THE HEALTH EFFECTS OF THE HUMAN VICTIMS OF THE CHERNOBYL CATASTROPHE

Collection of scientific articles, 2006

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Greenpeace greatly appreciates the noted submissions of the contributing authors of this report and the contributions of all those individuals that made this publication possible.

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This collection of articles was produced to advance the knowledge of information available in the scientific community concerning the effects on human health of the victims of the infamous Chernobyl catastrophe. This collection represents articles written by scientists who are specialists in their respective fields and have been working on Chernobyl health related issues for many years.
These Chernobyl related human health articles provide the reader with information regarding health impacts on the population in the most contaminated territories (Ukrainian, Russian, and Belarussian) and also includes the regions of some other affected European countries (Austria, Greece). The following articles were written in the 2006, with the exception of the article of August 2005 from Associate Professor Tilman Ruff.

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SOME ASPECTS OF THE HEALTH OF CHILDREN BORN AFTER THE CHERNOBYL CATASTROPHE

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Almost 20 years have passed since the large-scale man-made catastrophe at the Chernobyl nuclear power plant. We cannot forget this event as a result of the negative trends that we see in the overall health of different sectors of the Ukrainian population, and also because of the biological and medical effects of permanent exposure to low-dose radiation on living organisms, which have been discovered.

Research has shown that if a female organism is exposed to chronic or acute radiation in anamnesis, then her placenta accumulates radionuclides during pregnancy. Disturbances in blood circulation and dystrophic and involutive changes in the placenta are dose-related [1,2].

It has been proved that radionuclides accumulate in the placenta then penetrate into the fetus and cause fetal dysplasia resulting in structural and functional abnormalities in different organs and systems, including the skeletal system.

As a result of collaborative research with colleagues from the physics laboratory of Bristol University (under leadership of D. Henshaw) we were able to ascertain that the average level of uptake of alpha radionuclides in organs of deceased newborns is: ribs 1.01±0.24 Bq/kg, the internal part of spinal column 0.67±0.02 Bq/kg, dental germs 0.4±0.02 Bq/kg, liver 0.39±0.05 Bq/kg, tubular bones 0.32±0.02 Bq/kg, spleen 0.205±0.03 Bq/kg, thymus 0.14±0.015 Bq/kg (Lukyanova 2003, Lukyanova et al. 2005). [1,2].

Even these low doses can be significant for the continually growing and developing foetus.

It is known that new cells during their development are more sensitive to radiation than older cells. Because of higher atomic mass incorporated alpha radionuclides affect toxically osseous tissue and change metabolic processes.

Morphological examination of the osseous tissue revealed localized changes in blood circulation (dystrophic changes in the arteriolar walls), reduction in the number of osteoblasts, dystrophic changes to osteoblasts and osteoclasts which were smaller than usual and settled irregularly in 20% of cases. This proves development of dysplastic processes in osseous tissue of fetus. The apparent imbalance in the ratio of osteoblasts to osteoclasts would trigger destructive processes in the developing osseous tissue. This allowed to assume that structural and functional changes registered in osseous tissue of babies born after Chernobyl APP accident develop already on prenatal stage [1,2].

As the highest levels of radionuclide incorporation were found in the foetal osseous system and in the dental germs, we decided to study the status of the skeletal system. The study showed that children born after the Chernobyl accident underwent qualitative changes to the skeletal system structure from an early age. These changes were of mixed character and osteofibromatosis, osteopenia and osteoporosis were particularly apparent.

A trend of ongoing systemic dysplastic processes was found in children that were born after the Chernobyl accident, in chondral tissue (significant level of dysmesenhimoses, skeletal dysmorphism), osseous tissue (dysplastic osteofibromatosis, systemic hypoplasia of dental enamel), conjunctive tissue (significant levels of microangiopathy, fibrosis of arterioles and venules of liver, spleen, retina and mitral valve prolapse). These changes could indicate mesenchymal dysplasia, and variations in results related to groupings and gender in the conjunctive, chondral and osseous tissues could indicate heterogenic radiosensitivity of the children examined [3].

Most children in the group were found to have microcirculation disturbance and hypoxia , which initiate dystrophic processes in the osseous tissue (microangiopathies, lipid peroxidation, changes to the structural and functional properties of cell membranes and erythrocyte ultrastructure, a decrease in osmotic resistance and endurance of erythrocytes and lowering of their 2,3-diphosphoglycerate content).

The research showed changes in the normal development of the skeletal system: changes in structural and functional properties of osteoblasts, remodulation processes in osseous tissue and abnormalities in the formative phase of its mineralization combined with destruction of the osseous tissue.

The research also showed that the foetal teeth of the children examined incorporated α-radio nuclides irregularly and that this changed the rate at which teething took place. Specifically, it led to earlier second dentition followed by impairment of the condition of the periodontal tissue and early development of dental caries. This represents premature biological ageing of these tissues, and the changes to the osteogenesis process began as early as during the period of intrauterine development.

13.2% of children in the group lagged behind kids of the same age from "supposedly clean" regions in terms of biological age, and 46.9% of children overtook their contemporaries. This could indicate the existence of an early ageing process in children that were born after the Chernobyl accident [2-5].

It was demonstrated that exposure to radiation leads to the activation of osseous tissue remodeling processes. These processes cannot be related to so-called radiation "hormesis", as they have a negative impact upon the quality of neogenic osseous tissue and attainment of osseous mass peak in children born after the Chernobyl accident [2,3].

Based upon the data obtained from this group of children, research was conducted into the overall health and status of the skeletal system in the "first generation"- offspring of women who were acutely exposed to radiation in their childhood and adolescence as a result of the Chernobyl accident.

Indices regarding the antenatal and intranatal periods help to determine the child's future health status in many respects. It was established that women who received thyroid gland irradiation in their childhood experienced complications in pregnancy more frequently than women of the same age but from "supposedly clean" regions, and the complications were more likely to occur when the foetus carried was female.

Irradiation in childhood negatively influenced reproductive health and resulted in a very low pregnancy rate (25.8%). Variability depends on radiation dose (decreasing from 41% in those who received lesser doses to 12.5% in those who received large doses of radiation in childhood). This indicates the extreme radiation sensitivity of the female reproductive system in childhood and adolescence [6].

The high radiation sensitivity of the osseous system is indicated not only by the significant frequency of developmental problems with the skeletal and dental system, but also the 3-fold increase in the rate of development of osteoporosis in the women examined, which was clinically manifested as bone fractures before pregnancy in 11.1% of women (4.2% in the control group). A significant rate of nonspecific manifestations of hypocalcaemia during pregnancy- sural cramps, ossalgia, and dental caries in 74.2% (12.5% in the control group)- were also recorded [7,8].

These results indicate that in this group of women foetal development occurs under the very complicated conditions deriving from both maternal reproductive dysfunction and profound changes in mineral homeostasis. The birth rate of children with congenital anomalies was significantly higher in this group of women compared to female residents of "supposedly clean" territories, which can reflect the decompensation frequency of morphogenetic homeostatic adaptation of physical foetal development correction. Primary and secondary hypogalactia (lack of breast milk) occurred in one third (33.8%) of women, compared with 12.5% in the control group.

The first generation of children born from mothers irradiated in their childhood and adolescence was physiologically immature at birth. These children were frequently ill during their first year of life, and moreover, the somatic pathology was polymorphic, with early development of chronic forms. The proportion of healthy children was very low – 8% (in the control group – 15,6%).

In the first generation of offspring, dental caries developed during the first and second years of life and later on had greater prevalence than in children from "supposedly clean" territories (79,2%, in the control group – 47,5%). In morbidity structure in the first generation of irradiated mothers' offspring, diseases affecting the skeletal system were the 3rd most common effect in children (behind diseases affecting the digestive organs and those affecting the lungs) and were detected twice as often than in their contemporaries from "supposedly clean" regions. Ossalgia and fractures were 5 times more frequent [9,10].

The children's bodies in this group generally developed well, but they lagged behind the children of residents of officially "clean" regions.

It has been established that, in the first generation of children born frommothers irradiated in their childhood, early adaptive changes in the skeletal system are followed by quantitative changes to the osseous tissue structure, the character of which depends on the dose and kind of radiation that their mothers were exposed to in childhood, and also on the mothers' age at the period of irradiation. Higher radiation doses were linked to earlier osteofibrosis and osteoporosis development in offspring, especially in girls. Lower doses caused osteopenia and osteomalacia. Irradiation of mothers when young, irrespective of dose, resulted in osteofibrosis in the early childhood of offspring. Irradiation of mothers during puberty also promoted early development of scoliosis in offspring.

Based on biochemical markers of ontogenesis a modulation of osseous tissue formation was identified: changes of structural and functional properties of osteogenic cells, activation of osseous tissue remodeling process and fermentative phase of its mineralization, mixed destruction of osseous tissue.

Early histoarchitectonic changes of osseous tissue were followed not only by changes to the physical properties of the bone but also by disturbance of mineral homeostasis and changes in the structural and functional properties of osteogenic cells [6-10].

These changes to the osseous system and to the structuree of osseous tissue in this group of children can be interpreted as possible clinical and biological effects of ionizing radiation, as it was established that the nature of qualitative changes to the skeletal system in offspring depended on the doses of radiation their mothers were exposed to in childhood.

It is necessary to keep in mind that osteopenia – destruction of infant osseous tissue is very important clinically. This is due to the fact that changes in developing tissue would have more significant consequences in future than those, which are developing in already developed osseous tissue of adults.

The research carried out leads us to believe that the biological effects of irradiation of mothers during their own childhood are similar to those in the first generation of their offspring, although further investigations are required.

One issue of great importance to both the medical community and society as a whole is the genetic investigation of the Chernobyl Accident and its influence upon the health of future generations.

The assessment of the heritable mutation rate in seven hypermutable minisatellites loci has demonstrated that ionizing radiation does not have any significant influence upon the mutation rate in these loci in children of those affected by the Chernobyl accident.. The mutation process occurs only during the sperm cell maturation and does not affect gametal stem cells. The obtained data indicate that an increase in the heritable mutation rate is possible in a population, which was exposed to chronic low-dose radiation (even if received and reconstructed doses were not established clearly enough). Therefore, if the genetic effect of radiation on minisatellites loci is limited to the gamete meiosis stage than mutations induced by irradiation of parental organisms following the Chernobyl Accident, will be inherited by a very small number of children [11-13].

The effectiveness of similar research can be improved by investigating the mutation rate in additional genome loci.

In addition, it has been shown that in sons of men who worked in the Chernobyl nuclear power plant during clean-up works, the deletions in hot spots of genome on the long Y-chromosome arm have not been detected.

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ON THE ASSESSMENT OF ADVERSE CONSEQUENCES OF THE CHERNOBYL APS ACCIDENT ON THE HEALTH OF POPULATION AND CLEAN-UP WORKERS

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From 1987 onwards, studies on the effect of low-dose low-level irradiation on biophysical and biochemical parameters of the genetic and membrane apparatus of cells of organs of exposed animals have been carried out at the Emanuel Institute of Biochemical Physics, Russian Academy of Sciences

We have investigated the structural parameters of the genome (using the DNA binding to nitrocellulose filters method), structural parameters of nuclear, microsomal, mitochondrial, and plasmic (synaptic and erythrocyte) membranes (by the method of spin probes localized in various layers of membranes), the composition and oxidation degree of membrane lipids, and the functional activity of cells – the activity of enzymes, relationship between isozymic forms, and regulating properties. We have also investigated the effect of low-level irradiation on the sensitivity of cells, biopolymers, and animals to subsequent action of various damaging factors, including high-dose irradiation. The animals were exposed to a source of ^{137} Cs γ-radiation at the dose-rates 41.6 x 10^{-3}, 4.16 x 10^{-3}, and 0.416 x 10^{-3} mGy. The doses varied from 6 x 10^{-4} to 1.2 Gy.

As a result of the studies carried out, the following conclusions were made:

1. Low radiation doses actively affect the metabolism of animals and humans.
2. Over certain dose ranges, low-level irradiation has even greater effects than acute high-level irradiation.
3. The dose–effect dependence of irradiation may be nonlinear, nonmonotonic, and polymodal in character.

4. Doses that cause extreme effects depend on the irradiation dose-rate (intensity); they are lower at a lower intensity.
5. Low-dose irradiation causes changes (mainly, enhancement) to sensitivity to other damaging factors. [1,2]

The nonlinear and nonmonotonic dose–effect dependence that we obtained in our experiments with low-dose low-level irradiation is explained by changes in the relationship between damage and damage repair. With this kind of low-level irradiation, the reparative systems either are not initiated (induced), or do not function adequately, or are initiated with a delay, i.e., when the exposed object has already been damaged by radiation.

Recently, the absence of reparation at low irradiation doses was verified at cell level, [3] and the complex character of the dose dependence was confirmed [4]. Previously, we published a similar scheme of dependence of damages on irradiation dose, which was different for different dose ranges. According to the scheme, the quantitative characteristics were similar for the doses that differed by several orders of magnitude; in a certain dose range, the effect may have an opposite sign.

The results obtained and supported by numerous experiments are important because the above dose dependences made it possible to come to a conclusion about the radiogenic or non-radiogenic character of changes observed in an irradiated organism. The indisputable conclusion that if the effect increases with the dose it is evidence for its radiogenic nature is by no means in favor of an opposite statement, i.e., that the absence of a direct dose–effect dependence but its nonmonotonic character is evidence for the absence of a relation of the effect to irradiation.

In autumn 2005, an UNSCEAR Report, and publications by the IAEA, WHO, and the UNDP Commission were released which described the results of the analysis of the consequences of the Chernobyl APS accident, including its harmful effects on the health of the population and clean-up workers. The data recorded contradicts the conclusions made by many Russian scientists and other International organizations such as the American National BEIR Committee (on biological effects of Ionizing radiation) [5]. The controversy stems mainly from the underestimation and misunderstanding of the effects of low irradiation doses, the reluctance to apply other criteria to assess the consequences, and the (groundless) conviction that low doses cause either no damage or such minor damage that they may be ignored and disregarded.

When defining the irradiation risks, neither IAEA nor WHO took into account the phenomena associated with the action of low irradiation doses and increase the risks; these are the programmed death of cells (apoptosis), 'bystander effect', and radiation-induced instability of the genome, which, in turn, result in enhanced sensitivity of organisms to the action of other damaging factors and more serious forms of development of diseases unrelated to radiation exposure. The BEIR-7 reports on the sources of errors made while analyzing the state of health of irradiated contingents of people and on the danger of low-level ionizing radiation for health. In the Report, the conclusion made previously that there are no safe levels of radiation, i.e., even very low doses may cause cancer, has been confirmed.

Low-level radiation also causes other health disorders such as cardiac diseases and insults, hepatites, mental diseases, and others.

The factor of dose effectivenes and dose-rate for low doses was decreased from 2 to 1.5, which means that the anticipated amount of harmful effects of low doses on health is higher than it was considered earlier (see BEIR-7 Report, 2005).

Similar recommendations for assessment of low-dose risks were made by Russian scientists, who published five monographs on the effects of low doses of radiation on health.

We will emphasize some of the commentaries on the IAEA, WHO, and UNDP reports.

1. No consideration was given to changes in the morbidity rates, which, according to the experts, are related to the accident as a social (not only radiation) risk factor, i.e., stress caused by the accident, the need to migrate, changes in living conditions, radiophobia (fear of radiation), etc. The IAEA and WHO disregard these diseases as a result of the accident.
2. No consideration was given to those oncological diseases for which no usual dose–effect dependences were determined and can be explained in terms of conventional models, although the radiogenic nature of diseases caused by low irradiation doses should be determined by using specific biomarkers, in accordance with requirements of molecular epidemiology, but not on the basis of dose dependence.

3. No consideration was given to other somatic non-oncological diseases, although, according to L. Preston [6], the radiation component is an important factor for a great number of such diseases. Ivanov et al. [7] showed that cerebrovascular diseases affecting clean-up workers are radiogenic in nature. One cannot ignore the possibility that the incidence of these diseases has increased as a result of the accident. For example, the number of radiation-induced non-cancer thyroid diseases of children should be taken into account while summing up the results of irradiation effects on the health of people. The IAEA and WHO do not take them into account.

4. Neither IAEA nor WHO consider the high level of disabilities affecting clean-up workers. About 57% of clean-up workers were acknowledged as being handicapped; for 95% of them, their handicap is a direct result of the ChAPS accident.

5. At present, the problem of premature aging of clean-up workers is under wide discussion; there is a great difference between their biological age and their actual age. The phenomenon is not taken into account as relevant to their deteriorating health.

6. The IAEA and WHO consider only thyroid cancers as adverse effects on health of children irradiated after the Chernobyl accident. However, the deterioration of the health of children associated with the development of more than one chronic disease is not taken into account. The deteriorating health of the clean-up worker's children is not taken into account either.

One more source of errors in assessment of consequences of the accident lies in the selection of control groups. Usually, to determine the link between a disease and irradiation, two kinds of control are used: (a) the internal control, i.e., people of the same age and living under the same conditions as those under study but who received considerably lower irradiation doses than the group of people under study and (b) the external control, for which average values are considered that were recorded for the population of Russia and other regions. Each of the above approaches has advantages and drawbacks. However, it should be noted that if a dose–effect curve has no threshold but is appreciably nonlinear and has an extremum point in the range of low doses, the choice of the internal control may lead to a false decrease in the relative risk of morbidity for the group under study and make it look like irradiation has beneficial effects.

Note that the IAEA and WHO do not categorically deny the radiogenic nature of a great number of somatic diseases but do not consider them to be consequences of the ChAPS accident, although they do state that there is not enough statistical reliability in the results obtained.

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RISKS OF EYE PATHOLOGY WITH THE VICTIMS OF THE CHERNOBYL CATASTROPHE

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In this document, we will present the results of the long-term monitoring of the condition of the eyes of victims of the Chernobyl catastrophe. The patient examinations were conducted using our system of standard inspection and description of the condition of the eye. We have summarized the development of this system in another paper [1].

Ocular effects in patients as a result of the Chernobyl accident have been classified either as specific irradiation injuries, attributable only to radiation exposure, or ophthalmopathology that is observed under normal conditions, but for which radiation exposure is an important risk factor. This division is particularly apparent when examining the clean-up workers in Chernobyl.

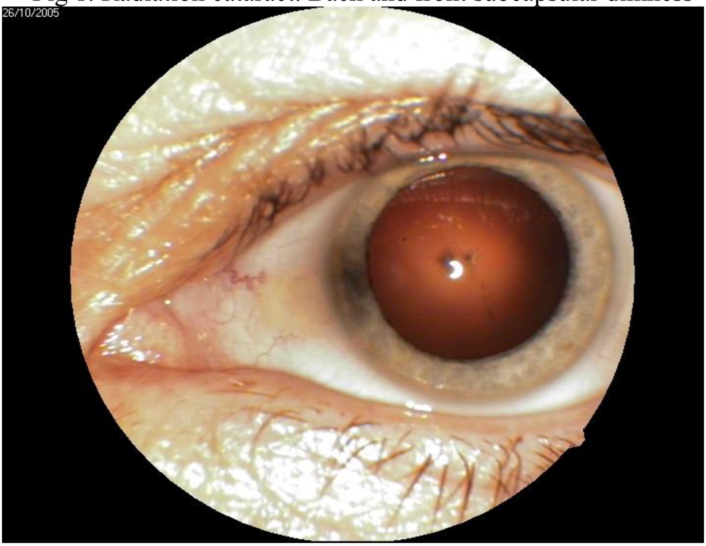
Therefore, firstly we will describe the results of our examination of the condition of eyes in clean-up workers.

The first group of radiation eye diseases includes radiation cataract and radiation chorioretinopathy including “chestnut” and “diffraction grating” syndromes. "Chestnut syndrome" is a type of radiation angiochorioretinopathy and was first recorded in autumn 1986, just a few months after the accident. Multiple microaneurisms, dilations and sacs in the retinal veins were found in the area around the macula in a shape similar to a chestnut leaf. In remote period - degenerate changes of retina in the form of chestnut leaves. "Diffraction grating syndrome", in which spots of exudate were scattered on the central part of the retina, was observed in an individual irradiated in special conditions, within direct sight of the exposed core of the 4th reactor [5].

Radiation cataracts (fig. 1) can be caused by high dose exposure, but also by doses of less than 1 Gy. Mathematical modeling data indicate that radiation cataracts are a stochastic effect of radioactive exposure. The absolute risk of radiation cataract is adequately described by non-threshold model, based on a whole-body external radiation dose and the exposure time. The relative risk per 1 Gy is 3.45 (1.34-5.55) [10,11].

The second group of pathologies - diseases which appear under normal conditions, but which are more widespread in radiation irradiated populations - is more significant. Radiation exposure caused by participation in emergency work at the Chernobyl NPP promotes the premature occurrence of involutional and dystrophic changes to the eyes, development of ocular vessel diseases, and leads to a significant dose-dependent increase in chorioretinal degeneration, such as age-dependent macular degeneration (AMD) and involutional cataracts. Central chorioretinal degeneration with clinical symptoms of age-dependent macular degeneration (AMD) was the most frequent form of retinal pathology in the later period (136.5±10.7 per 1 000 persons in 1993 and 585.7±23.8 per 1 000 persons in 2004). Involutional cataracts are the most widespread form of crystalline lens pathology. Their prevalence during the period of monitoring increased from 294.3±32.0 per thousand exposed individuals in 1993 to 766.7±35.9 per thousand in 2004 [1,5,7,12,14].

Fig 1. Radiation cataract. Back and front subcapsular dimness

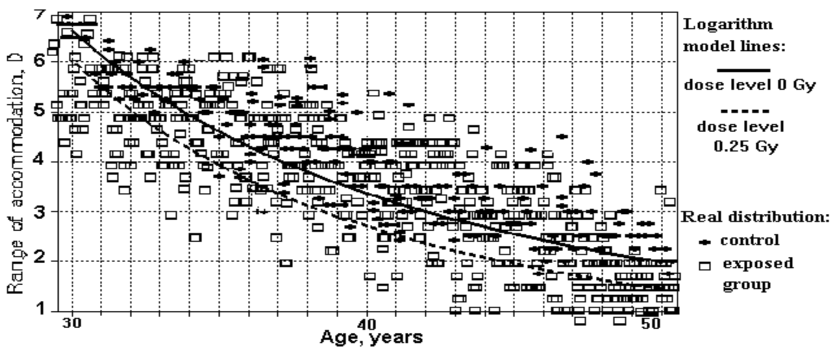


The age, time after exposure and the absorbed dose of external irradiation are the risk factors for involutional cataracts and central chorioretinal degeneration in clean-up workers, according to mathematical modeling data. Relative risk of age-dependent macular degeneration was 1.727 (1.498; 1.990) per year of calendar age, 6.453 (3.115; 13.37) per 1 $\sqrt{(d * t)}$, where d is the dose in Gy and t - time under risk in years [11].

Moreover, there was a high prevalence of dose dependent vitreous destruction, chronic conjunctivitis and benign neoplasm's of the skin of the eyelid [1,5,8]. Irradiated individuals also suffered a decrease in ocular accommodation ability (fig. 2) - of 0.78 dioptries per 1 Gy [20].

As a result of long-term monitoring of the eyes of irradiated populations and mathematical modeling of absolute risks of ocular diseases for radiation irradiated persons in the dose range 0.01-2.2 Gy, it was proven that in a remote period after a radioactive irradiation retinal angiopathy is the primary nosologic unit, whose rate of increase can be predicted with a statistically significant precision. A statistically significant increase of involutional cataracts risk can be expected by the fifth year after exposure and age dependent macular degeneration by six years after exposure. Radiation exposure promotes premature ageing of the eye [11].

Fig 2. Range of accommodation, D, in control group and in the exposed group. Lines - logarithm model lines, symbols - real distribution



We have also examined other categories of people exposed to radiation caused by Chernobyl catastrophe. These were adults and children from the radioactive contaminated territories, the people evacuated from the zone in around ChNPP and descendants of those exposed to radiation.

Ivankiv research into eye condition in children

In March 1991, we carried out an ophthalmologic examination of all children of school age (from 7 to 16 years) in 4 villages of the Ivankiv district of the Region of Kyiv [6,16]. The total number of children examined was 512. The villages located alongside differ only in the degree radioactive contamination of the soil. For the first villages inspected the level of soil contamination ^{137}Cs was: 12.4 Ci/km² average, max 8.0 Ci/km²; 90% index 5.4 Ci/km²; for the second these levels were, respectively, 0.89 Ci/km²; 2.7 Ci/km², and 1.87 Ci/km²: for the third 1.26 Ci/km², 4.7 Ci/km², and 2.1 Ci/km²; and for the fourth 3.11 Ci/km², 13.8 Ci/km², and 4.62 Ci/km². All other characteristics, such as chemical composition of soil, vegetation, way of life, peculiarity of nutrition, were identical in all villages. Genetically the inhabitants belong to the same population. The difference in the level of contamination may be attributed to the interaction between the wind that dominated over the region while radioactive clouds passed over the district. The situation in this region is valuable for scientific study as it establishes conditions, which may provide accurate investigative results.

To register the results we applied the system of objective description of the condition of the eye. This system was developed by the authors and makes it possible to define the localization, size, dimness intensity, and other changes to the lens.

In 1991 no cataracts were found. Typical lensopathies have been detected in 51% of those surveyed, and the frequency was the same in all villages. Atypical changes were found in the lenses of eyes in 61 children: density of back subcapsular layers, dimness in the form of small spots and points between the back capsule and the core, and vacuoles. A statistically significant difference in frequency of eye optical media changes in villages with high and comparatively lower levels of radioactive contamination has been established. ($\chi^2 = 9.12$, $p < 0.01$). The frequency of atypical changes of lens of the eye is connected with the average and, maximal level of soil contamination ^{137}Cs($r = 0.992$) [6,16].

The repeated investigation carried out in 1995 showed that the frequency of atypical changes to the lenses of eyes of inhabitants of villages with the average soil contamination over 2 Ci/km² increased to 34.9%. The increase of pathology frequency as compared with 1991 was significant ($\chi^2 = 5.17$; $p < 0.05$). In two girls, dimnesses suggesting the development of involutional cataracts were recorded (in 1991 early changes to their lens, such as density of cortical layers were recorded).

The increase in the frequency of diseases in inhabitants of villages with a level of soil contamination below 2 Ci/km² was not significant.

Just as in 1991, the frequency of lens pathology was higher in villages with a higher level of soil contamination with ^{137}Cs ($\chi^2 = 5.27$; $p < 0.05$). [2,6,16].

Other authors have obtained similar results, but their examinations were carried out only once [3].

Ovrouch - Boyarka comparative research into the condition of eyes in children - inhabitants of radiation-contaminated territories.

Between 1992 and 1998 the inhabitants of radiation-contaminated territories in Ovruch and Boyarka were subjected to research into the conditions of their eyes. Ovruch and Boyarka are town-type settlements. Ovruch is located in the 3 zone, the density of soil contamination ^{137}Cs being -185-555 kBq$*m^2$, Boyarka is located in the 4 zone, the density of soil contamination ^{137}Cs being 37-184,9 kBq$*m^2$. The third zone is the zone of voluntary migration into other regions; the fourth zone is an area of intensive radiation monitoring.

We have inspected 1948 children and teenagers, among them 461 inhabitants from Ovruch, and 1487 from Boyarka. The age of inspected people statistically did not differ.

When analyzing the spread of primary preclinical changes of lens of the eye we noted that in the third zone it was 234.27 per 1000, and in the fourth, 149.29. The relative risk was 1.6, CL = 1.3; 1.97, χ^2 =18.34, p<0,001.

The most significant lens disease was recorded in 1.34 children in 1000, in the fourth zone, and 6.51children in 1000 in the third. Thus, the changes of lenses are proved to occur more often in children who live on the territories with a higher level of radioactive contamination [17].

The spread of retinal diseases was 10.85 per 1000 inhabitants in the third radiation-contaminated zone and 2.02 in the fourth. In the third zone, angiopathy was present (6.51 in 1000) and 2 cases of congenital retinal degeneration were found in the fourth (this was the only angiopathy detected, 2.02 in 1000).

We have shown that children living in radiation-contaminated territories often show preclinical changes to retinal vessels, and these occur more often in more contaminated zones [13,18,19].

It was shown that the inhabitants of the third zone are more susceptible to myopia than those in the fourth zone. The relative risk of astigmatism is consistently higher in inhabitants between the ages of 8 and 12 in the third zone when compared with the same age group in the fourth zone (RR=1.6; CL –1.01; 2.55, χ^2 =3.95, p=0.047). At the same time, the relative risk of hypermetropia was less for inhabitants of the more contaminated zone (RR= 0.5; CL-0.3, 0.82, p<0.01) [2,13,18,21].

Adult population of radiation-contaminated territories

841 inhabitants of radiation-contaminated territories were examined between 1991 and 1997. The eye pathology structure of inhabitants of radiation-contaminated territories has been shown to change directly during the monitoring process due to increased risks of retinal diseases and involutional cataracts. An uncommonly early occurrence of such a pathology (even in the age group up to 30) was recorded. A high risk of chronic conjunctivitis and vitreous destructions was also recorded.

A comparative analysis of the distribution of eye diseases has been conducted. When comparing the results of the examinations of inhabitants in the third zone with those in the fourth one, a higher risk for residents of the third zone in a relatively young age group (up to 40 years) was shown. Thus, the relative risk of retinal diseases for inhabitants of the third zone was 1.47 (1.08; 1.99) when compared with the fourth zone.

It is recommended to continue the monitoring of eye diseases among the inhabitants of radiation-contaminated territories on a regular basis [4,9].

Monitoring the condition of eyes in the children of clean-up workers born after the catastrophe.

Monitoring of the conditions of the eyes of children of clean-up workers born after the catastrophe has been conducted since 1999. 2202 persons have been examined.

It was established that the risk of pathological changes to the retina in descendants of atomic irradiated people is significantly higher when compared with other groups of children. The data collected proves that continuous monitoring of the eye conditions of these categories of population is necessary. Further epidemiologic analysis of eye condition in the children of clean-up workers will first study the eye vessel system and retinal conditions and functional condition of vision organ [13,15].

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CHERNOBYL DISASTER AND HEALTH OF CHILDREN

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April 26th, 2006 is the 20th anniversary of the most extensive radiological disaster in modern history - the Chernobyl APS accident.

According to the international rating scale it is qualified as an accident of the seventh (highest) level. This accident brought about considerable environmental contamination, and, because of the global scale of influence over the population and the environment (radioactive deposits have been registered at a distances over 2 thousand km from the place of accident, on territories of 20 states), was named "Chernobyl disaster" [1,2].

The unprecedented situation exposed hundreds of thousand of children to an acute dose of radiation. They also continued to live, grow and develop under the conditions of long term (chronic) exposure to small doses of ionizing radiation and other detrimental factors of the post-Chernobyl period. The number of children born to parents, who have been exposed to radiation, is also growing with every passing year.

The citizens of Ukraine who suffered from the ChAPS accident, are classified into 4 groups of the primary account record: 1) persons who participated in the work of clean-up (liquidation) of radioactive material resultant from the accident; 2) those who were evacuated from the city of Pripyat and 30-km zone; 3) those who live on territories, polluted by radionuclides; 4) children who were born of parents classified under 1-3 groups of the primary account record.

Among various groups of the population exposed to the effect of ionizing radiation, children are given priority as far as observation is concerned. This is because growing and developing organisms are much more sensitive to the effects of radiation. Therefore, growing children belong to a critical group of the population that is likely to suffer the most from radiation exposure due to nuclear accidents.

It is postulated by the Law of Ukraine "On the status and social protection of the citizens who have suffered owing to Chernobyl accident", that salvage, treatment and rehabilitation of the children who suffered is a priority direction in all medical programs and measures associated with liquidation of Chernobyl accident consequences [3].

However, despite the great efforts aimed at exposed young people, to provide recovery of health, and maintenance of good health, the level of good health in these young people continues to fall in the post-accident period.

The percentage of "practically healthy" children diminished from 27.5 % in 1986-1987 to 7.2 % in 2003. The number of children with chronic diseases increased (from 8.4 % for 1986-1987 to 77.8 % in 2003), and the number of "children-invalids" among victims exceeded the population average in Ukraine by 4-fold [4]. The most detrimental shifts are noted in adolescents with high exposure doses to the thyroid gland. The percentage of "practically healthy" children among them is not more than 2.8 % [5].

Statistical data demonstrate an increasing rate of disease among exposed children during the post-accident period (from 455.4 % in 1987 up to 1383.45 % in 2004). At present, the diseases with most increased prevalence are diseases of the respiratory system; the nervous system; the digestive system; the skin; the subcutaneous connective tissue; infectious diseases; blood diseases and those of the haematological organs. There are also other types of diseases with increased prevalence, but the rates of increase are smaller with them [4].

The immune system is observed to be detrimentally affected – of children exposed to radiation due to the Chernobyl accident. The disturbed immune equilibrium, which can contribute to formation of many chronic diseases, is recorded in 82.5 % of them. Some specific features of somatic pathology development have been identified, namely, the multi-systemic, multi-organ nature of lesions, with a recurring course in their natural history, and with a relative resistance to therapy [5].

The children constantly residing in the zone of radionuclide pollution have been subdivided into 2 dose-based subgroups. Collective doses in subgroup I are 2.6 person-Sv, and 9.4 person-Sv in subgroup II. Reliable determination shows higher frequency of respiratory diseases (by 2.0 times), vegetovascular dysfunction (by 1.52 times), dysmetabolic disturbances and fibromatous tissues of the liver (by 1.4 and 2.3 times), higher quantities of eosinophilias (by 1.7 times) and lymphocytoses (by 2.5 times) in the subgroup of children with a collective dose 9.4 person-Sv. In the same dose-based subgroup more essential changes of immunity parameters of [4] are noted.

Of importance is evaluation of the state of hypophysial (pituitary)_-thyroid system disturbed functioning of which can serve as a pathogenic substrate of formation of many problems in children and adolescents who suffered owing to the Chernobyl accident.

Since 1986, the determined effects of exposure to radiation of the thyroid gland have been recorded: primary functional reaction was noted in 1986-1987, and formation of chronic autoimmune thyroidites started in 1990-1992 [6,7].

The nodal pathology of the thyroid gland (according to the ultrasound screening of children living in the polluted territories of Russia), was identified 5 times more often, than in the control. The echographic features of thyroid gland nodes were established, which can be subdivided under the category of formations with higher risk of oncology [8].

The growth of thyroid gland cancer rates among children and adolescents owing to influence of radioiodine is a proven fact nowadays [9]. As shown by the analysis of age structure of patients with primary diagnosis of thyroid gland cancer, the highest disease rates are recorded in children and adolescents (62.5 %). The majority of patients (60 %) were aged 0-4 years at the time of ChAPS accident. The prevalence of invasive forms of carcinoma (87.5 %) demonstrates high aggressiveness of tumor-formation process [10].

The peak of thyroid gland cancer morbidity among those who were children and adolescents at the moment of the accident is predicted to occur in 2001-2006.

Studies of radiation effect on the haematological system have not revealed exorbitant cases of cancer-induced haematological pathology at_children and adolescents living in territories polluted by radioactive nuclides. The leukemia and lymphoma case rate is within range of 2.9-6.6 on 100 thousand children, which corresponds to an average index across the Ukraine [7].

Studies of the adolescents, who have suffered due to the Chernobyl accident, have revealed social and psychological problems. They mention as significant factors of their vital perspective the serious illnesses (of themselves and of their relations), death of parents, short length of their own life and the like. These data reflect development of a "victim" identity in adolescents, characterized by pessimism, vital passivity, and absence of a structured picture of the future [11].

Thus, children and adolescents, who had been exposed to the influence of ionizing radiation and other detrimental factors of the Chernobyl accident, have entered an adult life more likely to have a poorer level of health, with more chance of having disease and a higher risk of oncological diseases (principally thyroid gland cancer). As well as these physical problems, they are also more liekly to have poor social and psychological adaptation with a developed "victim" identity.

Now, we will pay particular attention to the children exposed to radiation during the antenatal period, at the time of the ChAPS.

During the period after the Chernobyl accident we studied 1114 children exposed to radiation during antenatal period. Group I (basic) was composed of the children born from women pregnant at the moment of the accident and who had been evacuated from city of Pripyat; Group II (basic) – of the children born from women pregnant at the moment of the accident, who stayed living in II-III zone of radioactive contamination; and Group III - control – of the children born from women, living on "clean" territories.

It has been established that fetal exposure to radiation resulted in lower levels of good health in children at all the stages of postnatal development [12-15].

The chronic somatic pathology occurred in children more often at a fetal thyroid gland radiation exposure dose of over 0.36 Gy, and it was recorded almost in all children at an exposure dose above 1.0 Gy.

Disturbance of physical development in children exposed to ionizing radiation before the 16th week of fetal development (with an average exposure dose of 0.31 Gy) was observed more often than in the control. However, after 16th week of gestation (with an average dose of 0.85 Gy) frequent pathological findings were identified in the period of puberty. At a dose of fetal exposure to radiation of the thyroid gland over 0.76 Gy, disturbance of its echo structure at the expense of linear fibrosis elements was recorded in children more often, than at a dose under 0.36 Gy.

The exposure of the central organs of fetal immunogenesis (the thymus and the red marrow), to radiation, resulted in substantial disorders of the children's immune system. The functional activity of phagocytes, the T-cellular chain of immunity and dysimmunoglobulinemia were observed to be depressed. The interrelation was identified between the state of health, the thymus, the red marrow exposure dose and change of immunological parameters with factors of plural correlation of 0.78-0.87 [16-19].

Exposure of the fetus to medico-biological risk factors in a combination with radiation contributed to higher frequency of small anomalies of development. The number of these anomalies, on the average among children exposed to antenatal radiation, was 5.52 ± 0.22, compared to 2.95±0.18 (p<0,001) in the control group. The direct correlation was revealed between the number of small anomalies of child's development and exposure dose during fetal development (r=0,61).

At the age of 10-12 years – children exposed to antenatal radiation of red osteal brain, in doses of 10.0-376.0 мзв, had higher frequency of chromosomal aberrations, and this was found to be dependent upon dose [18,20], and in 15-17 year-old the residual cytogenetic effects were found to remain in 37.5 % of adolescents.

Children born from parents exposed to radiation (but not directly exposed to radiation themselves), also have a lower level of health. This is witnessed by higher total morbidity rates in these children, than across Ukraine as a whole, which, during the last 5 years vary within the limits of 1134.9-1367.2 ‰ (across Ukraine 960.0-1200.3 ‰). The share of practically healthy among them is 9.2 %. Among 13136 children born from liquidators of the 1986-1987 period, recorded in the State register of Ukraine, 1190 are registered as having congenital development anomalies (9.6 in 1000). The highest frequency was recorded in children born in the first post-accident years [21,22].

With the aim to evaluate possible genetic effects in the first generation of children of those exposed to radiation, the members of families of liquidators of 1986-1987 period were examined. Results of the study have shown that a phenotype of the majority of children born after their fathers participated in the liquidation of material resultant from the Chernobyl accident was characterized by presence of numerous small anomalies of development. The frequency of chromosomal aberrations [22,23] and mutations in micro-satellite-associated fractions of DNA was higher, than in their older brothers and sisters who had been born before the accident [24].

The higher level of mutations in micro-satellite fractions of DNA in the first generation of the parents exposed to radiation is mentioned by Y.Dubrova et al. [25-27].

Given the results noted above, we can classify children and adolescents exposed to radiation during the antenatal period, and also those children born to parents exposed to radiation (but not directly exposed to radiation themselves) into the group of mutation risk.

Conclusions:

The health status of the exposed children is characterized by steady negative tendencies:

- A steady trend of growth of various morbidities, and a reduced number of "practically healthy" is observed;
- The lowest level of health is revealed in adolescents with high exposure doses of the thyroid gland;
- Peculiarities of formation and course of chronic somatic diseases have been defined: arising at a younger age, multi-systemic, multi-organ nature of lesions, with a recurring course in their natural history, and with a relative resistance to therapy.
- Rising rates of thyroid gland cancer in those exposed to influence of radioiodine when children and adolescents are recorded;
- It was reliably identified that there is a correlation between an exposure of radiation during the fetal (antenatal) development and reduced states of health, physical development, formation of phenotypes with numerous small anomalies, and higher number of chromosomal aberrations in the somatic cells of children;
- There is phenomenon of genome instability in children born from those exposed to radiation, which is characterized by reduced adaptation potentials of an organism to the action of detrimental environmental factors,_as well as a predilection to multi-factorial diseases, formation of phenotypes with numerous small anomalies of development and-or congenital defects, higher frequency of

chromosomal aberrations in somatic cells and more frequent mutations in micro-satellite-associated fractions of DNA.

