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Study of genetic effects of radiation pollution from contaminated territories on biota and human

Abstract. An important element of the set of works to determine the degree of impact of radiation contaminated territory on the environment and public health is the conduct of ecological-genetic and medical-biological research in the region. Current publication is based on the results of scientific research to analyze the current state of the habitat in radiation-contaminated territories. Genetic impact of the combined effect of radiation and non-radiation factors, unlike other mutagens, have not been studied sufficiently, and the results of this kind of research are rather contradictory. Industrial factors, the forceful action of full elementary evolutionary processes (mutational process, migration, isolation, etc.), can lead to qualitative transformations of the gene pool of populations. The study of chromosomal aberrations in natural populations and the human body acquires a special practical and theoretical significance related to the influence of factors of the changing habitat. Research data obtained using modern physico-chemical (AA-spectrometry, radiology), cytological and molecular-genetic methods are presented with a complex of test systems in order to fully assess the effectiveness of the combined action of radiation and non-radiation factors. Observations in the field and lab facilitate establishing a previously unknown fact that complexes of soil animals with chronic irradiation with doses of 0.5-20 mSv/day experience clearly recorded oppression. Especially sensitive are earthworms *Eisenia fetida*. The quantitative dependence of the spectrum of structural and numerical aberrations of chromosomes was studied. The frequency of cells with chromosome aberrations averages 2.4%. Both structural (93.6%) and numerical aberrations (6.4%) of chromosomes were revealed. Among the cells with chromosome structure disorders, chromosomal type aberrations (67.04%) prevailed over chromatid (32.95%), which indicates a predominant radiation exposure.

Key words: cytogenetic, ecology, chromosome, population, molecular genetic, radiation genetic, earthworms, polyheta.

Introduction

In the past decade and a half, the concept of radiation-induced genome instability has been shaped and intensively studied. According to the literature, this phenomenon is the emergence of de novo multiple genetic changes (gene or chromosomal) non-clonal in approximately 10-30% of descendants of irradiated cells that survived after irradiation [1-3]; observed after irradiation not only at high, but also so-called low doses (200 cSv or less) of radiation [4; 5].

Today the problem of assessing the environmental hazard and the genetic efficacy of the combined action of low doses of mutagens, such as natural radionuclides and heavy metals, have a complex effect on living objects. The genetic effects of the combined action of these factors, unlike other mutagens, have been studied insufficiently, and the results of such studies are rather contradictory so-called anthropogenic factors, intensifying the action of all elementary evolutionary processes (mutational process, migration, isolation, etc.), can lead to qualitative transformations of the gene pool of populations [4; 6; 7]. Therefore, it

becomes necessary to study the effects of chronic exposure to ionizing radiation on natural populations in order to fully assess the effectiveness of the combined effect of radiation and non-radiation factors that are difficult to reproduce in the laboratory. The study of chromosomal aberrations in natural populations of organisms acquires a special significance in connection with the influence of factors of a changing habitat.

The growing development of the extractive industry in Kazakhstan requires further intensification of studies of migration patterns in natural ecosystems of heavy natural and artificial radionuclides, as well as the biological effects of ionizing radiation at the population and biogeocenotic levels.

The purpose of this publication – based on the results of scientific research to analyze the current state of the habitat in radiation-contaminated territories, namely, to give an ecological-genetic assessment of the consequences of radiation effect on biota and human.

Materials and methods

Conducted conventional cytogenetic (micronucleus analysis [8-11] in peripheral blood cells of humans). Cytogenetic analysis and photography were performed under a microscope (MicroOptix, Austria, 2013) [12]. In persons living in settlements adjacent to the source of pollution was carried out in clinics from the phalanx of the upper extremities (fingers), observing the principles of antiseptics. Blood smears were made on the prepared glasses according to the method for micronuclear analysis. Statistical processing of the results was carried out by conventional methods of biostatistics in biology and medicine [11; 13]. Molecular genetic RAPD-PCR analysis [14; 15].

A set of reagents QIAamp DNA Mini Kit (Qiagen, USA) was used for genomic DNA extraction.

