazakhstan due to high level of pollutant in the water [9].

To diagnose ecologically dependent diseases, it is necessary to consider the long-term effects of chemicals in low concentrations that cause non-specific, often reversible changes in the state of the body long before pathological disturbances occur. Therefore, when studying the impact of unfavorable environmental factors on the health of the population, it is expedient to identify primary, functional changes in the body, and not only the presence of pronounced effects and various diseases [7].

Thereby, there was a need for a comprehensive study of changes in the health status of the population on the basis of modern methodological approaches for obtaining evidential mechanisms of disease occurrence in the inhabitants of the Aral Sea region.

Research purpose

The study aimed to establish the cause-and-effect relationship between diseases formation among the adult population under the influence of environmental- hygienic factors in the Aral Sea region.

Research objectives

Identification of the dependence of the development of the main nosologies among the inhabitants of the Aral Sea region from environmental and hygienic factors by means of correlation analysis and predicting the change in the state of health by mathematical models obtained with the use of regression analysis.

Materials and Methods

Research design

The study was conducted in the frame of the scientific and technical program "Integrated approaches to managing the health of the population of the Aral Sea region." Medical examination (clinical and functional studies) of up to 5% of the adult population were conducted in the three zones: disaster zone (Aralsk and Aiteke-bi village (Kyzylorda) and Shalkar village (Aktobe)); ecological crisis zone (Zhalagash, Zhosaly, and Shieli villages (Kyzylorda)); pre-crisis ecological zone (Irgiz village(Aktobe), Ulytau village (Karaganda), and Aris(South Kazakhstan)). Atasu village (Karaganda) was chosen as a control.

Conditions and sampling technique

The data on the established physical diseases in the group of the examined people are reviewed and analyzed during a medical examination at the population level. The admission to the adult population group was carried out on the basis of stratification (by sex) and quota equal sampling for men and women in the following age groups: 18–29 years, 30–39 years, 40–49 years, 50–59 years, and 60–69 years in each village. The obtained results were entered into the developed unified map of the clinical examination that allowed to assess the state of health of a person living in an environment with an environmental load and to prescribe adequate methods of treatment more fully and comprehensively, taking into account the leading clinical syndromes characteristic for diseases (Certificate of state registration of rights for object of copyright No. 0313 dated February 17, 2016, and No. 1749 of August 16, 2016).

Inclusion criteria

The criterion for the inclusion of a person in the examination was the duration of residence in the area of the study for at least 5 years, the absence of contact in the workplace with production factors above Grade 2 hazard, and danger. The survey sample included persons of reproductive age from 18 to 69 years.

Statistical analysis

Statistical analysis was carried out in the program Statistica v.10 and Excel 2010. Electronic database was filled in the Excel environment, the coding of all diagnoses was carried out according to the International Classification of Diseases-10. An in-depth step-by-step statistical analysis was carried out, including frequency analysis, correlation, regression, and logistic analysis, based on the results of which the corresponding models were constructed.

Results and Discussion

At the stage of frequency analysis, the leading nosological forms of diseases among the

adult population at the population level have been identified. However, as such, regional features could not be identified, since the main disease classes were identified in the examined population in all the regions studied. In all inhabited regions, the most common diseases among the adult population were urogenital diseases (urolithiasis and chronic pyelonephritis), diseases of the digestive organs (chronic hepatopathy and chronic cholecystitis), circulatory system diseases (coronary heart disease – ischemic heart disease, atherosclerosis, and arterial hypertension), breathing organ diseases (chronic obstructive pulmonary disease – COPD and bronchial asthma), diseases of the blood and blood-forming organs (anemia, thrombocytopenia, and leukopenia), and musculoskeletal system diseases (osteoarthritis and arthritis).

At the next stage of establishing cause-and-effect relationship of the formation of ecologically-dependent non-infectious diseases of the therapeutic profile in the adult population of ecologically unfavorable territories of the Aral Sea region at the population level, a correlation analysis was carried out. The study of the linear and non-linear relationship of two quantitative variables was carried out based on the total hazard index (the sum of the multiplicities of the pollutants' doses) coming from the external environment in different ways and routes (inhalation and oral) per average person per day, average annual climatic factors, and chemical compounds.

Herewith, correlation analysis showed the presence of a direct expressed relationship in the development of anemia when the total dose of mercury was delivered (inhalation and oral intake) (r = 0.74 (r = 0.90, p > 99%), p > 95%), leukopenia, when the total dose of PCB (polychlorinated biphenyls) from the soil was received (r = 0.77 (r = 0.90, p > 99%), p > 95%), atherosclerosis of the vessels when the cobalt total dose was received (r = 0.72 (r = 0.90, p > 99%), p > 95%), and bronchial asthma with the effect of wind speed (r = 0.73 (r = 0.90, p > 99%), p> 95%) (r = 0.90, p > 99%).