Thus, the Chernobyl disaster has caused the deep disturbances of health of the exposed children's population, which will demand concentration of efforts and mobilization of the resources aimed for social, medical and psychological rehabilitation of children and adolescents.

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THE DECAY OF NUCLEAR POWER PLANTS

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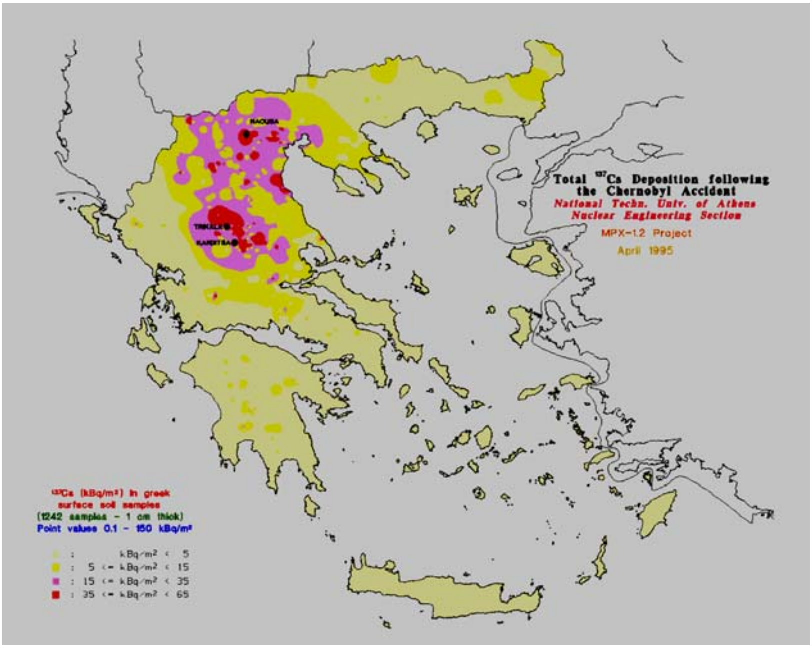
Research into Contamination in Greece



Several nuclear physics laboratories carried out research into contamination immediately after the Chernobyl accident, mainly through measuring radioactivity in several thousands soil samples. Among the contaminating radioisotopes, caesium-137 and its surface deposition was mostly studied throughout the Greek territory. Among others, two main laboratories comprehensively exhibited their studies by presenting a geographical distribution of surface deposited caesium-137 [1,2]. One of these maps, which depict the presence of caesium on the soil using four different colours, is shown here [1].

Health work

Although there were some rumours about radioactive victims, a health study based on case or epidemiological analysis has not been carried out.

Independently of the reasons why such studies have not been performed (e.g. lack of hospital data files, funds or policy), it is in any case very difficult to estimate any number of victims of radioactivity. This is because the low level dose is generally characterised by a long latent period (10 years), during which the symptoms are latent. For about 30 years after this latent period, the probability of more consequences appearing (cancer, for example) is consistently low. Now, since the accident, we have only spanned one third of this period so any estimations would be very preliminary. In addition, recent reports refer only to fatal cases and not to non-fatal ones, the number of which are expected to be relatively large but is not yet accurate. Nevertheless, in the second third of this 30-year period careful epidemiological studies should be carried out, mainly in the relatively highly contaminated regions.

The 20-year anniversary should not simply summarise what was done and what the health impacts of the incident were, but it should also review the actual nuclear situation at the NPP. This review is necessary because:

1. NPPs release radioactive gases into the atmosphere during "normal" operation.
2. The threat of another accident is always present, and the impact of such an accident is difficult to estimate and cannot be compared with conventional accidents.
3. The operation of a NPP requires, among other things, additional plants to extract, purify, enrich and produce the nuclear fuel. After it is burnt, reprocessing and depository plants are also required. Some of these plants, and the NPP itself, can create DU and plutonium for radioactive and nuclear weapons construction. In addition, all these units and the NPP emit a large amount of heat into the atmosphere (Heat pollution).
4. After a period of about 30 years, all NPPs should be dismantled and treated in the same way as used nuclear fuel, due to the radiation they emit (neutron activation). This procedure is rather costly and takes a long time. Note that after

approximately ten years half of all present NPPs (200) will reach this limit.

5. The advertised new 4th generation NPP will not significantly change this situation.

Today, NPPs are in decline and any attempts, especially from non-nuclear states, to install these plants are treated with suspicion.

Last, but not least, NPPs do not represent the peaceful use of nuclear energy in contrast with military use, as is frequently claimed, but they rather constitute the "other side of the same coin". Peaceful uses of radioactivity include medical, industrial, chemical, archaeological, trace analysis, etc applications.

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ANALYSIS OF MEDICAL AND IMMUNOLOGICAL EFFECTS ON LIQUIDATORS OF THE CHERNOBYL NUCLEAR POWER PLANT DISASTER AFTERMATHS IN THE LONG-TERM PERIOD BASED ON 20-YEAR MONITORING

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The delayed action is often manifested through the increasingly frequent clinical signs of dysimmunity, chronic bodily diseases and changes in the immunity status of liquidators. Since 1986, the Immunology Institute along with the Federal Medical and Biological Agency of Russia has been monitoring the health and the immunology status of the persons who participated in liquidation of the Chernobyl NPP disaster aftermaths. During the long-term period of the third and the fourth lustrums following the disaster, the monitoring mostly focused on liquidators from Moscow and Moscow Region, the Northwestern part of Leningrad Region and Krasnoyarsk Territory (see Fig. 1). The immunology monitoring was carried out under uniform methodology based on specialized clinical, immunology and allergenic surveys with the help of a uniform diagnostics card designed by the Immunology Institute for the detection of immunodeficiency and other evidence of the immune system dysfunctions at the pre-lab stage [10, 18-20, 29]. The main section of the screening is based on the clinical signs of immunodeficiency categorized by the leading immunopathological syndrome features as follow: infectious, allergic (atopic), infectious-allergic (a combination of the infectious and allergy syndromes) and autoimmune.

Fig. 1. Groups monitoring the liquidators of the Chernobyl NPP aftermaths.

City of Moscow and Moscow Region – Central Region – 585 persons.
North-Western part of Leningrad Region – 665 persons.
Krasnoyarsk Territory – 648 persons.
Long-term period of 1999–2004. Total of 1,982 persons subject to examination.

The infectious syndrome is inclusive of chronic, frequent, recurring pathological processes of bacterial, viral and fungal etiology, frequent acute respiratory viral infections recurring 3-4 times and more each year (Table 1). Other clinical immunopathological syndromes are inclusive of allergy diseases and reactions, autoimmune diseases and immunoproliferative conditions.

Allergenic examination included the collection of allergoanamnesis, skin tests using the domestic, epidermal, fungal and foodborne allergen indications, as well as identification of overall Immunoglobulin E (IgE). The study covered the most common chronic bodily diseases. The analysis also used the data from case records, annual standard medical examination by the Central Medical Department (CMD) experts and the results of instrumental examinations.

Dynamics in the Occurrence of Clinical Signs of Immunodeficiency Suffered by Liquidators of the Chernobyl NPP Aftermaths based on the 1997-2005 Monitoring Data

By the beginning of the third lustrum following the Chernobyl disaster, the liquidators from Moscow and Moscow Region (see Fig. 2) showed high rates and clinical signs of failure of the immune system – 84.88%. The dynamics of occurrence of clinical signs of immunodeficiency varied from 78.31% in 1999 to 88.54% in 2005, and were characterized by periodical increase of morbidity in 1999 and 2001 with a tendency toward certain decrease in 2000 and 2002. Availability of close value for the six-year period allowed to determine the average rate of occurrence of clinical signs of immunodeficiency with liquidators, which in 1997–2002 was 83.49% (435:521) or 834.9:1,000 and was higher than similar values with personnel employed at the nuclear power industry enterprises [4,5,8,11,13,14,16,18,22,23,25,26,31]. In 2003 the analysis revealed significant increase in the rate of clinical signs of immune system dysfunctions – up to 97.3% (107:110), whereas in 2004 they were revealed with all examined persons, which is mostly related to the increase of clinical signs of immunodeficiency resulting from the infection syndrome.

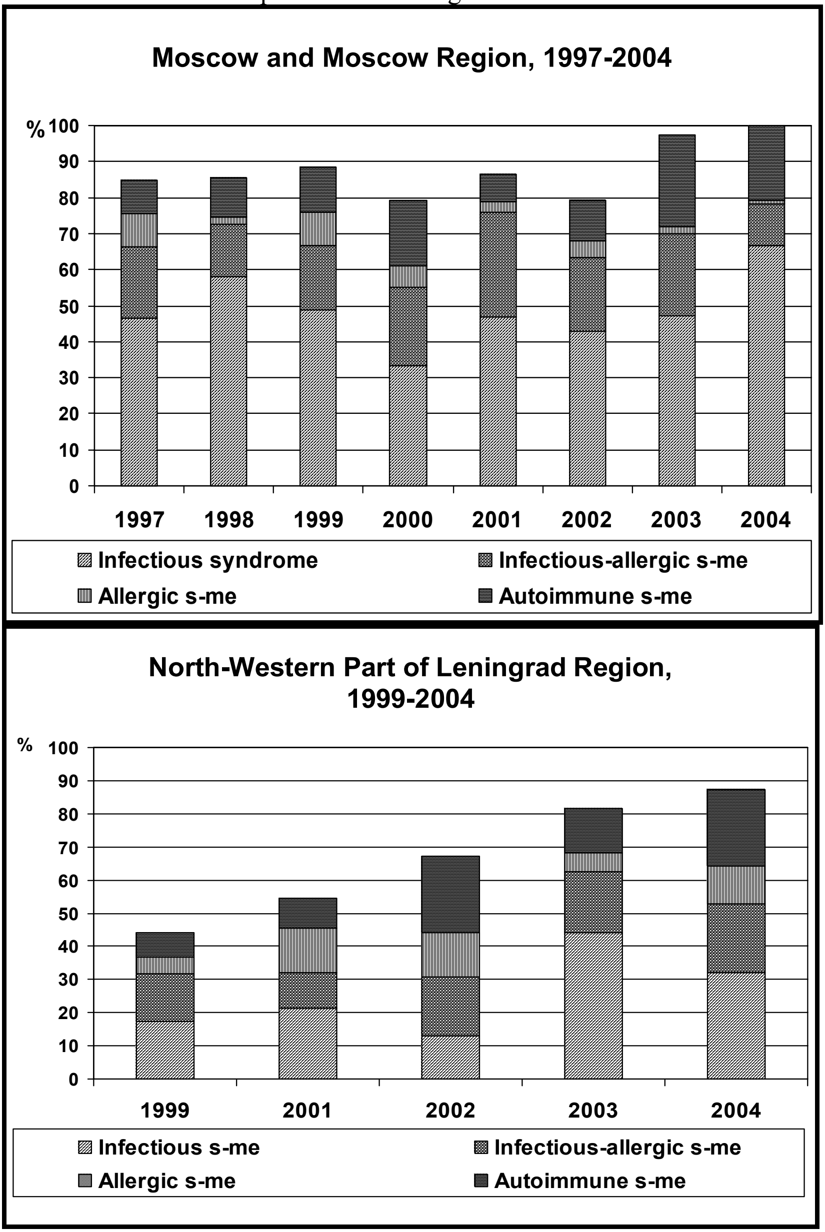
The infection syndrome is prevalent in the structure of clinical immune dysfunction suffered by liquidators from Moscow Region. Its rates were similar in 1997, 1999, 2001 and 2002 – around 42.75% – 48.96%. In 1998 the rates grew significantly up to 58.18% followed by reduction to 33.33% in 2000. The reduction in the rate of clinical signs of immunodeficiency resulting from the infection syndrome was accompanied by the increasing morbidity of the combined pathology of infection, allergicgenesis. The increasing frequency in occurrence of clinical signs of immunodeficiency based on both syndromes and the maximum combined value thereof was revealed in a group examined in 2001. The increasing frequency in occurrence for clinical signs of immunodeficiency resulting from the combined pathology based on infection and allergy syndrome from 1998 through 2001 were as follows: 14.55%→17.7%→21.84%→28.79%, which indicated the intensification of pathology. The occurrence of combined pathology based on infection and allergy syndrome in 2002-2003 was almost similar: 20.61%→22.72% against the values registered in 2000. Occurrence of allergy diseases without signs of infection within the liquidators residing in the city of Moscow and Moscow Region is fairly low. The analysis revealed high allergy diseases occurrence ratio and combined pathology based on infection, allergy syndrome due to the increased occurrence of infection and allergy diseases. Examination in 2000 revealed an increasing rate of autoimmune diseases, which occurred both in isolated cases and against the background of clinical signs of the immune system dysfunctions or in combination with other chronic pathologies revealed in 18.4% of the examined liquidators.

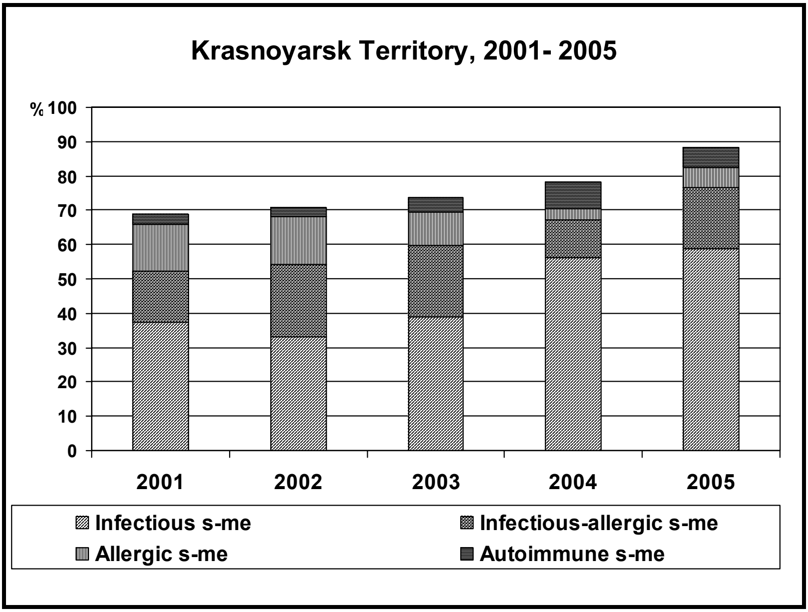
Most common nosological forms in 2000 were autoimmune thyroiditis and Type 2 diabetes requiring insulin (see Table 1). In 2003-2004 autoimmune disease rate grew by 25.45%–20.70% against 2000.

Clinical signs of immune pathology in liquidators residing in the Northwestern part of Leningrad Region were far less frequent than in Moscow Region during 1999, which was about 44.07%. Dynamics in frequency of clinical signs of immunopathological syndrome with liquidators residing in the Northwestern part of Leningrad Region was steadily growing in 1999-2004: 44.07%→54.5%→ 66.7%→81.7%→87.4% (see Fig. 2) and in 2003 it had reached the level for liquidators residing in Moscow Region (2002 data). The infection was another leading clinical syndrome of immunodeficiency (except for 2002), although its frequency during the said period was much lower – 17.51%→ 21.43%. In 2003 it grew to the value existing in Moscow and Moscow Region in 2001-2003.

The infection and allergy syndrome pathology were slightly lower in 2003, but the rates are also similar to those of liquidators residing in Moscow Region: 17.59% (2002) → 18.27% (2003) → 20.69% (2004). The cumulative allergy disease frequency in occurrence and the combined infection and allergy syndrome pathology values are very high. Allergic pathology is revealed in 1/3 of liquidators: 30.8% and 32.4%, of those examined in 2002 and 2004, and 1/4 (24.04%) in 2003. Liquidators from the Northwestern part of Leningrad Region, Moscow and Moscow Region suffered from autoimmune diseases more frequently, with two peaks: 23.15% (2002) and 22.99% (2004).

Fig. 2 Dynamics of GR Values and IPS Distribution among the Liquidator Groups from Three Regions of Russia

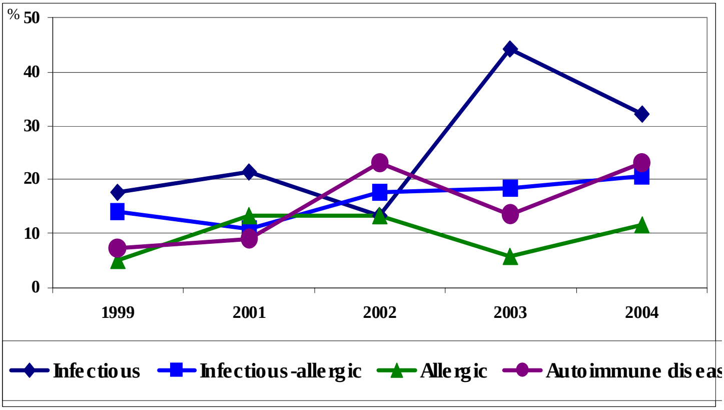




The increased rate of autoimmune pathology is the expected effect resulting from irradiation, which manifested itself to the maximum on liquidators residing in the Northwestern region 15-17 years after the emergency operations in the high radiation areas (liquidators residing in Moscow Region felt this effect 2 years sooner). Autoimmune thyroiditis prevails in the structure of autoimmune diseases.

The dynamics of immunopathological syndrome patterns for liquidators from the Northwestern part of Leningrad Region by the end of the second decade following the emergency period, specifically, in 2002-2004, was characterized by parallel changes in the frequency of allergy and autoimmune diseases, whereas in 2003 the values dropped a little against 2002 but increased in 2004, with a tendency toward slow increase of the combined pathology of infection, allergy syndrome, and an abrupt growth in the occurrence of clinical signs of the infection syndrome immunodeficiency in 2003 contrary to 2002 (see Fig. 3).

Fig. 3 Dynamics of Distribution of Immunopathological Syndromes in the Examined Groups of Liquidators of the Chernobyl NPP Aftermaths from the North-Western Part of Leningrad Region based on the 1999-2004 Monitoring Data

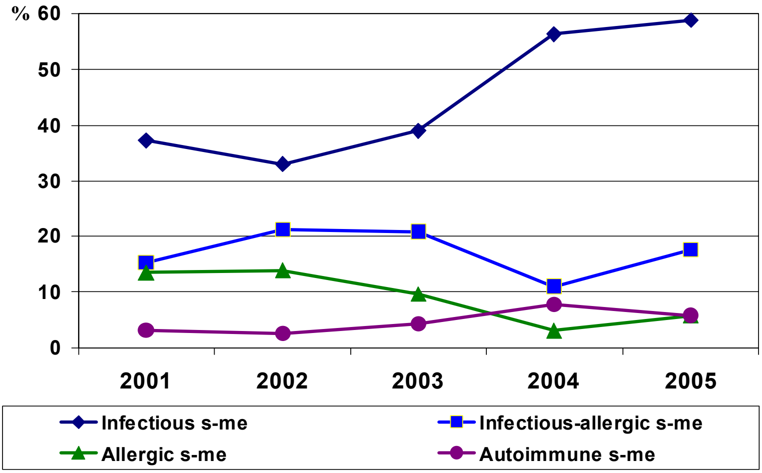


We believe, that a lower average rate of clinical signs of the immune system dysfunctions for liquidators from the Northwestern region before 2002 against the other two regions considered herein may be explained by a few reasons, which emphasize the importance of immunology monitoring:

- Since 1986, in addition to specialized examinations held on a more frequent basis, which had a big preventive effect, the liquidators from the Northwestern part of Leningrad Region took annual courses in preventive immunity.
- Specifics operations performed at the Chernobyl NPP to liquidate the aftermaths of the disaster.
- Regional specifics.
- Diagnostic opportunities of the CMD in conditions of a small town.

Analysis about prevalence of immunodeficiency and other clinical signs of the immune system dysfunctions among liquidators residing in Krasnoyarsk Territory includes the data on the remote period following the Chernobyl NPP emergency - from 2001 to 2005. Same as liquidators from the other two regions contemplated herein, liquidators residing in Krasnoyarsk Territory the monitoring revealed a tendency toward a steadily increasing rate in occurrence of clinical signs of immunopathology: 68.83%→70.62%→73.61%→78.13%→88.24% (see Fig. 4).

Fig. 4 Dynamics of Distribution of Immunopathological Syndromes in the Examined Groups of Liquidators of the Chernobyl NPP Aftermaths from Krasnoyarsk Territory based on the 2001-2005 Monitoring Data



The increasing occurrence of immunopathology is based on a significant growth in the occurrence of clinical signs of the infection syndrome immunodeficiency: 56.6% – 58.82% (see Fig. 4). As far as the occurrence frequency is concerned, the infection syndrome is followed by the combined pathology of the infection and allergy syndrome (17.65%). The distribution of AD was reducing up to 2004, followed by a slight rise in 2005. The occurrence in combined pathology of the infection and allergy syndrome has been changing as well. On the whole, the allergy pathology occurrence remains on a fairly high level – it was revealed in 1/4 of the monitored patients. The occurrence frequency of autoimmune diseases in Krasnoyarsk Territory is much lower (7.81% – 5.88%) compared to the liquidators residing in Moscow Region and the Northwestern region.

In the structure of immunodeficiency clinical signs in the infection syndrome, the most common in the fourth lustrum after the Chernobyl disaster, all three groups of liquidators are characterized by high occurrence of chronic, recurring and obstructive bronchitis (see Fig. 5, Table 1), frequent acute respiratory viral infections, chronic recurrent herpes viral infections (ChRHVI), frequent acute respiratory viral infections interfacing with ChRHVI, as well as chronic ENT infections.

Chronic obstructive bronchitis is one of the most common lung diseases. The occupation, close contact with industrial hazards, exposure to cold and smoking are very important factors promoting the occurrence of the chronic obstructive bronchitis. Rapid growth of chronic pulmonary diseases is observed around the world, which is specifically explained by the aggressive impact of industrial and domestic pollutants. The problem of chronic obstructive pulmonary diseases for Russia is becoming particularly pressing due to the aftermaths of the Chernobyl disaster, because 12 years thereafter the respiratory organs pathology among the liquidators reached the top of the morbidity structure (A.G. Chuchalin, 1998) [28].

The Pulmonology Research Institute revealed high occurrences of chronic bronchitis back in 1994 during the single-step epidemiological examination. According to the data provided by this Institute, the occurrence of chronic bronchitis among liquidators residing in Ryazan was 44.3%, and 34.9% among those residing in Vladimir [1,7]. In the same group of liquidators the researchers revealed high occurrences of long-standing acute respiratory viral infections (37.9%). 36.6% of liquidators suffered from acute respiratory viral infections 2 or 3 times a year [1]. According to our monitoring data, the higher rates for acute respiratory viral infections and chronic bronchitis can be explained by the more remote terms of examination. High frequency of respiratory diseases among the liquidators was based on the inhalation damage to the respiratory passages during the operations on liquidation of the disaster aftermaths. The average occurrence of the so-called "upper respiratory passages irritation syndrome" among those participating in liquidation operations in 1986 was 47.64% and depended on the exposure to γ-irradiation and the duration of works in the areas of enhanced irradiation, which increased with higher irradiation and longer terms of operations within the liquidation area [11].

Fig. 5 Structure of Clinical Signs of Immunodeficiency Infection Syndrome among the Chernobyl NPP Liquidators Residing in Moscow and Moscow Region

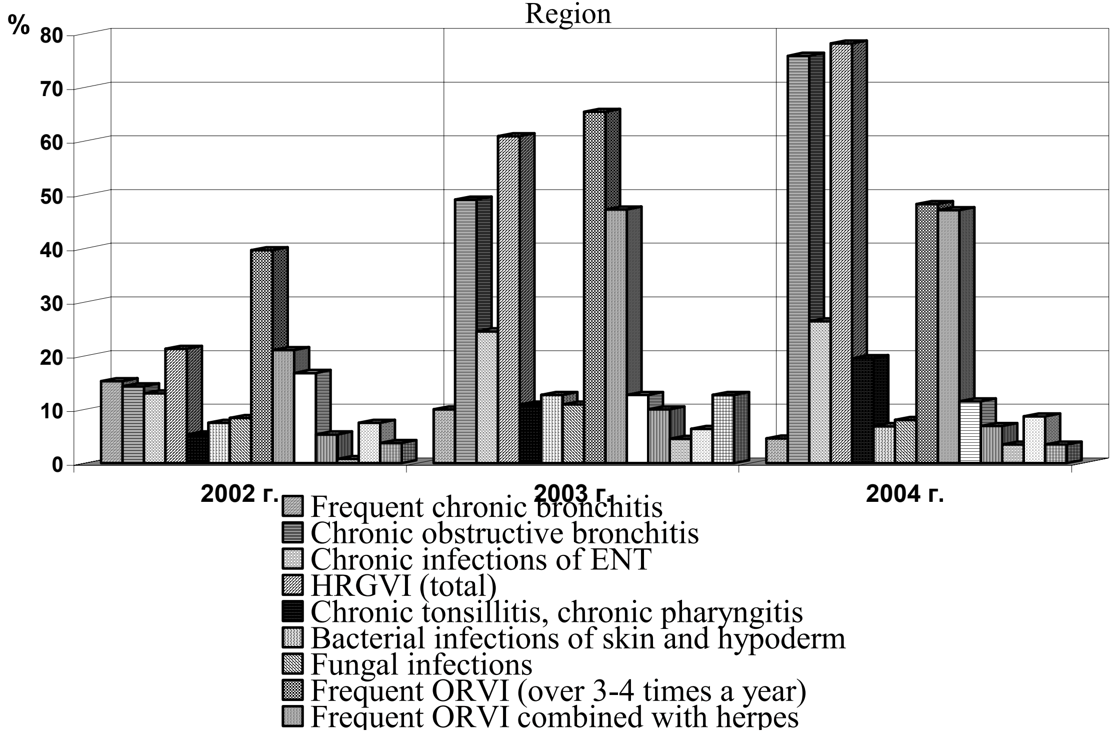


Table 1 – Structure and Dynamics of the Occurrence of Clinical Signs of Immunopathology among the Liquidators of the Chernobyl Disaster Aftermaths Residing in Moscow and Moscow Region - 2003-2004 Data

Ref. No.	**Clinical Signs of Immunopathology**	2004, n=87		2003, n=110	
		n	%	n	%
	I. Infection Syndrome:				
1	Frequent bronchitis (3 or more times a year)	9	10.34	11	10.0
2	Chronic obstructive bronchitis	68	**78.16**	41	**37.27**
3	Chronic obstructive pulmonary disease (COPD)	6	6.89	9	8.18
4	Frequent pneumonia	2	2.30	4	3.63
5	Frequent ENT infections (total)	24	**27.58**	28	**25.45**
6	Chronic tonsillitis	17	19.54	13	11.81
7	Chronic sinusitis	2	2.30	7	6.36
8	Chronic otitis/eustachitis/mesotympanitis/mastoiditis	3	3.45	4	3.63
9	Chronic pharyngitis, laryngitis and/or tracheitis	10	8.70	11	10.0
10	Fungal infections, seborrheal dermatitis, onychomycosis	6	6.89	9	8.18
11	Frequent acute respiratory viral infections (3 and more times a year)	42	**48.27**	73	**66.36**
12	Frequent acute respiratory viral infections without ChRHVI	1	1.15	18	16.36
13	Frequent acute respiratory viral infections with ChRHVI (total)	41	**47.12**	55	**50.00**
14	ChRHVI without frequent acute respiratory viral infections	28	**32.18**	15	13.6
15	ChRHVI (total, regardless of acute respiratory viral infections)	69	**79.31**	70	**63.63**

16	Bacterial gingivitis, stomatitis, periodontosis with frequent recrudescence	3	3.45	5	4.54
17	Intestinal dysbacteriosis	10	8.70	15	13.63
18	Chronic pyelonephritis	6	6.89	10	9.09
19	Chronic cystitis	6	6.89	4	3.63
20	Long-standing subfebrilitetis of unknown etiology	6	6.89	8	7.27
21	Caries multiplex with periodontosis	2	2.29	11	10.0
22	Bacterial infections of skin and hypoderm, chronic furunculosis	6	6.89	8	7.27
	II. Allergy Syndrome	1	1,15	2	1.81
1	Atopic dermatitis	1	1.15	3	2.72
2	Severe Atopic syndrome (SAS)	–	–	3	2.72
3	Atopic bronchial asthma	1	1.15	6	5.45
4	Pollen fever:	7	**8.05**	9	**8.18**
	Allergic rhinitis (seasonal)	3	3.45	4	3.63
	Allergic syndesmitis (seasonal)	4	4.59	6	5.45
	Pollen bronchial asthma (seasonal)	3	3.45	5	4.54
5	Chronic recurring urticaria, Quincke's edema	1	1.15	2	1.81
6	Food allergy, intolerance to food	1	1.15	4	3.63
7	Drug allergy, intolerance to drugs	7	**8.05**	16	**11.81**
8	Allergic rhinitis	6	**6.89**	9	**8.18**
9	Allergic syndesmitis, rhinosyndesmitis without sensibilization to the plant pollen allergens	1	1.15	4	3.63
10	Latent sensibilization to allergens	3	3.45	3	2.72
III. Autoimmune Syndrome					
1	Rheumatoid arthritis	1	1.15	3	2.72

2	Autoimmune thyroiditis	12	**13.79**	24	**21.81**
3	Rheumatism (rheumatic fever)	2	2.30	2	1.81
4	Chronic glomerulonephritis	1	1.15	1	0.9
5	Diabetes (Type II – requiring insulin)	1	1.15	1	0.9
6	Psoriasis	1	1.15	1	0.9
III. Lymphoproliferative Syndrome					
1	Lymphadenopathy	3	3.45	5	4.54
2	Polycythemia	1	1.15	0	0.0

This phenomenon was also promoted by reduction of cell-bound immunity in the first 12-18 months following the removal from the emergency response areas and the extensive imbalance within the system of cell-bound and humoral immunity [9,11]. The immunopathology structure, including allergy diseases, autoimmune pathology and clinical signs of lymphoproliferative syndrome among the liquidators residing in the city of Moscow and Moscow Region is shown in Table1. The revealed forms of allergy diseases are most frequently represented by pollen fever, drug allergy and intolerance, and the allergic rhinitis.

For liquidators from the Northwestern part of Leningrad Region the infection syndrome structure by the end of the fourth lustrum following the Chernobyl disaster is dominated by frequently recurring chronic bronchitis – 52.87%, followed by ChRHVI – 32.2%, frequent respiratory viral infections – 29.9%, frequent acute respiratory viral infections interfacing with ChRHVI – 18.4%, and ENT chronic infections – 20.7% (see Table 2, Fig. 6). The structure of allergy pathology is not profoundly different from liquidators residing in the city of Moscow and Moscow Region. The occurrence of certain nosological forms of allergy diseases varies depending on the composition of the examined groups. The nosological specter appears to be expanding, with prevailing pathology of mucosal damage: allergic rhinitis, rhinal syndesmitis and pollen fever. No atopical forms of skin diseases were revealed in 2003-2004, the occurrence of which in 2002 was 12.04%. The extent of revealed forms of autoimmune thyroiditis among the liquidators in 2004 was 183.9:1000.

Table 2 – Structure and Dynamics of the Occurrence of Clinical Signs of Immunopathology among the Liquidators of the Chernobyl Disaster Aftermaths Residing in Moscow and Moscow Region – 2001-2004

Ref. No.	**Clinical Signs of Immunopathology**	**2004** n=87	**2003** n=104	**2002** n=108	**2001** n=112
	I. Infection Syndrome:	%	%	%	%
1	Frequent chronic bronchitis	**52.87**	12.50	7.41	8.93
2	Frequent bronchitis with chronic infection of the ENT	0	0.96	–	2.68
3	Bronchitis with bronchospastic component and enhanced vulnerability to acute respiratory viral infections	0	0.96	1.86	1.79
4	Chronic obstructive bronchitis	**17.24**	**22.12**	5.56	3.58
5	Frequent chronic pneumonia	0	0	5.56	0
6	Frequent ENT infections	**20.69**	**25.96**	**25.0**	12.50
7	Bacterial infections of skin and hypoderm	3.45	1.92	2.79	2.68
8	Fungal infections	18.39	**23.08**	**15.74**	13.39
9	Frequent acute respiratory viral infections (over 3-4 times a year)	**29.89**	**9.62**	10.19	**19.64**
10	Frequent acute respiratory viral infections interfacing with herpes	**18.39**	**6.73**	4.63	2.68
11	Herpes without frequent acute respiratory viral infections	**32.18**	**20.19**	2.79	0.89

12	Gastroenteropathy with dysbacteriosis	4.60	5.77	2.79	1.79
13	Chronic pyelonephritis	9.20	13.46	2.79	2.68
14	Lymphadenopathy	0	0	0.93	0
15	Long-standing subfebrilitetis of unknown etiology	3.45	0.96	1.86	0.89
16	Periodontosis with frequent recrudescence	0	0.96	3.70	2.68
	II. Allergy Syndrome				
1	Atopic dermatitis	0	0	**12.04**	4.46
2	Severe Atopic syndrome (SAS)	0	0	0.93	–
3	Allergic syndesmitis	**5.75**	0	**10.19**	0.89
4	Allergic rhinitis	**5.75**	2.88	3.72	2.68
5	Rhinal syndesmitis	3.45	5.77	**10.19**	1.79
6	Recurring urticaria	0	6.73	–	5.36
7	Pollen fever	**10.34**	12.50	**10.19**	7.14
8	Bronchial asthma	**6.90**	5.77	6.48	2.68
9	Pre-asthma	0	0	1.86	1.79
10	Drug allergy, drug intolerance	**5.75**	**11.54**	**18.52**	**16.07**
11	Allergy to food	**6.90**	4.80	7.41	2.68
12	Latent sensibilization	3.45	5.77	9.26	8.93
13	Insect allergy	0	0.96	0.93	0.89
	III. Autoimmune Diseases				
1	Autoimmune thyroiditis	**18.39**	**11.54**	**14.81**	**8.04**
2	Diabetes	3.45	0	**6.48**	1.79
3	Rheumatoid arthritis	1.15	0.96	1.86	1.79
4	Systematic vasculitis	0	0	0.93	–

According to the clinical signs of immunodeficiency (infection syndrome), the most common diseases among the liquidators residing in Krasnoyarsk Territory are chronic bronchitis, frequently recurring as a single sign or interfacing with frequent ARVI or ENT diseases, chronic obstructive bronchitis, frequent ARVI, ARVI interfacing with ChRHVI and chronic pyelonephritis.

Same as in the other examined groups, since 2003 the research revealed the increasing frequency of obstructive bronchitis, however it is much lower in Krasnoyarsk Territory and the Northwestern part of Leningrad Region than in Moscow and Moscow Region. As far as the allergy pathology structure is concerned, unlike other groups under observation, here one reveals a higher rate of sensibilization to domestic and epidermal allergens, drugs, etc. In 2004 the research revealed a surge in the occurrence of bronchitis, which is typical for over 50% of the examined persons. However, the occurrence of allergy diseases within the examined group is much lower.

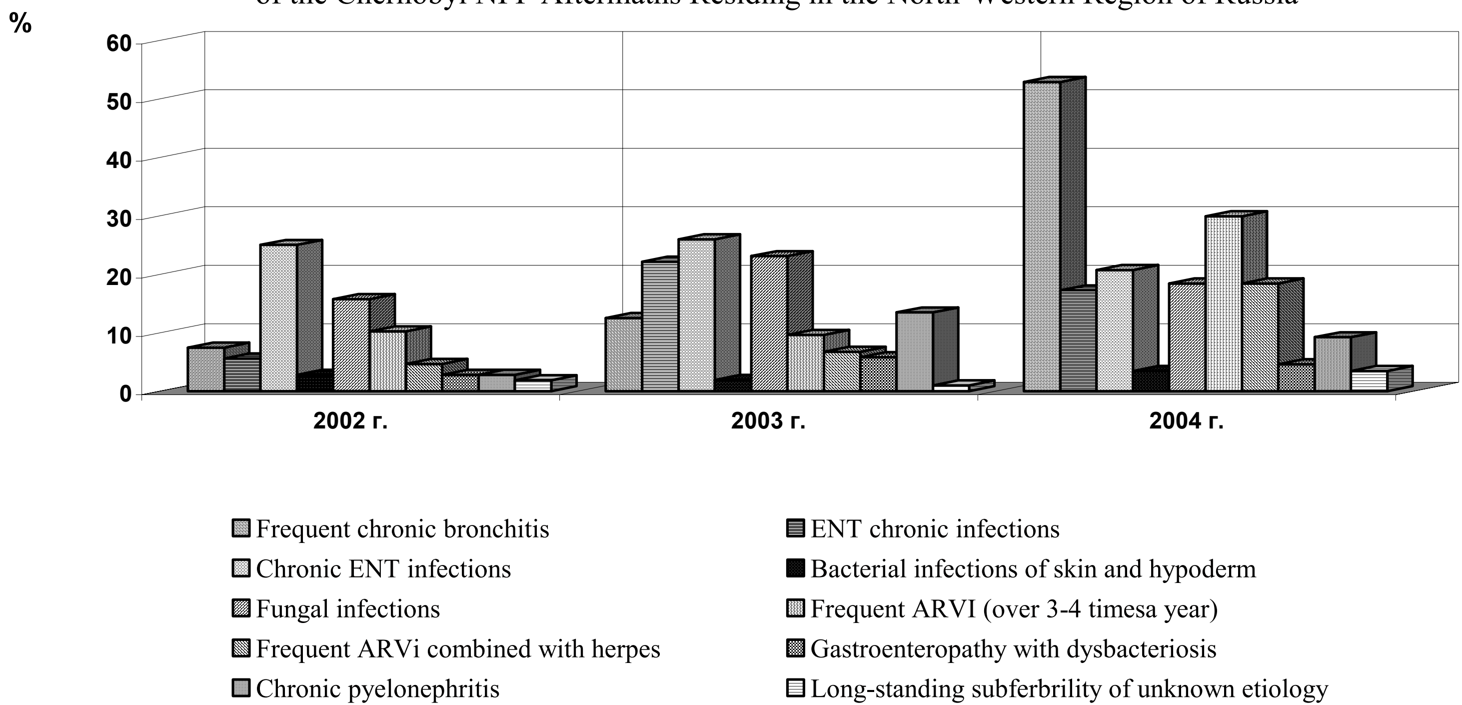
Based on the regional specifics, one may note that the index of clinical signs of immunopathology among the liquidators of the Chernobyl disaster residing in Krasnoyarsk Territory is similar to that of the personnel of the Mining Chemical Integrated Works (GHK) located in the same Territory. The qualitative distribution pattern of basic immunopathological syndrome is different. Clinical signs of immunodeficiency prevail in the liquidators immunopathological syndrome structure, whereas the total index for infection and combined pathology of the infection and allergy syndrome are very high.

The distribution of clinical immunopathological syndrome for the GHK personnel is fairly regular [31].

Dynamics of Occurrence of the Chronic Bodily Diseases

According to the monitoring of liquidators residing in three regions of Russia, chronic bodily diseases most often occur among the individuals who participated in liquidation of the Chernobyl disaster. The most common chronic pathology is observed among 95-98% of the examined individuals, while 80-84% individuals appear to have three and more chronic diseases (see Fig. 7). The dominant pathology among liquidators in the remote post-disaster period are the diseases affecting the circulatory system (circulatory system), such as: atherosclerosis, idiopathic hypertensia, coronary heart disease, cerebrovascular pathology, dyscirculatory encephalopathy (CVP:DEP). These are the diseases characteristic for middle-aged individuals. However, they occur among the liquidators of the Chernobyl disaster 10-15 years sooner.

Fig. 6 Structure of the Infection Syndrome Immunodeficiency Clinical Signs among Liquidators of the Chernobyl NPP Aftermaths Residing in the North-Western Region of Russia



The course of circulatory system diseases, especially the CVP:DEP, among the liquidators is characterized by seizures, memory corporals affecting attention, etc., and has clinical differences from the persons who have not participated in liquidation. Signs of hypercholesterolemia have also been revealed. The occurrence of lipid exchange disorders with the increased level of low-density lipids among the liquidators is three times higher than among the individuals who have not participated in liquidation. The increased rate of occurrence of middle age diseases indicate premature aging among liquidators.