Quantitative and qualitative assessment of the isolated DNA was performed using DNA photometer (Biofotometer Plus, Eppendorf, Germany) and electrophoretic analysis. PCR mixture with Taq polymerase, PCR Master Mix (Thermo Scientific, Lithuania) was used for DNA amplification of the studied and control samples. Amplification was performed automatically on the programmable amplifier Master cycler nexus Gradient (Eppendorf, Germany) using the Hot-start PCR method. Polymerase chain reaction was performed with ten-membered oligonucleotide primers synthesized in RSE Institute of General genetics and Cytology (Kazakhstan) on synthesizer ASM-800 of Bioset (Russia). The PCR reaction was carried out in the following temperature regime: initial denaturation at 94 °C for 2 min, 40 cycles consisting of four stages, including 45 sec at 92 °C, 30 sec at 37 °C, 15 C at 45 °C and 2 min at 72 °C. The reaction is performed during 10-minute elongation stage at 72 °C. Negative reaction control (contamination test) contained a reaction mixture without DNA addition.

Results and discussion

The content of γ -emitting radionuclides and radioactivity of the test objects. Observations and experiments in environment made it possible to establish a previously unknown fact that, under chronic irradiation with doses, such as 0.5-20 mSv/day, the complexes of soil animals undergo clearly recorded inhibition [11]. Particularly sensitive are earthworms [16].

As a result of determining the total level of total radioactivity of the test objects under study, the background level of β -radiation was detected in representatives of the ringed worms – *Nereis diversicolor* and *Eisenia fetida* (Table 1).

Table 1 – The total level of β -radiation test objects

Sample title	β -radiation, 1 / min * cm ² (SD± SE)	Sample title	β -radiation, 1 / min * cm ² (SD± SE)	Sample title	β -radiation, 1/ min * cm ² (SD± SE)
<i>Abramus brama</i>	0.88±0.003	<i>Unio pictorum</i>	0.86±0.004	<i>Nereis diversicolor</i>	1.24±0.005
<i>Sander lucioperca</i>	1.41±0.007	<i>Dreissena polymorpha</i>	0.86±0.003	<i>Eisenia fetida</i> (Earworms)	8.81±0.021
<i>Sander bersh</i>	1.42±0.007	<i>Nereis diversicolor</i>	6.24±0.021	<i>LD (limited Dose)</i>	5

Basically, the results on the content of γ -emitting radionuclides in test objects correlate with this indicator. Only in this case, the results

of all measurements are higher or close to the Limiting Dose (LD) with the exception of Cesium-137 (Table 2).

Table 2 – The content of γ -emitting radionuclides in test objects

Sample	The activity of radionuclides			
	Bk/kg		(SD \pm SE)	
	Cs-137	Ra-226	Th-232	K-40
<i>Abramus brama</i>	64.5 \pm 0.5	155 \pm 0.4	119 \pm 0.5	1296 \pm 12.3
<i>Sander lucioperca</i>	63 \pm 0.4	123 \pm 0.4	70 \pm 0.4	1124 \pm 12.4
<i>Sander bersh</i>	65 \pm 0.4	164 \pm 0.5	124 \pm 0.4	1300 \pm 11.9
<i>Unio pictorum</i>	109 \pm 0.5	31 \pm 0.3	43 \pm 0.4	625 \pm 9.9
<i>Dreissena polymorpha</i>	76 \pm 0.3	32 \pm 0.5	45 \pm 0.4	624 \pm 9.8
<i>Nereis diversicolor</i>	111 \pm 0.5	100 \pm 0.3	100 \pm 0.3	850 \pm 9.8
<i>Eisenia fetida</i>	125 \pm 0.4	185 \pm 0.6	169 \pm 0.5	1332 \pm 12.5
<i>Nereis diversicol</i>	89 \pm 0.5	29 \pm 0.4	40 \pm 0.3	594 \pm 12.3
Limiting Dose	370	32	45	700