Thereby, at this stage, a significantly significant correlation statistical relationship was established between the prevalence of non-infectious diseases and the dose load of chemical compounds on the average person, climatic factors, and chemical compounds. As a result of the conducted correlation analysis, the cause-and-effect relationships of health disorders in the Aral Sea region from the effects of various unfavorable environmental factors at the population level have been identified, and diseases which development is not associated with the studied environmental factors have been excluded.

At the next stage, multidimensional linear and non-linear regression analysis of data was carried out to check the statistical hypotheses obtained by correlation analysis, the relationship between the detected diseases and environmental factors at the population level. This stage is necessary for obtaining prognostic models and determining the contribution of individual factors to the development of the pathologies studied.

When regression linear analysis was carried out, the correlation interdependence between the development of some non-infectious diseases in the population of the Aral area of the studied regions and environmental factors was confirmed. Proposed predictive models were obtained using the least squares method. We obtained a prognostic linear model of the dependence of the prevalence of anemia on the total hazard index of mercury, that is, the sum of the multiplicities of the doses of mercury in the inhalation and oral route from the external environment to the body of the average person per day (rate of entry). Figure 1 shows the obtained predictive linear model of the dependence of the prevalence of anemia on the total mercury hazard index, that is, the sum of the multiplicity of doses of mercury in the inhalation and oral routes of entry from the external environment into the body of an average person per day (intake rate).

Anemia (with the influence of mercury) - Y = 9.78 * X + 10, where Y is the dependent variable (the number of people with the existing disease from 100 examined regions) and X is an independent variable
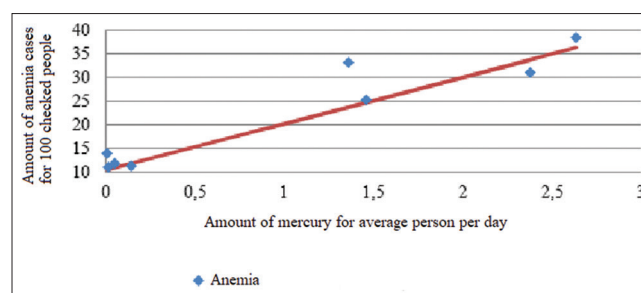

Figure 1: Predictive linear model for the development of anemia when mercury enters the body of an average person from the external environment per day

(various environmental factors, in this case – mercury). The model describes 74% of cases and determines that with an increase in X (mercury) per unit, Y (the number of people with anemia) increases by 10 units, that is, 10% of 100 people.

Abrupt effects on the development of aplastic anemia in the body are of mercury vapor, radiative impact and evaporation of oil products. In the blood, mercury is partially bound to proteins and shaped elements of the blood, from which it enters various organs and tissues. Thereby, organic compounds of mercury, due to high lipid solubility, easily enter through the hematological barriers, including through the blood–brain barrier to the brain, through the placenta into the fetus. Then, changes are added on the part of the blood in the form of base and eosinophilia, anemia, leukopenia, and less often agranulocytosis. The duration of clinical manifestations depends on the dose

and the duration of the effect of mercury on the body, but the symptoms, even in the absence of mercury in the body after specific treatment, can persist for up to 2 years and longer [10].

We also obtained a prognostic non-linear quadratic model for the dependence of the prevalence of leukopenia $Y = 399.99 * x^2$ on the total hazard index of polychlorinated biphenyls, that is, the sum of the multiplicities of doses of polychlorinated biphenyls with an inhalation and oral route from the external environment to the body of an average person per day (rate of entry). The model explains 77% of cases and determines that the probability of the disease development is increasing parabolically, which explains the fairly rapid increase in the number of cases of pathology detected with a small change in the concentration of the substance.

Figure 2 shows the obtained predictive nonlinear quadratic model of the dependence of the prevalence of leukopenia on the total hazard index for polychlorinated biphenyls, that is, the sum of the multiplicity of doses of polychlorinated biphenyls in the inhalation and oral routes of entry from the external environment into the body of an average person per day (intake rate).