Table 3 – Structure and Dynamics of the Occurrence of Clinical Signs of Immunopathology among the Liquidators of Chernobyl NPP Disaster Residing in Krasnoyarsk Territory - 2001-2004

Ref. No.	Clinical Signs of Immunodeficiency	2004	2003	2002	2001
		n=64	n=74	n=194	n=231
	I. Infection Syndrome:				
1	Frequent chronic bronchitis	**20.31**	12.16	8.25	12.12
2	Chronic bronchitis without frequent recrudescence	3.13	4.05	10.31	–
3	Frequent bronchitis with chronic infection of the ENT	–	2.70	3.61	5.19
4	Bronchitis with bronchospastic component and enhanced vulnerability to acute respiratory viral infections	–	5.41	4.12	2.16
5	Chronic obstructive bronchitis	**31.25**	**22.97**	7.22	9.52
6	Bronchitis (total)	**54.69**	**36.49**	**33.51**	**29.0**
7	Chronic pneumonia	–	1.35	–	–
8	Frequent ENT infections	**17.19**	**2.70**	**6.70**	4.33
9	Bacterial infections of skin and hypoderm	–	1.35	3.09	3.03
10	Fungal infections	–	6.76	**7.22**	5.19
11	Frequent acute respiratory viral infections (over 3-4 times a year)	**60.94**	**27.03**	**25.26**	**25.11**

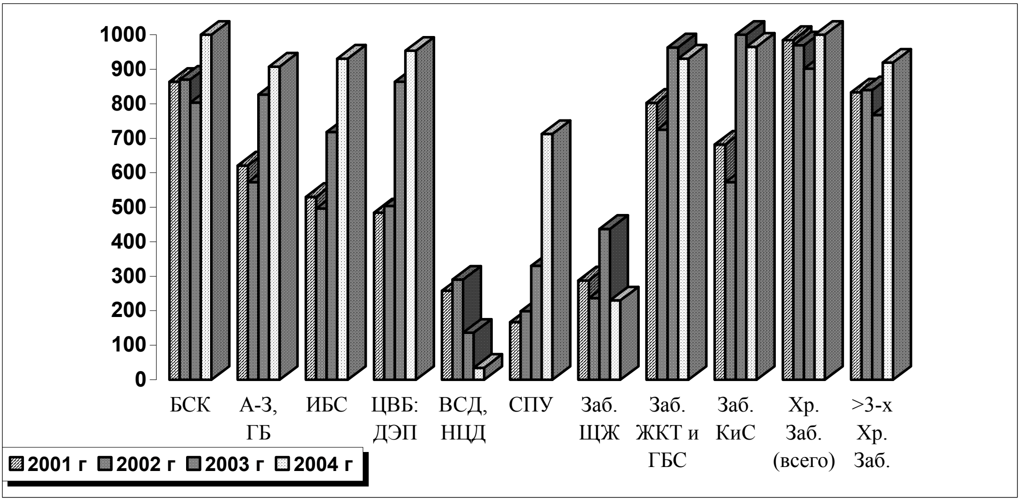
12	Frequent acute respiratory viral infections interfacing with ChRHVI	17.19	**14.86**	**7.22**	**9.09**
13	ChRHVI without frequent acute respiratory viral infections	3.13	4.05	1.55	–
14	Gastroenteropathy with dysbacteriosis	–	4.05	1.55	3.03
15	Chronic pyelonephritis, cystitis	3.13	**5.41**	3.09	6.06
16	Long-standing subfebrilitetis of unknown etiology	–	6.76	5.15	2.16
17	Periodontosis with frequent recrudescence	4.69	–	2.06	2.60
18	Lymphadenopathy	–	–	1.03	1.30
	II. Allergy Syndrome				
1	Atopic dermatitis	1.56	1.35	3.09	7.79
2	Weeping dermatitis	–	1.35	5.15	2.60
2	Allergic syndesmitis	–	–	2.58	0.43
3	Allergic rhinitis	–	–	4.64	5.19
4	Rhinal syndesmitis	–	5.41	6.70	7.79
5	Pollen fever	1.56	5.41	5.67	7.79
6	Bronchial asthma	3.13	**6.76**	3.09	2.16
7	Recurring urticaria	–	–	2.06	0.43
9	Sensibilization to allergens from domestic dust, drugs, etc.	1.56	**24.32**	**19.59**	**21.65**
10	Allergy to food	–	1.35	–	–
11	Latent sensibilization	1.56	6.76	5.15	3.46
	III. Autoimmune Diseases				
1	Autoimmune thyroiditis	1.56	2.70	2.06	0.87
2	Diabetes (Type I and II – requiring insulin)	6.25	0*	1.03*	0*
3	Rheumatoid arthritis	–	–	0.52	0.43
4	Rheumatism	–	–	–	0.43
5	Autoimmune glomerulonephritis	–	1.35	–	0.87
6	Psoriasis	–	1.35	0.52	1.30

*– Two cases of diabetes Type II in 2001 and 2003; four cases in 2002

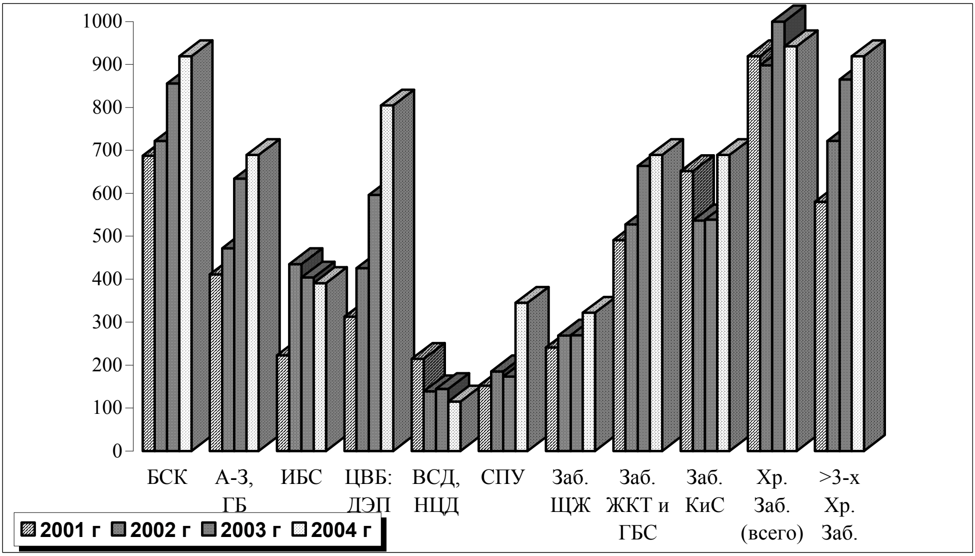
High occurrence of chronic pathology among liquidators residing in the city of Moscow and Moscow Region was observed by the beginning of the fourth lustrum following the Chernobyl disaster [12,15,17]. Analysis of the dynamics of the occurrence of the most common chronic bodily diseases in 1997–2002 and, especially, in 2003–2004 (the fourth lustrum) revealed significant growth virtually by all classes of diseases (see Fig. 6). 100% of the examined individuals had chronic bodily diseases. Significant growth of diseases affecting the circulatory system has been revealed in all nosological forms related to atherosclerosis. Circulatory system diseases are revealed in 98.2% of individuals within the examined group. The frequency of atherosclerosis with idiopathic hypertensia and coronary heart disease grew 1.47 times against 2002; cerebrovascular disease – 1.74 times; 82.7% individuals suffer from systematic atherosclerosis and idiopathic hypertensia. Digestive system diseases have been revealed in 96.4% patients. Gastrointestinal tract diseases accounted for the most significant growth of: 51.88%→95.45%. 100% of the examined individuals suffer from the musculoskeletal system diseases, including 91.8% – deforming osteochondrosis; 39.1% of which had deforming osteoarthrosis and/or chronic polyarthritis. Among other nosological forms of diseases in 2003 the researchers revealed the increasing occurrence of thyroid gland disease, mostly due to the autoimmune thyroiditis, pathology of visual organs of non-infection etiology, urolithiasis and benign neoplasm (papilla, basalioma, adenoma, etc.), which were found in over 1/3 of the individuals under examination. The occurrence of circulatory system diseases of all nosological forms increased in 2003–2004, same as overall index of CD and polymorbidity syndrome, i.e. individuals suffering from over three CD at a time. The data provided herein is sufficient proof of dramatic deterioration of health of the liquidators in 2003–2004 against the period between 2002-2001. It should be noted that the growth of pathology is observed both in clinical signs of immunodeficiency and in chronic bodily diseases.

Fig. 7 Occurrence Rates for the Most Common Chronic Bodily Diseases among the Liquidators of the Chernobyl Disaster (per 1,000 persons)

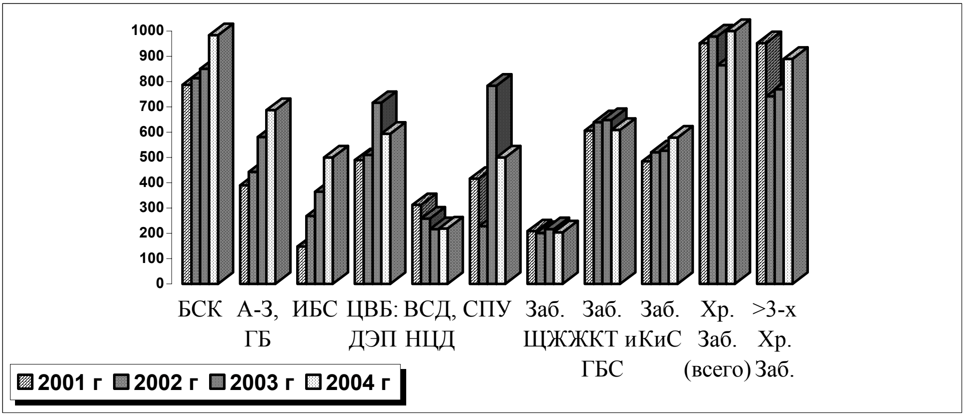
Moscow and Moscow Region



Northwestern Part of Leningrad Region



Krasnoyarsk Territory



Legends:

БСК – Circulatory system diseases
А-З – Allergy diseases
ИБС - Coronary heart disease
ЦВБ:ДЭП – CVP:DEP
ВСД, НЦД – VVD, CPN
СПУ –Ppost-oncotomy conditions
Заб. ЩЖ – Thyroid gland diseases
Заб. ЖКТ и ГБС – Digestive tract and hepatobiliary diseases
Заб. КиС – Diseases of bones and joints
Хр. Заб.(всего) – Chronic diseases (total)

The occurrence of certain classes of chronic bodily diseases among the liquidators residing in Moscow Region is higher than in the Northwestern region and in Krasnoyarsk Territory, especially by specific nosological forms of the circulatory diseases, which may be attributed to the “large megalopolis” effect. However, overall chronic pathology index is similar in all three groups under examination (see Fig. 7).

One examined individual had very similar signs of over three chronic bodily diseases at a time. Similar data was also obtained from the analysis of disease rates among the liquidators residing in St. Petersburg and other territories of the Northwestern region, which indicate that the incidence rate in St. Petersburg by a variety of disease classes is 1.4-3.3 times higher than in Leningrad Region, Novgorod Region, Pskov Region and Tver Region [30].

Dynamics of the occurrence frequency for the circulatory diseases (circulatory system diseases) and other chronic pathologies among liquidators residing in Moscow Region is represented on Fig. 8. The data therein indicate a negative situation, especially in terms of atherosclerosis, coronary heart disease (coronary heart disease) and dyscirculatory encephalopathy (CVP:DEP) against the reduction of occurrence of functional disorders (vegetative-vascular dystonia, cardiophyshoneurosis - VVD, CPN), which proves the progressive deterioration of the cardio-vascular system among the liquidators of the Chernobyl disaster. In 2002 there was a tendency toward reduction of the occurrence of certain circulatory system diseases, such as atherosclerosis and idiopathic hypertensia, coronary heart disease as well as CD gastrointestinal tract, bones and joints. This may be due to the specific composition of the examined groups, as well as mortality among the liquidators resulting from the multiple organ pathology.

Reduction in the occurrence of functional disorders was also revealed based on the data of the N.E. Meskikh Medical and Dosimetric Register (Obninsk, 1999) [10]: for the period of 1991-1997 and up to 1998, the CPN occurrence frequency reduces from 41% to 13%, which, on the whole, indicates the increasingly heavy flow of pathology, increase of the share of diseases with a pronounced organic pathology, which often results in disability.

The occurrence of coronary heart disease among the liquidators during this period grew from 20.0% to 58.9% in 1998 and was the most common in overall circulatory system diseases structure leading to disability. The occurrence of encephalopathy of various etiologies in 1998 grew to 61.5% against 25% in 1991-1997. The occurrence of ailments as nasty as acute cerebral circulation disorder grew from 4% to 10%. The author explains the early development of this pathology among the liquidators (especially in 1986) by the data available in specialized literature on the early development of atherosclerotic damage to coronary and cerebral vessels among individuals residing in the streets affected by irradiation.

Fig. 8 Dynamics of the Occurrence Rates for BCD, Digestive Apparatus and Musculoskeletal System Diseases among Liquidators of the Chernobyl Disaster residing in Moscow and Moscow Region over a Remote Period of 1997-2004 (per 1,000 persons)

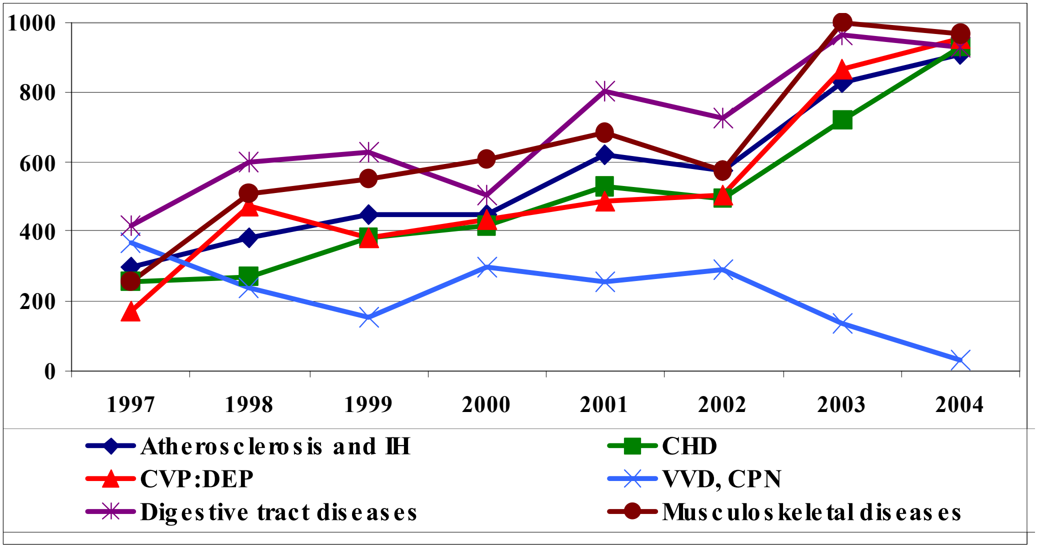


Table 4 – Frequency of CD among Individuals Participating in Liquidation of the Chernobyl Disaster Currently Residing in Moscow and Moscow Region Based on the 2001-2004 Monitoring Data

Ref. No.	Disease	2004		2003		2002		2001	
		n=87	%	n=110	%	n=133	%	n=66	%
Circulatory System Diseases		87	**100.0**	108	**98.18**	114	**85.71**	56	**84.85**
1	Atherosclerosis + idiopathic hypertensia	**79**	**90.80**	91	**82.72**	75	**56.39**	41	**62,12**
2	Coronary heart disease	**75**	**86.20**	79	**71.81**	65	**48.87**	35	**53,03**
3	VVD, CPN	**3**	**3.45**	10	**9.09**	34	**25.56**	18	**27,28**
4	CVB: dyscirculatory encephalopathy	**84**	**96.55**	100	**90.91**	66	**49.62**	32	**48,49**
5	Varicosity of the lower extremities	4	4.60	4	3.64	4	3.01	1	1,52
Neuropsychic Diseases		72	**82.75**	88	**80.0**	55	**41.99**	27	**40.91**
7	Asthenia, neurasthenia	40	**45.97**	59	**53.63**	27	20.30	10	15.15
8	Undue fatigability syndrome	62	**71.26**	69	**62.72**	26	19.55	12	18.18
9	Organic brain diseases, psycho-organic syndrome	12	13.80	16	**14.54**	17	**12.78**	6	**9.09**
10	Polyneuropathy	6	6.89	10	9.09	2	3.03	2	1.50
Digestive System Diseases (total)		80	**91,95**	106	**96.36**	96	**72.18**	52	**78.79**
11	**Diseases of the digestive tract** (chronic gastritis, gastroduodenitis, peptic ulcer	80	**91.95**	105	**95.45**	69	**51.88**	43	**65.15**
12	Hemorrhoids	2	2.30	5	4.54	5	3.76	1	1.52
13	Chronic cholecystitis, cholecystopancreatitis	40	**45.97**	54	**49.09**	54	**40.60**	28	**42.42**

14	Chronic pancreatitis	5	5.74	10	9.09	–	–	–	–
15	Adipoid hepatosis, adipose degeneration of lever	18	20.68	19	17.27	7	5.26	7	10.61
Musculoskeletal System Diseases		83	**95,40**	110	**100.0**	88	**66.17**	49	**74.24**
16	Vertebral column osteochondrosis deformans	83	**95.40**	101	**91.81**	75	**56.39**	45	**68.18**
17	Chronic polyarthritis, osteoarthrosis	31	35.63	43	39.09	19	14.29	6	9.09
18	Arthralgia, osteoalgia, myalgia	52	59.77	60	54.54	23	17.29	16	24.24
Other Chronic Pathologies									
19	Multiple caries	2	2.29	11	10.0	8	6.02	9	13.64
20	Thyroid gland disease with AT	26	**29.88**	47	**42.72**	40	**30.08**	**20**	**30.30**
21	Visual organ pathology w/ unknown etiology	9	10.34	55	**50.0**	13	9.77	6	9.09
22	Irradiation cataract	4	4.59	9	8.18	5	3.76	3	4.55
23	Perceptive hearing loss	4	4.59	7	6.36	2	1.50	–	–
24	Dyshidrotic eczema (non-allergic)	1	1.15	4	3.63	1	0.75	2	3.03
25	UL	16	18.39	29	**26.36**	21	16.03	11	16.67
26	HPN	6	6.89	5	4.54	–	–	–	–
27	Adiposis	11	12.64	8	7.27	–	–	–	–
28	Diabetes Type II	3	3.45	5	4.54	4	3.01	1	1.52
29	Benign tumors	21	**24.13**	39	**35.45**	8	**14.10**	9	13.64
30	Conditions after removal of malign tumors	3	3.45	3	2.72	2	1.50	2	3.03
31	**Three or more diseases at a time (SPM)**	80	91.95	110	**100.0**	112	**84.21**	56	**84.85**

32	**Chronic diseases** (total)	87	100.0	110	**100.0**	129	**96.99**	65	**98.48**

According to the data obtained in 2004, the occurrence frequency grew for chronic bodily diseases and, essentially, the Circulatory system diseases, which were revealed in 100% of the examined liquidators residing in the city of Moscow and Moscow Region. This being the case, the research revealed the growth in all nosological forms of circulatory system diseases interfacing with atherosclerosis, while the occurrence of VVD and CPN was reducing (see Tables 4 and 5; Fig. 7 and 8). The circulatory system diseases structure shows a tendency toward the growth of atherosclerosis, including atherosclerosis interfacing with idiopathic hypertensia (idiopathic hypertensia) of II and III degree, atherosclerosis without idiopathic hypertensia, coronary heart disease and cerebrovascular pathology along with decreasing occurrence of VVD, CPN among those examined who do not have atherosclerosis, and CVP:DEP – without atherosclerosis and dyslipidemia. The occurrence of neuropsychic diseases with a certain growth tendency in 2003-2004 has comparable indices. The frequency of occurrence of the digestive system and the musculoskeletal system, as well as polymorbidity among the group of liquidators examined in 2004 showed a tendency toward certain reduction against 2003, which can be explained by the composition of the examined groups.

Table 5 – Structure and Frequency of Occurrence of the circulatory system diseases among the Liquidators of the Chernobyl NPP Aftermaths residing in the city of Moscow and Moscow Region based on the 2003-2004 Monitoring Data

Disease	**2004**		**2003**	
	n=87	**%**	**n=110**	**%**
Circulatory System	**87**	**100**	109	**99,09**
Atherosclerosis with and without idiopathic hypertensia	79	**90.80**	90	81.82
Atherosclerosis (total)	77	**88.50**	69	**62.72**
Idiopathic hypertensia (total)	48	**55.17**	67	**60.90**

Idiopathic hypertensia I – total	7	8.04	17	15.45
Idiopathic hypertensia II – total	36	**41.38**	48	**43.63**
Idiopathic hypertensia III – total	5	5.74	6	5.45
Idiopathic hypertensia I – without atherosclerosis	2	2.29	7	6.36
Atherosclerosis + idiopathic hypertensia I	5	5.74	10	9.09
Atherosclerosis + idiopathic hypertensia II	36	**41.38**	36	**32.72**
Atherosclerosis + idiopathic hypertensia III	5	5.74	4	3.63
Atherosclerosis without idiopathic hypertensia	31	**35.63**	23	**20.90**
Examined individuals without idiopathic hypertensia and atherosclerosis	8	**9.19**	20	**18.18**
Coronary heart disease	75	**86.20**	79	**71.81**
VVD, CPN	3	3.45	10	9.09
CVB: dyscirculatory encephalopathy	84	**96.55**	100	**90.90**
CVP:DEP without atherosclerosis и dyslipidemia	2	2.29	28	**25.45**

Up to 2000, the indices for thyroid gland disease (ЩЖ) were fairly stable (1/4 of the examined individuals) with a slight rise in 2001. During the period of 2001-2002 the ЦЖ pathology occurrence was at the rate of 30%, with maximum rise to 42.72% in 2003. In 2003 the thyroid gland disease incidence was 427.2:1000 against 300.8–303.0:1000 in 2002–2001. The growth was based on the increasing detection of autoimmune thyroiditis, which was diagnosed in 29.09% (32:110) cases. Nodular or diffused forms of thyroiditis were observed in 15.45% (17:110) of cases. In 2004 the ЦЖ occurrence was lower than in 2003 and reached the level of 2001-2002.

According to the data above, the dynamics of blood circulation CD among the liquidators, including atherosclerosis +

idiopathic hypertensia, coronary heart disease and CVP:DEP, in 2004 was growing by all nosological forms, while the occurrence of VVD and CPN was going down (see Fig. 8). As far as the 2003-2004 occurrence is concerned, the CVP:DEP and atherosclerosis were increasing side-by-side. Moscow Region is second to none of the other monitored groups of liquidators both in terms of frequency of chronic bodily diseases and the growth rate of pathology.

The liquidators residing in the Northwestern part of Leningrad Region in the third lustrum following the Chernobyl disaster were less exposed to CD and clinical signs of immunodeficiency compared to liquidators residing in the city of Moscow and Moscow Region [12]. In the fourth lustrum the liquidators residing in the Northwestern part of Leningrad Region appear to be more frequently prone to chronic pathology. By 2004, the chronic bodily diseases were found in 94.25% of the examined individuals, whereas polymorbidity syndrome was found in 91.95% of the examined individuals (see Table 6, Fig. 7). There appears to be a tendency toward steady growth in the percentage of persons having three or more chronic bodily diseases, which is indicative of deterioration of the liquidators' health. The circulatory system diseases have become increasingly frequent and by 2003-2004 the frequency in occurrence was 858.8 – 942.5:1,000, which is close to the index of circulatory system diseases among the Moscow and Moscow Region liquidators in 2002-2003. The circulatory system diseases structure is also dominated by atherosclerosis, idiopathic hypertensia and CVP:DEP, the frequency of which in 2003 grew 1.34 and 1.40 times correspondingly against the number of individuals examined in 2002. The highest increase rate was revealed for cerebrovascular pathology (see Fig. 9), the frequency of CVP:DEP in 2004 in 2004 was almost two times higher, followed by the digestive system diseases (1.74 times). Over 50% of those examined in 2002-2003 (80.5% in 2004) appeared to suffer from the disease of bones and joints: deforming osteochondrosis, osteoarthrosis, muscle-joints pain syndrome, etc.

On the whole, as far as the occurrence among the liquidators residing in the Northwestern region is concerned, the period between 1999-2004 is dominated by circulatory system diseases, followed in 2003 by the digestive system diseases, with diseases of bones and joints being the second 'runner-up'. It should be noted that while the

CD of the musculoskeletal system and the digestive systemin 2002 had very similar values and ‘competed’ in terms of the occurrence, in 2003–2004 the CD of the digestive system left the CD of musculoskeletal system behind. Among liquidators residing in the city of Moscow and Moscow Region, the CD of the digestive system in 2001 and 2002 were ahead of the CD of the musculoskeletal system. In 2003 a similar situation was present in the Northwestern part of Leningrad Region.

Table 6 – Frequency of the CD among Individuals Participating in Liquidation of the Chernobyl Disaster Currently Residing in the Northwestern Region Based on the 2001-2004 Monitoring Data

Disease	2004, n=87		2003, n=104		2002, n=108		2001, n=112	
	q-ty	%	q-ty	%	q-ty	%	q-ty	%
Blood Circulation Diseases	82	94.25	89	85.58	78	72.22	77	68.75
Atherosclerosis, idiopathic hypertensia	60	68.97	66	63.46	51	47.22	46	41.07
Coronary heart disease	34	39.08	42	40.38	47	43.52	25	22.32
VVD, CPN	10	11.49	15	14.42	15	13.89	24	21.43
CVB: dyscirculatory encephalopathy	70	80.46	62	59.62	46	42.59	35	31.25
Neuropsychic Diseases	41	47.13	36	34.62	28	25.93	28	25.0
Asthenia	15	17.24	16	15.38	10	9.26	10	8.66
Organic brain diseases, psycho-organic syndrome	5	5.75	6	5.77	3	2.78	2	1.79
Undue fatigability syndrome	30	34.48	18	17.31	20	18.52	17	14.06
Digestive System Diseases	80	91.95	69	66.35	57	52.78	50	44.64

Diseases of the digestive tract (gastritis, gastroduodenitis, peptic ulcer, chronic colitis, etc.)	60	68.97	59	56.73	51	47.22	41	36.61
Cholecystitis, cholecystopancreatitis	22	25.29	27	25.96	21	20.59	16	14.29
Chronic hepatitis, hepatosis	7	8.05	10	9.62	6	5.56	7	6.25
Musculoskeletal System Diseases	70	80.46	56	53.85	58	53.7	70	62.50
Osteochondrosis deformans	60	68.97	50	48.08	50	46.30	63	56.25
Chronic polyarthritis	4	4.60	2	1.92	7	6.48	7	6.25
Muscle-joints pain syndrome	15	17.24	6	5.77	9	8.33	21	18.75
Osteoarthrosis	14	16.09	11	10.58	7	6.48	12	10.71
Vein diseases	17	19.54	16	15.39	11	10.19	4	3.57
Thyroid gland diseases (hyperplasia, autoimmune thyroiditis)	17	19.54	28	26.92	29	26.85	27	24.11
Psoriasis	0	0	1	0.96	4	3.72	4	3.57
Multiple caries	1	1.15	0	0	4	3.72	1	0.89
Visual organs diseases	8	9.20	9	8.65	9	8.33	9	8.04
Irradiation cataract	0	0	0	0	5	4.63	4	3.57
UL	2	2.30	11	10.58	12	11.11	11	8.59
Benign tumors	10	11.49	13	12.50	18	16.67	15	13.39
Conditions after removal of malign tumors	5	5.75	4	3.85	3	2.78	3	2.68
Three or more diseases at a time	80	91.95	90	86.54	78	72.22	65	58.04

Chronic diseases (total)	82	94.25	104	100.00	97	89.81	103	91.96

Dynamics of changes in frequency of circulatory system diseases among liquidators residing in the Northwestern region (see Fig. 9) were characterized by a relatively uniform, albeit significant and steady increase of atherosclerosis, idiopathic hypertensia (in the period of 1994–2004) and CVB (1999–2004), as well as two peaks of coronary heart disease in 1999 and 2002, and a slight reduction of the coronary heart disease frequency in 2003-2004 against 2002. Changes in frequency of VVD and CPN were emphasized by the increasing occurrence in the period between 1988 and 1994, i.e. the earlier terms following the participation in liquidation activities, with the peak of occurrence in 1994, followed by reduction during 1994-1999, and doubling back in 2001 against 1999, however still much lower than the 1994 level, and again followed by reduction during the period of 2001-2004.

The dynamics of incidence of the digestive system diseases among the liquidators residing in the Northwestern region was characterized by a continuous and steady growth in 1988-2004, with the peak of the DAD occurrence in 2004. The dynamics of frequency of the bones and joints diseases was also characterized by a continuous, albeit faster, growth up to the year of 2001 followed by a slight drop in 2002, holding on a similar level in 2003 (against 2002) and resuming its growth in 2004.

The increasing rate of the digestive system CD was revealed in both groups under examination 0 the liquidators from the Northwestern part of Leningrad Region and liquidators residing in the city of Moscow and Moscow Region, which lasted until 2003. However, the incidence of such diseases in Moscow Region is much higher (1.45 times), whereas in 2004 it is at level with the Northwestern region. Frequency in CD of bones and joints among the liquidators from Moscow Region in 2003 was almost 2 times higher, although in 2004 the gap is closing considerably (95.40% – 80.46%).

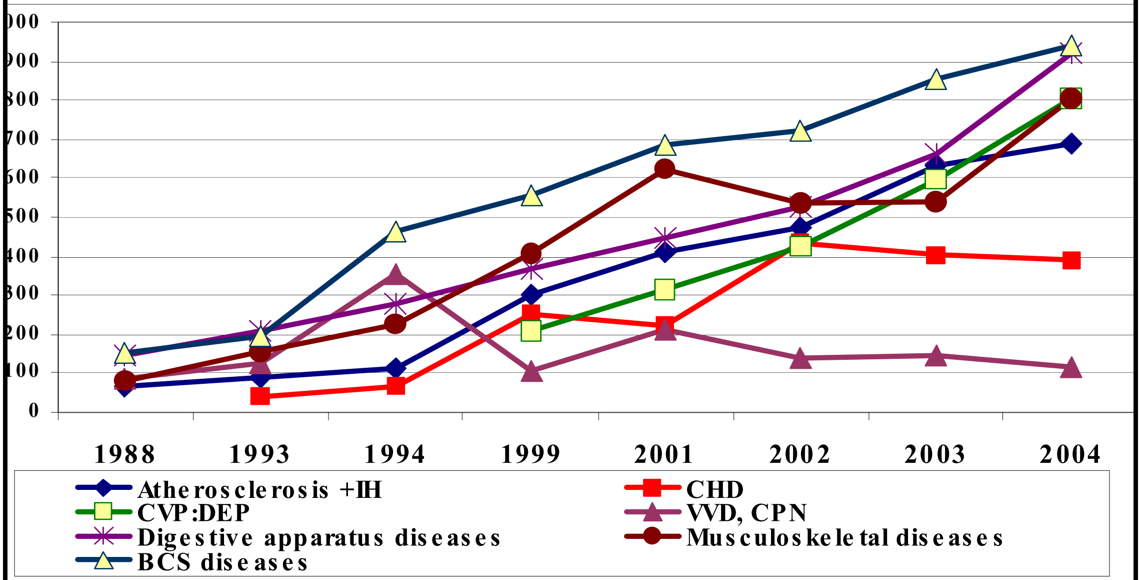
Analysis of incidence in chronic pathology among the liquidators residing in Krasnoyarsk Territory (see Fig. 10, Table 7) also revealed high frequency of CD – 95.24% (220:231) in 2001, and 97.94% (190:194) in 2002. The difference in frequency of 3 or more

CD at a time: 93.1% in 2001, and 74.23% in 2002, which is largely due to the difference in composition of the examined groups. The average age of liquidators having CD at the date of examination in 2001 was 50.63±0.63; whereas those having 3 or more CD – 50.76±0.64, i.e. the values are identical and the percentage of CD does not depend on the age of liquidators. The CD occurrence frequency among the liquidators residing in Krasnoyarsk Territory as of 2002 was consistent with that of liquidators residing in Moscow Region. However, there are some discrepancies in the frequency of occurrence of 3 and more CD at a time.

According to the 2001-2002 monitoring data on liquidators residing in the city of Moscow and Moscow Region, 3 and more CD at a time occurred in 84.85%–84.21%. The frequency among liquidators residing in Krasnoyarsk Territory is almost similar to that of the Northwestern region – 72.22% or 742.27:1,000 and 722.22:1,000 accordingly. The group examined in 2003, CD was diagnosed in 86.49% cases, which is lower than the values effective in the preceding years. The significant difference in the frequency of the CD occurrence is most likely based on a much smaller group examined in 2003 against the number of liquidators examined in 2001-2002. The 2003 polymorbidity rate is consistent with the 2002 values, with an upward tendency.

The CD structure for liquidators residing in Krasnoyarsk Territory (as well as in other groups) is dominated by circulatory system diseases: atherosclerosis, idiopathic hypertensia, CVP:DEP and coronary heart disease. Based on the data of biannual observation, the occurrence of developed circulatory system diseases is 787.88:1,000 (2001) and 814.43:1,000 (2002). The average age of liquidators suffering from atherosclerosis, idiopathic hypertensia and arterial hypertension is 51.75±1.02; CVP:DEP – 51.84±0.87; clinical signs of a psycho-organic syndrome – 50.12±1.30. These diseases naturally manifested themselves much sooner. They belong to the "middle-age" diseases, dominate in all groups of liquidators, and indicate that biological age is surpassing the passport age, which means premature ageing.

Fig. 9 Dynamics of Incidence of the BCS and Diseases of the Digestive Apparatus and Musculoskeletal System among Liquidators Residing in the North-Western Region (per 1,000 persons) in 1988–2004



Premature ageing of liquidators in just 7-10 years after the Chernobyl disaster was also revealed by the experts of Kharkov Medical Radiology Research Institute, Ukraine [21]. The early manifestation of an age-based pathology, such as cerebral atherosclerosis and idiopathic hypertensia, promoting the frequent infarctions and apoplexy resulting from extended effect of small irradiation dosages (both ionizing and non-ionizing), was pointed out by Y.G. Grigoryev in his works [3]. Byelorussian research workers also report the development of premature ageing syndrome [2].

Changes in the eye-ground, such as incipient phacosclerosis, retinal angiodystrophy, incipient cataracts (both irradiation and geriatric) and presbyopia, also prove the fact of premature ageing of liquidators. Acceleration of the ageing processes is also manifested through reduction of the top cortical functions. The liquidators suffer from enhanced psycho-emotional tension, anxiety reactions, and reduced adaptive capabilities along with inadequate assessment of their own health status. Deterioration of health, inability to perform prior assignments at the same rate and the same scope and loss of job resulted in psychological discomfort, perplexity, pessimism and social maladjustment, which added up to a closed circle of problems hard to solve in conditions of social disadaptation and promoted misbalance in functioning of the basic vital systems of the body and accelerated ageing.

Table 7 – Frequency of the CD among Individuals Participating in Liquidation of the Chernobyl Disaster Currently Residing in Krasnoyarsk Territory Based on the 2001-2004 Monitoring Data

Disease	**2004, n=64**		**2003,n=74**		**2002, n=194**		**2001, n=231**	
Circulatory System Diseases	63	98.44	63	85.14	158	81.44	182	78.79
Atherosclerosis, idiopathic hypertensia	44	68.75	43	58.11	86	44.32	90	38.96
Coronary heart disease	32	50.0	27	36.49	52	26.80	34	14.72

CVB: dyscirculatory encephalopathy	38	59.38	53	71.62	99	51.03	113	48.92
VVD, CPN	14	21.88	16	21.62	50	25.77	72	31.17
Neuropsychic Diseases	34	53.13	61	82.43	70	40.72	103	44.59
Psycho-organic syndrome	6	9.38	19	25.68	28	14.43	41	17.75
Undue fatigability syndrome	32	50.0	58	78.38	44	22.68	96	41.56
Asthenia	8	12.50	10	13.51	18	9.28	19	8.23
Polyneuropathy	1	1.56	2	2.70	8	4.12	7	3.03
Thyroid gland diseases (without autoimmune thyroiditis)	13	20.31	16	21.62	39	20.10	48	20.78
Digestive System Diseases	39	60.94	48	64.87	124	63.92	140	60.61
Diseases of the digestive tract	30	46.88	35	47.30	82	42.27	94	40.69
Cholecystitis, cholecystopancreatitis	19	29.69	34	45.95	80	41.24	90	38.96
Chronic hepatitis, hepatosis	5	7.81	12	16.22	12	8.69	16	6.93
Musculoskeletal System Diseases	37	57.81	39	52.70	101	52.06	112	48.49
Osteochondrosis deformans	33	51.56	36	48.65	86	44.32	105	45.45
Chronic polyarthritis, osteoarthrosis	3	4.69	6	8.11	16	8.25	21	9.09
Osteoarthrosis	2	3.13	1	1.35	3	1.56	20	8.66
Muscle-joints pain syndrome	13	20.31	3	4.05	13	6.70	20	8.66

Palmar fibromatosis	–	–	–	–	2	1.04	1	0.43
Vascular diseases	2	3.13	3	4.05	8	4.12	22	9.52
Multiple caries, periodontosis	–	–	1	1.35	8	4.12	16	6.93
Benign tumors	6	9.38	10	13.51	8	4.12	12	5.19
Conditions after removal of malign tumors	2	3.13	3	4.05	8	4.12	3	1.30
Visual organs pathology, non-infection etiology	9	14.06	12	16.22	12	6.19	44	19.05
Irradiation cataract	7	10.94	2	2.70	4	2.06	11	4.76
Acoustic organ pathology, non-infection etiology	1	1.56	3	4.05	3	1.55	2	0.86
Anemia	1	1.56	0	0	2	1.04	1	0.43
Diabetes Type II	3	4.69	2	2.70	4	2.06	2	0.86
Other	–	–	19	25.68	27	13.92	61	26.41
Three or more diseases at a time	57	89.06	57	77.03	144	74.23	220	95.24
Chronic diseases (total)	64	100.0	64	86.49	190	97.94	220	95.24
Apparently healthy	0	0	0	0	4	2.06	3	1.30

Compared to the 2001-2002 data, the 2003 CD Structure for liquidators residing in Krasnoyarsk Territory shows a steady tendency toward the increase of circulatory system diseases interfacing with atherosclerosis, especially CVP:DEP along with reduction of VVD, which also confirms ageing of liquidators (Table 7). Frequency of cerebrovascular pathology increased 1.46 times in 2003 amounting to 716.2:1,000. Observation during three years of the remote period indicate that CVP:DEP was prevailing in the structure of circulatory system diseases among the liquidators residing in Krasnoyarsk Territory, along with a fairly high frequency in occurrence of atherosclerosis and idiopathic hypertensia, and a lower frequency of coronary heart disease against the remaining two groups. Up to 2003, atherosclerosis and idiopathic hypertensia prevailed in the circulatory system diseases structure for liquidators residing in the city of Moscow, and only in 2003 did CVP:DEP go to the top in terms of frequency in occurrence, albeit remaining too close to atherosclerosis and idiopathic hypertensia values: 863.6 – 827.2 : 1,000. Even though all three examined groups demonstrate annual growth of the occurrence frequency for specific nosological forms of diseases interfacing with atherosclerosis, this pathology is more common among liquidators residing in the city of Moscow (Table 4 and Table 5).

The monitoring reveals high morbidity of the digestive system, bones and joints with pain syndrome. Average age of liquidators who suffer prolonged pains in bones, joints, column by the date of examination in 2001 was 49.08±1.03 years, and those diagnosed to have osteochondrosis deformans – 50.75±0.86. The frequency of the digestive system diseases in 2003 remained on a high level: 648.7:1,000; including the digestive tract diseases (47.30%) and hepatho-biliary system (51.4%). As far as the frequency in occurrence is concerned, the digestive system diseases are second in the chronic pathology structure, and as far the growth rates are concerned, in the last three years they have similar values, therefore one can say they remained at the same level. The incidence rates in the digestive system diseases are almost similar among the liquidators residing in Krasnoyarsk Territory and the Northwestern part of Leningrad Region, dragging far behind from those in Moscow and Moscow Region. The bone and joints are the third group of diseases in the chronic pathology structure, with identical values in 2002-2003. Compared to other groups of chronic diseases of the musculoskeletal system, the incidence rates are similar in Krasnoyarsk Territory and the Northwestern part of Leningrad Region, but in Moscow Region they are almost twice as high.

According to the 2004 monitoring data, all 1005 examined liquidators were diagnosed to have chronic somatic pathology (Table 7). The polymorbidity rates appear to be increasing as well. The frequency in chronic bodily diseases increases primarily due to the increasing incidence of circulatory system diseases, which are diagnosed in 98.44% (63:64) of the examined liquidators. The circulatory system diseases structure is dominated by atherosclerosis and idiopathic hypertensia, followed by CVP:DEP and coronary heart disease. The occurrence varies for coronary heart disease↑ and cerebrovascular pathology↓. The incidence of chronic diseases of the digestive system, the digestive tract, as well as diseases of bones and joints remain fairly stable with a certain tendency toward the increase of the overall index.