According to the data presented in the Table 2, the activity of Cesium-137 in all test objects is significantly lower than LD. The activity of Potassium-40 in mollusks and gadflies is less than the LD, while in other organisms it is much higher. The activity of Radium-226 and Thorium-232 in the tissues of the *Sander bersh*, *Dreissena polymorpha* are within the LD. Therefore, of all studied fish species, pike perch accumulates less radionuclides, although as an active predator, this species should receive more radionuclides from food. Apparently, low activity are associated with the presence of the molecular mechanism for removing radionuclides from the body. Among invertebrates, the number of studied radionuclides (except for cesium) is significantly higher than the LD. In species more closely contacting with the soil and the ground: the *Eisenia fetida* earthworm and the polychaetes (*Nereis diversicolor*). Apparently, this is due to the subsidence and accumulation of radionuclides at the bottom and in the coastal soil, from which they enter the body of the above species with food. The presence of high activity of Radium-226 in the studied objects is explained by the presence of this isotope in all mountain and sedimentary rocks. Accordingly, this radionuclide always accompanies the pollution of the mining industry. Being in a dissolved state in water, radium forms the so-called secondary materials, which is part of the salts of lead, calcium, barium, etc. Referring to the group of alkaline earth

metals, radium is an analogue of the elements of biological accumulators of copper and magnesium. Thorium-232 and Potassium-40 are low-toxic radionuclides, but at high activity that were found in invertebrate test objects, these isotopes contribute to the irradiation of organisms. Thus, on the basis of data on the content of radioisotopes in the body of hydro species, one can judge about the unfavorable radiation situation in the waters of the Northern Caspian. Of particular concern are the large concentrations of radionuclides in earthworms, which indicates that the soil in the studied area is radioactively contaminated. Accordingly, it can be assumed that radionuclides enter the food products of the region's population not only with commercial fish, but also along the following chain: soil – plants – livestock – meat and dairy products. It is these groups of organisms that can be recommended as bio indicators of radioactive contamination of the soil.

The effect of radiation on the body of animals and humans. Assessing the impact of factors that pollute the human environment, genetic consequences should be included. Among the factors leading to chromosome abnormalities, ionizing radiation is of particular importance, since all types of radiation cause chromosomal aberrations in human germ cells and somatic cells [17].

Cytogenetic analysis in rodents. Catching rodents big gerbil and small *R. opimus* was carried out

with live bait from adjacent to the tailing dump areas and were taken as control from the Balkhash zone. Following the standard (conventional) methods cytological preparations for chromosome analysis and samples for DNA extractions were conducted accordingly (molecular genetic research).

To establish the mutagenic potential, a test was used to account for chromosomal and genomic mutations in bone marrow cells. The obtained data on the assessment of the potential mutagenic hazard of contamination of the tailing dump and surrounding areas with oil and petroleum products using as a test object of big gerbil (*R. opimus*), showed that in all four points of the rodents studied, there are changes in both the frequency of aberrant cells and types of chromosomal abnormalities.

Cytogenetic studies of large gerbils (*R. opimus*). The karyotype of the great gerbil (*R. opimus*) consists of 40 chromosomes (Figure 1). 8th chromosome is a large submetacentric or metacentrics. 15 pairs of chromosomes gradually decrease in size and form are submetacentric or metacentric. One pair of chromosomes is the smallest in size and morphologically they are acrocentric chromosomes.



Figure 1 – Karyotype of a big gerbil (2n=40)

The maximum values of the studied cytogenetic parameters were observed in heavily polluted areas. In animals caught near the tailing dump, the frequency of chromosomal aberrations in the bone marrow of the gerbil is $(5.03 \pm 1.3)\%$ at $t=3.83$; $p<0.003$, which exceeds the spontaneous level by 2.5 times. Rodents living in the neighborhood, in the adjacent territory to the tailing dump really detect individual variability in cytogenetic damage. The level of cytogenetic disorders in *R. opimus*, living in the surrounding area, 1.5 times lower than in rodents from the tailings. In the studied animals of the adjacent territory at a distance of 500 m (place 1, 2), the frequency of metaphase cells with aberrations was $(4.97 \pm 1.21)\%$ at $(t=2.58$; $p<0.01)$, 2,3 times higher than spontaneous level, and points 3.4 (1000 m) – $(4.05 \pm 1.02)\%$ at $(t=2.01$; $p<0.05)$, 1.5 times higher than the level of spontaneous chromosomal mutations.