It is believed that up to now, up to 80% of the total amount of polychlorinated biphenyls produced worldwide has been released into the environment,
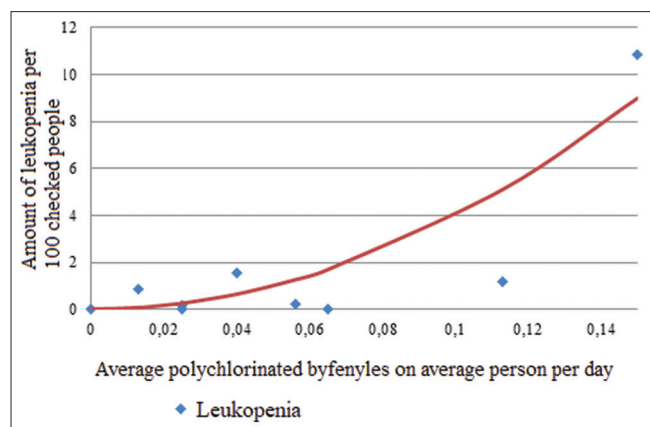

Figure 2: Predictive nonlinear quadratic model of leukopenia when polychlorinated biphenyls enter the body of an average person from the external environment per day

most of which has been released into fresh and marine waters. The formation of polychlorinated biphenyls from organochlorine pesticides in the upper atmosphere, under the influence of ultraviolet rays, is possible. Decomposition of organochlorine pesticides to the simplest biphenyls can also occur in seawater. Over many years of intensive use of polychlorinated biphenyls in industry in many countries around the world, huge amounts of these compounds have been released into environment and at the present time, contamination with these xenobiotics affects the entire biosphere. Along with organochlorine pesticides, polychlorinated

biphenyls are the most common products that pollute water in natural reservoirs.

We believe that leukopenia with subacute action of polychlorinated biphenyls is due to the depressive influence of the toxicant on bone marrow hematopoiesis, which is consistent with Mufazalova [11].

In the territory of the Aral Sea, sources of contamination with polychlorinated biphenyls of soil, bottom sediments, and surface waters of the Syr Darya River are highly mineralized, containing pesticides, collector-drainage water from rice, cotton irrigated massifs, and fields of various vegetable crops. Associated petroleum gas in the Kumkol field is not disposed of, contaminating soil and surface water. The growth of the number of pollutants is associated with the disaggregation of organizations and enterprises, the creation of new forms of ownership; commissioning of new mini-boiler houses, thermal power station, gas station, and oil industry.

The prognostic linear model of the dependence of the prevalence of atherosclerosis $Y = 1{,}1 * X + 14{,}45$ on the total index of cobalt hazard, that is, the sum of the multiplicities of doses of cobalt in the inhalation and oral route from the external environment to the body of an average person for a day describes 72% of the cases and determines that the probability of occurrence increases in direct proportion and linearly depending on the studied metal concentration, that is, with a change in X (cobalt) by 1, Y (the number of people with atherosclerosis) increases by 1.1, or by 1.1% of 100 examined. Most metals are essential, that is, vital. They are not synthesized inside of the body and must come from the environment. Many essential metals are needed in small doses – they are microelements that act as coordinators of enzymes, vitamins in the body: Cobalt, B12, chromium provide glucose tolerance, iron, and copper are involved in the formation of hemoglobin. Cobalt reduces the absorption of calcium and phosphorus [12]. At the same time, atherosclerosis is characterized by impaired lipid metabolism and the accumulation of insoluble precipitate of crystalline calcium phosphate on atherosclerotic plaques, even in the early stages of atherosclerotic lesions. The change in the physiologically necessary amount of calcium intake and its Vitamin D3 synergist both decrease and increase – leads to pathology [13]. Thus, the association of cobalt accumulation in atherosclerotic plaques is obvious (Figure 3).

A prognostic non-linear model of the dependence of the prevalence of bronchial asthma $Y = 0.25 * X$ with the influence of average annual wind speed indicators on the average human organism describes 73% of cases and determines that with an increase in the independent factor in 10 times, the dependent one will increase in 3 times. The climate of the studied territories is characterized by winds of the eastern, northeastern, and southern directions at a speed of 1–8 m/s; southeast, west, and southwest
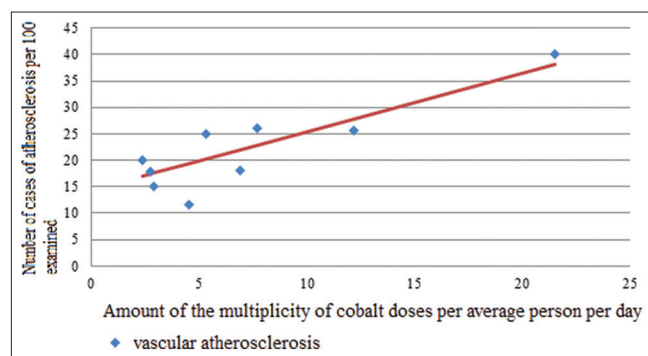
Figure 3: Predictive linear model for the development of atherosclerosis when cobalt enters the body of an average person from the external environment per day

directions at a speed of 1–5 m/s; west, east, and southwest directions at a speed of 1–10 m/s. The main characteristics of the wind are speed and direction (Figure 4).