Therefore, by age 50 the liquidators have a whole gamut of chronic diseases affecting a lot of organs and systems, and the pathology has a poly-system and poly-morbid nature. Our data on high frequency of chronic diseases, as well as their steady growth and dominance of the circulatory system diseases among the liquidators is consistent with the examination results in Byelarus, Ukraine and Latvia [2,24,27]. The VCERM (All-Russia Center for Ecological and Radiation Medicine) experts also reveal multiple organ pathologies among the liquidators. Multiple vegetovascular dysfunctions with CPN and VVD occur in 76% of liquidators; the digestive tract diseases are diagnosed among 63% of individuals with coronary heart disease; external respiration dysfunctions or a diagnosed chronic bronchitis occur in 75% of the examined individuals. Pathology of musculoskeletal system and ailing joints occur in 95% of liquidators, and psychological status deviations have been revealed in 98% of cases [7].

The following data serves to demonstrate the extent of discrepancy between the CD incidence data applicable to the liquidators and other groups of patients. The circulatory system diseases occurrence among the Krasnoyarsk Territory GHK personnel is 281.9:1,000 [18, 31]. This value is 3.02 times lower (851.4:1,000) than with the liquidators. The circulatory system diseases structure is dominated by VVD (137.3:1,000) and atherosclerosis interfacing with the idiopathic hypertensia (127.7:1,000). The atherosclerosis interfacing with the idiopathic hypertensia occurs in liquidators residing in this region at the rate of 581.1:1,000 (2003) and 687.5:1,000 (2004), which is, accordingly, 4.55 and 5.38 times higher. For the Cherepovetsk Metallurgical Plant personnel employed in the chemical and metallurgical processing of uranium and in contact with the small-dosage radiation factor by way of profession, the circulatory system diseases incidence rate was 246.3:1,000, which is consistent with similar values for the GHK personnel [31]. The occurrence of chronic diseases of the digestive system among the examined GHK personnel was 424.1:1,000, whereas among the examined residents of this region it was 344.0:1,000, and the liquidators residing in Krasnoyarsk Territory this index was 648.7:1000, which is 1.55 times higher than for the personnel and 1.9 times higher than for the population. The rate of occurrence of chronic diseases of the digestive system among the liquidators is 1.77 times higher than that of the GHK personnel and 1.8 times that of the population; osteochondrosis deformans – 2.35 and 2.64 correspondingly. Comparison of frequency in cerebrovascular pathology among the Chernobyl disaster liquidators, the examined groups of the GHK personnel and the population of Krasnoyarsk Territory demonstrates disparate indices. CVP:DEP is diagnosed among the liquidators at the rate of 716.2:1,000 (2003), whereas for the GHK personnel this index is 31.3:1,000 and for population – 72.0:1,000, which means that the CVP:DEP occurrence frequency among the liquidators is 22.9 times higher than that of the GHK personnel and 9.95 times higher than that of the population. These figures are thoroughly convincing of the extent of hardship experienced by the Chernobyl disaster liquidators and prove how badly their health has deteriorated.

Occurrence of chronic somatic diseases among the liquidators residing in Moscow and Moscow region depending on disability or unavailability thereof

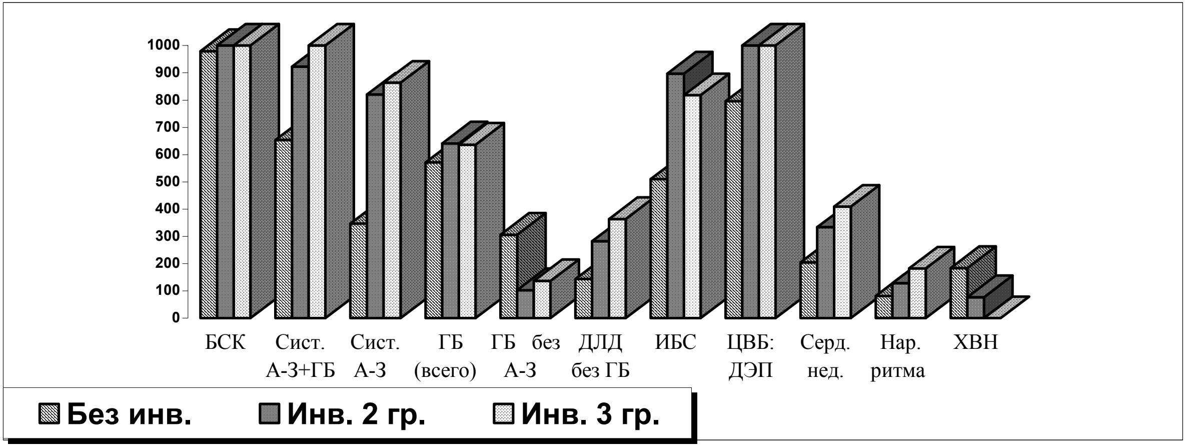
The research involved matching of the frequency in occurrence for chronic bodily diseases most common among liquidators having disability group II and III, as well as liquidators who were not disabled resulting from operations at the Chernobyl NPP (see Fig. 10). The matching revealed discrepancies based on the circulatory system diseases most common among the liquidators, which most frequently cause disability. On the whole, circulatory system diseases have been revealed in 100% of the disabled liquidators, regardless of disability group, and in 97.96% liquidators who were not disabled. The average age of liquidators having disability group II was 60.7±1.55 years (ranging from 42 to 82 years); disability group III – 50.3±2.20 years (34-68 years); not disabled individuals – 50.7±1.11 years (37-68). The higher occurrence frequency for circulatory system diseases interfacing with atherosclerosis, specifically, constitutional atherosclerosis with IH, coronary heart disease and cerebrovascular pathology is found in the groups of disabled individuals: atherosclerosis with IH is found among liquidators having disability group III, who are 10 years younger (according to their passport data) than individuals having disability group II.

Constitutional atherosclerosis and dyslipidemia without IH were also frequently diagnosed among the disability group III individuals. Arterial hypertension without atherosclerosis is more often found among liquidators without established disability. Significant differences between the groups of the disabled liquidators and the group of liquidators who were not disabled resulting from the performance at the Chernobyl NPP are identified by the frequency of coronary heart disease. The difference between disability groups II and III is negligible. However, the coronary heart disease occurrence is higher among the disability group II individuals. Cardiac insufficiency and arrhythmia are also frequently diagnosed among the disabled liquidators, and more frequently occur among the disability group III liquidators. Chronic vascular insufficiency with leg cramps is more often found among liquidators who have no disability status, whereas varicosity of lower extremities is found among the disability group II liquidators.

Cerebrovascular disease is very often found among all liquidators: 100% of the examined individuals having disability group II status were diagnosed to have CVP:DEP.

However, over 80% of liquidators without disability status appear to have cerebrovascular pathology as well. At the same time, vegetative-vascular disorders with symptoms of VVD and CPN are found only among the liquidators who have no disability status (20.4%). Apart from the circulatory system diseases, the differences in the occurrence frequency for chronic bodily diseases among the liquidators having disability group II and III are revealed by the following nosological forms (see Fig. 11).

Fig. 10. Structure and Occurrence Frequency of circulatory system diseases among Chernobyl NPP Disaster Liquidators Residing in the City of Moscow and Moscow Region Based on the 2003 Monitoring Data



Legends:

БСК – blood circulatory system diseases

ГБ – idiopathic hypertensia

Сист. А-З – systematic atherosclerosis; **ГБ** – hypertensive disease

ДЛД – dyslipidemia

без - without

ИБС – coronary heart disease

ЦВБ:ДЭП – cerebrovascular pathology: dyscirculatory encephalopathy

ХВН – chronic venous insufficiency; **Нар. ритма** – rhythm disturbance

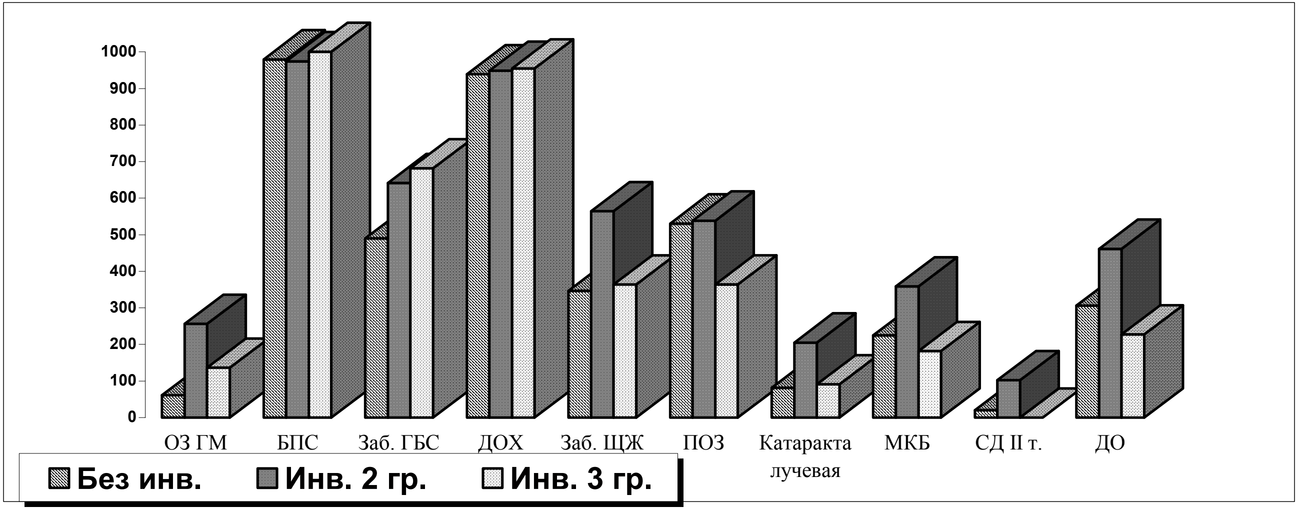
Серд. нед. – Cardiac insufficiency; **Без инв.** – No disability status; **Инв. 2 гр.** – II-group disability; **Инв. 3 гр.** – III-group disability

The liquidators having disability group II status slightly suffer more often of organic brain disease, psycho-organic syndrome, chronic pancreatitis, hepatosis and adipose degeneration, diseases of joints, thyroid gland + autoimmune thyroiditis, pathology of visual organ of non-infection etiology, irradiation cataract, urolithiasis, diabetes and proliferative benign tumors. Frequency of clinical signs of the undue fatigability syndrome and asthenia within all examined groups is rather consistent, although slightly more often revealed among individuals who have disability group II status. Liquidators having disability group III status are more often diagnosed for nosological forms of diseases comprising the circulatory system diseases structure, as well as chronic gastritis/gastroduodenitis, peptic ulcer, chronic cholecystitis and cholecystopancreatitis. Chronic diseases of the digestive system are most frequently diagnosed within each group, regardless of disability status.

Despite the high occurrence among the Chernobyl disaster liquidators, these diseases less frequently become the cause of disability than the blood circulation diseases. Hepatho-biliary system diseases, such as chronic cholecystitis and cholecystopancreatitis, are much more often observed among the liquidators who have a disability status. Diseases of bones and joints with muscle-joints pain syndrome and the frequently occurring column osteochondrosis are very often diagnosed in each group regardless of a disability status or absence thereof; chronic polyarthritis is more frequently observed among the disability group II liquidators.

Thyroid gland diseases + autoimmune thyroiditis, irradiation cataract, urolithiasis, Type II diabetes (requiring insulin) and proliferative diseases are more often diagnosed among liquidators, who acquired the disability status following their liquidation activities at the Chernobyl NPP.

Fig. 11 – Chronic Diseases Occurrence Frequency with Liquidators Residing in Moscow and Moscow Region, regardless of Disability Status – based on the 2003 Monitoring Data



Legends:

OBD *– organic brain diseases*

DAD *– digestive system diseases*

HBSD *– hepatobiliary system diseases*

COD *– column osteochondrosis deformans*

TGD *– thyroid gland diseases*

PVO *– pathology of visual organs*

UL *– urolithiasis*

D II t. *– diabetes Type II*

BT*– benign tumors*

Prevalence of Immunodeficiency Clinical Signs with Chernobyl Liquidators from the City of Moscow and Moscow Region Depending on Disability or Unavailability Thereof

It was established that liquidators of disability group II considerably developed more often chronic and recurring bronchitis, as well as chronic obstructive pulmonary disease, while chronic obstructive bronchitis occurs is almost as frequent with the liquidators of disability group II and those with disability group III (see Fig. 12). On the whole, frequent ear, nose and throat infections are diagnosed in liquidators with Invalidity status obtained after participation in Chernobyl NNP disaster liquidation (32.0%) compared with the liquidators having disability status (18.64%) irrespective of the group. To this regard, liquidators of disability group II are diagnosed with frequent ear, nose and throat infections 2.5 times more often than persons of disability group III, while such diseases as chronic tonsillitis and chronic sinusitis are more frequent with non-disabled Chernobyl aftermath liquidators. Liquidators of disability group II, as compared to liquidators of disability group III, twice as frequently suffer from fungal infections and onychomycosis. Disability status is in no way linked to such frequent clinic signs of immunodeficiency as frequent ARVI, including those combined with ChRHVI. Prevalence of frequent ARVI combined with ChRHVI, as well as ChRHVI irrespective of localization is somewhat higher with the liquidators of disability group III.

Therefore, much fewer differences are revealed in terms of occurrence frequency of clinical signs of infection-generated immunodeficiency with Chernobyl NPP aftermath liquidators depending on their disability status than in terms of their chronic bodily pathologies. Even fewer differences between liquidators depending on their disability status are revealed in terms of occurrence frequency in allergic pathologies. Main differences include more than twice as large prevalence of bronchial asthma with the liquidators with disability status (13.56%) as compared to those without such status (6.0%), severe atopic syndrome (14.29%) with persons of disability group III, and allergic rhinitis with persons of disability group II (15.8%) also compared to those with no disability status (6.0%). Comparison in prevalence of autoimmune pathologies with groups of Chernobyl NPP aftermath liquidators revealed the main differences related to the occurrence frequency of autoimmune thyroadenitis. The highest frequency of this pathology is revealed with the liquidators of disability group II (31.6%), second-ranking frequency – among those of disability group III (19.05%) and the lowest frequency was revealed with the liquidators with no disability status (14.0%).

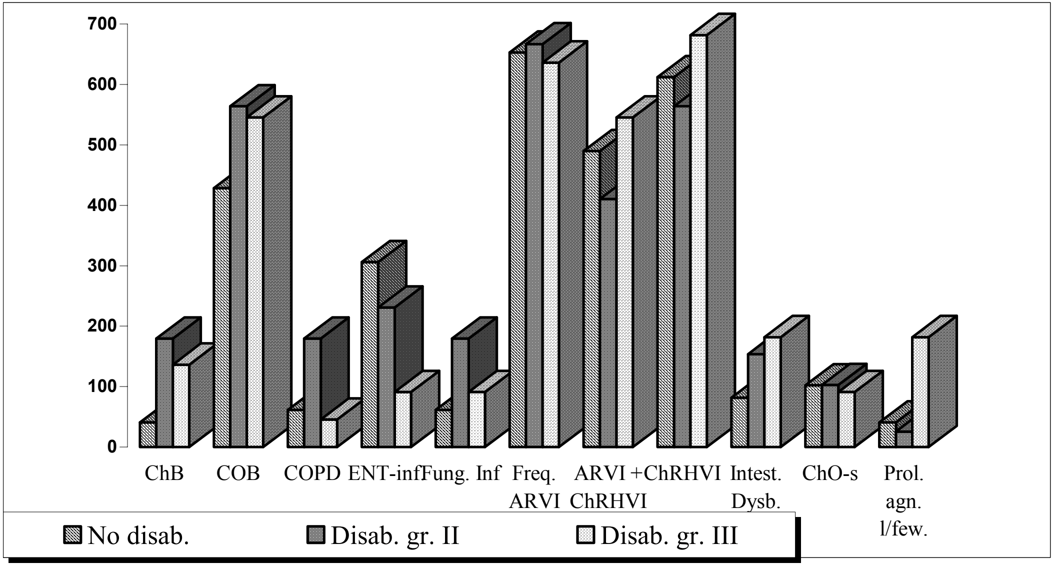
In summary, greater difference between HSZ frequency and clinical signs of infection-generated immunodeficiency (except for chronic obstructive pulmonary disease) and allergic pathology with groups of liquidators having disability status as compared to the liquidators, who haven't obtained any disability as a result of participation in Chernobyl NPP aftermath liquidation, allows concluding that chronic bodily diseases are the basic reason of liquidators' disability.

Dynamics of Change in Immunological Status of the Liquidators from the North-Western Region based on the 1997-2005 Monitoring Data

Laboratory immunoassay is the second element of immunological monitoring and includes determination of white blood (leukocyte) count, relative and absolute lymphocyte content, total population of T-lymphocytes (CD3+), sub-populations of T-helpers (CD4+) and cytotoxic T-lymphocytes (CTL–CD8+), immunoregulation index (CD4+/CD8+), natural killers (CD16+) and phagocytic activity of neutrophils (PhAN) with latex. The following markers of cellular activity were determined: CD25+, CD95+, HLA-DR+ and activated T-lymphocytes.

Measurement of the humoral component of immunological status included determination of B-lymphocytes (CD19+), the level of immune serum globulins of three major classes M, G and A by the method of Mancini and the overall IgE level. Laboratory verification of immunodeficiency and determination of persons with depressed and increased immunological status employs the principle of sigma deviations: lower (↓) and higher (↑) than reference values [21]

Fig. 12 – Prevalence of Immunodeficiency Clinical Signs with Chernobyl Liquidators from the City of Moscow and Moscow Region Depending on Disability or Unavailability Thereof, 2003



Legends:

ChB – *chronic, recurring bronchitis*
COB – *chronic obstructive bronchitis*
COPD – *chronic obstructive pulmonary disease*
ENT-inf. – *chronic, recurring ear, nose and throat infections*
Freq. ARVI – *frequent acute respiratory virus infections*
Fung. inf. – *fungal infections*
Intest. dysb. – *intestinal dysbacteriosis*
ChP-s – *chronic pyelonephritis*
Prol. agn. l/few. – *prolonged agnogenic lowgrade fever*
ChRHVI – *chronic recurring herpesviral infection*

In the course of immunoassay of the liquidators residing in the North-Western region carried out in earlier period of 1995, significant changes were revealed inclusive of deficiency of T-cell component, imbalanced indexes of cytotoxic cells: CTL deficiency and increased level of natural killers, reduction of B-lymphocytes and deficiency of immune serum globulins (IgG). Monitoring carried out in 1999 revealed significant fluctuation of indexes combined with imbalanced cellular, phagocytic and humoral components of immunological status. Imbalanced condition of cellular component manifested itself in proved increase of lymphocyte percentage, dissociated indexes of T-cell-bound immunity including deficiency of T-lymphocytes (%) and CTL–CD8+(%), increased absolute values of CD3+, CD4+ and immunoregulation index as well as considerable reduction of NK-cells as compared to 1995 indexes (see Fig. 15). Disimmunoglobulinemia was revealed based on the indexes of serumal IgM (↑), IgG (↑) and overall IgE (↑↑). Average indexes of PhAN were credibly higher. As compared to earlier periods after Chernobyl NPP disaster, the increased PhAN was revealed in 1992 followed with stable and proved reduction in 1993, 1994 and 1995 as compared to the periods of PhAN increase [12].

Based on 2001 monitoring data, the liquidators (as compared to control group) were characterized with reliable reduction of absolute indexes of T-lymphocytes (%), T-helpers (%), immunoregulation index, as well as increase of cytotoxic cells: CTL – CD8+ and NK-cells both in relative and absolute terms, PhAN, level of serumal IgM and IgG (see Fig.13). Dynamics of the immunological status, as compared to 1999, was characterized by proved reduction of [those increased in 1999] relative indexes of lymphocytes, T-helpers, immunoregulation index, PhAN (which remained increased as compared to the control level), serumal IgA and proved increase of – CD8+, CD16+, B-lymphocytes (%) and level of serumal IgM, IgG. An express misbalance was observed in all components of the immune system, as well as considerable fluctuations in characteristics of cytotoxic cells, deficiency of T-cell component in terms of indexes of T-lymphocytes, T-helpers and immunoregulation, as well as disimmunoglobulinemia with increasing level of IgM, IgG, and percentage of persons with ↑ IgE and ↓ of serumal IgA.

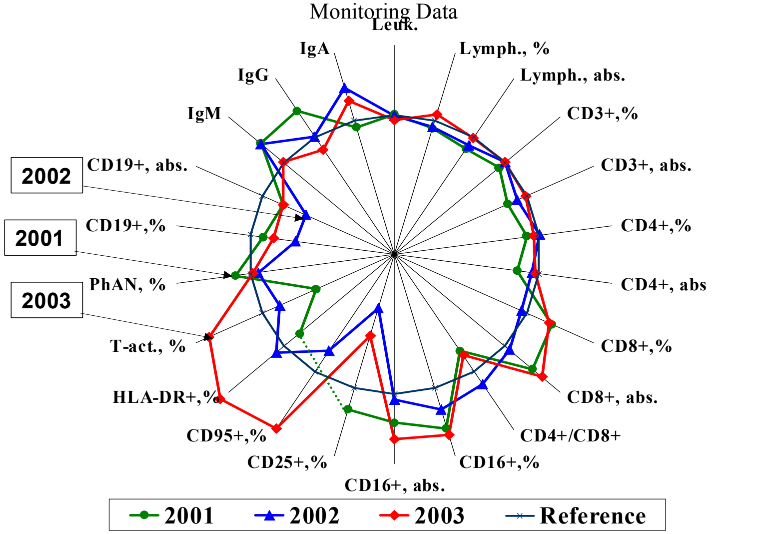
Monitoring carried out in 2002, as compared to the findings of the previous survey carried out in 2001, revealed a number of changes in the indexes of T-component characterized with the proved increase in percentage of T-lymphocytes and T-helpers to the control level, as well as immunoregulation index and CTL in relative and absolute terms. Proved change of cellular activity markers was also registered: considerable reduction of the early activation marker CD25+, indicating to the reduction of cellular component activity at the level of reception to interleukine-2, increase in average indexes of the cellular activation late marker– HLA-DR+, as well as T-activated lymphocytes along with reduction in B-lymphocyte indexes. Disimmunoglobulinemia manifested itself in multi-directional change of the humoral component indexes and was registered when comparing the character of change in serumal Ig observed during the monitoring carried out in 2002-2001 with the indexes registered in 2001-1999. Persons examined in 2002 were characterized by proved reduction of serumal IgG and overall IgE, as well as increase of serumal IgA. Stable disimmunoglobulinemia is one of the signs of immune system ageing. As compared to the indexes registered in 1999-2001 and level of control values observed with persons examined in 2002, PhAN was depressed.

Dynamics of cell-bound immunity indexes observed with the group of persons examined in 2003 (see Fig. 13) was characterized with change in indexes of cytotoxic cells (↑), activation markers (↑), reduction in indexes of humoral immunity and increase of overall IgE. Cellular component indexes testify to the reduction in percentage of lymphocytes, CTL and NK-cells in relative and absolute terms, as well as depressed immunoregulation on account of increased CD8+ and early lymphocyte activation marker CD25+ as compared to the indexes registered in 2002, though average values of CD25+ were low as before. The immunological status of persons examined in 2003 is characterized by a considerable intensification in expression of CD95+ and HLA-DR+ molecules, as well as T-activated lymphocytes in terms of average values. Deficiency of B-lymphocytes was still there, but as compared to the indexes registered in 2002, average values are definitely higher. As compared to the indexes of the previous surveys, average values of serumal immunoglobulins of all three classes were definitely reduced, and as compared to the control values – the level of serumal IgG was also reduced. In comparison with the findings of monitoring carried out in 1999-2003, a steady disimmunoglobulinemia was observed, which testifies to the liquidators' immune system ageing.

For the purposes of comparison, a group of persons from among the Special Risk Department (SRD) and population of the same town were examined in 2003. As compared to SRD staff, liquidators were characterized by definitely higher absolute values of lymphocytes, T- and B-lymphocytes.

As compared to the town's population, liquidators are characterized by definitely higher absolute values of NK-cells with

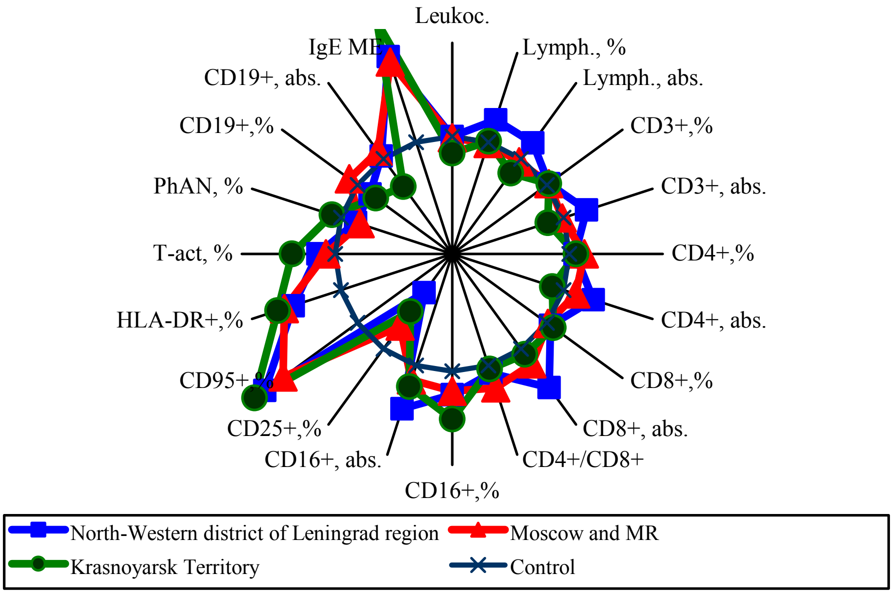
Fig. 13 Dynamics of Immunological Values Observed with Liquidators of Chernobyl NPP Disaster Residing in North-Western part of LR Based on the 2001-2003 Monitoring Data



the trend of CD16+ percentage increase, as well as increased expression of CD95+, late activation marker indexes HLA-DR+ and T-activated lymphocytes. In terms of humoral component indexes, proved differences between the liquidators and town's population are manifested in the following indexes: serumal IgM (↓), IgA (↑) and overall IgE (↑). As compared to population members, SRD representatives are characterized by definitely reduced indexes of B-lymphocytes and serumal IgM, as well as definitely increased values of T-activated lymphocytes. All examined groups, especially liquidators and SRD representatives, are characterized by very low average values of activated lymphocytes. Increased activation markers being the sign of strenuously functioning immune system manifest another significant difference between the immunological status of Chernobyl disaster liquidators and the same of town's population.

Dynamics of immunological values observed in 2004 with liquidators residing in North-Western region (see Fig. 14) was characterized with proved increase in cellular component indexes: relative and absolute values of T-lymphocytes and T-helpers, NK-cells with dissociated relative and absolute values, lymphocytosis available, multi-directional change of cellular activity markers: increased CD95+ expression, tendency towards reduction of HLA-DR+ and T-activated lymphocytes, though, as compared to the control level, these indexes remained increased as before, proved reduction of PhAN, low level of CD25+ expression, deficiency of B-lymphocytes and high values of overall IgE.

Fig. 14 Dynamics of Immunological Values Observed with Liquidators of Chernobyl NPP Disaster Residing in Northwestern Region, Moscow and

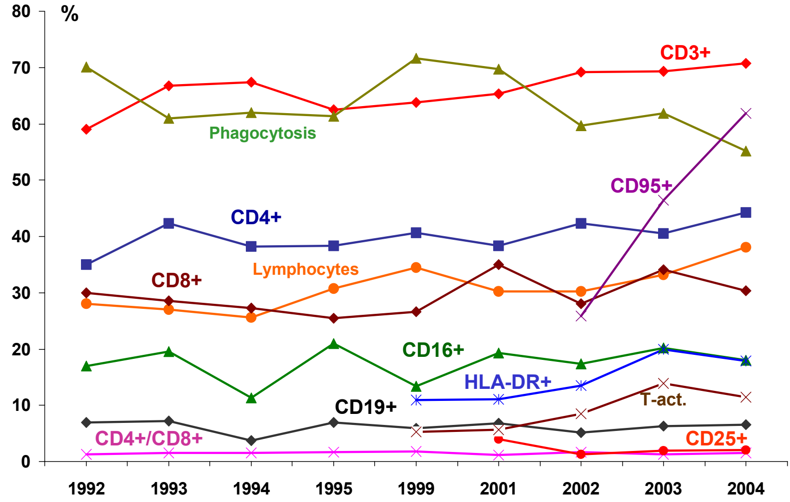


Moscow Region Based on the 2004

On the whole, dynamics of immunological values registered in the course of long-term monitoring (1992 – 2004) is characterized with the following changes (see Fig. 15):

1. Immunodeficiency by T-lymphocyte indexes registered in 1992, 1995, 1999 and 2001, which tended to reduce from 1995 to 2001, by T-helper indexes registered in 1992, 1995 and 2001, depressed immunoregulation observed in 2001 and 2003;
2. Spontaneous fluctuations of NK-cells with increased values registered in 1993, 1995 and 2001, 2003 and considerable reduction of CD16+ in 1994 and 1999;
3. Fluctuations of CTL – CD8+ from 1999 to 2004 with their dynamics coinciding with the same of natural killers (CD16+) within the period and prior deficiency of CTL (1995-1999);
4. Reduction of early activation markers registered in 2002-2004 as compared to those registered in 2001 and very low average values of CD25+ in 2002 – 2003;
5. Gradual increase of late activation marker indexes HLA-DR+ from 2001 to 2003 with their maximum value at the upper bound of reference values registered in 2003 and tendency towards reduction in 2004;
6. Coincidence of T-activated lymphocyte dynamics with the same of HLA-DR+;
7. Increase in lymphocyte percentage from 2001 to 2004;
8. Continuous increase in CD95+ expression from 2002 to 2004 with considerable excess of the reference level in 2004;
9. Significant increase in phagocytic activity of neutrophils from 1995 to 1999 with further drop of PhAN from 1999 to 2002, especially drastic towards 2004;
10. Disimmunoglobulinemia registered throughout the survey period with the tendency of increase in the level of serumal IgM from 1995 to 2001 and steady values of disimmunoglobulinemia in 2001-2002 with further reduction to the reference level; tendency towards increase in serumal IgG also from 1995 to 2001 and further reduction to 1995 level by 2003; tendency towards increase in serumal IgA from 1995 to 2002, its reduction in 2001 and equal values in 2003 and 1999;
11. Increase in overall IgE: by average indexes – highest in 2001, by quantitative distribution of increased indexes – in 1999-2001 (46.55–41.07%).

Fig. 15 Dynamics of Immunological Values Registered with Chernobyl Disaster Liquidators Residing in North-Western Part of Leningrad Region, Depending on Survey Year



According to results of frequency analysis, dynamics of immunological values registered in the period from 1995 to 2004 with Chernobyl NPP aftermath liquidators residing in North-Western region was characterized in 1995 with a great share of persons with deficiency of T-cell component: T-lymphocytes with 1/3 of examined persons, T-helpers and CTL with 1/4, B-lymphocytes with 1/3, and increased NK-cell values with more than 40% examined persons. In view of the share of persons with normal values registered, the most frequently deviating immunological characteristics were NK-cells, normal indexes of which were registered with 51.6% of examined persons only; these were followed by T-helpers with normal values of CD4+ being 58.6% and T- and B-lymphocytes. Normal values of these parameters were registered with 65.1% and 66.9% of examined persons respectively.

In 1999, the tendency was revealed toward reduction of share in persons with deficiency of T-cell component and their considerable increase along with reduction of B-lymphocytes and NK-cells. The reduction of share of persons with normal B-lymphocyte values was also observed: 66.9%→56.6%. Distribution of NK-cells as compared to 1995 values showed an express imbalance with a significant change of correlation between increased and reduced CD16+ values. Percentage of persons with increased overall IgE was very high (46.55%), with such IgE increase being revealed both with AD registered and in absence thereof. The indexes of overall IgE were relatively low (≤45 ME) with 1/5 of examined persons, which indicates to disrupted cell cooperation in immune response, as well as reduction of tolerance to unlike antigens. Increase of overall IgE may serve an evidence of endotoxic condition developed due to the impact of radiation disaster risk factors, as well as indicate to post-exposure long-term changes in allergic reactivity. On the whole, percentage of persons with immunological deviations was very high in 1999.

The group of liquidators examined in 2001 was also characterized with imbalanced system of cell-bound immunity, however of different nature as compared to 1999: a significant growth of percentage of examined persons with increased number of cytotoxic cells was observed: NK-cells (41.82%) and T-killers (36.4%) along with reduction in percentage of persons with normal values of the said characteristics, inadequate distribution of T-cell sub-populations with more than 40% of examined persons, 37.6% of which demonstrating deficient immunoregulation. 30% of examined persons were still characterized by B-lymphocyte deficiency (see Fig. 16). As in 1999, imbalanced system of humoral immunity was characterized not only by quantitative B-cell immunodeficiency, but also with disimmunoglobulinemia by Ig indexes in the four classes being determined.

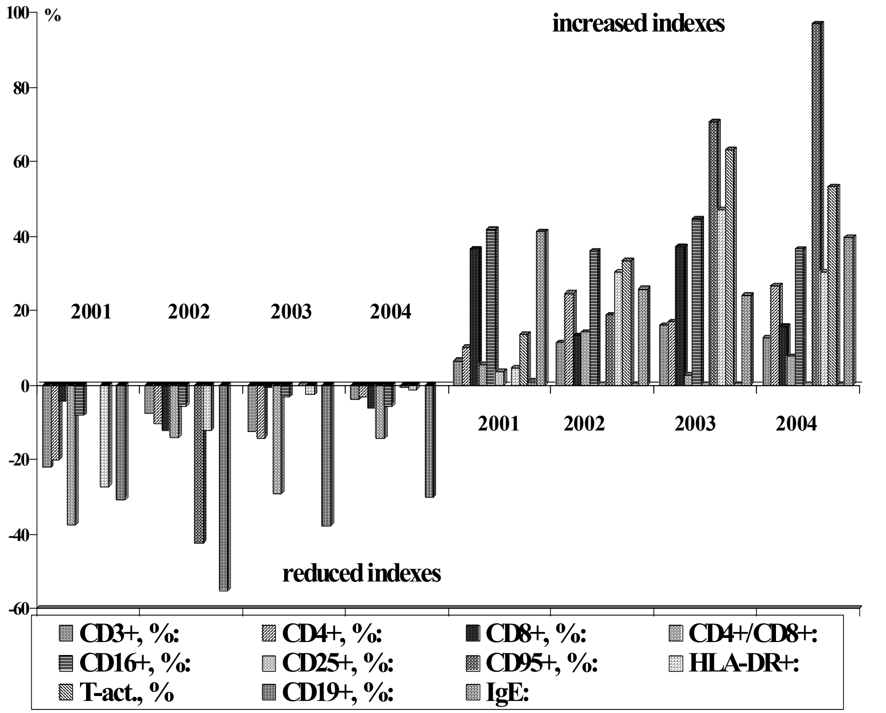
Immune status of liquidators from the Northwestern region examined in 2002 was marked by even greater share of persons with B-lymphocyte deficiency (55.24%). Throughout the survey period from 1995 to 2003, quantitative deficiency of B-lymphocytes with their function being preserved was registered with more than 1/3 – 1/2 of examined persons, but in 1999 and especially in 2002 they were characterized with the highest indexes of B-cell immunodeficiency. Percentage of persons with increased number of NK-cells was high as before (35.85%) while percentage of T-killers reduced considerably – 13.2%. The tendency was revealed toward reduction in percentage of examined persons with normal level of T-helpers on account of increase in number (%) of persons with increased CD4+. There was a big percentage of persons (42.5%) with depressed CD95+ expression and its increase with almost 1/5 of persons examined in 2002.

In 2003, a great percentage of persons with increased CTL (37%) and NK-cells (44.54%) was registered; more than 70% were characterized with increased activation markers HLA-DR+ and CD95+; more than 60% of examined persons were characterized with high indexes of activated T-lymphocytes. As compared to 2002 indexes, these percentage ratios are very high. Besides, 1/3 of liquidators examined in 2003 were characterized with deficient immunoregulation, which is also likewise twice as large as the previous index. More than 1/3 had continued B-lymphocyte deficiency. 23.93% of liquidators had increased overall IgE level, which corresponds to 2002 index, while 29.06% of examined persons (34:117) had a low IgE level. As compared to the examined SRD representatives and town's population, percentage of persons with high indexes of overall IgE was considerably (three times) higher among liquidators. The dynamics of quantitative distribution of persons with changed (↑↓) indexes in 2004 is mostly characterized by a considerable growth in percentage of examined persons with increased CD95+ expression (96.93%↑) with a tendency toward reduction of percentage of persons with ↑ HLA-DR+ (47.06%→30.06%) and ↑ T-activated lymphocytes(63.03%→53.37%), though percentage of persons with these increased characteristics remains high. Noteworthy is the cyclic character of increase in percentage of persons with increased indexes of cytotoxic cells and CD8+, CD16+ (↑ in 2001 and 2003), T-helpers (↑in 1999, 2002 and 2004) and (↓in 2001 and 2003) with its further reduction, as well as percentage of persons with deficient immunoregulation (in 2001 and 2003), and since 2002 – significant reduction in percentage of examined persons with increased activation markers. In case of cyclic fluctuations of NK-cells, even in "reduction" periods, percentage of persons with increased values: 35.85% and 35.58% remains quite high. Immunological dynamics observed with liquidators residing in the Northwestern region from 1995 to 2004 does every year reflect imbalanced major components of the immune system, thus convincingly proving the degree of immunogram distortion (see Fig. 13, 14). The most frequently deviating parameters include cytotoxic cells CD16+, CD8+, T-helpers, B-lymphocytes and overall IgE; in 2002 – CD95+; since 2003 – CD95+ and T-activated lymphocytes.

Immunoproliferative Disorder

In view of a high percentage of persons with increased activation markers in 2003, as well as increased indexes of cytotoxic cells, deficient immunoregulation and B-lymphocytes, cyclic fluctuations of CTL and CD4+/CD8+ and growth of increased NK-cell values, we analyzed the immunological dynamics observed with liquidators residing in the North-Western region who suffered from proliferate diseases – benign tumors.

Fig. 16. Percentage of Persons with Changed Immunological Indexes in Surveyed Groups of Chernobyl NPP Disaster Liquidators Residing in the North-Western Part of Leningrad Region, Based on 2001-2004 Monitoring Data



According to 2003 monitoring data, the immune status of liquidators diagnosed with proliferate processes of nonmalignant nature was characterized by lymphocytosis: average values of lymphocyte percentage were at the upper border of physiological standard and definitely higher than reference values and the same parameter observed with other chronic bodily diseases and clinical signs of immunodeficiency. Indexes of T-cell component, as compared to other clinical signs of immunodeficiency tended to reduce (CD3+, CD4+) along with inadequate distribution of T-cell sub-populations and proved reduction of CD4+/CD8+(↓); throughout the three years of monitoring, average indexes of NK-cells exceeded the upper border of normal values with an express tendency toward increase in 2003, and definitely they considerably exceeded the reference level. PhAN indexes are also definitely reduced as compared to 2001 indexes; annual reduction of values was observed. Cyclic fluctuations of CTL and immunoregulation index, which are also observed with other signs of immunodeficiency and chronic diseases, were also registered. The increase of lymphocyte activation markers is also registered: intensification of CD95+ expression, late activation marker HLA-DR+ and act T-lymphocytes along with low values of early activation marker CD25+, which was registered earlier in case of chronic pathology. Simultaneous increase of all three activation markers: CD95+, HLA-DR+ and act. T-lymphocytes with liquidators is registered in 38.66% cases (46:119). Simultaneous increase of CD95+ and HLA-DR+ is observed with 41.18% (49:119); CD95+ and activated T-lymphocytes – with 59 persons: 49.58%. It follows that activation processes get intensified on account of both apoptotic and late activation of cells. Probably, the indexes of activation markers, as well as the same of cytotoxic cells, develop spontaneous fluctuations from high to reduced values and further surveys may reveal both activation “fall” by markers, which were increased in 2003, and their further intensification. Since these indexes were included into later monitoring terms for the purpose to assess liquidators’ immune status, the truth will be revealed in the course of dynamic observations. In terms of humoral immunity, there are no significant differences in comparison with other pathological processes and chronic diseases.

Consequently, according to 2001-2003 monitoring data, in case of non-malignant proliferative conditions, two patterns of immunological change are developed, which cannot be revealed with other signs of immunodeficiency and chronic diseases:

- Lymphocytosis,
- Reduction in indexes of T-cell component of immune status: CD3+ and CD4+;
- Inadequate distribution of T-cell sub-populations;
- Deficient immunoregulation;
- Increase of NK-cell number;
- Reduction of PhAN, as well as immunological changes, which, based on 2003 monitoring data, were observed with other pathological conditions;
- Cyclic fluctuations of CTL and immunoreactive insulin;
- Increase in lymphocyte activation markers: intensification of CD95+, HLA-DR+ expression and activated T-lymphocytes;
- Low values of early activation marker CD25+.