The quantitative and qualitative composition of cytogenetic disturbances revealed in this work according to dislocation from the source of pollution in the studied points testifies to the presence of strong clastogenic effects of pollutants here. The studied mutagenic factors radionuclides, heavy metals and others are the cause of the high frequency of chromosomal mutations of *R. opimus* in the surveyed areas. However, it is difficult to say which of these mutagenic environmental factors caused the observed changes [18]. However, the revealed level of genetic disorders in wild rodents with appropriate extrapolation can be considered as the real maximum mutagenic effect of environmental factors in relation to people living in these areas [19-21].



Figure 2 – Chromosome of metaphase cell with terminal deletion in big gerbil

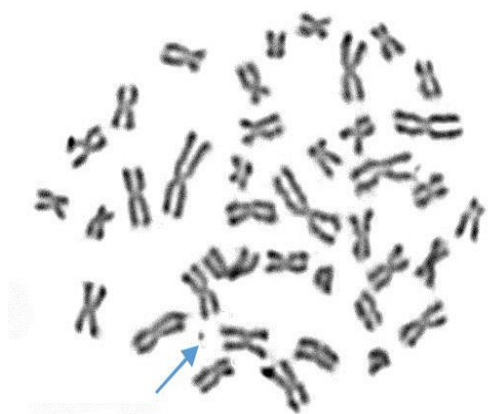


Figure 3 – Metaphase cell with diploid set of chromosomes ($2n=38$)

Chromosomal rearrangements play an important role in karyotype divergence and population adaptation in many animal and plant species, and there are differing views on the role of chromosomal polymorphism in natural populations.

Micronuclear test. We examined the inhabitants of the settlements adjacent to the source of pollution of the coastal zone of the Caspian sea, using a micronuclear test. Table 3 presents the results of micronuclear test of people living in settlements: the city of Aktau and towns: Mangystau-1 village, Mangystau-5 village, Baskuduk village and Akshukur village.

Table 3 – The amount of blood examined erythrocytes with micronuclei in patients

Place of observation	Quantity of patients	Number of analyzed erythrocytes, in thousands	Erythrocytes with micronuclea	
			Absolute number	% (SD± SE)
Control group	35	482.4	2	0.415±0.01
Industrial chemistry metallic plant, Aktau city	10	1819.622	2029	3.693± 0.35
Baskuduk village	5	1180.5	1037	1.224±0.07
Mangystau-5 village	5	1158.9	1057	1.225±0.06
Akshukur village	11	2368.3	1797.2	4.256±0.03
Mangystau-1 village	6	1235.6	1225	1.513±0.06

As follows from Table 3, the maximum frequency of cytogenetic disorders in persons living in the area of the Aktau (uranium enterprises) was detected in the age group up to 60 years and ranges from 0.199 – 0.287, which is slightly lower than the age group over 60 years – from 0.189 to 0.201, and the minimum frequency in children is 0.102.

According to this test similar results were obtained from residents of other settlements adjacent to the source of pollution (total residents – 33). In particular, residents of Baskudyk village have the highest frequency of cells with disorders MN found in children under the age of 5 years (0.236-0.244), and in the age group of 31-40 years it is slightly lower (0.175-0.193).

A sufficiently high frequency of cells with MN in the blood of the examined residents of Mangystau – 5 in the age group 30-45 years and ranges from 0.208-0.221, and in persons over 45 years within 0,197 was revealed. In persons living in the village of Akshukyr, the number of cells with MN is: in the group over 60 years in the range 0.163-0.184; in the

age of 50 years-from 0.196 to 0.204; in the group of 20-23 years-from 0.213 to 0.25; in children-0.228. The number of erythrocytes with micronuclei in the blood of the examined art. Mangystau-1, up to 30 years ranges from 0.196-0.255, and in the group over 50 years – from 0.184-0.198.