When analyzing its effects on the bronchopulmonary system, it is difficult to pick out any
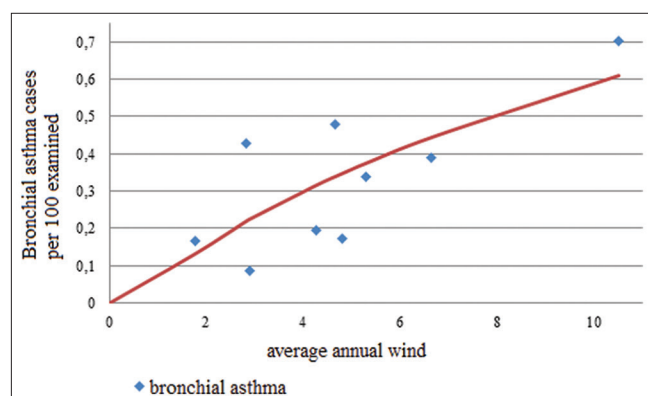

Figure 4: Predictive non-linear model of bronchial asthma with the influence of wind speed on the body of an average person

specific mechanisms. In the work of Melnikova [14], for patients with bronchial asthma, a relationship was found between the increase in exacerbations and the increase in wind speed (r = 0.73 (r = 0.90, p > 99%), p > 95%). Similar results were obtained by other authors, for patients with bronchitis and bronchial asthma, were established a relationship between exacerbations with atmospheric pressure, an increase in absolute and relative humidity, and a decrease in air temperature. The important role of meteo-factors in the formation of exacerbations of bronchial asthma is shown, in particular, the occurrence of seizures in women depends on the increase in wind speed (private correlation coefficient r = 2.26) [15]. A strong relationship between wind speed and atmospheric pressure in men in winter was found [16]. According to modern beliefs, bronchial asthma is an example of an environmentally caused disease, the nature and course of which is largely determined by the state of the environment. The factors of the external environment are considered

as trigger and inducer stimuli [17]. According to the WHO experts, the exacerbation of bronchial asthma is associated with unfavorable weather conditions, however, these factors have been subjected to a deep and systematic study. Nevertheless, the treatment plan for patients with bronchial asthma includes an item that provides for monitoring the state of the environment and correction of patient behavior in accordance with this [18].

As a result of the obtained reliably significant correlation and regression models at this stage was identified a preliminary estimated list of four diseases that can be included in the list of ecologically dependent non-infectious diseases at the population level:

1. Anemia, which develops when the sum of the multiplicities of doses of mercury is received with an inhalation and oral route from the external environment to the body of the average person per day (rate of entry).

2. Leukopenia, which develops on the receipt of the sum of multiplicities of doses of polychlorinated biphenyls with an inhalation and oral route from the external environment to the body of an average person per day.

3. Atherosclerosis, which develops when the sum of the multiplicities of doses of cobalt that comes from an inhalation and oral route from the external environment to the body of an average person per day.

4. Bronchial asthma, which develops under the influence of average annual wind speed indicators on the body of the average person.

During the medical examination by a therapist from 6501 examined people, in nine inhabited areas of the Aral Sea region, anemia was detected in 1711 people (26.3%), leukopenia in 115 persons (1.8%), atherosclerosis in 1802 people (27.7%), and bronchial asthma in 31 people (0.5%). However, it should be noted that during construction of models at this stage, we used a linear and non-linear dependence of the construction of predictive models with a given level of reliability of 95%. In our analysis, obtained models describe from 72 to 77% of cases. Therefore, it was necessary to build models that would meet 95% of the level of reliability.

At the next stage, a logistic analysis of the data was conducted to determine presence or absence of significant effect of environmental, biological, and social factors on the development of the disease at the individual level. The study was conducted on individual potential doses of multicenter chemicals that enter the human body for a certain period of residence (accumulation of chemicals in the body for a certain time) in the region. This analysis is the most in-depth and complex, however, as a result, it gives information on the evaluation of the probability of the disease development from a wider range of components at the individual level. As a result of the obtained reliably significant results of regression

logistic analysis, we have obtained a model for the development of vascular arteriosclerosis, depending on several factors for separate individuals:

Where, Y is the probability of the development of the disease when exposed to factors: X1 – age, X2 – blood cholesterol, X3 – triglyceride levels in the blood, and X4 – cobalt accumulation in the body of the individual during their residence in the region.