It appears that availability of both signs in immune status allows referring the examined persons to the highly vulnerable group in terms of possible development of proliferative disorders. Even earlier, when monitoring the liquidators for the purpose to reveal the negative impacts of Chernobyl nuclear disaster, with the liquidators from North-Western part of Leningrad region we observed spontaneous fluctuations of cytotoxic cells, mostly natural killers as the risk factor of possible development of proliferative conditions (see Fig.15). In the course of monitoring carried out in 2004 several persons with above-indicated immunological changes diagnosed with a number of disorders, including malignant diseases (gastric adenocarcinoma and prostate cancer, which for a number of years was preceded by benign hyperplasia; bladder cancer with recurrent course, B-cell lymphoma etc). In comparison with the character of immunological parameters deviations in previous years (1999-2002), we are inclined to unite all the changes observed with the immune status into the immunological description of proliferative disorder provided below. Persons developing such changes should be considered as endangered in terms of tumoral diseases.

IMMUNOLOGICAL DESCRIPTION OF PROLIFERATIVE DISORDER

- Lymphocytosis (during 2-3 years)
- High (max) values / deficiency of CD3+
- Spontaneous fluctuations (↓↑↓↑) of cytotoxic cells CD8+ and CD16+
- Deficient immunoregulation CD4+/CD8+(↓↓)
- Deficiency/ significant increase of NK-cells during 2-3 years, negative dynamics toward increase
- significant increase (growth) of activation markers:
  - CD95+ expression from (↓↓) to (↑↑↑),
  - late activation marker HLA-DR+(↑),
  - activatedT-lymphocytes
- PhAN reduction
- B-lymphocyte deficiency

Such persons should undergo in-depth clinical-and-instrumental examination twice or three times a year, especially in cases of “target organs”, i.e. some chronic disease that may develop into neoplastic process. This is a highly vulnerable group in terms of negative consequences of the nuclear disaster.

Monitoring carried out in 2004, in cases of proliferative disorders, revealed the tendency toward leukocyte increase and lymphocyte percentage reduction as compared to 2003 lymphocytosis, but with excess of the reference values; the tendency toward increase in number of T-lymphocytes, T-helpers and immunoregulation index along with proved reduction of absolute values of CTL–CD8+, reduction of NK-cells, the average values of which definitely exceeded the reference level (see Fig. 18). As compared to 2003 values, there was proved reduction of T-activated lymphocytes and PhAN, intensified expression of CD95+ and increased level of overall IgE. As compared to immunological indexes of the whole examined group of liquidators, there are no proved differences. The tendency is observed to the increase of leukocytes, reduction of lymphocytes (%) and certain redistribution of correlation between T-cell sub-populations during proliferative disorders, but normal values of immunoregulation index in the both groups being compared. Immunograms taken from persons with proliferative disorders examined in 2004, in many respects coincides with the immunogram taken from all examined liquidators, in spite of a great difference in number (10 and 159 persons) and character of pathology, i.e. There are signs of changes observed no only with proliferative conditions, but also typical for immunological dynamics of the whole observed group.

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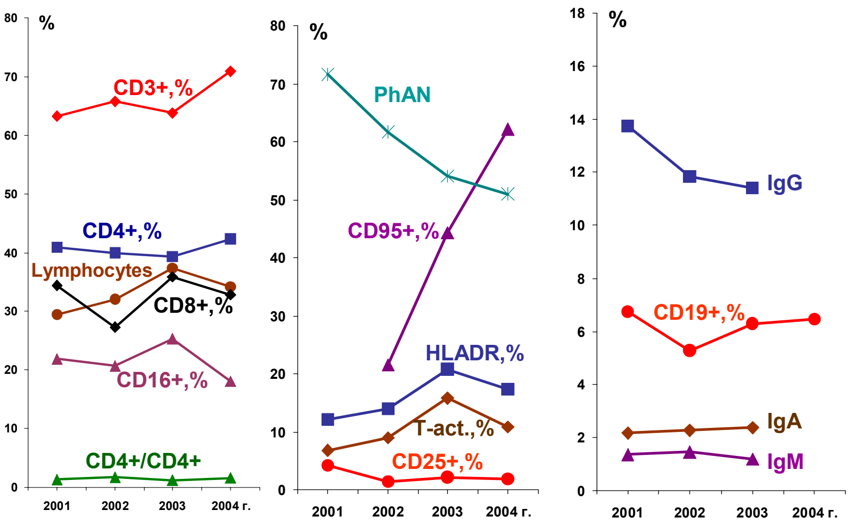
Fig. 18. Dynamics of Immunological Indexes Observed with Chernobyl NPP Disaster Liquidators Residing in the North-Western Part of Leningrad Region Diagnosed with Proliferative Disorders, Based on 2001-2004 Monitoring Data



On the whole, immunological dynamics with non-malignant proliferative disorders are characterized apart from the above-mentioned changes, by continuous and drastic increase in CD95+ expression, and the same drastic fall of PhAN along with reduction of other cellular activity markers from 2003 to 2004: HLA-DR+, T-activated lymphocytes and low values of early activation markers CD25+. Intensification of CD95+ expression is accompanied with increase in indexes of T-cell component CD3+ and CD4+ manifested in erratic values of cytotoxic cells, reduction of serumal IgG and increase of overall IgE (see Fig. 18).

Dynamics of Immunological Indexes Observed with the Liquidators Residing in the City of Moscow and Moscow Region, Based on 2001-2004 Monitoring Data

Comparison of immunological parameters registered with Chernobyl NPP disaster liquidators residing in the Northwestern region, city of Moscow and Moscow region throughout the four-year monitoring revealed a multidirectional character of changes by most of immunological parameters. CTL fluctuations do not coincide: with the liquidators from the Northwestern region, the increase was registered in the period between 2001-2003, with the liquidators from the city of Moscow and Moscow region – in 2002; while reduction with regard to increased values, down to normal levels of average values with the liquidators from the Northwestern region was observed in 2002; CTL percentage with the liquidators from the city of Moscow and Moscow Region corresponded to normal values in 2001 and 2003, while the same were definitely increased in 2002. In the same manner, there is no coincidence between the periods of change in immunoregulation index and the opposite type of deviation in relation to CTL. The second difference is revealed in the character of dynamics of cellular activity markers, which are also characterized by multidirectional change: Indexes of lymphocyte early activation markers are considerably higher with the liquidators from Moscow, while the same indexes are low with the liquidators from the Northwestern region. The indexes of other cellular activity markers: CD95+ expression, HLA-DR+ and T-activated lymphocytes with the liquidators from the Northwestern region in 2002-2003 exceed the same indexes observed with the liquidators from Moscow Region (except for HLA-DR+ in 2002). In 2001, average values of HLA-DR+ and T-activated lymphocytes registered within liquidators from both regions were at the same level. In the group of liquidators from the city of Moscow and Moscow Region, increased values of CD25+ were registered with more than 1/4 of examined persons.

Difference in the character of deviation is also observed by other markers however with greater increase in CD95+ and HLA-DR+ with liquidators residing in the Northwestern region and T-activated lymphocytes – with those residing in Moscow region. Disimmunoglobulinemia was registered in the both groups. Monitoring data obtained in 2002-2004 testify to an imbalance in the system of cellular and humoral immunity, changes in the indexes of T-helpers, significant fluctuations in cytotoxic cells, increasing activation markers and disimmunoglobulinemia.

Comparison with earlier monitoring periods allows concluding that the liquidators from the city of Moscow and Moscow region never developed such spontaneous fluctuations of NK-cells, as the liquidators from the Northwestern region did, and since 1999 the same correlation was observed in respect to CTL, which earlier definitely tended toward reduction (see Fig. 19). The change in CTL–CD8+ observed with the liquidators from the city of Moscow and Moscow region from 1997 to 2004 was characterized with two periods of growth in 1998 and in 2002 and reduction to normal level of average values in 2000-2001 and 2003. Indexes of NK-cells with the liquidators from the city of Moscow and MOSCOW REGION from 1997 to 2001 were reduced, and from 2001 to 2004 these indexes tend to increase, however being definitely lower than in 2002 as compared to the liquidators from the Northwestern region. Along with low level of natural killers registered with the liquidators from Moscow region as compared to other groups of liquidators, the occurrence of clinical signs of immunodeficiency was much higher throughout the monitoring period.

Dynamics of quantitative distribution of persons with changed (↓↑) immunological indexes (see Fig. 20) testifies to the increase in percentage of the examined persons with increased T-helpers, NK-cells, CD95+ and CD25+ expression (by 2004), reduction in percentage of persons with depressed CD95+ expression and increased CTL. The frequency of increase in IgE with persons examined in 2003 tends to reduce as compared to 2002 index, but as compared to 2000-2001 data, the said indexes are in many ways the same. 2003-2004 indexes are of comparable level. Multi-directional character of deviation is revealed by the following indexes: CD4+/CD8+ (↓) in 2002, (↓↑) in 2003 with lower frequency of deviation, (↓↑) in 2004 with higher frequency of deviation and CD95+ expression: (↓) in 2002, (↓↑) in 2003, (↑↑) in 2004 with growing percentage of the examined persons with increased indexes.

When comparing the immune status of the liquidators residing in the Northwestern region, city of Moscow and Moscow region throughout the four years of monitoring, one may conclude that reaction type of the liquidators from the Northwestern region in 2001 may be characterized as deficient by most of cell-bound immunity indexes: lymphocytes, T-lymphocytes, T-helpers, immunoregulation index, along with increased cytotoxic cells CD8+, CD16+ and PhAN (see Fig. 21). Humoral component of the immune status was characterized by deficient B-lymphocytes, moderate reduction in serumal IgA and increase in IgM and IgG.

Cellular activity indexes were characterized with a moderate reduction of early and late activation markers: CD25+, HLA-DR+

and T-activated lymphocytes as compared to the reference level. Immunological dynamics 2002 is characterized by increased indexes of T-cell component: CD3+, CD4+ with dissociated relative (N) and absolute (↓) of values, reduced CTL (%), increased CD4+/CD8+, reduced level of NK-cells and PhAN. Dynamics of humoral component was characterized by development of greater deficiency of B-lymphocytes and multi-directional changes in serumal IgG (↓ down to N) and IgA (↑). Changes in activation markers were characterized by low values of CD95+ and CD25+ expression with the tendency of HLA-DR+ increase. Major feature of immunological dynamics 2003: even greater, as compared to 2001, excess of cytotoxic cells and activation markers CD95+, HLA-DR+ along with low values of CD25+. By the indexes of humoral component: continued deficiency of B-lymphocytes and disimmunoglobulinemia with IgM level reducing down to N, deficient IgG and increased level of IgA. Reaction type of the liquidators from the North-Western region in 2004 (see Fig. 14) is characterized as activated by cellular component indexes: lymphocytes, T-cell component indexes, NK-cells with dissociated relative and absolute values, cellular activity markers: CD95+, HLA-DR+, T-activated lymphocytes along with reduced values of PhAN and CD25+, deficient B-lymphocytes and high level of overall IgE.

Fig. 19 Dynamics of Immunological Indexes Observed with Chernobyl NPP Disaster Liquidators Residing in the City of Moscow and Moscow Region, Based on 1997-2004 Monitoring Data

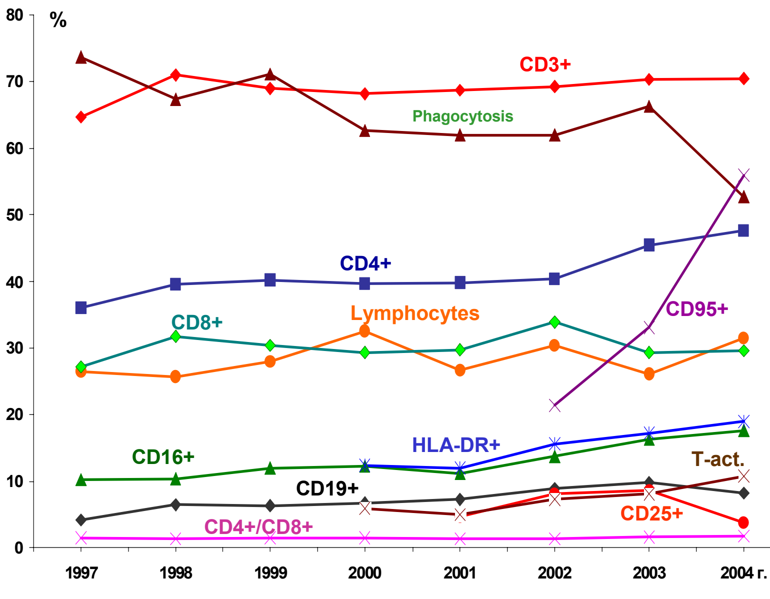


Fig. 20. Percentage of Persons with Immunological Changes in the Examined Groups of Chernobyl NPP Disaster Liquidators from the City of Moscow and Moscow Region, 2001-2004

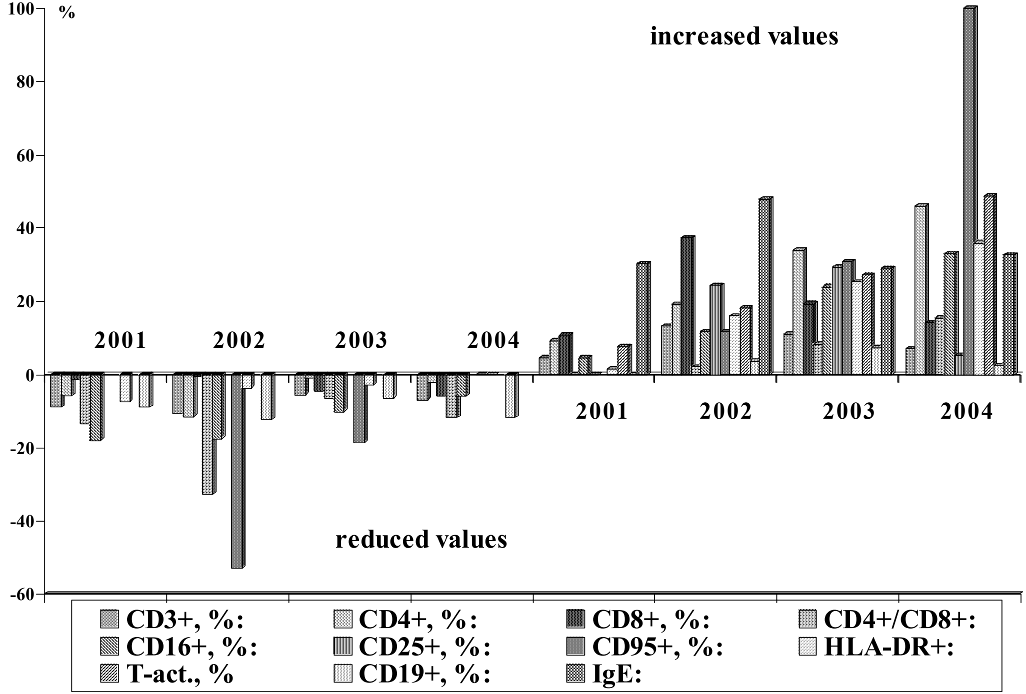
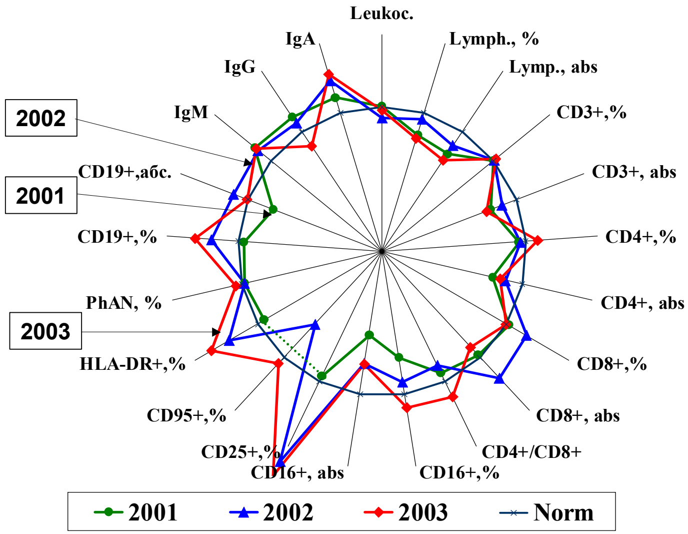


Fig. 21. Immunological Dynamics Observed with Chernobyl NPP Liquidators Residing in the City of Moscow and MR, Based on 2001-2003 Monitoring Data



Immune status of the liquidators from the city of Moscow and Moscow Region in 2001 was also characterized by deficient cell-bound immunity with dissociated relative and absolute values of T-cell component and B-lymphocytes, deficient immunoregulation, NK-cells and moderate increase in serumal IgM, IgG, IgA and early activation marker CD25+ (see Fig. 21). Immunological dynamics in 2002 is characterized by a lower degree of cell-bound immunity deficiency along with persisting dissociation in relative and absolute values of T-cell component, uniform increase in indexes of humoral component by all examined parameters. By cellular activity indexes – intensification of CD25+ and HLA-DR+ expression and reduction of CD95+. The line of cellular component in 2003 observed with the liquidators from the city of Moscow and Moscow region is in many ways similar to the line of reaction type in 2001 with greater dissociation in relative and absolute values of T-cell component: CD3+, CD4+, CD8+ and CD16+, as well as deficiency in absolute values, increased immunoregulation index, PhAN, NK-cells (%) and growing values of cellular activity markers, increase in B-lymphocytes with dissociated values:↑ relative and N-level of absolute values, as well as disimmunoglobulinemia: IgG↓, IgM↑ and

IgA↑. Distinctive feature of 2003 dynamics – inverted type of change in cytotoxic cells in relation to 2002 indexes: CD8+ (↑) – in 2002 and (N→↓) – in 2003; CD16+(↓) – in 2002 and (↑-%,↓-abs.) – in 2003. Immunological reaction type with the liquidators from Moscow region in 2004 is also characterized as activated cellular component indexes, but differs by normal level of lymphocytes, T-lymphocytes, no dissociation of relative and absolute values and lower degree of CD25+ reduction (see Fig. 14). It also differs from the indexes of the Northwestern region by CD19+ indexes (↑). Despite the tendency toward reduction of the early activation marker observed with the liquidators from the city of Moscow and Moscow region, while CD25+ indexes registered with them continue to be definitely higher as compared to the liquidators from the North-Western region along with higher indexes of CD95+ expression with the liquidators from the North-Western region, i.e. By CD25+ and CD95+, reproducibility of differences is observed. Activated type of cellular component registered with the liquidators from Moscow region includes increasing T-helpers, cytotoxic cells and cellular activity markers. Along with certain differences in the indexes of cellular component, a similar type of deviation in activation markers CD95+(↑) and HLA-DR+(↑), as well as T-activated lymphocytes (↑), PhAN (↓) and overall IgE (↑) were revealed.

Comparison of immunological indexes of the two regions allows concluding that, in the beginning of the fourth lustrum, the reaction type of immune status is closer to deficient or "insufficient" by cellular component and, by the end of the fourth lustrum since 2003, the shift toward activation was observed.

In order to compare the immunological description of proliferative disorder, which was prepared based on long-term examination of the liquidators from the Northwestern region, we provide the data relating to immunological dynamics with non-malignant proliferative conditions registered with the liquidators from Moscow region. In case of benign tumors, immunological dynamics also in many ways imitates major patterns of change in immunological parameters with chronic pathologies and differs radically from the same parameters observed with the liquidators from the Northwestern region.

Major differences:

- Unlike the liquidators, from the Northwestern region, no lymphocytosis observed;

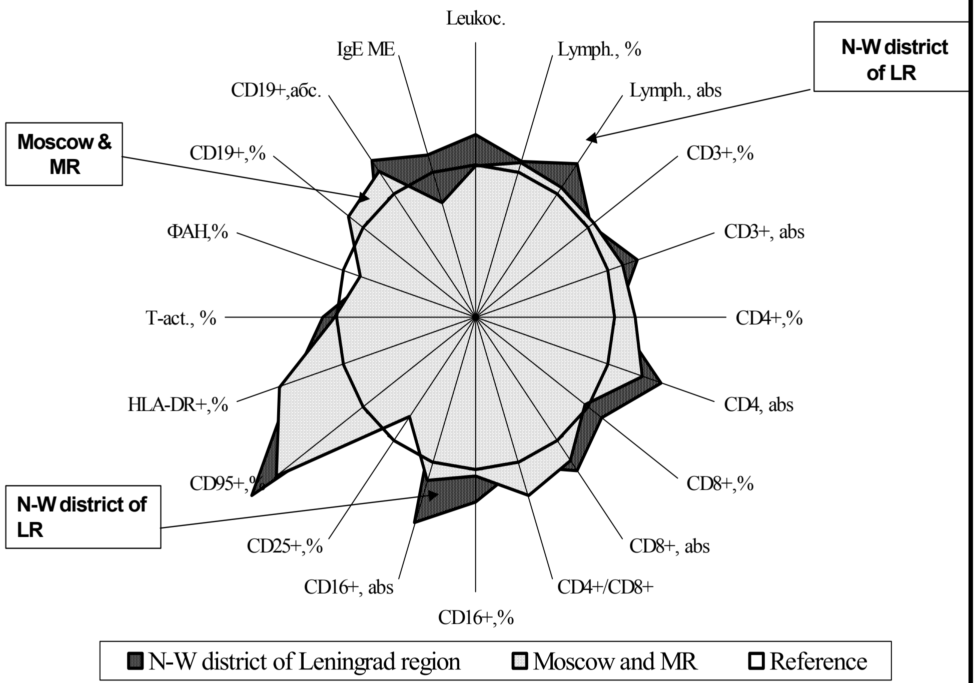
- No reduction in the indexes of T-cell component of the immune status observed: CD3+ and CD4+; indexes of T-lymphocytes coincide with reference values, while the indexes of T-helpers tend to increase;
- No disruptions in T-cell sub-populations, immunoregulation index corresponds to normal values;
- Significant differences are revealed in NK-cell indexes with a significant excess of reference values observed with the liquidators from the Northwestern region;
- PhAN indexes registered with the liquidators from the city of Moscow and Moscow region correspond to normal indexes, while the same registered with the liquidators from the Northwestern region were reduced in 2003;
- No coincidence in CTL fluctuations: with the liquidators from the city of Moscow and Moscow region, the period of increase falls at 2002, while with the liquidators from the North-Western region – at 2001 and 2003; periods of reduction in relation to increased values, respectively, with the liquidators from the city of Moscow and Moscow region – at 2001 and 2003, with the liquidators from the North-Western region – at 2002;
- Indexes of CD25+ early activation markers registered with the liquidators from the city of Moscow and Moscow region tend to increase;
- Average values of all activation markers registered with the liquidators from the Northwestern region considerably exceed the same registered with the liquidators from the city of Moscow and Moscow region.

Consequently, according to 2003 monitoring data, as opposed the liquidators from the Northwestern region, the liquidators from the city of Moscow and Moscow region do not develop the same complex of immunological parameters typical for non-malignant proliferative conditions. Dynamics of change in immunological parameters with the liquidators from the city of Moscow and Moscow region mostly coincides with the dynamics registered in case of other pathological conditions. Monitoring carried out in 2004 revealed a great similarity, in cases of proliferate disorders, of immunological indexes within the examined persons from both regions (see Fig. 22), especially by cellular activity markers – in terms of CD95+ expression and HLA-DR+. Certain differences in immunograms taken from the liquidators residing in the North-Western and Moscow regions were manifested by increased leukocytes and, respectively, absolute values of cellular component and B-lymphocytes, as well as higher values of overall IgE registered with the liquidators residing in the Northwestern region along with the tendency toward increase of B-lymphocytes (%) and T-helpers (%) observed with the liquidators from city of Moscow and Moscow Region. Proved differences were revealed only by the marker of early lymphocyte activation, the indexes of which were considerably lower throughout the four-year monitoring in the group of persons from the Northwestern region and allowed revealing the proved tendency of reduction in the Moscow region group. Increase in the values of late cellular activation marker 20 years after Chernobyl NPP disaster is prognostic alerting sign in terms of oncogenesis.

Immunological Dynamics Observed with Chernobyl NPP Disaster Liquidators Residing in Krasnoyarsk Territory Based on 2001-2004 Monitoring Data

Reaction type of the liquidators from Krasnoyarsk Territory, based on 2001 monitoring data, may be characterized as moderately activated by most of cell-bound immunity indexes: lymphocytes, T-helpers, CTL, natural killers with higher increase of cytotoxic cells CD8+ and CD16+ (see Fig. 23). Humoral component was characterized with a moderate deficiency of B-lymphocytes (%) with normal absolute values, increased serumal IgG and the tendency toward reduction of serumal IgM and IgA. The level of CD95+ and CD25+ expression correspond to reference values, while the indexes of HLA-DR+ and act. T-lymphocytes were increased. As in other groups of liquidators, the immune status of liquidators residing in Krasnoyarsk Territory is characterized with progressively increasing level of overall IgE.

Fig. 22. Immune Status Observed with Chernobyl NPP Disaster Liquidators residing in the North-Western Part of Leningrad Region, the City of Moscow and Moscow region, 2004



Reaction type of the immune status observed with the liquidators in 2002 and 2003 in terms of cell-bound immunity markers was characterized by similar values and differed from 2001 values by leukocyte reduction, dissociated indexes of lymphocytes, T-lymphocytes, T-helpers, NK-cells, PhAN, deficient B-lymphocytes, similar values of CD25+ and HLA-DR+, as well as intensified CD95+ expression in 2003. Differences were determined by the level of serumal immunoglobulins: in 2002 – IgG (↑↑) and IgA (↑); in 2003 – IgG (N) and IgA (↑↑). The level of IgM was also increased in 2002 and 2003 with the tendency of higher increase in 2003. Comparison with the immunological dynamics observed with the liquidators from the N-W region, city of Moscow and MOSCOW REGION allows concluding that the liquidators from Krasnoyarsk Territory showed no significant changes in activation markers, which are expressly manifested in the immune status of the liquidators from the Northwestern region.

Dynamics of quantitative (percentage) distribution of persons with changed (↓↑) immunological indexes is characterized by increased frequency of B-cell immunodeficiency, especially in the autumn period of 2002, intensified CD95+ expression, and, in the period of the latest surveys, by fluctuations in the indexes of NK-cell deviations, mainly with increased level and more frequently in 2001 and 2004, by high percentage of increased CTL in 2001 with further tendency to reduction of the index and growing percentage of the increased values in 2004 (see Fig. 24). More than 1/3 of the persons examined in 2003 had increased T-helpers and more than 40% of liquidators had high level of overall IgE (autumn 2002) along with its reduction in 1/4–1/3 of cases in other monitoring periods. 1/4–1/3 of the liquidators from Krasnoyarsk Territory had increased indexes of T-activated lymphocytes.

Monitoring carried out in 2004 was characterized by significant growth of percentage of examined persons with increased values of cellular activity markers: HLA-DR+ and CD95+ and T-activated Lymphocytes and cytotoxic cells, largely of NK-cells, the values of which exceed normal level with more than a half of examined persons. Throughout the monitoring period, percentages of persons with increased T-helpers remain at comparable level. The most frequently deviating immunological characteristics (with the tendency toward increase) include CD95+, T-activated lymphocytes and natural killers.

Comparison of immunological reaction type observed with the liquidators from all three regions monitored in 2001-2004 allows concluding that the common feature of monitoring carried out in 2004 (see Fig. 14) is a considerable increase in cellular activity markers HLA-DR+ and CD95+, as well as T-activated lymphocytes along with low values of early activation marker CD25+, which indicates to reduction of T-regulating mechanisms, and along with PhAN reduction with the liquidators from the N-W and Moscow regions and somewhat increased values registered in Krasnoyarsk territory, as well as increased level of overall IgE and NK-cells. All the said deviations are most expressly manifested with the liquidators from Krasnoyarsk Territory, whose immune status was characterized by the least changes until 2004. Prior to 2004, immunograms taken from the liquidators residing in these regions showed certain differences, but later on these regional differences were leveled down giving place to a number of general patterns of immune status formation regardless of region of residence that require accumulation of facts and further analysis.

Immunological Indexes Observed with Liquidators Depending on Disability Status

Analysis covered the immunological indexes registered with the liquidators from the city of Moscow and Moscow region with their disability status established after participation in Chernobyl NPP disaster liquidation based on examinations carried out in 2002 and 2003. Analysis of quantitative distribution of persons with changed immunological characteristics among examined in 2003 persons referred to disability group II and suffering from, as a rule, more severe diseases, allows revealing considerably greater percentage of persons having lymphopathy both by relative (29.7%→13.6%) and by absolute (40.5%→18.2%) values and with CD95+ expression depressed more than twofold. All liquidator groups contain a high percentage of persons with increased CD4+, CD16+, CD25+, CD95+, HLA-DR+ and T-activated lymphocytes, as well as overall IgE and, to a lesser extent, serumal IgA.

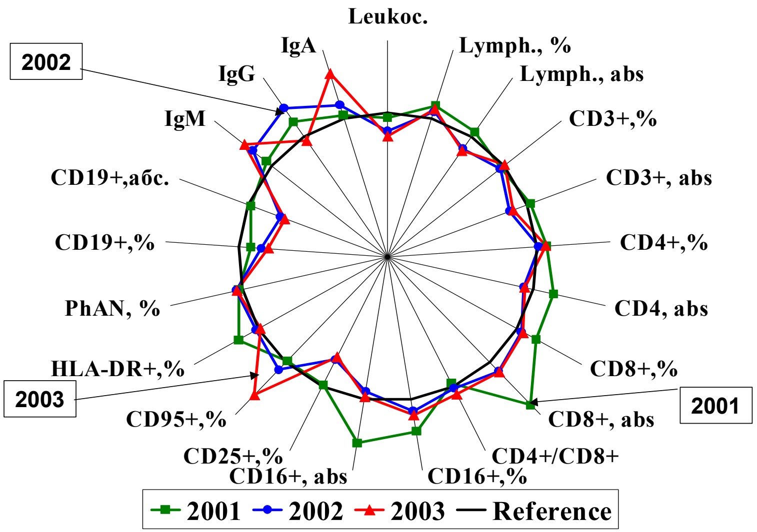
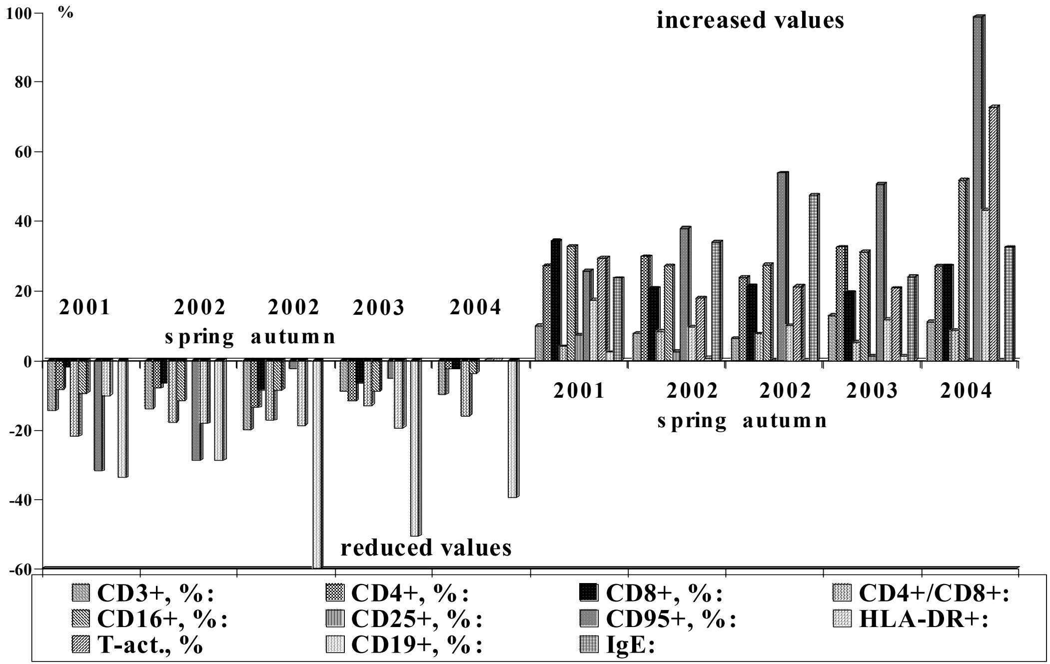


Fig.23. Immunological Dynamics Observed with Chernobyl NPP Disaster Liquidators Residing in Krasnoyarsk Territory, 2001-2003

Differences between liquidators referred to disability groups II and III are determined by the following parameters: III-group liquidators have deficient natural killers, which is not revealed with examined persons referred to disability group II; higher percentage of persons with increased T-cell component: T- lymphocytes, T-helpers and CTL, overal IgE and serumal IgA, with intensified CD95+ expression and late activation marker HLA-DR+. II-group liquidators include, apart from the above-mentioned, the highest percentage of persons with increased level of early activation marker CD25+. Significance of these differences requires further accumulation of data and analysis thereof, since in 2002 another type of deviation of many parameters was observed. Though even 2002 data demonstrate that percentage of persons with increased activation markers: CD25+ and T-activated lymphocytes is quite high: CD25+ in case of II-group disability, T-activated lymphocytes and HLA-DR+ in case of III-group disability. More than a half of examined persons from each group had reduced CD95+ expression. In 2002, the increase in percentage of persons with ↑ serumal IgA and ↑overall IgE was revealed. Some 36-39% of persons have increased values of CTL – CD8+ irrespective of disability group.

Fig. 24. Percentage of Persons with Immunological Changes in the Examined Groups of Chernobyl NPP Disaster Liquidators from Krasnoyarsk Territory, 2001-2004



Increase of NK-cells was observed with more than 1/5 of examined persons referred to disability group II, while deficient natural killers were revealed in same frequency with persons referred to disability group III. Higher frequency of CTL increase with persons of disability group III, and NK-cells – in case of II-group disability was also revealed during 2003 monitoring, as well as higher frequency of deficient natural killers in case of III-group disability. Higher frequencies of ↑ IgE in case of III-group disability, as well as correlation of activation markers in case of II-group and III-group disability are also revealed. Consequently, reproducibility of differences in the character of deviation of key immune cells is also revealed with liquidators referred to disability groups II and III.

However, liquidators having no disability status are also diagnosed with considerable deviations in immunological indexes. In the year of 2002, deficient immunoregulation was revealed in 1/3 case, and more than a half of examined persons had ↓ CD95+, 1/4 of examined persons had– ↑ CD25+ and more than 1/3 – ↑ CTL. Increased overall IgE is quite frequently revealed as well. In the year of 2003, as with the liquidators referred to disability groups, growing percentage of persons with increased indexes by many parameters (except for overall IgE and CD8+) was observed. Immunological deviations registered with the liquidators having no disability status have the same reasons as the same registered with the liquidators referred to disability groups: impact of risk factors induced by radiation disaster, numerous chronic diseases and clinical signs of immunodeficiency etc. Among liquidators having no disability status, there are persons, who did not request medical assistance in proper time and did not formalize their disability status – either out of fear to lose job or for some other reasons, but whose health status allowed them being formally referred to disability group. Further on, disability status was not formalized due to changes to the laws relating to causal relation of diseases with Chernobyl NPP aftermath.

In summary, one can conclude that all groups of liquidators, irrespective of their region of residence and regardless of disability status, very frequently suffer from chronic diseases and clinical signs of immunodeficiency. A certain pattern can be delineated: separate nosological forms of circulatory system diseases, such as systematic atherosclerosis with IH, atherosclerosis without arterial hypertension, cardiac insufficiency, rhythm disturbance, dyslipidemia without IH occur more frequently with the liquidators referred to disability group III despite the fact that they are 10 years younger than the liquidators referred to disability group II. Liquidators referred to disability group III suffer from more frequent clinical signs of immunodeficiency, such as frequent ARVI combined with ChRHVI and ChRHVI without frequent ARVI. Hepatobiliary pathologies and chronic digestive tract diseases are somewhat more frequently revealed in case of III-group disability. Other chronic diseases such as coronary heart disease, organic cerebral diseases, thyroid disorders, non-infectious eye pathologies, urolithiasis, diabetes and benign tumors are more frequently revealed with liquidators referred to disability group II. Data obtained confirms early development of atherosclerosis and, consequently, accelerated ageing of the liquidators, as well as dependency relation between age and degree of noci-influence of disease-producing factors of Chernobyl disaster: the younger the age when a person entered Chernobyl NPP zone and participated in the aftermath liquidation, the earlier (by 10 years) manifestations of such severe diseases as systematic atherosclerosis and chronic diseases typical for the elderly occur. In case of III-group disability, somewhat more frequent immunological deviations are revealed, including T-cell component indexes, activation markers: intensified CD95+ expression and HLA-DR+ and T-activated lymphocytes, increased IgA and overall IgE (2003).

Liquidators being monitored develop the following signs of immunological ageing: growing percentage of cells ready for apoptosis (↑CD95+), which results in the prevalence of “negative” activation of immunocompetent cells and, finally, to development of secondary immunodeficiencies requiring respective correction; changes in cellular activity markers (HLA-DR+↑, T-activated lymphocytes↑, CD25+↑↓); increase of T-helpers indirectly testifying to immune system activation; imbalanced T-cell component, which is responsible for high frequency of immunodeficiency clinical signs with leading infectious syndrome; reduced production of γ-IFN indicating to reduced functional activity of NK-cells typical for the elderly; disimmunoglobulinemia; imbalanced cell-bound immunity in case of CHD and CVP:DEP etc. Very significant deviations by numerous parameters of immune status with all groups of examined liquidators, especially with the liquidators referred to disability group III, who are 10 years younger, testify to the fact that the biological age significantly exceeds the chronological age. As is well known, premature ageing is one of the effects of small-dose radiation exposure.

Almost 20 years have passed since the Chernobyl tragedy, but contradictions as to assessment of the aftermath still persist. Based on the data obtained by us, as well as information provided by experts from other institutions dealing with Chernobyl-related issues, one can conclude that the damage inflicted on health of Chernobyl disaster liquidators is enormous. Chernobyl-related problems are long-term in their nature and, in view of specific consequences affecting everyone who went through this disaster; we all should go on with our investigations, further accumulation of facts and in-depth analysis thereof.

Major Conclusions

1. During the fifth lustrum after Chernobyl Nuclear Power Plant disaster, the persons who participated in the liquidation developed increasingly frequent and prevalent chronic diseases. Revealed indexes testify to negative state of affairs and testify to significant deterioration of liquidators' health.
2. Circulatory system diseases are the dominating pathologies registered with liquidators in long-term period. Increasing frequency and prevalence of diseases typical for the elderly: atherosclerosis and IH as well as diseases associated with atherosclerosis: CHD and CVP:DEP testify to the liquidators' premature ageing. In the structure of circulatory system diseases, CVP:DEP and atherosclerosis with IH prevail. High frequency of chronic diseases, including circulatory system diseases associated with atherosclerosis resulted from high prevalence of clinical signs of infection-induced immunodeficiency, frequent viral respiratory infections combined with ChRHVI, as well as protracted disadaptation syndrome.
3. Comparison of examined groups of liquidators, GHK personnel and population of Krasnoyarsk Territory allowed revealing multifold excess of chronic pathology occurrence with Chernobyl NPP disaster liquidators: as compared to the personnel by BCS diseases – by 3.02 times, by atherosclerosis and IH – by 4.55 times, by CVP:DEP – by 22.9 times; as compared to population, the excess by these pathologies is,

respectively, 2.6 times, 3.30 times and by CVP:DEP – by 9.95 times. Other classes and separate nosologic forms of diseases also reveal significant excess in prevalence among liquidators.

4. During the long-term period (2001-2003) that elapsed after Chernobyl NPP disaster, all three monitored groups of liquidators were assigned their own immune reaction type along with changes typical for each region. While the frequency of immunodeficiency clinical signs and prevalence of chronic diseases are higher among the liquidators residing in the city of Moscow and Moscow region, the most significant changes, based on the indexes being monitored, are revealed with the liquidators from the Northwestern region. All the three groups were diagnosed with quantitative and immunoregulatory imbalance with increasing indexes of cellular activity: CD95+, HLA-DR+, T-activated lymphocytes, fluctuations in cytotoxic cells most expressly manifested with the liquidators from the Northwestern region. Disimmunoglobulinemia with multi-directional changes in serumal Ig and deficient B-lymphocytes are also frequently revealed.