Many authors [8; 9; 11; 14] evaluated the micronucleus test as a convenient method of screening substances, allowing to quickly determine the presence or absence of cytogenotoxicity and mutagenicity of various compounds. Comparison of the results of this study with the literature data indicates the adequacy of the results obtained by us, that is, the induction of pollutants, in our case radionuclides and chemical contaminants, in human peripheral blood cells leads to violations of genome stability.

As follows from the analysis, a clear dependence of cytogenetic disorders on the micronucleus test (MN) from the age of the examined is not observed. In turn, there is an increase in the frequency of cells with cytogenetic disorders (MN), depending on the location of the village from the source of pollution,

in particular, the tail of the Koshkar-Ata. Thus, the greatest frequency is found in persons living in the area GHS Aktau and towns have Baskuduk, Akshukur that corresponds to the data of radiation ecological surveys of these territories.

Molecular genetic analysis of the population living in Mangystau region by DNA repair genes XRCC1 and XRCC3. To analyze the state of re-

pair systems of the organism in the inhabitants of Mangystau region, polymorphism of genes XRCC1 Arg194Trp (rs1799782) and XRCC3 Trp241Met (rs861539) were studied. A group of people living in Almaty region was used as a control. The results of electrophoretic analysis of restriction products after PCR-analysis are presented on Figures 4 and 5.

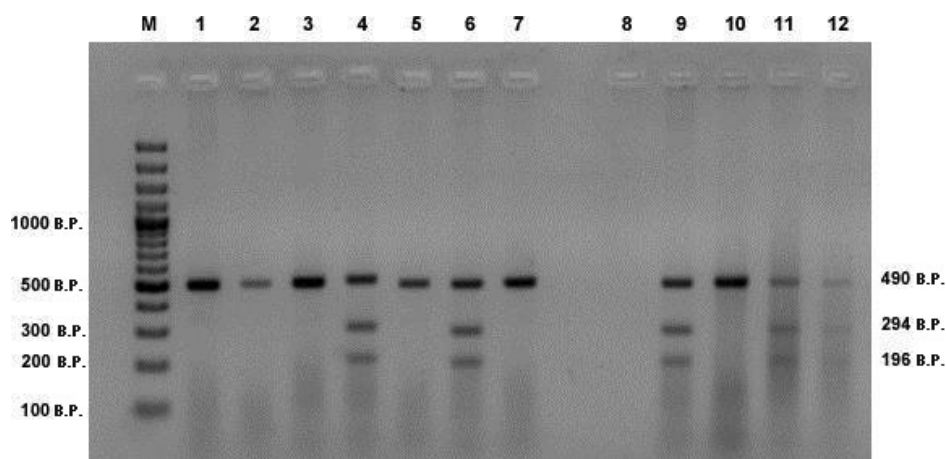


Figure 4 – Electrophoresis products in a polymorphic restriction site 194Arg/ Trp of the XRCC1 gene. Note: M: molecular DNA marker. Homozygotes by normal allele XRCC1 194 Arg/Arg – 1, 2, 3, 5, 7, 10 heterozygotes XRCC1 194 Arg/Trp – 4, 6, 9, 11, 12