$$Y = \frac{\exp(-2.2567 + 0.0089 * X_1 + 0.0084 * X_2 + 0.0081 * X_3 + 0.0571 * X_4)}{1 + \exp(-2.2567 + 0.0089 * X_1 + 0.0084 * X_2 + 0.0081 * X_3 + 0.0571 * X_4)}$$

Obviously, the development of arteriosclerosis of blood vessels is due to age, lipid metabolism, and the effect of cobalt on the cardiovascular system of the organism [12], [19], [20]. Moreover, taking into the account values of the investigated parameters and the obtained equation coefficients, it can be concluded that the age of the individual has more significant effect on the development of arteriosclerosis of the vessels, then one of the increases in the dose of cobalt, and the aggravating factor is the violation of lipid metabolism in the body. The increase in cobalt by 5 units leads to an increase in probability by 3%, the chance increases by 1.33 times. All the factors are related to the probability in direct proportion, that is, as the value of the factor increases, the probability value increases. We also obtained a model for the development of anemia, depending on several factors for individual individuals, which had the following form:

$$Y = \frac{\exp(1,062 + 0.196 * X_1 + 0.035 * X_2)}{1 + \exp(1,062 + 0.196 * X_1 + 0.035 * X_2)}$$

Where, Y is the probability of the development of the disease under the influence of factors: X1 – quality of nutrition (1 – good, 2 – satisfactory, and 3 – poor) and X2 – accumulation of mercury in the body of an individual during their residence in the region.

It is obvious that the development of anemia is connected to the quality of nutrition and the cumulative effect of mercury in the body of the individual on the hematopoietic system of the body. Moreover, taking into account, the values of the investigated parameters and the obtained coefficients of the equation, it can be concluded that the quality of food consumed by an individual exerts a more significant influence on the development of anemia, and the accumulated amount of mercury in the body is an aggravating factor. The increase in mercury per unit leads to an increase in probability by 1%, the chance increases by 1.03 times. Accumulation of mercury is associated with probability of the development of anemia in direct proportion, that is, as the value of the factor increases, the probability value increases [21].

As a result of the obtained reliably significant results of regression logistic analysis, the proposed list

of ecologically dependent diseases decreased at this stage to two nosologies: Anemia and arteriosclerosis of blood vessels.

When analyzing the data obtained by logistic regression, no statistically reliable results were obtained, this suggests that at the moment, it was not possible to identify a factor that allows constructing a prognostic model for the emergence of the remaining two nosologies (leukopenia and bronchial asthma) at the individual level among the inhabitants of the Aral Sea region.

Conclusion

Health reflects the state of the ecosystem as a whole; it is a generalized indicator of the quality of the habitat and its impact on people's livelihoods. The state of health, as an ecological-pathological issue, is relevant in the last decade and the assessment of the role of adverse effects on the human body related to environmental pollution is a major task of medical science at the present stage.

At the present stage, public health is determined by the level of environmental safety and disease prevention. About 80% of contemporary human diseases are the result of environmental stress. There are practically no areas where the problems of medical ecology do not sound unsettling, and in the conditions of environmental ill-being, the environmental impact on health is increased to 50% or more. It was noted that the reserves for reducing mortality and increasing life expectancy lie in solving the problem of limiting the impact of unfavorable environmental factors.

The enormous social and economic importance of this problem dictates the need for its timely solution, which will allow not only to justifiably reduce sickness rate but also to manage the risks of diseases developing due to environmental factors, and to make timely both medical and management decisions.

Thus, our multidimensional statistical analysis (correlation, linear and non-linear regression, and logistic) allows us to determine in stages the presence of the influence of the environmental factor on the development of a particular nosology and determine the significance of this influence, and also to estimate the prognosis for the increase in sickness rate with an increase in the level of the environmental factor.

Presented results on the sickness rate of the Aral Sea population require, first of all (in addition to preventive measures and rehabilitation) active actions aimed at improving the environment and environmental safety of the population, as well as unifying the list of health indicators for the population and environment, for subsequent medical and social activities (privileges,

guarantees, compensation payments, and specialized targeted medical assistance).

When carrying out medicodiagnostic studies, regional features have not been identified, but leading nosologies from the main classes of diseases have been identified throughout the Aral Sea region.

As a result of the multivariate statistical analysis, two nosologies have been identified that can be included in the proposed list of ecologically dependent diseases depending on several factors: Anemia (quality of nutrition and accumulation of mercury in the body during the stay) and arteriosclerosis of the vessels (age, cholesterol and triglycerides in the blood, and accumulation of cobalt in the body during residence).

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