5. Immunological indexes revealed by the end of 20-year period elapsed after Chernobyl NPP disaster with all three monitored groups testify to similar reaction types of immune status formation along with considerable increase in cellular activity markers, largely in late activation marker HLA-DR+ and apoptotic activity by CD95+ expression being potentially dangerous in terms of oncogenesis.

6. Based on long-term monitoring of Chernobyl NPP disaster liquidators, the immunological description of proliferative disorder was developed, including lymphocytosis (during 2-3 years); maximum indexes of T-lymphocytes or deficiency thereof; deficient immunoregulation CD4+/CD8+ (↓↓); spontaneous fluctuations (↓↑↓↑) of cytotoxic cells CD8+, CD16+ along with deficient or significantly increased NK-cells during 2-3 years and negative dynamics toward increase. Significant increase and growing indexes of activation markers are also observed: CD95+ expression from (↓↓) to (↑↑↑), late activation marker HLA-DR+(↑), T-activated lymphocytes negative dynamics of PhAN (↓) and deficient B- lymphocytes.

7. Liquidators referred to disability group III, who are 10 years younger than liquidators referred to disability group II (in chronological terms), more frequently suffer from such nosological forms of circulatory system diseases as systematic atherosclerosis with IH, atherosclerosis without arterial hypertension, cardiac insufficiency, rhythm disturbance, dyslipidemia without IH etc. Besides, liquidators referred to disability group III suffer more frequently from clinical signs of immunodeficiency, infectious diseases combined with ChRHVI, with herpes simplex viruses participating in atherogenesis. These findings testify to development of premature atherosclerosis and accelerated ageing of the liquidators as well as dependency relation between age and degree of noci-influence of disease-producing factors of Chernobyl disaster: the younger the age when a person entered Chernobyl NPP zone and participated in the aftermath liquidation, the earlier (by 10 years) manifestations of diseases typical for the elderly occurred.

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CYTOGENETIC EFFECTS IN HUMAN AS THE RESULT OF THE CHERNOBYL ACCIDENT

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Summary

The Chernobyl accident significantly complicated the ecological situation in Ukraine. The existing environmental pollution, which was already rooted in the background, promoted in great part that the Ukrainian population come into contact with one of the most powerful universal mutagens - ionizing radiation, which can cause genetic damage in all living beings, including human.

As such, it was essential that the Chernobyl accident victims be medically monitored using cytogenetic monitoring – the study of the frequency and spectrum of chromosome aberrations in human peripheral blood lymphocytes with the help of classical (conventional cytogenetics, G-banding analysis) and new (FISH-WCP) research methods.

A report included the results of this monitoring, which was conducted by the scientists from the cytogenetic lab of RCRM AMSU since January 1987 until now. The results indicated that among the exposed groups of high priority were patients recovering from acute radiation sickness, such patients included clean-up workers mainly from the 1986 and 1987 cleanup efforts, Chernobyl power plant personnel, Sarcophagus workers, self-settlers from the 30-km exclusion zone and children and adults from areas of mandatory and voluntary evacuation.

The data received about the dose-dependent rise of the frequency of chromosome aberrations in examined groups had been in agreement with the results of other authors and confirmed that in fact there was an increase of the somatic chromosome mutagenesis intensity; which was induced by Chernobyl accident factors, on the background of general ecological and social despondency that allows to consider this accident as a new ecogenetic factor for population of Ukraine.

It has been shown that even so called “low” human doses of ionizing radiation under prolonged exposure can be "doubling" on cytogenetic criteria and induce specific chromosome damage in cells-indicators (human peripheral blood lymphocytes), which are not only biomarkers of radiation mutagenic exposure, but cause the death or functional disturbance of target cells (somatic and germinal). This can be the basis for the origin of stochastic and possibly some nonstochastic effects of mutational characters (particularly multifactorial pathology).

The most important areas for further scientific investigation are the in-depth study of the radioinduced, so called “disgenomic effects” (adaptive response, chromosome instability - delayed, hidden, transmissible - and "bystander effect”) as well as the comparison of primary structure chromosomal damage with known harmful health effects due to human irradiation. Such research will provide the opportunity to obtain unique data, from the contribution of radiogenic genomic injuries to the outcome of delayed medical consequences of radiation accidents.

The Chernobyl accident significantly complicated the ecological situation in Ukraine and on the background of already existing environmental contamination, promoted that great part of the Ukrainian population become increasingly in contact with one of the most powerful universal mutagens - ionizing radiation. This type of radiation can cause genome damages in all living beings including human. As it is known, only radioinduced genetic damage can be base for the appearance and development of both stochastic effects (hereditary pathology, oncological pathology) and non-stochastic effects with mutational characteristics (multifactorial pathology, congenital malformations).

Therefore, it becomes necessary for Chernobyl accident victims to be under medical observation by selective cytogenetic monitoring – the study of the frequency and spectrum of chromosome aberrations in human peripheral blood lymphocytes with the help of classical (conventional cytogenetics, G-banding analysis) and new (FISH-WCP) methods of the investigation.

Such monitoring has been conducted in the cytogenetic lab of RCRM AMSU since January 1987 till now, among priority groups of the Ukrainian population that suffered from the influence of the Chernobyl accident effects - patients recovering from acute radiation sickness, clean-up workers mainly from the 1986-1987 years, children from areas of mandatory or voluntary evacuation, evacuees, people living or working in the 30-km. zone of alienation (including Sarcophagus); the majority of whom (liquidators, children and adult population of the Ukrainian territories contaminated with radionuclides) one can suppose have been under the influence of low intensity radiation , with doses mainly less than 25 sGy.

It had been established that in all examined groups, a high level of cytogenetical markers of irradiation has remained. Its mean group values depended on the character and intensity of radiation exposure and its individual values probably were conditioned by the individual susceptibility of human organism to the identical radiation exposure.

A number of articles on the results of the cytogenetical examination of Chernobyl accident victims (mainly liquidators of different years as well as children and adults from territories of the Commonwealth of Independent States and some countries of Western Europe such as Germany and Austria) had been published by 2005 in some near by (Ukraine, Russia, Belarus, Estonia, Latvia) and some remote (Germany, Italy, Great Britain, the Netherlands, USA, Israel) countries. Radioinduced cytogenetic effects had been revealed in the majority of the examined groups, the extent of its expression depended on the intensity, duration, conditions of irradiation, time following the accident and in some cases on specific treatment of radiation-induced injuries [1-10].

The results obtained from the selective cytogenetical monitoring (which are indicators of general mutagenic load for the examined contingents) had been in agreement with the data received by colleagues from Ukraine and other countries, and this confirmed the fact that there is a dose-dependent increase in the intensity of somatic chromosome mutagenesis in humans, which was induced by Chernobyl accident effects on the background of general ecological and social despondency, which allows to consider this accident as a new ecogenetic factor for the population of Ukraine.

It has been shown that prolonged exposure of even so called “low” doses of ionizing radiation can induce specific chromosome damage in human peripheral blood lymphocytes and more than double the increase of spontaneous chromosome mutations. Such primary damages of the genome at the chromosome level are not only biomarkers of radiation exposure and biodosimeters of absorbed radiation, but by causing the disturbances of the normal function of target cells, can also be the basis for finding stochastic and possibly, some non-stochastic post-radiation effects with genetic components.

Interindividual variability in frequency of radio-dependent chromosome aberrations that have been observed under even identical conditions of irradiation can serve as an indicator of human individual sensitivity to mutagenic factors including ionizing radiation.

At the same time, the data obtained allows to suggest that there are such lower levels of irradiation in which cytogenical effects in some individuals are either not induced; or are induced but can be repaired; or are not identified by current approaches and methods which is a limiting factor in studying the cytogenical effects of low radiation doses.

The most important and perspective areas for further scientific research in the field of human radiation cytogenetics are profound studies of radioinduced “digenetic effects” (adaptive response, "bystander effect” or chromosome instability: delayed, hidden, transmissible); which we have been doing during the last several years [11-13], and also comparison of primary structure chromosome damage with developed harmful health effects due to human irradiation.

Such investigations will enable to get unique data about contribution of radiogenic genomic injuries to realization of delayed medical consequences of radiation accidents, which will finally allow basing scientific measures directed for minimizing of such consequences.

A cardinal solution of that problem can only be possible within the frames of a well-financed international scientific-technical program what will allow joint efforts of scientific groups working in this field.

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SOLID CANCER INCIDENCE IN VARIOUS GROUPS OF POPULATION AFFECTED DUE TO THE CHERNOBYL ACCIDENT

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Introduction

Malignant tumours including leukaemia are the most significant after effects of radiation exposure. The main sources for evaluation of risk of occurrence of malignant neoplasms are studies in A-bomb victims in Japan [1], nuclear tests [2] and patients exposed to radiation at medical diagnostics and therapeutic procedures. According to studies performed earlier, risk of fatal cancer is evaluated as 10-12% per 1 Gy [2].

Radiation exposure due to the Chernobyl accident may not be completely comparable with types of irradiation mentioned above, because the radiation exposure was too much lower doses and existed for a much longer time period. That is why the risk of fatal cancer due to the Chernobyl accident is evaluated is more than twice lower, at 5% per 1 Gy [3]. As in another exposed cohorts, the effects of irradiation may be postponed, and observed only after few decades after exposure. There are significant problems in estimation of cancer effects following the Chernobyl accident, and this has caused much debate. To substantiate estimates reliably, there is a need to evaluate doses received by the main groups of affected population and monitor these groups over time. These main groups are defined as: Chernobyl accident recovery operation workers (CAROW), who participated in recovery operation works in 1986-1987; evacuees from Prypyat town and 30 km zone; and the population still living in the territories that were most heavily contaminated with radionuclides.

The results represented below are based on the study of cancer incidence, in the groups mentioned above, during almost 20 years of follow-up since the Chernobyl accident.

Materials and methods

The current study was started to investigate the frequency of malignancies, after irradiation occurred of a significant part of Ukrainian population due to the Chernobyl accident [4-6].

A local cancer registry was established in 1987 for residents of the territories that were most heavily contaminated with radionuclides, to collect information on all retrospective (since 1980) and current cancer cases in Luginy, Narodichy, Ovruch districts of Zhytomir region and Borodyanka, Ivankov, and the Polesskoye districts of the Kiev region. These six districts are referred to in the text below as territories that are the most heavily contaminated with radionuclides. Besides this, the information on all cancer cases in the former Chernobyl district for 1981-1985 was collected as well and included in the database of the local cancer registry. At the time of the accident, the total number of this population was 360,700 including 74,400 children aged between 0-14 years [6].

In 2004, the population of six districts excluding unpopulated now Chernobyl district was 211,700 including 34,000 children [7]. In the procedure of data collection, all medical documents (including emergency notifications of new cancer cases, and death certificates) were obtained from all medical institutions where these patients were diagnosed and treated. These documents were crosschecked to eliminate duplicates and a final database was compiled. There were 19, 836 new cases of cancer registered in total, since 1980.

Annual age-specific and age-standardized (by direct method) incidence rates were calculated for 1980-2004 and compared with corresponding rates for Kiev, Zhytomir regions (to which the studied districts belong) and then compared to the Ukraine as a whole. The age structure of the USSR population in 1979 (according to the All-Union census) was used as a standard.

The data of the State registry of Ukraine on Chernobyl victims was used to investigate cancer incidence in CAROW 1986-1987 and evacuees. These data were compared with the database of the National cancer-registry. After this procedure all duplicates and cases without a validated diagnosis were eliminated. During 1990-2004, there were 6,221 new cases of cancer registered in CAROW and 2182 in evacuees [8-12].

The analysis of data on the following cohorts was performed: the data on CAROW of 1986-1987 years of participation, those who reside in Dnepropetrovsk, Donetsk, Harkov, Kiev, Lugansk regions and Kiev city (that totally amounted to 106,844 in 2004); and evacuees from Prypyat and the 30 km zone, who resettled in all territory of Ukraine (and they amounted to 56,175 in 2004). The indirect method of standardization was used for analysis of cancer incidence in these two groups. As a standard against which to compare, the age-specific incidence rates in Ukraine in 1998 was accepted.

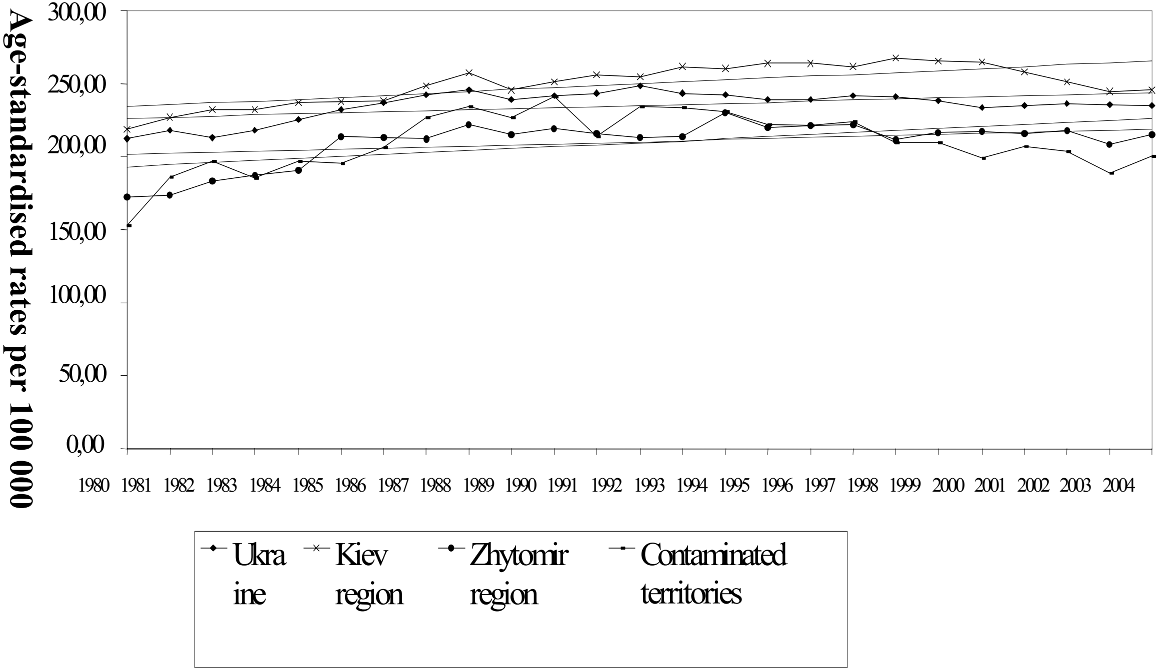
Results

Cancer incidence rates in the populations, which are still living in the territories most heavily contaminated with radionuclides is presented in the fig. 1 [9,13]. For comparison the data for Kiev, Zhytomir regions and Ukraine as a whole is presented there as well. During 1980-2004 the cancer incidence rate in contaminated territories was somewhat lower than that in other compared areas.

At the same time, the time trends of cancer incidence rate were similar in all the compared territories in that the annual standardized incidence rates had a gradually increasing trend. However, after 1998 the trend showed some decrease of incidence rates in all observed compared territories. There is no significant difference between their regression coefficients.

Comparison of standardized incidence ratios (SIR) in different groups of affected population (table 1) suggests a lack of statistically significant difference in cancer incidence, when comparing both "evacuees" and "residents of contaminated territories" to the national level. But in CAROW the cancer incidence is higher than the national level (and this difference is statistically significant).

Fig. 1. Cancer incidence rate in Ukraine, Kiev, Zhytomir regions and the territories most heavily contaminated with radionuclides in 1980-2004. Regression coefficients: Ukraine - 0,75±0,24, Kiev region. – 1,31±0,27; Zhytomir region – 1,38±0,32; contaminated territories – 0,71 ± 0,56).



Almost 20 years after the Chernobyl accident, some particular forms of malignant tumors are of great interest, because radiation is known to be significant causative factor for them. They are thyroid cancer, breast cancer, lung cancer, stomach cancer, colon cancer, ovary cancer and some others.

It is now indisputable that exposure to radiation was the cause of a dramatic increase in the thyroid cancer incidence rate (fig. 2). In Ukraine as a whole, this increase was twice the expected level in males and three times higher the expected level in females. Fig. 3 shows that the level of this cancer was 5 and 6 times the expected level, in Kiev city and Kiev region, respectively. This was where a significant part of the population of Prypyat town and the residents (who lived within 30 km zone) were relocated [9].

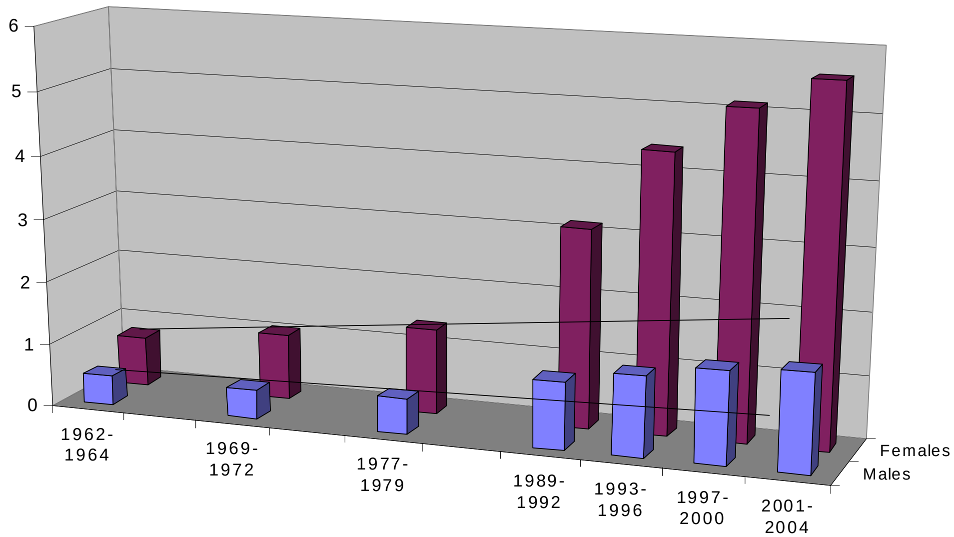
Regression coefficients that reflect time trends are: Ukraine 0,12±0,01; Kiev region – 0,41±0,07; Kiev city – 0,52±0,05; Zhytomir region – 0,22±0,03; contaminated territories – 0,41 ± 0,06. The first thyroid cancer cases in children up to 14 years old living in contaminated territories were registered in 1990 [4]. Betwee 1980 - 1990 (1980 was the the first year included in data collection) this pathology was not registered in the territory under study.

Since 1990 the increase of thyroid cancer incidence rate was noted not only in children, but also in adolescents and adults. One of the studies was performed in Chernigov, Kiev, and Zhytomir regions during 1990-1999, where radioactive iodine fallouts were observed [10,12]. The thyroid glands of the population were irradiated mainly due to this radioactive isotope of iodine, in fallout. This study showed correlation between the level of radioiodine fallout and thyroid cancer incidence rates for the first time. Truncated age-standardized incidence rates in territories with levels of contamination <100 kBq/m^2 did not exceed 2 cases per 100 000 in males and 5 cases per 100 000 in females. However, in territories with medium and high levels of contamination (100-200 kBq/m^2 and >200 kBq/m^2 respectively) significant increases of thyroid cancer incidence rates were observed. This observed increase consisted of 4 cases per 100 000 in males and 16 cases per 100 000 in females in 1998-1999. It was shown that the appearance of excess cases of of the thyroid gland cancer (due to the effect of exposure to radioiodine) has a tendency to increase over time [10,12].

Table 1 – Standardized incidence ratios (SIR) for all forms of cancer (Code ICD-9 140-208) in different groups of Ukrainian population affected by the Chernobyl accident

Group of observation and time period	Number of person-years of observation	Actual number of cases	Expected number of cases	SIR (%)	95% confidence interval
Residents of contaminated with radionuclides territories (males + females) 1990-2004	3,413,232	11,221	13,211	84,9	83,4-86,5
CAROW 1986-1987 years of participation (males) 1990-2004	1,228,422	5,396	4,603	117,2	114,1-120,3
Evacuees from Prypyat and 30 km zone (males + females) 1990-2004	796,653	2,182	2,599	83,9	80,4-87,5

Fig. 2 – Age-standardized average annual thyroid cancer incidence rates in Ukraine in separate time periods (males and females)



Comparative analysis of thyroid cancer incidence rate in different groups of affected population (table 2) suggest that the most significant increase of thyroid cancer (compared to national level) in the period 1990-2004 was in CAROW (8.0 times normal), and evacuees (5.1 times normal). This rate of increase in thyroid cancer appearance was seen to increase over time. In 1998-2004 it was higher – 9.1 and 6.0 times the normal national level, respectively.

The statistically significant increase, over normal, of incidence for thyroid cancer (1.6 times) was registered for the time period 1990-2004 in residents of the territories that were most heavily contaminated with radionuclides [9].

When we consider other forms of malignant neoplasms, we should pay particular attention to female breast cancer, which belongs to the group of radiation sensitive tumors. In the areas that were most contaminated with radionuclides territories, the incidence rate of this pathology was almost stable during 1980-1992 (fig. 4) and had a lower incidence rate than in larger compared areas

(Ukraine, Kiev and Zhytomir regions).

In 1992-2004 the breast cancer incidence rate in contaminated territories increased to be close to the rate of large compared areas [13].

Concerning female breast cancer incidence in all groups of affected population, it should be noted that it exceeded the national level only in CAROW. In 1990-2004 the SIR was 190.6% (95% confidence interval 163.6-217.7%), so these results show that breast cancer rates were 1.9 times higher in the CAROW group over that time period. An analysis of SIR in two other groups (evacuees and residents of contaminated territories) of affected population gave controversial results. According to the local standard, the SIR shows a statistically significant increase of actual breast cancer numbers compared to expected local numbers. However, comparison with the national level does not give evidence to conclude a statistically significant result overall.

At the same time, the increase in female breast cancer incidence rate in all three groups of victims during the period of observation is obvious. When we consider other malignant tumours, we must remember that they may have much longer latent development periods after radiation exposure, so persistent observation for them must be continued for a much longer time.

Conclusions

The study of cancer incidence in the main groups of population affected by the Chernobyl accident (CAROW of 1986-1987; evacuees from Prypyat' town and 30 km zone; and the population still living in the territories most heavily contaminated with radionuclides) showed peculiarities of the incidence rates of cancer frequency. The CAROW were the only group to have a higher incidence rate for all cancers studied, compared to the national average level, (particulary those CAROW who participated in recovery operation works in 1986-1987).

Fig. 3 – Thyroid cancer incidence rate in Ukraine, Kiev, Zhytomir regions, Kiev city and the territories most heavily contaminated with radionuclides in 1980-2004. Regression coefficients: Ukraine 0,12±0,01; Kiev region – 0,41±0,07; Kiev city – 0,52±0,05; Zhytomir region – 0,22±0,03; contaminated territories – 0,41±0,06.

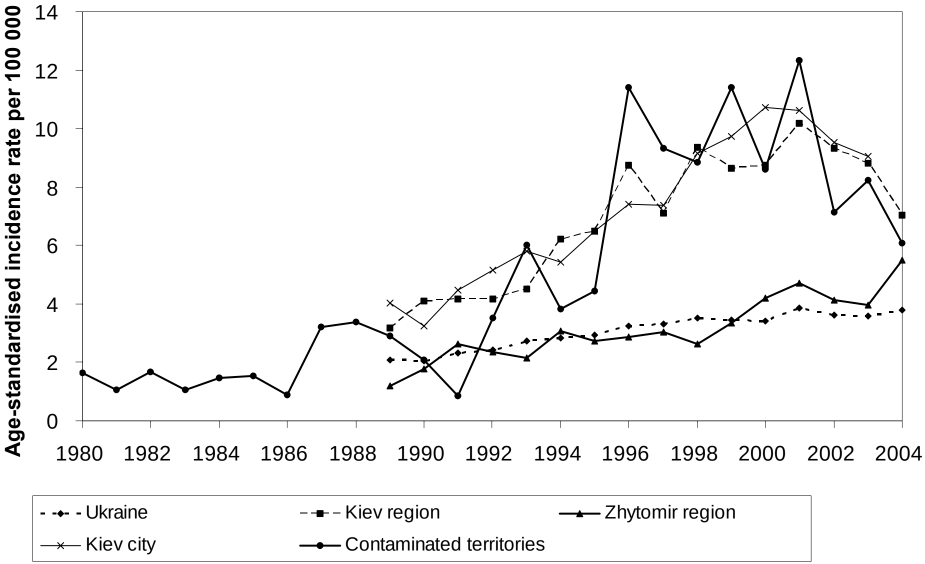
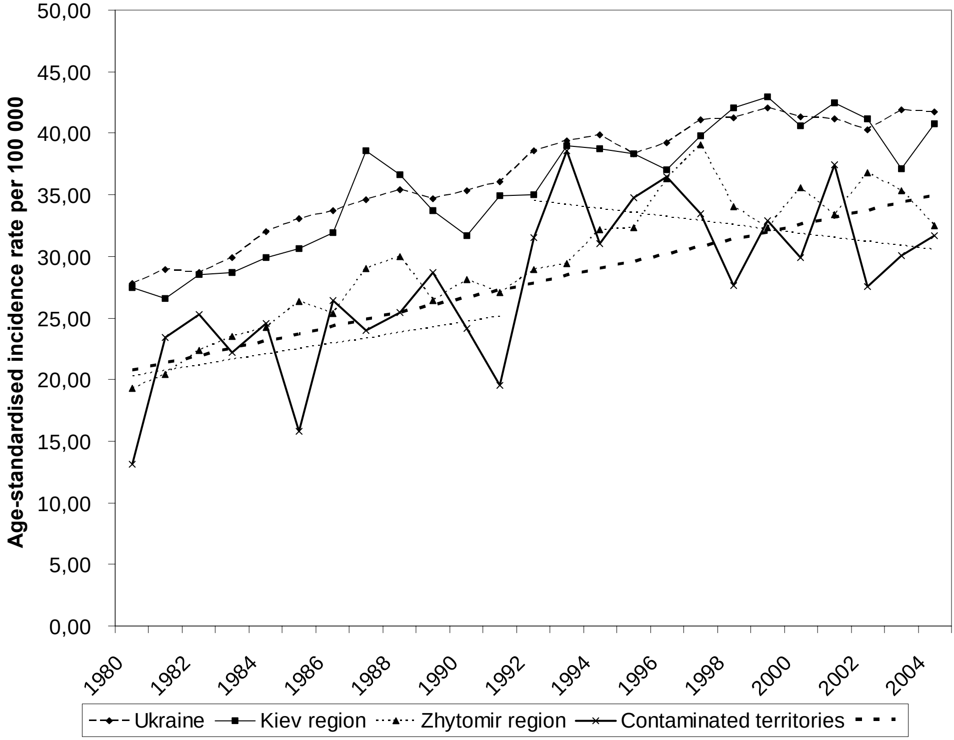


Table 2 - Standardized incidence ratios (SIR) for thyroid cancer (Code ICD-9 193) in different groups of Ukrainian population affected by the Chernobyl accident

Group of observation and time period	Number of person-years of observation	Actual number of cases	Expected number of cases	SIR (%)	95% confidence interval
Residents of contaminated with radionuclides territories (males + females) 1990-2004	3,413,232	247	151.4	163.1	142.7-183.4
CAROW 1986-1987 years of participation (males) 1990-2004	1,228,422	164	20.5	800.7	678.2-923.3
Evacuees from Prypyat and 30 km zone (males + females) 1990-2004	796,653	174	34.0	511.3	435.3-587.2

Fig 4 – Female breast cancer incidence rate in Ukraine, Kiev, Zhytomir regions, Kiev city and the territories most heavily contaminated with radionuclides in 1980-2004. Regression coefficients: Ukraine - 0,60±0,04; Kiev region. – 0,61±0,07; Zhytomir region. – 0,66 ± 0,07; contaminated territories: in 1980-1991- 0,44 ± 0,37; in 1992-2004 - (-0,34) ± 0,25; in 1980-2004 - 0,59 ± 0,13.



In all groups under study, significant increases of thyroid cancer incidence rates were observed. These increased rates may be associated with fallouts of radioactive iodine. This increase was found not only in children, but also in adolescents and adults. Following exposure to radioiodine, the occurence of extra thyroid cancer cases has a tendency to increase over time.

There is some tendency of increases seen for female breast cancer rates. However, there is a necessity for the further monitoring of other malignant tumour cases to reveal any possible rate increases due to radiation exposure, and so there is also a need for improving the quality of malignant tumour data collection in the future.

The small number of cases of several forms of cancer and migration suggest the necessity to perform this monitoring not only in contaminated areas. Particular attention should be paid to places of current residence of persons who were exposed to radiation, but who then were moved outside of contaminated zone.

The solution to these problems could be effected, with the assistance of the "State registry of Ukraine", coordinating with the National cancer registry and regional cancer registries. The information about exposed radiation doses received would be very important to evaluate risk of developing radiation induced malignant tumours.

Because the latency period of different forms of radiation-induced-cancers vary, there should not only be focus on thyroid, breast cancers and leukaemia, but also to lung, stomach, colon, ovary, bladder, liver cancers and multiple myeloma. We should pay particular attention to young age groups (at the moment of accident), i.e. persons who were subjected to radiation in utero, in early childhood and teenagers.

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CHRONIC OBSTRUCTIVE PULMONARY DISEASE IN CLEAN-UP WORKERS OF CHERNOBYL CATASTROPHE, WHO UNDERWENT TO RADIONUCLEADES INHALATION

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The complex integrated characteristics of 20 years study of persons with pulmonary diseases who suffered from Chernobyl catastrophe was performed. These studies are based on epidemiological, clinical, functional, immunological, morphological, electron microscopy data and helped to evaluate peculiarities of patients whose chronic pulmonary diseases had started after the external radiation and radionuclides inhalation. Pulmonary system was one of the main "targets"- tissue of such exposure realizing in chronic obstructive pulmonary disease (COPD) during the first 3-5 years after the Chernobyl accident among the clean-up workers of Chernobyl Catastrophe. Pathomorphosys and peculiarities of COPD are studied at the clean-up workers of 1986. COPD is a part of multiple organ failure as a result of homeostasis disturbances with the immune transformation (predominance of depressive changes at the initial phase and cytotoxic and immune complex reactions - at the remote period). Clean up workers have hypotonical dyskinesia of trachea membrane at the beginning with the transformation to the total bronchial obstruction at the remote period. Bronchoscopic study showed diffuse atrophic endobronchitis with considerable sclerotic changes of mucous membrane and bronchial deformation. Morphological examination showed chronic endobronchial inflammation with expressed regeneration injury of bronchial epithelium, pathology of microcirculation, damage of mucociliary system, basic membrane disturbance, and local immunity insufficiency. Bacteriological research discovered 2-4 bacterial species in endobronchial outwashes. The electron microscopic study detected deep invasion of microorganisms in bronchial mucosa because of bronchial epithelium injury. Key words: ionizing radiation, pathomorphosys, chronic obstructive pulmonary disease, clean-up wokers of the accident at the Chernobyl nuclear power plant, ventilating function of the lungs, bronchofiberscopy, bronchial mucosae.

Introduction

A great amount of radioactivity released into environment and spread by air-dust for a long distance due to the Chernobyl Nuclear Power Plant accident, which was one of the greatest technogenic ecological catastrophes in the human history. This caused both external and internal (first of all by inhalation) ionizing irradiation of population in the low doses [1,2,3]. According to the different estimations [4] more then 200 000 people of different categories were irradiated by radionuclide inhalation.

The most numerous and staggering category among them are clean-up workers especially those who has been participating in these works in April – May 1986 and till the time, the object "Shelter" has been built – spring 1987 [5,6].

There is no doubt that at these conditions radionuclide inhalation was one of the main ways of incorporation at clean-up workers of ChNPP accident [2,3,7]. And radionuclide inhalation was the main way of irradiation within the bounds of 30 km zone round ChNPP. These peculiarities caused stochastic and nonstochastic effects of ionizing radiation influences on clean-up workers bronchopulmonary system [7]. So, topicality of this item is doubtless.

Scientific Centre for Radiation Medicine Academy of Medical Sciences of Ukraine and Institute of Ecology Problems of Men have been making research during 20 years after disaster to find out the influence of Chernobyl damaging factors on man's bronchopulmonary system. This research is connected with the epidemiological data analysis, bronchopulmonary system state monitory in those who suffered due to Chernobyl Catastrophe, studying of Chronic obstructive pulmonary disease (COPD) clinical feature peculiarities and its pathomorphosis in the conditions of radionuclide inhalation.

Results

Long–term (1996-2004) pulmonology checkup results more then 16 000 (16133) clean-up workers of ChNPP accident of 1986 at the SCRM outpatient department show reliable unswerving chronic bronchitis and COPD morbidity rate at this category of patients (Fig.1).

Relative risks analysis due to the data of clinical epidemiological study (1992 – 2004) of 7665 clean-up workers of ChNPP accident COPD patients, men, was provided in RSRM AMS of Ukraine (Fig. 2). The results showed reliable relation of pathology appearance with the whole body irradiation dose level higher then 0.25 Sv (control group of patients had body irradiation dose level less then 0,05 Sv).

Figure 1. Results of long-term pulmonological monitoring liquidators of the Chernobyl Catastrophe at the SCRM outpatient department

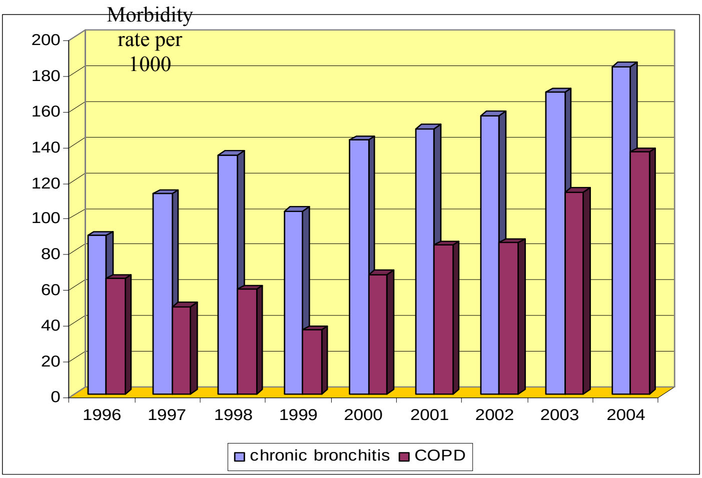
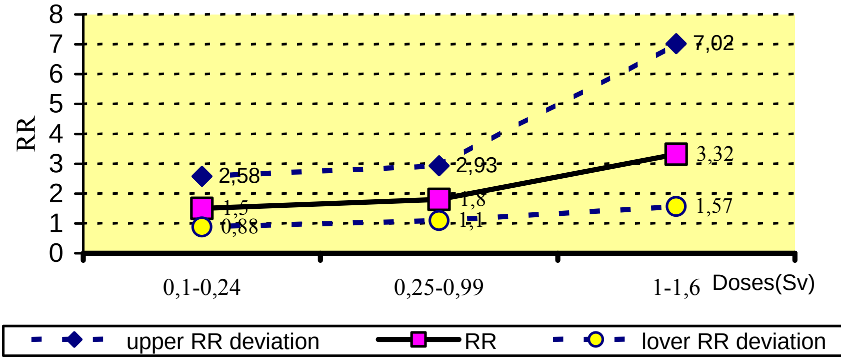


Figure 2. Relative risks and 95 % confidence interval of relative risk of COPD morbidity among males clean-up workers of 1986-1987 with different doses of whole body irradiation (Buzunov V.P., Krasnikova L.I., Sushko V.A., SCRM of AMS of Ukraine, 2005).



During 1987-2005 p. a complex pulmonological study was carried out among 2736 patients with chronic obstructive pulmonary disease (COPD) – 2427 clean-up workers of Chernobyl NPP accident, who have been participated in this works during 1986 (including 82 patients, who had acute radiation sickness, and 11 patients with “hot particles” incorporation (mostly ^{137}Cs, ^{60}Co) with the doses of external irradiation from 2 to 76 cSv (with the exception of acute radiation sickness reconvalescents) and 309 COPD patient without radiation influence.

The priority data were received, which made it evidence of COPD pathomorphosis in case of air-dust and other damaging factors in clean-up workers of ChNPP accident, who were involved into these works in 1986 [9,10].

According to the received data, clean-up workers of accident on the ChNPP directly during the works and in the nearest period after works in zone of ChNPP had cough syndrome without sputum. The subsequent currency of disease was characterized by "poverty" of a clinical picture with progradiate development of obstruction and formation of dyspnea. Later on the pathology got features of chronic obstructive lung disease with the appropriate clinical triad: cough, sputum, and dyspnea in a combination with the obstructive and mixed ventilating disorders.

The structure of bronchoobstructive syndrome in liquidators of accident on the ChNPP has been changed from the syndrome of isolated obstruction of small bronchus occurred and the hypotonic dyskinesia of membranous parts of trachea and the main bronchial tubes to the syndrome of total generalized obstruction.

Endoscopic research of tracheobronchial tree has allowed to establish, that for the given category of patients the most typical changes of bronchial wall is diffuse atrophic bronchitis, which is characterized by thinning of mucous membrane, sharper in comparison with norm of cartilaginous skeleton evidence, pauperization of vascular figure. The basic endoscopic type of bronchus mucous changes was sclerotic, accompanied by deformation of tracheobronchial tree. Fine light pink longitudinal gentle circulary-directed connective scars on a mucous membrane mainly at segmentary and subsegmentary bronchial low lobes tubes ostium characterize this type of changes. Expressiveness of inflammatory process testifies to a low degree of activity of productive inflammatory process in overwhelming majority of cases and, is coordinated to the prevailing form and type of pathological changes in tracheobronhial mucous in liquidators of accident on the ChAPP, suffering from COPD [11].

The results of bronchofibroscopic studying of tracheabronchial tree mucousa in COPD patients – clean-up workers of ChNPP accident, have shown, that primary endoscopic variant of a chronic bronchitis is chronic diffuse 1 stage of inflammation atrophic endobronchitis with catarrhal-sclerotic type of changes.

It was testified also, that COPD is the part of polyorganic disorders, which is caused by the specific changes of immune mechanisms: from the prevalence of radiation-caused immunologycal insufficiency primary after irradiation to the cytotoxic, and also immunecomplex reactions in the period of the remote consequences.

By means of pathomorphological analysis it was found out the combination of insufficiency of inflammation with the reduced quantity of T-lymphocytes which was accompanied by decrease of the maintenance on a cell surface of functionally active receptors - CD3, CD2, HLADR. Decrease of CD3 + T- lymphocyte maintenance at the surveyed patients in the first period correlated with the increased number of somatic mutations in T-cellular receptor locus that testifies to value of radiation-induced processes in formation of functional insufficiency of T-cells [12,13].

In clean-up workers dysregenetory changes of superficial epithelium were combined with it basal cellular hyperplasia. The great amount of supervisions showed the basal cellular hyperplasia, which was accompanied by planocellular metaplasia of bronchus superficial epithelium. Subsequently, combinations of basal cellular hyperplasia with secretory-cellular and, even, with hyperplasia of ciliary epithelium manifested and appeared more and more typical. Two kinds of abnormalities in basal cells were found: firstly, those predetermined neoplastic transformations, and, secondly, pathology of cambial layer characterized by modified, functionally "insolvent" (planocellular metaplasia) or "poor" epitheliocytes populations (mucous, ciliary).

Damage of microvessel channels of bronchus mucous membrane have been verified during all supervision period. The sclerotic changes of bronchial tubes walls (all layers accessible by biopsy research) form the basis of chronic bronchitis progressing in patients exposed to radiation influence [13].

Structural substratum of chronic inflammatory process in bronchial tubes mucous membrane is characterized by low intensity of inflammatory-cellular infiltration, in particular, immunecompetentive cells. Transformed manifestations of reactance facilitate microbes' invasion. Over the last two years the fungous infection is more and more frequently verified. Taking into account the fact that planocellular metaplasia and cellular atypia are precancer conditions, examination of clean-up workers of the ChNPP in 1986-87 requires pulmooncological vigilance.

The diagnostic algorithm and its methodology were created to provide for optimal diagnostic, treating and prophylactics, as well as expert tactics for COPD patients, who suffered from Chornobyl Catastrophe.

Conclusion

In conditions of combined influence of external irradiation and mixture of radionuclide pulmonary system was one of the main "targets"-tissue of such exposure realizing in chronic obstructive pulmonary disease (COPD) during the first 3-5 years after the Chernobyl accident among the clean-up workers of Chernobyl

Catastrophe. The analysis of dosimetric and clinical-epidemiological data indicates, that the basic risk group in terms of realization of stochastic and not stochastic effects of ionizing radiation influence and radionuclides inhalations in conditions of the Chernobyl accident are clean-up workers of the ChNPP in 1986-1987.

Chornobyl Catastrophe caused growing up of pulmonary diseases morbidity rate in those, who suffered after disaster.