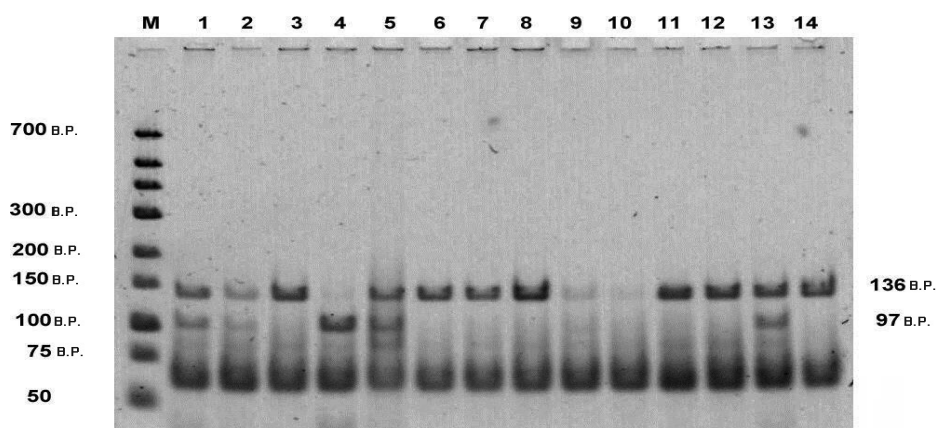


Figure 5 – Electrophoresis products of the restriction in the polymorphic site 241 Thr/Met XRCC3 gene. Note: M: molecular DNA marker. Homozygotes by normal allele XRCC3 241 Thr/Thr – 3, 6, 7, 8, 9, 11, 12, 14 heterozygotes XRCC3 241 Thr/Met – 1, 2, 5, 13 homozygotes by mutant allele XRCC3 241 Met / Met – 4

The research method “case-control” is an effective method for epidemiological assessment of the relative effect (hazard ratio). The most important and crucial point of this study is the formation of groups for analysis.

As a criterion, we considered living in an ecologically unfavorable region of Kazakhstan near the Koshkar-Ata tailing dump.

The case study group was formed from representatives living in the Mangystau region (95 people) (Table 4).

Table 4 – Frequencies of polymorphic alleles of XRCC1 Arg194Trp and XRCC3 Trp241Met genes

gene	Alleles of gene	Allele frequency			
		Group “case”	Group “control”	Data NCBI/NIH	
				Asian Populations	European Populations
XRCC1 Arg194Trp	Arg	0.95	0.951	0.761 – 0.711	0.948 – 0.908
	Trp	0.205	0.049	0.239 – 0.289	0.052 – 0.092
XRCC3 Trp241Met	Thr	0.874	0.837	0.942 – 0.889	0.571 – 0.500
	Met	0.126	0.163	0.058 – 0.110	0.429 – 0.500

The mean age in this group was 35.16 ± 1.16 years. The gender composition of the experimental group is 85% of women and 15% of men. The selection of the control group was based on the analysis of the database of biological samples (personal data and clinical examination data) of the laboratory of molecular genetics of the Institute of General genetics and Cytology, Almaty, Kazakhstan. Clinical material from these people was collected in 2008-2014 in the course of scientific projects of the Institute of genetics and Cytology, Almaty, Kazakhstan. Blood and DNA samples are stored in the Biological bank at $-20\text{ }^{\circ}\text{C}$ and $-80\text{ }^{\circ}\text{C}$. The control group included healthy individuals living in ecologically favorable areas of Almaty region. The control population of conditionally healthy donors was selected in the maximum possible accordance with the personal data of the surveyed group according to age and gender criteria. A total of 92 peripheral blood samples were collected for the control group. The mean age in the control group was 36.99 ± 1.02 years. The gender composition of the control group is 78% women and 22% men. The Student's t-test was used to determine the statistical significance of the differences in the studied samples. The differences were considered to be significant, starting with $p < 0.05$, that is, when the probability of differences was equal to or greater than 95%. The analysis of the experimental and control cohorts showed that the differences of the compared values in Table 4 are not statistically significant, since in all cases $p > 0.05$.

According to international experts, the threshold dose for deterministic (acute, immediate) effects is 0.2 Gr. Therefore, at lower doses, the only type of radiological consequences are stochastic (remote) effects – oncological and hereditary diseases. Considering the range of such small doses, it is more correct to speak of low radiation levels (LRL), implying not only the absolute value of the dose, but also the low intensity of radiation exposure – a low dose rate [4; 5].

All information about the long-term effects of LRL in humans was obtained either by extrapolation of experimental data on animals, or as a result of direct radiation-epidemiological studies. The main source of the latter is the data of acute single exposure of high dose rate in atomic catastrophes (Hiroshima and Nagasaki, Chernobyl, Fukushima, and other). The quantitative parameters of the probability of development of the stochastic effects of an LRL are characterized by a number of important radiobiological parameters. However, due to the lack of specific data, these effects have not been accurately determined to date and remain a subject of discussion.