The analysis of anamnestic data indicates that in clean-up workers directly during and at the nearest period after the works in the ChNPP zone coughing syndrome without sputum features was observed. Subsequently, disease course was characterized by "poverty" of clinical picture with progradiate development of obstruction syndrome and dyspnea formation. With time course, the pathology obtained features of chronic obstructive lung disease with appropriate clinical triad: cough, sputum, and dyspnea in combination with the obstructive and mixed ventilating disorders.

Macromorphological study of tracheobronchial tree mucous of clean-up workers with COPD established that the basic endoscopic variant of bronchial damage is chronic diffuse of 1st stage inflammation atrophic endobronchitis with catarrhal-sclerotic change of mucous membrane.

Pathomorfological researches of bronchobiopsy materials allows to systematize structural equivalents of clinical pathomorfisis of COPD in patients - clean-up workers as transforming of regeneratory processes, features of microvessels damage, fibrillogenesis disorders and modification chronic inflammatory process.

Thus, the given data indicate that for victims of the ChNPP accident (primarily clean-up workers) presence of bronchological pathology in the form of chronic obstructive lung disease with some special clinical, endoscopic, pathomorphological and immunological features appeared typical. That requires the adequate methodology elaboration of diagnostics and treatment of bronchopulmonary diseases for the given contingent.

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RADIOLOGICAL CONSEQUENCES OF THE CHERNOBYL ACCIDENT IN AUSTRIA

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Austria ranks among the countries that have been strongly affected by the fallout of radioactivity from the Chernobyl disaster. The average contamination with Cesium-137 (and Cs-134) from Cernobyl in Austria was 23,4 kBq/m². With this amount of contamination Austria follows the Ukraine, Belarus and Sweden as the fourth ranked concerning the fallout from the Chernobyl disaster.

The contaminated air from Chernobyl came to Austria in two waves: first via Turkey and Romania to the southeast of Austria, the second cloud came from the east and hit the regions north of the Alps. The geographical distribution correlates significantly to the rainfalls during the last days of April and the first days of May 1986. The actual contamination differs from nearly nil (no rain) to 200 kBq/m² (heavy thunderstorms).

In the eastern part of Austria during the first weeks following the accident, vegetables such as spinach and salad were prohibited from being sold to the public. Milk was contaminated for more than one year - especially milk from Alpine regions.

In regions without precipitation (especially the eastern part of Austria) Iodine-131 concentration of air was high at the time the radioactive cloud passed through (approximately 1-2 days). Physicians in these regions report that the number of people with thyroid diseases has increased since 1990.

A simple analysis of existing data for thyroid cancer conducted by our Institute in 1998 indicates that in regions in which the gamma dose was high in the first days following the accident the incidence rate of thyroid cancer in 1995 was higher than in the other regions of Austria.

During the years 1997 and 1998 various Austrian media reported an increase of thyroid cancer, leukemia and non-Hodgkin's lymphoma. Since the media compared only case numbers, these observations cannot be taken seriously, however it should prompt investigation by the authorities.

The Federal Health Ministry of Austria did not investigate incidence rates of thyroid cancer and leukemia with reference to the Chernobyl impact in Austria. The STATISTIK Austria/Österreichisches Krebsregister (= Austrian Institution collecting all statistical data for the Austrian government and other costumers) provide many health related data which could be used to investigate correlations between radiation exposure of the population in Austria caused by the Chernobyl disaster and the health of the population, but the Austrian administration did not seem to be interested in investigation of the facts.

One reason for this hesitation is that in the 1980s the cancer registration system was changed which makes comparison of the data before and after the nuclear accident difficult. A recent study made by the University of Salzburg (Austria) compared large regions in Austria (countries) (Austria is a federal Republic consisting of 9 Bundeslaender/countries) with highly contaminated parts followed by another without relevantly contaminated regions. This analysis based on the average contamination in the countries did not show significant differences in health data. This setting was probably not refined significantly enough.

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MORBIDITY AMONG PERSONS EXPOSED TO RADIATION AS A RESULT OF THE CHERNOBYL NUCLEAR REACTOR ACCIDENT

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A considerable amount of scientific research in the past years analyzing the state of health of persons who were exposed to radiation caused by the Chernobyl nuclear reactor accident proved sickness rate among them to be much higher than the Russian average.

This prompts the question of whether there is causality in the emergence of diseases among citizens exposed to the harmful effects of the catastrophe. The Russian interdepartmental expert panel of the Russian Scientific Radiology Center of the Ministry of Health of the Russian Federation investigates this issue.

This article uses data of sickness rate, disablement and mortality of persons who participated in the liquidation of the after-effects of the Chernobyl nuclear reactor accident. These data were acquired in detailed analyzes of medical-expert documents, researched in 2004.

Altogether 1,000 medical records of (mostly male) liquidators were researched. These medical records included detailed excerpts from surgery documents (or in some cases the entire document), excerpts of sanitary treatments or analyze, referrals for medical examination, or, in the case of death, the autopsy protocol. In cases where it was necessary to specify the diagnosis, the Council transferred the patients to the best-qualified medical facility. Given the meticulousness of the primary medical documents as well as the experts' advanced level of training (the Council was composed of leading specialists from various medical fields), the credibility of the diagnosis could be significantly increased [1].

It should be noted that only the main diseases causing invalidity or death were examined; accompanying diseases were not investigated.

Ranked first (63%) are blood-circulation diseases [2].

Among the causes of death of liquidators, ranked first are diseases of the cardiovascular system.

Among afflictions of the blood circulation system, most common are ischemic heart diseases (72%).

It is worth noting that the ischemic heart disease developed early among liquidators who were on service most notably in 1986. This can be explained by the early development of atherosclerotic lesions of coronary and cerebral vessels in persons who were exposed to radiation [2].

The second most common disease of the cardiovascular system is idiopathic hypertensia (38%), ranked third is vegetative-vascular dystonia (12,9%) [2].

Neuropsychic diseases rank second (18%) among all diseases. The most widespread disease in this group is encephalopathy of various origins (34%). The frequency with which this disease occurred grew significantly in 2004, as compared to 1991-1998 (from 25% to 34%) [3].

In addition, serious affects such as severe disturbances of cerebral blood flow became more widespread (10% in 1998 and 17% in 2004).

Neuropsychic dynamic damages - neuroculatory dystonic became much more frequent (from 41% in 1991-1997 to 13% in 2004. This overall is evidence of more serious clinical courses of psychoneurological diseases among liquidators, shown by an increasing distribution of diseases with pronounced organic afflictions, quite often leading to disability in the given category [3].

The third most common disease are malignant neoplasms (6.8%), and it is the second most common cause of death (26.3%).

Among liquidators the most widespread were malignant neoplasms in kidney and urinary bladder, totalling 17.6% of all cancer diseases, which is twice as high as the average in Russia (7,5%).

The second ranked in frequency was malignant tumours in three localizations: respiratory organs, stomach and hemoblastosis (9%). Compared to the Russian average among liquidators, malignant tumors in the thyroid gland were diagnosed (almost three times) more frequently, tumours in haematogenic and lymphatic tissues (more than two times higher), tumours in larynx, and prostatic glands. The following types of tumours were found to be less frequent (one and a half times) than in the remainder of Russia: cancer of the lung and less so for stomach tumours and tumours of large intestine [2].

Analysis of the distribution of cancer diseases among liquidators who died revealed that the majority was afflicted with lung cancer while was stomach cancer followed second. This is consistent with data regarding the remainder of Russia. Third ranked was hemoblastosis, which exceeded more than two times the all-Russian level. Among tumours in other parts of the body, most widespread were brain tumors, tumors in the thyroid gland, kidneys, urinary bladder and larynx.

Affliction of the gastrointestinal tract rank fourth (6.4%) within the entire range of liquidators' diseases. Stomach ulcers make up the highest proportion with 53.9% among the afflictions of digestion organs.

Furthermore, attention must be given to the increase in liver diseases in 2004 as compared to 1991-1997. Until 1997 liver pathology was basically determined by chronic hepatitis (5%), however after 1998 a considerable proportion was made up by a more serious disease – liver cirrhosis [3].

Of all liquidator deaths diseases of the digestion organs caused 10.6%. These diseases now rank third in the range of diseases, after cardiovascular diseases and cancer.

Accordingly, a substantial portion in the range of the liquidators' diseases is composed of blood circulation system and neurologic-mental diseases (63% total).

Over the last several years, in this range of diseases, the proportion of serious diseases (ischemic heart disease, cerebrovascular accident, encephalopathy) increased, whereas the proportion of dynamic diseases with a relatively favorable course decreased (cardiopsychoneurosis, vegetative-vascular dystonia).

Regarding liquidators with cancer, ranked first is malignant neoplasm of respiratory organs (36.2%) and of digestion organs (28.3%).

A large proportion (64.7%) of liquidators of working age are invalids. The most common causes of death among liquidators include diseases of the blood circulation system (63%) and malignant neoplasm (26.3%). Remarkably few deaths among liquidators were caused by diseases of the gastrointestinal tract (7%), lung diseases (5%), injuries and poisoning (5 percent), and tuberculosis (3%) [2].

Twenty years have passed since the Chernobyl catastrophe, but the study of its negative health effects is still prevailing (suggest using "continuing" instead of "prevailing"). The liquidators are among those citizens most intensely exposed to the harmful effects of the accident.

Thus the study of morbidity and fatality of liquidators is of the highest importance, as it is the basis for developing and carrying out complex medical and social measures aimed at minimizing the negative health consequences of the accident, not only for the liquidators, but also for the population as a whole.

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SUPPLEMENTARY INFORMATION REQUESTED OF THE MEDICAL ASSOTIATION FOR PREVENTION OF WAR (AUSTRALIA) AT INQUIRY PUBLIC HEARING, 19 AUG 2005

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Introduction

At the Committee's public hearing in Melbourne on 19 Aug 2005, Associate Professor Tilman Ruff was requested by the Committee to provide:

1. Further information and references regarding the health consequences of the Chernobyl disaster; and
2. A reference to the most recent Carnegie Endowment for International Peace report on nuclear, biological and chemical threats, which discusses the situation regarding laser enrichment of uranium in various countries, and related proliferation concerns

This information is provided here, and a further paper written recently for the Association by Professor Frank Barnaby, is enclosed. Entitled 'Safeguards and plutonium reprocessing', this provides further background on the matter of plutonium and reprocessing of spent nuclear fuel, discussed with the Committee during its 19 August hearing.

Health consequences of the Chernobyl disaster

Introduction

During representatives of MAPW's appearance before the Committee hearing on 19 Aug 05, the Chair invited A/Prof Ruff to explain the discrepancy between a United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) assessment he cited of 31 immediate deaths and an increase of some 800 cases of thyroid cancer diagnosed in children, only about 10 of which had been fatal, and the higher numbers, at least 6000 deaths (and a documented up to a 34-fold increase in thyroid cancer rates) A/Prof Ruff described in his submission.

The figure of 6000 deaths cited and referenced is a low-end figure very likely to substantially underestimate the scale of the health consequences of the disaster.

Since the hearing, a major multi-agency UN report was released on 5 Sep 2005, by the International Atomic Agency (IAEA), World Health Organisation (WHO) and United Nations Development Programme (UNDP). This 600 page report is the work of the Chernobyl Forum, made up of 8 agencies – IAEA, WHO, UNDP, Food and Agriculture Organisation (FAO), United Nations Environment Programme (UNEP), United Nations Office for the Coordination of Humanitarian Affairs (UN-OCHA), UNSCEAR, the World Bank, and the governments of Belarus, Russia and Ukraine. Its (conservative) estimate is 4000 deaths attributable to the disaster over the lifetime of emergency workers and local residents in the most contaminated areas – quite similar to the estimate cited in the MAPW submission.

The Committee Chair's suggestion of about 40 total deaths caused by the Chernobyl disaster is quite inaccurate and a misleading interpretation of the evidence.

A summary of the key findings of the recent Chernobyl Forum report, and a review of its strengths and weaknesses are presented to the Committee to provide a framework to understand the consequences of the world's worst civilian nuclear disaster.

‘Chernobyl’s legacy: health, environmental and socio-economic impacts’ - The Sept 2005 Chernobyl Forum Report[1]

Major findings

The summary of major findings is contained in the Press release announcing the Report[2].

Radiological and health

- Major releases of radionuclides continued for 10 days after the core meltdown on 26 April 1986 and contaminated more than 200,000 square km of Europe
- Strontium-90 and cesium-137, with half-lives of around 30 years, persist and will remain a concern for decades to come. Cesium, present especially in milk, meat, fish and some plant foods, remains the most significant concern for internal human exposure
- About 100,000 people of the 5 million living in the most contaminated areas received more than the recommended maximum radiation dose limit of more than 1mSv annually
- Although plutonium isotopes and americium-241 will persist for thousands of years, their contribution to human exposure is thought to be low
- A total of about 4000 deaths attributable to the disaster are expected over the lifetime of emergency workers and local residents in the most contaminated areas, including:
    - Some 50 emergency workers who died of acute radiation syndrome
    - 9 children who have died of thyroid cancer
    - An estimated 3940 deaths from radiation-induced cancer (a 3% increased incidence in overall cancer deaths),

[1] Available at: http://www.who.int/ionizing_radiation/a_e/chernobyl/-EGH%20Master%20file%202005.08.24.pdf

[2] IAEA, WHO, UNDP. Chernobyl: the true scale of the accident. 20 years later a UN report provides definitive answers and ways to repair lives. (Press release). 5 Sep 2005, 11 pp.

including leukemia among the following 600,000 people:

- 200,000 emergency workers exposed over the period 1986-7
- 116,000 people evacuated
- 270,000 residents of the most contaminated areas

- Among emergency and recovery operation workers ('liquidators'), an increase in leukemia, solid cancers and cardiovascular diseases has already been identified

Social

- Relocation proved a 'deeply traumatic experience' for some 350,000 people
- Poverty and lifestyle diseases are severe and persistent, the effects of the disaster compounding adverse social and economic consequences following the break-up of the former Soviet Union. Poverty is especially acute in affected areas
- Adverse mental health consequences including depression, 'paralysing fatalism', reckless risk-taking behavior and substance abuse have been extensive and persistent in affected communities
- Anxiety over health effects of radiation shows no signs of diminishing and may even be spreading

Environment

- Increased mortality in conifers, invertebrates and mammals and reproductive losses in plants and animals were seen in areas up to 20-30 km distant from the reactor
- Agriculture was hard hit, with 784,320 hectares taken from production. Countermeasures applied on more than 3 billion ha of agricultural land in Belarus, Russia and Ukraine was needed to minimize the amount of products with radionuclide concentrations above action levels. Some agricultural lands in Belarus, Ukraine and Russia are still out of use and will need to remain so until remediation can be undertaken
- In Western Europe, a range of countermeasures are still being used for animal products from uplands and forests
- Timber production was halted in 694,200 ha of forest

- Restrictions on harvesting of firewood and food products such as game, fish, berries and mushrooms are still needed in some areas though they are often disregarded by the population, especially in low-income areas

Economic losses

- A variety of estimates from the 1990s placed the costs over 2 decades at hundreds of billions of dollars [These are not further developed, elaborated upon or updated in the Report].

The damaged reactor

- The protective shelter or sarcophagus built over the damaged reactor was erected quickly and imperfectly and did not allow collection of complete data on the stability of the damaged reactor
- Some structural parts of the shelter have corroded, and the main potential hazard posed by the shelter is the possible collapse of its top structures, with further release of radioactivity
- Strengthening of those unstable structures has been performed recently, and construction of a new structure covering the existing shelter that should serve for more than 100 years is planned to start in the near future. It will hopefully allow dismantlement of the current shelter, removal of the radioactive fuel mass, and eventually, decommissioning of the damaged reactor
- A comprehensive strategy is still to be developed for dealing with the high level and long-lived radioactive waste from past remediation activities. Much of this waste was placed in temporary storage in trenches and landfills that do not meet current waste safety requirements. For example, they are without engineered barriers, proper design documentation, or hydro-geological investigation.
- The other 3 RBMK reactors (Units 1-3) at the site are shutdown with a view to being decommissioned, and 2 additional reactors (Units 5 and 6) that had been near completion were abandoned in 1986 following the disaster. Thus major radioactive waste management tasks remain at the site.

Report of the UN Chernobyl Forum Expert Group 'Health': Health effects of the Chernobyl accident and special health care programmes. Working Draft 31 Aug 2005[3].

Key findings of this section of the Chernobyl Forum report are presented with some comment.

Most affected populations

- 30 immediate deaths among power plant employees and firemen occurred with days–weeks, 28 due to high radiation exposure
- About 240,000 recovery operation or clean-up workers (also called liquidators) undertook mitigation activities at the reactor and in the 30 km surrounding 'exclusion zone' in 1986-7; and these activities continued on a large scale until 1990, involving 600,000 identified personnel in the 3 most affected countries [Other estimates which include personnel from other countries of the former USSR suggest that such personnel number in total around 800,000 eg in the background material for a forthcoming conference on the health of liquidators to be held in Switzerland[4]]
- About 116,000 residents of highly contaminated areas were evacuated in 1986 and a further 220,000 after this time, across the 3 republics of Belarus, Russia and Ukraine
- Iodine blockade with stable iodine to reduce thyroid radiation doses from ingested iodine-131 (I-131) must be given immediately after exposure to be effective – this was effectively implemented in Poland, but not for the majority of the affected population in the

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[3] Available at: http://www.who.int/ionizing_radiation/a_e/chernobyl/-EGH%20Master%20file%202005.08.24.pdf

[4] 'Health of liquidators (clean-up workers), 20 years after the Chernobyl explosion' is a conference to be held on 12 November 2005 at University Hospital, Bern, Switzerland, organized by Physicians for Social Responsibility/International Physicians for the Prevention of Nuclear War Switzerland and the Faculty of Medicine of the University of Bern. For further information see: www.ippnw.ch

former Soviet Union. Indeed, high doses of stable iodine administered too late to block radioactive iodine uptake may have increased radiation doses (p 68)

- ‘Contaminated areas’, defined as those where cesium-137 (Cs-137) deposition was more than 37 kBq per square meter (m^2), (or 1 microcurie per $m^{2)}$ are variably described as containing 5 million (p 4), 6 million (p 27) or 6.8 million (p 144) residents in different places in the report.

Dose estimations

- Much uncertainty and inconsistency exists in relation to assessments of thyroid radiation doses in the 3 most affected republics (p 17)
- Doses to recovery operation workers estimated by different methods involve uncertainties of between 10% and a factor of 5 (p 23)
- National registry data in the 3 most affected countries cover less than half of the recovery operation workers, and do not contain information on affiliation or type of work carried out (p 25)
- Falsification of Registry data is thought to have occurred for about 10% of the military workers (p 25); and for the remainder of the military workers, the doses are thought to have been systematically overestimated by about a factor of 2.[This would tend to underestimate dose-related health effects]. Doses from internal irradiation ‘have not been given much attention’ and limited information is available on beta radiation to the skin and eye (p 25)
- Internal doses from strontium-90 and plutonium-239 have received limited attention (p 28)

Thyroid cancer

- An unexpectedly early and marked, dose-related rise in incidence of thyroid cancer in children and also in liquidators has unequivocally been observed in all 3 most affected republics, with odds ratios in exposed children up to over 100 (p 38)
- There is also evidence that in territories with severe iodine deficiency, the increased risk of thyroid cancer was further increased by a factor of between 2 and 3.2 (p 38, 46)

- Pooled analysis of groups exposed to external radiation during childhood and adolescence in various parts of the world shows thyroid cancer risk still increased at the longest period of observation, about 45 years, with the greatest risk at about 15-30 years after exposure. More than 15 years after the Chernobyl disaster, thyroid cancer incidence is still highly elevated, and it is likely that it will continue at this current high rate for at least the next decade (p 44)

Leukemia and non-thyroid solid cancers

- Data with considerable methodological limitations and lacking dose information for children exposed in utero are nevertheless suggestive of an increase in leukemia (p 84), and a case-control study in Ukraine suggested an increase in leukemia in exposed children (p 86)
- Recent data suggest a 2-fold increase in leukemia (other than chronic lymphocytic leukemia) among Russian liquidation workers exposed to estimated total external doses of 150-300mGy (p 87)
- As noted in the report (p 91), solid cancers from Chernobyl radiation exposure would be expected to only now begin to appear, following a typical minimal latent period of 10-15 years. [Thus, most cancers that will be caused by Chernobyl radiation are yet to occur, and long-term, high-quality disease surveillance will be required.]
- To date, there has been relatively little study of solid cancers other than thyroid cancer in Chernobyl-exposed populations, however at least 2 significant studies have been reported. Cited in the report (p 92) is a descriptive epidemiological study in Belarus and Ukraine undertaken in collaboration with the International Agency for Research on Cancer (IARC) and the Finnish Cancer Registry. The results indicate a significant increase in incidence of pre-menopausal breast cancer incidence among women exposed before the age of 45 y in the most contaminated compared with less contaminated districts.
- An important study not referred to in the Report, despite having been published in October 2004, almost a year before the release of the draft Report, is an assessment of data from the Belarus national Cancer Registry, which compares baseline incidence rates for various cancers and overall cancer in 1976-85, with rates observed

in 1990-2000[5]. Data are disaggregated by sex and region, allowing comparison between high and low exposure regions; and linkage with a national registry of those most affected by Chernobyl – liquidators (about 120,000), evacuated persons, and those still living in contaminated territories.

A statistically significant increase in cancer incidence, averaging 39.8%, was observed in all regions, but was most pronounced in Gomel region, the most contaminated region, with an increase between the 2 time periods of 55.9%. Compared with adults in the least contaminated region (Vitebsk), in the period 1997-2000 (an anticipated 11-15 year latency period), male liquidators had statistically significantly raised risk of cancers of all sites, and for colon, lung and bladder cancer, with relative risks shown in Table 1.

Table 1. Relative risk (RR) in cancer incidence (truncated age-standardised rate for ages 20-85 per 100,000 population) in liquidators, 1997-2000, compared with control adults in least contaminated area (Vitebsk), Belarus Source: Okeanov et al 2004

	Incidence in controls	Incidence in liquidators	RR	95% confidence interval
All sites	373.3	449.3	1.20*	1.14 – 1.27
Breast (female)	58.6	61.3	1.05	0.81 – 1.35
Lung	52.4	67.3	1.28*	1.13 – 1.46
Stomach	41.7	44.9	1.08	0.92 – 1.26
Colon	17.0	22.3	1.31*	1.03 – 1.67
Rectum	19.0	18.4	0.97	0.77 – 1.23
Kidney	14.8	17.9	1.21	0.97 – 1.50
Bladder	10.9	17.0	1.55*	1.21 – 1.99

**Statistically significant differences*

Even though thyroid cancer represents only 0.4% of the total cancers recorded, an increase in the exposed adult population is clearly discernible, with a standardized incidence among the adult

5 Okeanov AE, Sosnovskaya EY, Priatkina OP. A national cancer registry to assess trends after the Chernobyl accident. Swiss Med Wkly 2004;134:645-9.

population aged over 30 years of 1.24 per 100,000 population in 1980, 1.96 in 1990, and 5.67 in 2000. Among liquidators, the rate was 24.4 per 100,000 for the period 1993-2000.

While longer follow-up and data from additional populations will be useful, and controlling for confounding factors such as smoking would be desirable, these data are biologically highly plausible and indicate an increase in a diverse range of solid tumours among the most exposed populations, especially liquidators

- As noted in the Report, even if effects due to low and moderate radiation doses may be difficult to detect given the high incidence of cancer overall, and its multiple causes other than ionizing radiation, even a small increase in relative risk can result in a substantial number of cases when applied to a large population

Non-cancer diseases

- **The eye**
  - Several studies in Ukraine among liquidators and exposed children show an association of posterior subcapsular cataracts with Chernobyl radiation exposure, consistent with other evidence, at relatively low doses, of the order of 250 mGy (p 107)
- **Cardiovascular diseases**
  - In Ukraine and Belarus, there are no large epidemiological studies on radiation and cardiovascular disease, however in Russia, data are available on 4995 deaths among a cohort of 60,910 emergency workers, which demonstrated a significant dose-related excess relative risk (RR) for death from cardiovascular disease, with an excess RR coefficient per Sv of 0.54 (95% CI 0.18-0.91) (p 111). Despite the known inaccuracies and limitations of radiation dose data recorded in Chernobyl State Registers, these findings are consistent with the published data for Japanese atomic bomb survivors (p 112)
- **Cytogenetic markers**
  - A variety of types of chromosomal abnormalities in circulating blood lymphocytes have been shown to serve as biological dosimeters for assessing radiation doses received, either immediately following exposure or retrospectively. While a number of studies have been conducted, primarily to

estimate absorbed radiation doses, in liquidators and residents in highly contaminated communities, these have not been systematically used on a large scale and have not been coordinated with data on health outcomes (p 116).

- **Infant mortality**

- Considerable uncertainty and unexplained fluctuations and changes are noted in a range of observed reproductive and child health outcomes. Cases of Down's syndrome in Belarus have fluctuated widely over time (p 123-6). A steady increase over time in 9 types of congenital malformations has been reported in both low and high contamination areas in Belarus since the disaster (p 123-4). The birth rate in Ukraine has declined by about 30% during the 1990s, apparently as a result of induced abortions – in 2000, there were 113 induced abortions per 100 live births and this ratio continues to increase (p 123).
- The most significant finding is probably the high infant mortality rates, which the Report notes have generally decreased in non-contaminated areas, and less so in highly contaminated areas (pp 125,127, 129). The reasons for this remain unexplained. Though the Report states that the increase in infant mortality in most heavily contaminated areas is not statistically significant, an upward trend in those areas during 1990-7, while the rate elsewhere is declining, is strongly suggestive of an adverse effect on infant mortality in the most contaminated areas in the period 4-11 years after the disaster, and aggregated data in a larger population may be more definitive. The causes of the high infant mortality in the 3 most affected countries are not elucidated in the Report.

- **Mental health**

- Increased levels of depression, anxiety, unexplained physical symptoms, subjective ill health, and self-identification as 'invalid' and 'victim' have been documented in a range of Chernobyl-exposed populations (p 132-3). Suicide is reported as the leading cause of death in Estonian clean-up workers (p 133)
- The Consensus Expert Assessment in the Report concludes (p 134-5):

The mental health impact of Chernobyl is the largest public health problem caused by the accident to date. The magnitude and scope of the disaster, the size of the affected population, and the long-term consequences make it, by far, the worst industrial disaster on record. Chernobyl unleashed a complex of events and long-term difficulties, such as massive relocation, loss of economic stability, and long-term threats to health in current, and possibly, future generation, that resulted in an increased sense of anomie and diminished sense of physical and emotional balance... the high levels of anxiety and medically unexplained physical symptoms continue to this day.

...

The accident has had a serious impact on mental health and well being in the general population. Importantly, however, it appears that this impact is demonstrable mainly at a subclinical level.'

Mortality caused by ionizing radiation

As there is nothing that biologically unequivocally identifies cancers, cardiovascular events, or other stochastic (probabilistic) health outcomes - the probability of which is increased following radiation exposure - as being caused by radiation exposure, the Report states (p 137): 'In reality, the actual number of deaths caused by this accident is unlikely to ever be precisely known.' Indeed it cannot be any other way.

- **Acute radiation sickness (ARS)**
  - ARS was originally diagnosed in 237 emergency workers, later confirmed in detail in 134, of whom 28 died in 1986 and 19 more died between 1987 and 2004 (p 138)
- **Emergency workers**
  - National registries in the 3 most affected countries include dose and medical information for 550,000 emergency workers and more than 1.5 million people living in contaminated areas. Age-matched control and dose-response

studies on liquidators have only been conducted in Russia (p 138) [but note published Belarus data referred to previously which is not included in the Report].

- Evidence to date in this group indicates:
    - An increase in leukemia incidence with an excess relative risk per sievert (ERR/Sv) of 6.7 (95%CI 0.8 – 23.5)
    - An increase in mortality due to solid cancer, with an ERR/Sv of 2.11 (95%CI 1.3 - 2.9)
    - Increased mortality due to cardiovascular disease with ERR/Sv of 0.5 (95%CI 0.2 – 0.9)
- The estimate of 4.6% of all deaths in the Russian liquidators being attributable to radiation-induced cancer and cardiovascular disease over the period 1991-8 underestimates the overall impact by:
    - Considering a period during which excess cancers have just started to occur
    - Considering only external and not internal radiation doses
    - Importantly, the relative risk assessment is based on an inappropriate baseline – the Russian general population. The Report shows (Figs 16.1 and 16.2, p 139) data, which only begin in 1991 (rather than going back to 1986 as would be much more useful). In 1991 there was a substantial healthy worker effect – the standardized mortality ratio in these generally young (mostly between 20 and 40 years, p 163), healthy, (mostly male) workers was under 0.65 ie their mortality rate was 35% less than that of the general population. Over the period shown, till 1998, this healthy worker effect lessens and by 1997 almost disappears.

      The substantial diminution of the healthy worker effect 5-11 years after the disaster begs the question of whether it had already declined from 1986 to 1991, and in any case will substantially underestimate any adverse health effects. A more appropriate baseline would be age, sex and occupation-matched military, nuclear power and emergency service workers who were not exposed to significant Chernobyl radiation. There should be no technical reasons why such a more appropriate control group could not be utilised.

- The number of deaths attributable to radiation exposure in the liquidators described in this section (Chapter 16) of the Report relates to only approximately one-third of the Russian emergency workers (and less than 10% of the total number of liquidators), over a 7 year period 1991-8, an observation period extending only slightly longer than the recognized minimum latency period of about 10 years for many of the cancers.
- It is rather surprising (p 142) that the relatively simple task of applying the Russian mortality data to liquidators from the other countries is yet to be done

Populations of contaminated areas

- The conclusions presented in this section of the Report (16.2.3) do not reflect information in other sections of the report noted above, or other data, which were available to the Report's authors well before its release in draft form (such as the published cancer registry data from Belarus outlined previously). This section of the Report states that the only malignancy, which has shown a statistically significant increase to date, is thyroid cancer in children and adolescents (p 143). This ignores evidence cited in the Report of increased incidence in leukemia in liquidators and probably in children, increase in thyroid cancer in adults, and increase of overall cancer and cancers of a range of other sites in adults in Belarus, especially in highly contaminated regions.
- Table 16.4 (p 145, adapted as Table 2 below) of the Report summarises predictions of excess deaths from solid cancers and leukemia in exposed populations. It contains errors as it is not clear which of 'solid cancer' and/or 'leukemia' applies to the 3 time periods listed for each group. The denominators included are not consistent with other sections of the report eg the number of evacuees is given as 135,000; elsewhere the figure of 116,000 is used. Similarly, residents of other contaminated areas other than the most contaminated zones (SCZs) are given here as numbering

6,800,000; elsewhere in the Report figures of 5 and 6 million are used for this (somewhat arbitrarily defined) group.

- Assuming that the first 2 periods for each population group refer to solid cancers and leukemia, respectively, over the lifetime of those alive at the time of the disaster, gives a total number of estimated deaths from malignancy of 3960 (not 3940 as quoted in the accompanying press release) for 200,000 liquidators who worked during 1986-7 (no more than 1/3 of the total number), evacuees and residents of the SCZs. However, another 4970 deaths are estimated in the residents of other contaminated areas.

Table 2. Predictions of excess deaths from solid cancers and leukemia over lifetime (up to 95 years) in populations exposed as a result of Chernobyl disaster (drawn from Report Table 16.4, p 145)

Population	Population size	Average dose	Predicted excess cancer deaths	Total predicted excess malignant deaths
Liquidators 1986-7	200,000	100 mSv	Solid 2000 Leukemia 200	2200
Evacuees from 30 km zone	135,000	10 mSv	Solid 150 Leukemia 10	160
Residents of SCZs	270,000	50 mSv	Solid 1500 Leukemia 100	1600
Subtotal				*3960*
Residents of other 'contaminated zones'	6,800,000	7 mSv	Solid 4600 Leukemia 370	4970
Total				8930

- These estimates are incomplete in a number of respects:
    - The number of liquidators included (200,000) is only a small fraction of the total number mentioned elsewhere in the report (600,000) in the 3 most affected countries. Yet even this number is incomplete, as liquidators are known to have come from other countries, such as Estonia and Lithuania, and elsewhere have been estimated to number around 800,000. These are generally the most exposed group.
    - The estimates omit Chernobyl radiation-attributed cardiovascular deaths (estimated in the Russian liquidators for the period 1986-1998, p 141) to comprise 2.0 % of all deaths, in comparison with 2.6% of all deaths estimated to be due to Chernobyl-related malignancy ie in this group, the excess of cardiovascular deaths is almost as large as the excess of cancer deaths. These data also omit other non-malignant causes of death such as suicide
    - These estimates omit the less exposed countries, particularly of Europe, which although generally involving quite low exposures, involve at least many tens of millions of people, so even small increased risks can be associated with a large number of attributable cases of disease
    - Internal exposures are not considered
    - Exposures for those born since 1986 and future generations are not considered
- These estimates are therefore quite incomplete and underestimate the health consequences of the disaster

Specific comments in relation to the Report and accompanying press release

The Health Effects report is designated as 'Working Draft, August 31, 2005', and is an incomplete, provisional document eg under 'Foreword' is written only 'to be inserted'. No overall summary or conclusions are presented.

The 11 page press release embargoed for 5 Sep 05, announcing the Chernobyl Forum's Report, was issued by IAEA, WHO and UNDP, titled ‘Chernobyl: the true scale of the accident’ and subtitled: ‘20 years later a UN report provides definitive answers and ways to repair lives’. This release rather than the Report itself seems to have been the basis for most of the media coverage of the Report. The first 2 paragraphs of the release state:

‘A total of up to four thousand people could eventually die of radiation exposure from the Chernobyl nuclear power plant (NPP) accident nearly 20 years ago, an international team of more than 100 scientists has concluded.

As of mid-2005, however, fewer than 50 deaths have been directly attributed to radiation from the disaster, almost all being highly exposed rescue workers, many of whom died within months of the accident but others who died as late as 2004.’

From the above review of the Report’s key findings in relation to health outcomes, it is apparent that these widely quoted statements are at odds with the findings of the Report and convey a misleading understatement of the effects of the disaster. The impression that ‘*As of mid-2005, however, fewer than 50 deaths had been directly attributed to radiation from the disaster…’* is in contrast to the Report’s estimated 8930 deaths expected in the 3 most affected countries among 200,000 liquidators, 135,000 evacuees and 7,070,000 residents of the most contaminated areas, within the lifetime of those exposed. The figure of 50 deaths is highly selective, relating only to deaths from acute radiation sickness.

A more complete approach to total cancer deaths is reflected in a US Dept of Energy study which applied radiation risk estimates more conservative than those used today to the estimated collective exposure in the Northern Hemisphere of 930,000 person-gray over a 50 year period, on the basis of the total inventory of radionuclides released and their dispersal across the Northern Hemisphere[6]. In this study, 17,400 excess cancer deaths over a 50-year period were estimated, with 63% of these occurring outside the (then) USSR, mostly elsewhere in Europe. These estimates ignore non-cancer effects and those occurring over a longer timeframe.

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[6] Anspaugh LR, Catlin RJ, Goldman M. The global impact of the Chernobyl reactor accident. Science 1988; 242:1514-9.

WHO's lack of leadership in radiation health and the vexed relationship between WHO and the IAEA

An important contextual matter in relation to the Report and assessment of Chernobyl health consequences is the diminished independence and leadership of WHO in relation to radiation health matters in general and the health dimensions of the Chernobyl disaster in particular. These deficiencies have, in the absence of feasible alternative explanations, been attributed in large part to WHO's problematic and inherently contradictory relationship with the IAEA.

One expects that WHO, as the world's lead technical international health organization, acts with objective, independent, scientific rigour; and that it would take the lead on assessing health consequences of major international events. Unfortunately, in relation to radiation health matters, WHO has played a diminished role compared with its leadership and activity in other health areas. This applies in relation to the Chernobyl disaster, as evidenced by:

- WHO was not substantially involved in assessing or seeking to minimize the health consequences of the disaster in the first 5 years following it. A statement from WHO accompanying the Chernobyl Forum Health Report titled 'WHO's role in the assessment and mitigation of the health effects of the Chernbyl accident'[7] makes no mention of any WHO activities prior to 1991.
- The lead agency for essentially all major conferences and UN agency reports on the Chernobyl disaster has not been WHO, but the IAEA. A variety of other UN agencies such as UNSCEAR and the International Agency for Research on Cancer (IARC), as well as national and regional organizations, have often played a more important role than WHO.

The IAEA spans inconsistent roles as both nuclear proliferation watchdog; and promoter of 'non-military' nuclear technology, including nuclear power, and involving largely the same materials, technology, and expertise as nuclear weapons development and production.

[7] www.who.int/ionizing_radiation/a_e/chernobyl/en/print.html accessed 21.9.2005

Article 1 of the Agreement between the IAEA and WHO (which came into force on 28 May 1959) established that the 2 organisations '…will act in close co-operation with each other and will consult each other regularly in regard to matters of common interest.' It appropriately asserts the independence of WHO's work by stating:

' … it is recognized by the WHO that the IAEA has the primary responsibility for encouraging, assisting and coordinating research and development and practical application of atomic energy for peaceful purposes throughout the world *without prejudice to the right of the WHO to concern itself with promoting, developing, assisting and co-ordinating international health work, including research, in all its aspects*.'[Emphasis added]

Article III.2 specifies: 'Subject to such arrangements as may be necessary for the safeguarding of confidential material, the Secretariat of the International Atomic Energy Agency and the Secretariat of the World Health Organisation shall keep each other fully informed concerning all projected activities and all programmes of work which may be of interest to both parties', and Article III.3 stipulates '…consultations regarding the provision by either party of such special information as may be of interest to the other party'. Such consultation and communication is appropriate for two UN agencies.

However, other parts of the Agreement inherently compromise WHO's independence in relation to nuclear and radiation matters:

'Whenever either organisation proposes to initiate a program or activity on a subject in which the other organization has or may have a substantial interest, the first party shall consult the other *with a view to adjusting the matter by mutual consent'* [Article I.3, emphasis added].

Further, Article III.1 outlines circumstances in which confidentiality may be exercised:

' The IAEA and the WHO recognize that they may find it necessary to apply certain limitations for the safeguarding of confidential information furnished to them. They therefore agree that nothing in this agreement shall be construed as requiring either of them to furnish such information as would, in the judgement of the party possessing the information, constitute a violation of the confidence of any of its Members or anyone from whom it has received such information or otherwise interfere with the orderly conduct of its operations.'

These provisions do not reinforce fundamental principles of accountability, transparency, or public provision of information; and do not justify confidentiality on the basis of public safety, as may temporarily be warranted, but on the basis of weaker, largely internal, organizational considerations.

The frequent deferral by WHO to IAEA as the lead agency in relation to Chernobyl consequences, the paucity and lateness of WHO involvement in evaluating and responding to the health consequences of the disaster, and the inappropriate downplaying of these consequences in the public communication around the recent Chernobyl Forum Report represent a compromised role of WHO, contrary to its global health leadership mandate.

Perhaps the most telling indicator of WHO's weak contribution and leadership on assessing Chernobyl disaster health consequences is the fact that I could only find 3 substantive WHO documents specific to Chernobyl included in the over 420 references in the Health Report.

Nor is the Chernobyl situation unique in this respect. It is germane to note that other highly radiation exposed populations in the former Soviet Union include those in the vicinity of Soviet nuclear test sites, particularly Semipalatinsk, in Kazakstan. Independent, rigorous, peer-reviewed, well-conducted and internationally coordinated studies whose methods and findings should be promptly publicly available are needed in these populations, preferably led and co-ordinated by WHO. Yet again substantive WHO engagement and leadership appear to be absent.

General comments on the Report's context, strengths and limitations

Almost 20 years after the world's worst industrial disaster and worst non-military nuclear disaster, much of the available data on health consequences is weak, with a patchwork of different organizations utilizing different, non-standardised methodologies, and significant deficiencies exist in consistent and reliable radiation dose estimates, fundamental to accurate risk assessment. As outlined in this review, there is significant variation, both within the Report itself and between the Report and other sources, in the basic demography of population groups most affected.

Data on very few health outcomes, collected with sound and consistent methodology, are available for all the most affected areas. For example, the Report notes that information on liquidator mortality data are available mostly from Russia, on malformations mostly from Belarus, and on infant mortality mostly from Ukraine (p 105). Most data were collected in different ways in different places. This diminishes the ability of data to be pooled, its power to identify efects, the precision around estimates, and the reliability and strength of conclusions which can be drawn. The body of the Report, in contrast to the accompanying press release, highlights in some detail how incomplete and inconclusive the available data are, and highlights multiple ongoing researches needs. It is in no way a definitive account of the health consequences of the disaster. The range of effects which have been already demonstrated are therefore of even greater significance in terms of their likely true extent.