If we consider that the human genome contains up to 100,000 genes, then the potential number of possible mutations, as well as various radiation genetic disorders, can be enormous, especially since there are no specific radiation mutations. Irradiation only increases the likelihood of the manifestation of all categories of hereditary disorders that occur in natural conditions – Mendelian, chromosomal and multifactorial [15].

In the process of evolution of the species under consideration, such a mechanism in humans has reached a maximum, ensuring the leveling of genetic effects in LRL. Without a doubt, the validity of the proposed mechanism needs experimental confirmation. The latest data on the assessment of the minimum significance of radiation genetic risk and provide grounds for a confident conclusion that this risk, as a factor taken into account when regulating LRL has firmly shifted to a much less significant place compared to radiation-carcinogenic risk. In this regard, there are two independent, albeit interrelated research aspects of radiobiology: basic research – the study of the effects of ionizing radiation at the molecular and cellular levels and applied – recording effects at the organismic and population levels to assess radiation safety [22].

It is important to keep in mind that it is impossible to evaluate the response of the whole organism in the field of an LRL under the conditions of a variety of other factors, based solely on radiobiological knowledge of the effects at previous levels of biological organization. The fact is that with the modern possibilities of registering the most diverse indicators of the action of radiation, the dose ranges at the cellular and organismic levels are very different. If this is not taken into account, then there are conclusions about the harm to human health of radiation in the range of so-called “ultra-low” doses. Knowledge of the effects of radiation on humans with an LRL (low exposure levels – up to 100 background levels) are given by radiation epidemiological studies.

Information on the effect of LRL for the population of Kazakhstan needs to develop a separate program in relation to the specific conditions of uranium mining activities, guaranteeing the technical conditions of radiation safety, ensuring compliance with radiation hygiene standards for external and incorporated exposure to different types of ionizing radiation. This program should be based on the data of modern scientific studies, taking into account the limits of applicability and significance for radiation safety of a person of relevant results at the molecular and cellular levels. The relevance of such a work program is evidenced by the materials of the 55th session of UNSCEAR, held from May 21 to 25, 2007 in Vienna (Austria) [13]. As was noted at this session, the exposure of occupational groups and the risk to the population of adjacent areas in the mining industry is a particular problem today, when very large amounts of waste rock are formed, containing even low concentrations of ^{238}U and ^{232}Th and their decay products. Although, on average, radiation doses of miners are insignificant, amounting to several micro-Sieverts (mSv) per year, in some cases they can reach several milli-Sieverts, which already represents a radiation risk [17; 24]. Japanese scientists studied the chromosomes in the blood leukocytes of people exposed to the atomic bombardment of Hiroshima and Nagasaki, and showed that chromosomal rearrangements are characteristic of human leukocytes even after at least three decades after the explosion.

When conducting cytogenetic analysis of leukocytes of people who received radiation, it turned out that all irradiated people had leukocytes, among which more than 10% had chromosomal rearrangements [6; 24-26]. The results of epidemiological and experimental studies indicate the induction of genome instability in the offspring of parents exposed to ionizing radiation. This genomic instability is pri-

marily manifested by an increase in the rate of mutation and an increase in the risk of tumor and other pathologies in the offspring [8; 17]. Studies of many scientists have shown that the phenomenon of genomic instability is found in the populations of distant descendants irradiated. At the same time, the appearance of different types of chromosomal aberrations in cells and an increase in the overall level of chromosome abnormalities are noted. It was revealed experimentally that prolonged low-intensity irradiation can cause a significant increase in the number of cells with chromosomal aberrations and reciprocal chromosomal translocations not only in the exposed but also in their descendants of the first [16; 25; 26], and especially the second generation. To date, cytogenetic studies of the patterns of action of a wide variety of gene toxically agents and accumulated a sufficiently large amount of factual material on the dynamics of the yield and diversity of types of chromosomal aberrations, which are difficult to replicate double-stranded DNA breaks. The work of many scientists [16; 26] is devoted to the study of new molecular mechanisms of the formation of cytogenetic damage.

Conclusion

On the basis of data on the content of radioisotopes in the body of hydro species (fish's, mollusk's, polychaetes), one can judge about the unfavorable radiation situation in the waters of the Northern Caspian. Of particular concern are the large activity of radionuclides in body of polychaetes and earthworms, which indicates that the soil in the studied area is radioactively contaminated. It is these groups of organisms that can be recommended as bio indicators of radioactive contamination of the soil.

The studied mutagenic factors radionuclides, heavy metals and others are the cause of the high frequency of chromosomal mutations of wild mouse (*R. opimus*) in the surveyed areas. The level of cytogenetic disorders in *R. opimus*, living in the surrounding area, 1.5 times lower than in rodents from the tailings. In the studied animals of the adjacent territory at a distance of 500 m (places 1, 2), the frequency of metaphase cells with aberrations was $(4.97 \pm 1.21)\%$ at $(t=2.58; p<0.01)$, 2,3 times higher than spontaneous level, and points 3.4 (1000 m) – $(4.05 \pm 1.02)\%$ at $(t=2.01; p<0.05)$, 1.5 times higher than the level of spontaneous chromosomal mutations [18]. However, the revealed level of genetic disorders in wild rodents with appropriate extrapolation can be considered as the real maximum mutagenic effect of environmental factors in relation to people living in these areas.

As next test-system for examined the inhabitants of the settlements adjacent to the source of pollution of the coastal zone of the Caspian sea was used a micro-nuclear test. Was obtained the maximum frequency of cytogenetic disorders in people living in the area of the Aktau (uranium enterprises) was detected in the age group up to 60 years and ranges from 0.199 – 0.287, which is slightly lower than the age group over 60 years – from 0.189 to 0.201, and the minimum frequency in children is 0.102. According to micronuclear test similar results were obtained from residents of other settlements adjacent to the source of pollution (total residents – 33). In particular, residents of Baskudyk village have the highest frequency of cells with disorders (MN) found in children under the age of 5 years (0.236-0.244), and in the age group of 31–40 years it is slightly lower (0.175-0.193). A sufficiently high frequency of cells with MN in the blood of the examined residents of Mangystau – 5 in the age group 30–45 years and ranges from 0.208-0.221, and in persons over 45 years within 0,197 was revealed. In persons living in the village of Akshukyr, the number of cells with MN is: in the group over 60 years in the range 0.163-0.184; in the age of 50 years-from 0.196 to 0.204; in the group of 20-23 years-from 0.213 to 0.25; in children – 0.228. The number of erythrocytes with micronuclei in the blood of the examined art. Mangistau-1, up to 30 years ranges from 0.196-0.255, and in the group over 50 years – from 0.184-0.198.

The results of molecular genetic investigation by electrophoretic analysis of restriction products after PCR-analysis the state of repair systems of the organism in the inhabitants of Mangystau region polymorphism of genes XRCC1 Arg194Trp (rs1799782) and XRCC3 Trp241Met (rs861539) was obtained. The study of the distribution of genotypes in people living near radiation-contaminated areas of Western Kazakhstan showed that the distribution of the mutation genotype (TRP/TRP) gene XRCC1 Arg194 total-1.7%, and the gene XRCC1 arg 399Gln(English/English) – 8.6%, XRCC3Thr 241Met – (Met/Met)-7% and XPD751Gln – 5.2%-contaminated areas of Western Kazakhstan showed that the distribution of the mutation genotype (TRP/TRP) of the gene XRCC1 Arg194 total – 1.7%, and the gene XRCC1 arg 399gln(ENG/ENG) – 8.6%, xrcc3thr 241met – (Met/ Met) – 7% and XPD751Gln – (Gln/Gln) – 5.2%. The research method “case-control” is an effective method for epidemiological assessment of the relative effect (hazard ratio). The most important and crucial point of this study is the formation of groups

for analysis. As a criterion, we considered living in an ecologically unfavorable region of Kazakhstan near Koshkar-Ata tailing dump. In order to explain the possible causes of surprising interspecific quantitative differences in the manifestation of radiation-genetic consequences.

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