It is important to recognize (as the Report does), the fundamental principle that, particularly in relation to diseases, which have multiple causes and changing epidemiology, lack of demonstration of an effect does not equate to absence of effect.

Particularly in the critical early days, weeks and years following the disaster, there existed strong elements of political cover-up and obfuscation which both hampered measures, which could have protected people, and ongoing objective assessment of health consequences. A few examples will serve to underscore this:

- In the most affected countries, distribution of stable iodine, which could have minimized much of the harm from ingestion of short-lived I-131, was too late to be effective - indeed may have been harmful – and was not available at all to most of those who were significantly exposed
- The first reports of a major radioactive contamination event came not from Belarus, Ukraine or Russia, but from a nuclear power plant in Sweden, where contamination was detected on the clothing of incoming workers[8]
- Prof Yuri Bandashevsky, head of the Gomel State Medical Centre in one of the most contaminated regions of Belarus, paid for

[8] Anon. Chernobyl. Bulletin of the Atomic Scientists 1996;52(3):20.

his work on the effects of internal radiation with an 8-year prison term, and was adopted by Amnesty International as a prisoner of conscience, believing that his conviction was ‘related to his scientific research into the Chernobyl nuclear reactor catastrophe of 1986 and his open criticism of the state authorities’[9].

Subsequently, and at the opposite extreme, there were some exaggerated claims of harm resulting from the disaster, in part probably driven by a desire to attract international resources to deal with its consequences, particularly in the context of the significant economic downturn resulting from the disaster, and the strains associated with break-up of the former USSR. As noted in the Report, there is ‘some evidence from Belarus, Russia and Ukraine of the manipulation of diagnoses allowing persons to be recognized as a Chernobyl invalid without proper justification in order to obtain social benefits’ (p 172).

The political, governmental, social and economic upheaval associated with the break-up of the former Soviet Union compounded the difficulties of conducting well-organised and long-term health studies and introduced a wide range of additional potentially confounding health effects, including an overall significant reduction in life expectancy, particularly among adult males – 6 years in Ukraine, 9 years in Russia - which would have the effect of shortening the period of older age when the risk of cancer is greatest and a radiation-related increase would be most evident, and therefore diminishing observed effects.

In the survivors of Hiroshima and Nagasaki, an early peak of leukemia 5-10 years after the exposure was followed by a steady rise in solid cancers and non-cancer disease incidence, which is still increasing. Children have a higher sensitivity to radiation than adults – the same radiation dose in boys in the first year of life produces 3-4 times the cancer risk as between the ages of 20 and 50 years; and

[9] Schneider M. The Chernobyl disaster. A human tragedy for generations to come. In: International Physicians for the Prevention of Nuclear War, PSR/IPPNW-Switzerland. Rethinking nuclear energy and democracy after September 11, 2001. IPPNW Global Health Watch Report No. 4. Cambridge, MA; IPPNW, 2004:7.

infant girls have almost double the risk of boys[10]. For both these reasons, the greatest radiation-related increase in cancer and other diseases in those exposed following the Chernobyl disaster is yet to occur, and cancer cases among those exposed to Chernobyl fallout as children can be expected to continue to accrue till the 2060s and 2070s.

Health assessment of the long-term impacts of the disaster also needs to take into account potential exposures, especially internal exposures, from long-lived isotopes such as Cs-137, Sr-90, Pu-239 and Am-240, in future generations living in contaminated regions, particularly given recycling of radionuclides within the biosphere, and bioaccumulation of some, such as Cs-137. Such long-term exposure pathways have scarcely been investigated and the Chernobyl Forum report does not address them.

The Report also does not address the health consequences of the disaster outside the most affected countries. Even though exposures of the large populations of Europe generally involved low radiation doses and therefore the incremental risk of adverse health effects is small, because they affect a very large number of people, the total number of excess cases, eg of cancer, attributable to Chernobyl exposure, even though not directly measurable, is considerable, as demonstrated in the US DOE study cited.

The limitations of the Report can perhaps best be illustrated if one adds to the Report's estimated number of 8930 excess cancer-related deaths over the lifetime of those most exposed in the 3 most affected countries (but involving no more than one-third of the total liquidators) (Table 2), some conservative estimates for other groups:

- As many cancer deaths in the 400,000–600,000 additional liquidators for whom risk estimates have not yet been made (p 142) as in the Russian cohort for which they have: 2200 x 2-3 = 4400 – 6600.
- The Report (p 141) estimates that in Russian liquidators 2.0% of radiation-related deaths were due to cardiovascular disease and 2.6% to cancers. If one applies this ratio to the whole cohort of 600,000-800,000 liquidators, as above in relation to

[10] The National Academies. BEIR VII: health risks from exposure to low levels of ionizing radiation. Washington DC; National Academies Press, 2005.

cancers, one can estimate 2200 x 3-4 x 2.0/2.6 cardiovascular deaths among all the liquidators: 5077 – 6769.

- The same number of cancer deaths outside the 3 most affected countries as in the 1988 US DOE report (based on 50 year dose commitment): 10,920;
- An additional 20% of cancer deaths related to exposures occurring in future generations: 0.2 x (8930+(4400-6600)+10,920)= 4850-5290.

This yields an estimate (rounded to 3 figures) of 34,200 – 38,500 deaths.

This does not include any non-cancer effects other than in liquidators, and even in this group includes only cardiovascular deaths, and not those due to suicide, other mental health problems, substance abuse or any other causes; or any possible genetic effects.

And of course in addition to the burden of excess mortality is the substantial and long-term burden of illness and ill health. As noted in the WHO statement accompanying the draft Health Effects Report[11]:

'The Chernobyl disaster was a human tragedy, resulting in large-scale displacement of populations, the contamination of vast areas of land, the loss of livelihood and the mental trauma suffered by people who had to be evacuated because of severing links with their home and social networks. The victims of the tragedy were confronted by situations they could not understand and against which they had no means of defense.'

Conclusions

Despite the considerable limitations in quality and extent of data available on health outcomes of the Chernobyl disaster, multiple confounding factors, lack of leadership by WHO, and the fact that most health consequences beyond the acute phase of the disaster are still to occur, the Report documents numerous health consequences of the disaster, and estimates that about 9000 excess deaths can be

[11] WHO. WHO's role in the assessment and mitigation of the health effects of the Chernobyl accident. www.who.int/ionizing_radiation/a_e/chernobyl/en/print.html. Accessed 21 Sep 2005.

expected only in the most affected areas among those alive at the time of the disaster. This estimate includes only 200,000 of the 600,000 to 800,000 liquidators, who were the most heavily exposed group.

A conference on ‘Health of liquidators (clean-up workers), 20 years after the Chernobyl explosion’ organized MAPW’s Swiss sister organization Physicians for Social Responsibility/ International Physicians for the Prevention of Nuclear War Switzerland is being held on 12 Nov 05 at the University Hospital in Bern, Switzerland.

By any standard, as the report notes, the Chernobyl disaster was the world’s worst industrial disaster, with serious economic, social, environmental and health consequences, which will continue to accrue over many years hence.

GENE POOL CHANGES AFTER ECOLOGICAL CATASTROPHE

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ABSTRACT

Analysis of the population-genetic consequences of technogenic catastrophes, e.g., Chernobyl, represents special interest in connection with development of global ecological changes and rising technogenic contamination. Research of dynamics of cytogenetic anomalies in bone marrow cells of different *Rodentia* species (trapped in the alienation zone near Chernobyl's NPP in 1994-2001 in places with different levels of contamination from 5 up to 1000 Ci/km2) and in peripheral blood cells of cattle generations of experimental herd (Pripjat, 200 Ci/km2) were carried out. The changes of genetic structure in cattle generations were analyzed employing family analysis of allele's transfer in structural genes and ISSR-PCR markers. An increased number of mutant animals were not detected, but reversal of the genetic structure of cattle, from the genetic structure of their initial breed to one typical for a more primitive breed, was revealed. Our results indicate that ionizing radiation does not induce new genetic anomalies but allows realization of inherently unstable species- and individual-specific genetic characteristics.

INTRODUCTION

Life on Earth has arisen and developed in the presence of the natural radioactive background (RB), a constant external abiotic factor. RB for humans, calculated for an altitude of 1 meter above ground, fluctuates worldwide around an average annual exposure of 3.5 mSv (Masse R., 2000). Exposure to natural sources is characterized by very large fluctuations, not excluding a range covering two orders of magnitude. The existence of territories on

Earth in which RB is up to a hundred times more than the global average [9], testifies the relativity of concepts of injuring doses of ionizing radiation.

The genetic consequences of living in radioactive regions have been investigated for many years. The broad research into human populations in the areas with increased RB (for example, several states in India, Ramsar in Iran), where the exposure dose of the population for one year is between 35 and 260 mSv, has not revealed an increased level of hereditary diseases in the populations [3,6].

Sudden significant elevation and persistence of sub-lethal radioactive exposure caused by human error as in Chernobyl can be considered a "changed" ecological condition. The abruptness of the change, and not just the change itself, is a real long-term problem related to the Chernobyl accident. The "novelty" of ecological conditions caused by human activity is a trait specific to modern times. Chernobyl serves as an invaluable model for the study of effects of rapid changes in the environment on the well being of humans and ecosystems.

Investigations into cytogenetic anomaly frequencies in somatic cells related to ionizing irradiation in the last 50 years were widely conducted on the people, plants, small-sized *Rodentia* species and others. The high individual variability in tested species in the same conditions, and also the absence of precise relations between quantity of cytogenetic damages in somatic cells and doses of ionizing irradiation were the singularity of the accumulated data. Usually it is assumed that the increased accuracy of methods will allow more precise correlations between low doses of irradiation and induced mutation events to be revealed. The first data confirming this hypothesis were obtained by Dubrova et al. [1] and concerned the occurrence of new minisatellite loci mutations in children of clean-up workers. However, the increase of mutation frequencies was observed only in 3 out of the 8 microsatellite loci investigated [1]. In other research [13], the increase of new mutations was detected by RAPD-PCR, but not by ISSR-PCR DNA markers. So, revealing mutation events on DNA level in these investigations was determined by specificity of variability in investigated minisatellite loci [1] and in DNA fragments, as well as by particular decanucleotide or microsatellite invert repeats (RAPD-PCR, ISSR-

PCR) [13]. Hence, as in cytogenetic investigation, DNA marker analysis fails to provide unambiguous data about genetic effects of low doses of ionizing irradiation, which would not depend on specificity of initial-variability of separate character.

We propose several methods to solve this problem. First, we need to define markers of individual "resistance" to ecological change and evaluate the changes in the fitness of genotypes facing changed conditions. This could be done by analyzing generation-to-generation changes in the allelic composition of populations of several species reproducing under conditions of ecological catastrophe (it is impossible in human populations because of their large lifespan). It is reasonable to expect that a set of molecular genetic markers distributed across the genome whose variability has nonrandom character in generations under conditions of increased ionizing radiation can be identified.

Thus, we propose our model of the control of population-genetic changes around Chernobyl using several species, for example, the *Rodentia* species. As a result of the high breeding rate of this species, it is a convenient subject for direct cytogenetic analysis of dividing cells in bone marrow and population genetic research. Its disadvantages include a short reproductive cycle, a complex migration processes, and the fact that it is impossible to analyse these animals under field conditions.

Another good object for such investigations is the cattle at the Novoshepelichi experimental farm (Pripjat). Advantages of this object: each animal has strictly determined genealogy and is useful for family analysis; all generations born after the Chernobyl catastrophe in conditions of a zone of alienation of Chernobyl's accident are available. A cattle of the same breed in relatively uncontaminated regions is available as control. A large quantity of molecular genetic markers in cattle is available and their localization in chromosomes in cattle is well characterized. In addition, the similarities between cattle and humans in terms of gene syntheny are also of note. The shortfalls of this object include the low number of offspring and special service required.

MATERIAL AND METHODS

ANIMALS

The mice of laboratory lines BALB/c (35 animals), C57BL/6j (35 animals) and CC57W/Mv (27 animals) were investigated in two age groups (2-3 month and 12-18 month) under control conditions (vivarium of Institute in Kiev, Ukraine [4] and their sibs in an experimental vivarium near Chernobyl's NPP, in which they were exposed to chronic low ionizing irradiation (around 0,6 Sv,). The investigation was carried out between 1993 and 1999 in different seasons.

Representatives of *Microtus oeconomus* (10 animals)*, Clethrionomys glareolus* (29 animals) and *Microtus arvalis* (43 animals) were trapped in different parts of the alienation zone around the Chernobyl NPP, each with different levels of radio nuclide pollution ranging from high (Red Forest, 1000 Ci/km^2), middle (Janov, near 200 Ci/km^2) and to low (Ivankov, Nedanchichi 1-3 Ci/km^2) levels.

Cytogenetic and population-genetic investigation was carried out on Holstein cattle at Novoshepelichi farm, located within 5 km of the Chernobyl nuclear power plant (near 200 Ci/km^2). As a result of the accident the zone showed dramatically increased ionizing radiation (~200 Ci/km^2*).* These cattle are referred to as the "exposed" group. The parent generation (FP), born in "pure" zones and parents to the experimental herd in the Novoshepelichi farm, included two subgroups:

(1) A bull, *Uran,* and three cows *-Alfa, Beta* and *Gamma* - kept in 1987 near the Chernobyl reactor where the accident happened in 1986. These animals (FP) were the parents of the F1, F2 and F3 generations, born in "Novoshepelichi".

(2) Another subgroup of cows (FP) brought to Novoshepelichi from "pure" zones of Ukraine in the years 1990-1993 were the parents of other Fl and F2 generations, born in an experimental farm near the Chernobyl reactor.

In both subgroups, FP as well as F1 and F2 cows mated exclusively with only one bull –*Uran* - belonging to FP. In summary, the experimentally exposed herd included 17 parents, 96 animals F1 and 50 F2 (first and second generations born in conditions of chronic influences of low doses of ionizing irradiation).

Cattle of the same breed kept in an uncontaminated region (Dnepropetrovsk, Ukraine) served as a control group, 46 animals in total. The cattle group (36 animals), of the Grey Ukrainian breed, (from "pure" Kherson region, Ukraine) was included in analysis as an example of a more primitive breed to be compared with the Holsteins.

CYTOGENETIC INVESTIGATIONS

The preparations of bone marrow cells of representatives of the *Rodentia* species and peripheral blood cells of cattle (with the use of short cell cultivation throughout 72 hours with phytohemagglutinin) were obtained by a standard technique without colchicine. In *Rodentia* species, the bone marrow from the back legs was washed away using a hypothonic solution (0,54 %), fixed by a mix of methanol spirit and ice acetic acid (3:1). The fixing solution was changed three times. Cells were then spread onto cold glass slides, dried and colored using Gimsa dye ("Merck", Germany), and then further analyzed using a Karl Ceiss binocular microscope at a magnification of 1000. Metaphase plates were photographed using a "Micrat-300" film. The frequency of metaphase plates (in %) with following cytogenetic characteristic was counted (in %): metaphase with aneuploidy, polyploidy (PP), chromosome aberrations (CHA), interchromosome associations on a type of Robertsonian translocation (RB), with asynchronous separation of centromere chromosome region (ASCR). Aneuploidy was evaluated in two variants: general aneuploidy (A1) and aneuploidy (A2) of one chromosome ($2n\pm1$).

The quantity of metaphase plates (MI) in 1000 cells, binuclear leukocytes (BL) and leukocytes with the micronuclei (LM) calculated on the same preparations in cells with saved cytoplasm (in ‰). Additionally the smears of cattle peripheral blood were done and frequency of MI, BL, LM and the erythrocytes with micronuclei (EM) in them was analyzed. Statistical reliability of the differences between groups was evaluated using our Student criterion (t_S).

POPULATION-GENETIC ANALYSIS

In cattle, we used the electrophoretic method of protein separation in vertical PAGE gels according to Gahne's modified technique (Gahne et al., 1977) for the analysis of the polymorphism of transferrin (TF), posttransferrin-2 (PTF-2) and receptor of vitamin D (GC) loci. The analysis of hemoglobin (HB), ceruloplasmin (CP), amylase-1 and purin nucleoside phosphorylase (PN) loci was carried out by a method of horizontal starch gel electrophoresis with subsequent histology-chemical dyeing using the standard techniques [5].

Polymorphism kappa-casein genes were investigated with the use of PCR-RFLP analysis. For PCR-amplification of a fragment of a kappa-casein gene used the following primers: Bocas A: 5 ' - ATGTGCTGAGCAGGTATCCTAGTTATGG - 3 ' and Bocas B: 5 ' - CCAAAAGTAGAGTGCAACAACACTGG - 3 ', picked up so that the DNA fragment between them included Pst I site specific for A and B allelic variants [14]. PCR-amplification carried out in the following mode: denaturation - 60 sec at + 92 C, subsequent 35 cycles - 60 sec at + 62 C, 90 sec at + 72 C. 5 mcl of amplified product was used for restriction analysis which was carried out within 4 hours at + 37 C with restrictase Pst I in the buffer of firm Sibenzime in volume 15 mcl. Allele CSN3 A contains the site to restrictase Pst I, and B – don't contain. The restriction products divided by a method of electrophoresis in 1,5%-s' agarose gels with addition of ethidium bromide and testing under ultra-violet light. The mix for PCR contained in all cases 50 ng of DNA, 15 pmol of each primer, 2,5 mcl 10 x buffer (700 mmol/l TRIS-HCL, pH 8,8 at +25oC, 170 mmol sulfate ammonium, 1,7 mg/ml BCA, 0,3 mmol/l Mg2Cl), on 200 mcmol/l desoxinucleoside triphosphates, and also on 1,5 U of Taq polymerase ("Bion", Moscow). PCR was carried out in volume 25 mcl in thermocycler PTC-100 MJ Research, Inc. (USA).

We used also the method proposed by Zietkiewicz E. et al. [15] for PCR-amplification of DNA fragments, flanked by microsatellite repeats (ISSR-PCR), using dinucleotide repeats - $(CA)_{10}G$, (CG)9G and three nucleotide repeats - $GT(CAC)_7$, $(CAC)_7T$, $(AGC)_6C$, $(AGC)_6G$ - as primers

The statistical analysis (accounts of allelic and genotype frequencies, genetic distances based on M.Nei's method, estimation of gene balance according to Hardy-Weinberg's law, cluster analysis) was carried out using the standard computer program "BIOSYS-I". The statistical reliability between frequencies of allelic variants and phenotypes on various loci was calculated uisng Fisher's criterion.

RESULTS AND DISCUSSION

1) Constitutive (inherited) mutations

Our results indicate the absence of constitutive mutations in the Chernobyl NPP alienation zone in *Rodentia* species and increased resistance to radiation between 1994 and 2001, along with a higher frequency of cells with cytogenetic anomalies in bone marrow cells. The constitutive mutations were not detected under exposure of mice lines (C57BL/6, BALB/c, CC57W/Mv) to increased (approximately 100 times) level of ionizing radiation in special vivarium [4], in species of red and common voles, and in oeconomus voles, surprisingly, including those, trapped in the Red Forest.

In cattle, in one animal (from 160 investigated) a mutation in the transferrin gene was revealed in the second animal generation, which was born in conditions of increased contamination by radionuclides (200 Ci/km2).

Carriers of the Robertsonian translocation were not detected in mice and cattle in the Chernobyl zone, in spite of the high presence of such mutation even in "pure" zones in the genomes of species with acrocentric autosomes.

2) Cytogenetic anomalies in somatic cells

Laboratory lines of mice

In laboratory experiments on mice lines (in special vivarium near Chernobyl's reactor), we observed an increase of cytogenetic anomalies in the bone marrow cells subjected to ionizing radiation (near 0,6 Sv). However, only those types of cytogenetic anomalies, which were spontaneously highly variable in an age- or season-dependent manner in the same mice lines not subjected to radiation, were increased. For example, from 8 investigated cytogenetic characters only the frequency of binucleated leukocytes (BL) and leukocytes with micronuclei (LM) varied in relation to the season in which the analysis took place (winter, summer and autumn) and the age of BALB/c mice kept under control conditions, and only BL and LM were increased in BALB/c exposed experimental population. Under control conditions, only aneuploidy (A1 and A2 types) was varied in relation to the season in which the analysis took place and the age of the C57BL/6j mice, and only aneuploidy increased in the exposed population. The increase of LM and metaphase plates with chromosome aberration (CHA) in old mice and in winter in comparison with summer was revealed in CC57W/Mv mice, and CHA and LM were increased in CC57W/Mv mice in special Chernobyl's vivarium. Moreover, in the group of "old" linear mice CC57W/Mv (aged 16-18 months), some cytogenetic anomalies (LM) were less frequent (5.0±0.8‰) than in the mice of the same age in the control group (9.0±1.2‰). This corroborates the findings of an increased rate of cell division (MI, updating of cell populations in bone morrow and elimination of defect cells) in Chernobyl's animal populations (7.0±1.8‰) in comparison with the control group (4.0±0.7‰).

Therefore, our results indicate that ionizing radiation does not induce new anomalies in laboratory mice, but strengthens the process of inherently unstable line-specific cytogenetic characteristics in the mice breeds investigated.

Species of voles

In other experiments, three species of voles (*Microtus arvalis, Microtus oeconomus, Clethrionomys glareolus*) were investigated. Among them, the evolutionary youngest species of common vole (*Microtus arvalis*), characterized by comparative high karyotype instability in the area, was the most sensitive to ionizing radiation [7].

This interspecies comparison thus confirmed that an increase in ionizing radiation does not induce new genetic damage, but destabilizes the preexisting genomic "hot spots" that are either species-specific (and more characteristic to evolutionarily young species) or genotype-specific (for example, different laboratory breeds of mice).

We have discovered a selection of radiation-resistant animals in environments with a high level of radionuclide contamination. Among red and common voles trapped in Chernobyl's contaminated zone in places with high (Red Forest, 1000 Ci/km2) and medium (Janov, near 200 Ci/km2) levels of radiation, in 1994-1996, or 16-20 generations after the explosion, increased frequency of cytogenetic anomalies in bone marrow cells was revealed. In bone marrow cells of *Microtus arvalis,* trapped in contaminated zones in 1996, the frequencies of aneuploid metaphases (A2, 2n±1) and LM were 17.9±4.4% and 6.8±0.5‰ in comparison with A2=8.6±2.8% and LM=3.0±0.4‰ in control group (trapped in “pure” zones). In voles of *Clethrionomys glareolus* in these zones in 1996, the frequency of metaphases with chromosome aberration was 7.3±3.4%, in comparison with 1.2±0.7% in animals from “pure” zones. In 1999-2001, after 26-30 generations, nothing to distinguish these groups from the control groups in terms of the frequency of cytogenetic anomalies in bone marrow cells was revealed in animals trapped in Red Forest. So, the frequencies of A2 and LM in *Microtus arvalis* were 3.1±0.8% and 3.1±0.5‰; CHA in *Clethrionomys glareolus* – 0.9±0.3%.

The greatest level of radiation-resistance was foun in the Red Forest (1000 Ci/км2). The slower speed of such selection was observed under middle level of radionuclide contamination. In 1999, in locations with a radioactive contamination level of 200 Ci/км2 (Janov), higher individual variability and increased frequency of cytogenetic anomalies in comparison with the control group from the “pure” zone (lower than 5 Ci/km2) and population from a Red Forest in 1999-2001 year were revealed. For example, the frequency of metaphases with CHA in bone marrow cells of *Clethrionomys glareolus,* trapped in 1999 y in Janov, was CHA=8.1±4.0%.

Cattle

In the parent cattle generation in the experimental economy “Novoshepelichi”, the frequency of leukocytes with the micronuclei (LM) in blood smears was significantly higher ($P < 0,001$) than in the first, in the second and in the third generations of animals that were born in the zone of increased radionuclide contamination. This characteristic in the cattle of the third generation was significantly lower ($P < 0.001$) than in the second generation. 6 animals from parent generation (LM=4.5±0.3‰), 15 cattle from F1 generation, born in an experimental farm (LM=1.1±0.8‰), 12 animals form F2 generation (3.0±0.3‰) and 3 animals from F3 generation (1.5±0.4‰) were included in the analysis. The frequency of binuclear leukocytes (BL) in smears of peripheral blood was also significantly higher in the parent generation than in the first and in the second generations of animals.

That is, on the frequencies of cytogenetic anomalies in smears of peripheral blood in generations of cattle, which were born in conditions of increased ionizing radiation, the clear increase of radio resistance of animals was observed also.

We also investigated also the fertility of cows (according to the average number of calves produced oer cow per year) in parent and F1 generations. The fertility of cows in the first generations after the Chernobyl explosion on the experimental farm located in the contaminated zone was reduced by approximately five times in comparison with the parent generation (on average, from 0.93 up to 0.12 calves per cow per year). So, 16 cows of the parent population produced 96 calves (0.93±0.03 calf per cow per year); 20 of them (21%) died before reaching an age of three months. However, there were no sterile cows in the parent population. In F1, between 36 cows 21 ones (58%) were sterile; only 15 cows of F1 gave birth to F2 generation calves: 50 calves (27♀ and 23♂) in 8 years. 13 of them died before reaching an age of three months (26%).

If we calculate for all 36 cows of F1, the cow's fertility decreased from 0,93 in the parent cow generation to 0,12 calves per cow per year in F1 cows. If we calculate the number calves produced by the 15 fertile cows of the F1 generation, the decrease would be less, 0,73±0,06 calves per cow per year, but some fertility decrease (t_S=2,86; P<0,01) was revealed.

Four F2 cows in summary produced 10 calves (F3) for 4 – 2 years, in average, 0,94±0,06 calf per year per cow. This means that we can assume thatthe fertility of F2 cows could increase in comparison with F1 cows (t_S=2,67; P<0,02).

The data obtained can result from selection pressure in F1 generation, related with new conditions of cattle reproduction (the increase level of ionizing irradiation), which lead to elimination of some genotypes.

3) Population-genetic changes in cattle's generations

Analysis of the allele inheritance in different genes and DNA fragments, flanked by microsatellite loci (ISSR-PCR) in cattle's generations that were born under increased radionuclide contamination was carried out. Data on allele frequencies observed in the control group and exposed groups of cattle are presented in Table 1. The homozygosity of HB locus and low level of polymorphism in PN locus are the specific traits of the Holstein breed in different countries. This was also true for the exposed experimental herd and hence the data of HB and PN loci was not included in the following comparative analysis of the genetic structures of cattle groups. It is interesting that the mean heterozygosity in the exposed group (by one sire, bull *Uran)* was not lower than that in the control group sired by a number of bulls (Tab.1). The investigations covered allelic variants of the following polymorphous loci traced in the exposed group: *TF, CP, GC, AM-I, PTF-2,* and *CSN3.* At the *TF locus* three allelic variants -A, D1 and D2 - were found. The rare allele Tf E and specific for ancestor breed Grey Ukraininan allele Tf F were not revealed in the experimental herd. Two allelic variants were revealed at the *CP* locus - A and B. Polymorphism at the GC locus was due to two alleles: A and B. *AM-I* was represented by variants B and C. *PTF-2* locus showed fast and slow allelic variants - F and S, respectively. *CSN3* had two variants - A and B. For the first time an animal was revealed to have a constitutive mutation, the carrier of a unique variant at the *TF* locus, having electrophoretical mobility different from the other five *TF* variants, including the parental and rare ones, revealed in a Holstein from the “pure” zone (Tf E) and in a Grey Ukrainian (Tf F). Mutated allele (mut) had a faster electrophoretic mobility than allele E, but slower than allele D2. Its genetic nature was confirmed by data on its inheritance (Tab.2). A similar allelic variant was not found neither in literature nor in the control animals (bred in a relatively clean environment), thus confirming the uniqueness of the mutation. Based on the available data, it is not possible to establish precisely whether the mutation came from the dame or the sire. One may only assume that the mutation had appeared in cow No.49 (FI. the daughter of cow Beta) and next was inherited by No. 113 (F2) and her daughter No. 155 (F3), but did not appear in any other progeny of Beta and Uran (Tab. 2).

The distribution of allelic variants at the loci studied in parents and their progeny of different generations is presented in Tables 2 and 3. An analysis of the transfer of allelic variants from heterozygous parents to their progeny was carried out. Theoretically, both alleles have an equal chance of being transferred from the parents to the offspring.

In the parent generation (FP), the genetic structure was described as the sum of 13 different mother genotypes and 13 identical genotypes of the bull Uran, which was the father in all cases (Tab. 1). Excess heterozygosity was observed in some loci. However, in the parent group excess heterozygosity in the TF locus was revealed in Uran's Tf AD1 genotype (Chi-square=15.384; p=0,002), but in F1 – on Tf AD2 genotype (Chi-square=8.975; p=0,030). In four out of the six loci investigated significant deviations were found from the expected parent → offspring transfer values in two generations, However the preference for Tf D2 allele transfer from mothers to offspring was only obvious for AMI and *CP* loci (t_S=2,0, P<0.05 and t_S=2,8, P<0.01, respectively) and only in FI derived from cows *Alfa* and *Gamma* (Tab. 2,4). In general, in the case of the *TF* locus in FI, allele A was more often transferred to the offspring from the sire (AD1 genotype) while allele D2 was transferred from the dames. In F2 the allelic transfer from *Uran* was closer to that expected (Tab. 2, 3, 4). In case of CSN3 locus an increase of B allele frequency in F1 in comparison with FP was also observed, but the differences were smaller (t_S=1,77, P<0.10). It is very important to note that the comparative high frequencies of allele D2 in TF, B in AMI, B in CSN3 loci are the specific traits of gene pools of ancestor Grey Ukrainian breed (Tab.1). So, the data obtained demonstrated some shift of gene pools in F1 offspring, born in conditions of ionizing irradiation, from parent generation to ones, typical for more primitive cattle breed, Grey Ukrainian.

An analysis of the changes in allele frequencies occurring over the two generations demonstrated a clear disturbance in their distribution in F1, as compared to that characteristic for the parent (FP) generation. In generation F2, the frequencies observed were close to those expected. The reason for the inheritance disequilibrium observed in F1 may be related to a change in selection, or the decrease in fertility of F1 cows. Effects of abiotic stress may lead to selection in different stages of offspring forming from parental generation, which was subjected to an increased level of ionizing irradiation in the alienation zone around Chernobyl. Thus, the change of environment could directly affect the preferable reproduction of some genotype combination of the parent animal gametes, and also change the pattern of genetic structure in F1. The effect of the environment on preferable genotype reproduction is most clearly demonstrated in the disruption of the expected allelic transfer.

Despite close inbreeding in the exposed herd (one bull serving several generations), the heterozygosity at the loci analyzed in generation F2 was close to the mean heterozygosity in Fl. In the case of the *PTF-2* and *CSN3* loci the mean heterozygosity in F2 was even higher than that in FP. Therefore, over the two progeny generations examined the principal effect of inbreeding (increase in the number of homozygotes) was not observed. This phenomenon may possibly be explained by the involvement of mechanisms preserving a stable heterozygosity level, expressed as a disrupted allelic transfer from the parents to the offspring.

Thus, under changed environmental conditions the disrupted transfer of certain alleles from the parents to the offspring leads to significant differences in allele frequencies from those expected in F1 and to a stabilization of these differences in F2.

The comparison of genetic structure of the same molecular-genetic markers between Holstein and Grey Ukrainian cattle breeds from "pure" zones, parent generation of experimental herd and their children (born under the influences of ionizing irradiation) demonstrated the shift of the offspring's genetic structure in some loci from typical ones for parents (belonging to Holstein breed) to those more typical of a more primitive, ancestor breed, Grey Ukrainian cattle.

In a previous paper the increase of frequencies of cytogenetic anomalies, which did not lead to cell death (such as inversions, inserts, reciprocal translocations) in the blood cells of children (14 – 16 years age) who received the dose of ionizing radiation (0,3-0,4 Sv) in utero was revealed [10]. Obviously, it is related to the clonal cell expansion after exposure to ionizing irradiation. Our data about the cattle fertility decrease in F1 allows us to assume that children exposed to low doses of ionizing radiation in utero could face reproductive problems in the future.

The analysis of polymorphism and heritability of some molecular genetic markers of anonymous sequences in DNA (ISSR-PCR) was carried out using the method described by Ziętkiewicz *et al.* [15]. The fol1owing sequences were used as primers: dinucleotide repeats – (CA) 10G, (CG) 9G and trinucleotide repeats – GT (CAC) 7, (CAC) 7T, (AGC) 6C and (AGC) 6G.

The amplification spectra were analyzed for two families in the exposed group -from cows *Alfa* and *Beta* mated, as always, with *Uran.* In the case of dinucleotide repeat (CA) 10G, in the amplification spectra of all investigated animals, eight distinct DNA fragments were observed -from 750 to 1900 bp. These fragments were seen in all animals, both in the parents and in the offspring, and neither individual variation nor the occurrence of new variants was observed in the progeny. The same pattern was observed when (CG) 9G primer was used -the amplicon spectra had six precisely identified fragments, each of 650-1500 bp in length. Neither individual variation nor differences of amplicon spectra from parental variants were found when using the trinucleotide repeat (CAC) 7T as a primer, and ten fragments were recorded in its amplicon spectrum -400-1600 bp long. Thus, considering each fragment of amplified DNA as a separate locus, it was possible to conclude that in all 24 DNA *loci* and in all animals analyzed no individual variation appeared and no new mutation variants occurred in the progeny born under increased ionizing radiation.

The use of three other primers, consisting of trinucleotide microsatellite repeats –GT (CAC) 7, (AGC) 6C and (AGC) 6G – resulted in the formation of polymorphous spectra of amplification products. Using the GT (CAC) 7 primer produced ten fragments 650-2000 bp long, in the spectra of amplification products. The 2000 bp fragment was absent in cow *Alfa* and in her FI offspring (Nos. 120 and 105). The progeny of cow *Beta* (No.113 and 155, respectively) were also lacking this fragment. Fragments 1800 and 1700 bp long were absent in F2 and F3 (No.113 and 155, respectively) of cows *Alfa* and *Beta.* The 1500 bp fragment was absent in cows Nos. 49, 113, 144 and 155 *(Beta's* progeny), while fragment 1400 bp -in No.105 *(Alfa's* progeny). Thus, among ten fragments (loci) of GT (CAC) 7 primer, five appeared polymorphous as they were present or absent from the amplicon spectra. Based on the data obtained, one may conclude that *Uran* was heterozygous with respect to the 2000 bp fragment, *Alfa* was homozygous as regards the absence of the fragment, while *Beta* homozygous as regards its presence. The distribution of this fragment in the progeny was close to that expected.

The use of the (AGC) 6G primer resulted in a wide spectrum of amplification products, consisting in total of 27 fragments (600-

2600 bp) from different animals. Again no amplification products, which would point to the occurrence of mutations, were found. Altogether, with the existing polymorphous spectra in different animals the use of these two trinucleotide primers resulted in 49 amplification products.

The most complex spectrum of amplification products was observed with (AGC) 6C primer. Two amplification products were revealed in *Alfa's* daughter No.105 that were absent in both parents. A poor reproducibility of the amplification spectra in this case was also marked. One may assume that such complexity of the amplification spectra and poor reproducibility were caused by the primer itself, in particular by the presence on its 3' end of the nucleotide combination GCC, which promotes formation of a "mini-pin". It could result in a poor annealing accuracy. For this reason it proved necessary to make a special family investigation establishing whether the new bands in animal No.105 were a result of mutation events or artefacts of an inaccurate reannealing of the primers.

In total, using two dinucleotide and three trinucleotide primers, 73 amplification products were found in the progeny of cows *Alfa* and *Beta* mated to the bull *Uran.* No changes were observed which could be interpreted as a new mutation. Two unique bands found in one offspring of *Alfa* with the (AGC) 6C primer could be the effect of the reduced accuracy of annealing, and thus requires further research. Interesting is the high heterozygosity of *Uran,* shown by the analysis of polymorphous spectra of anonymous DNA fragments and by the polymorphism of structural genes. It is possible that the prolonged and successful fertility of the bull under both increased ionizing radiation and inbreeding was caused by his high heterozygosity.

It is important to note the observed shift of a genetic structure in cattle generations in the direction of the less specialized forms matched the data appearing in the literature concerning a decrease in the number of behavioural specialized functions in voles (more primitive relatives of burrows) in conditions of increased radio nuclide contamination [8], and also the data collected by Danish investigators regarding the disturbance of functions of associative thinking in Danish children after the first air explosions of nuclear bombs and after the Chernobyl accident [11].

All these appearances corresponded to a rule of I.I. Shmalgauzen [12] that any change of the environment may lead to preferable reproduction of the more primitive forms within a species. Thus, the main problem after the Chernobyl catastrophe, as well as other ecological changes, lies not in the occurrence of the new mutant organisms, but in the long-term changes to the genetic structure of populations and, as a result, to the appearance of the new interspecies interactions between the less specialized (marginal) representatives of each species in species communities.

Conclusions

1. The Chernobyl catastrophe meant that the populations of different organisms were subjected to doses of ionizing radiation, which were new to them.
2. The increased level of ionizing radiation did not induce qualitatively new damages of the genetic material, but increased chromosomal instability in those species or at those cytogenetic anomalies that have been determined to be *apriori* more prone to appearance of cytogenetic defects than others. This provides a basis for the hypothesis that evolutionary younger species are more sensitive to the change of ecological conditions at the chromosome rearrangement level in comparison with older ones.
3. Effects of detrimental environmental changes have deferred realization in generations. A decreased reproduction rate was observed in cows which were born in first generation in of the alienation zone around Chernobyl's NPP, possibly in connection with the particularities of mammalian oogenesis (maturation of ooblasts to meiotic stage before birth). Strong selection for radionuclide resistance in voles emerged through approximately 26 generations after the beginning of the ionizing radiation exposure. This was dose-dependent.
4. No increase was noted in the quantity of constitutive mutations in investigated genes, ISSR-PCR markers or chromosomes in analyzed species (cattle and *Rodentia* species).
5. In various generations of cattle, a disturbance of the equiprobable transmission of alleles of a number of molecular genetic markers, an increase in heterozygosity and radio resistance were observed.

6. In family analysis the changes of genetic structure in cattle generations of experimental farm "Novoshepelichi", the shift of gene pool from typical for specialized parent dairy breed Holstein to that characteristic for the less specialized breeds was revealed (decrease in level of specialization)

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ASSESSMENT OF CHERNOBYL MEDICAL CONSEQUENCES

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Resume. Prognoses of medical effects of the Chernobyl accident for 1986-2056 in Belarus and other countries of the world are discussed in the present report. It is shown that as a result of irradiation approximately 270,000 malignant neoplasms has to be expected in countries affected by the Chernobyl accident in this period of time including approximately 140,000 thyroid cancers, approximately 120,000 other solid cancers and approximately 10,000 leukemia. The number of fatal malignant neoplasms in all these countries in the period 1986-2056 can be approximately 93,000 cases. This figure includes approximately 13,700 fatal thyroid cancers, 71,000 other solid cancers and 8,000 leukemia. According to estimated results radiation risks of malignant neoplasms in Belarus and other countries of the world caused by the Chernobyl accident are by some factors higher than radiation risks established for survived inhabitants of Hiroshima and Nagasaki. This means that radiation risks found for atomic bomb survivors are not relevant for normal populations affected by long-term irradiation at low doses and low dose rates.

Introduction.

The Chernobyl NPP accident has become the most severe technical accident in the history of humankind. It took place on April 26, 1986, during an electromechanical experiment. The aim of the experiment was a determination of the amount of electrical energy produced by the electrical generator in the process of an idle turbine rundown. The program of the experiment did not take into account a number of important physical and thermal-hydraulic peculiarities of the reactor and the whole reactor unit. This caused some wrong operations of the personnel and as a result the total destruction of the active core of the forth unit of the Chernobyl NPP as well as considerable damage of the third unit of the plant. The witnesses of the Chernobyl NPP accident claim that destruction of the Chernobyl reactor occurred as a result of at least two consecutive explosions [1]. Specialists believe that the first explosion was caused by an explosion-like formation of vapour in the active core of reactor. This caused complete displacement of water from reactor and nuclear explosion in the drained active core [2]. The power of this second explosion is estimated to be approximately 0,28 kilotons TNT [3], which is by 50 times less than the power of the atomic bomb dropped on Hiroshima.

The destruction of the Chernobyl reactor caused the release of a huge amount of radioactive substances into the environment. They spread far beyond the borders of the nuclear plant [4]. These substances were deposited in many countries of the Northern Hemisphere causing considerable radioactive ecological problems. However, Belarus suffered most severely from the Chernobyl NPP accident than any other country of the world. Comparison of densities of the isotope ^{137}Cs deposition in different countries of the world allows to draw such conclusion. This isotope was chosen after the Chernobyl NPP accident as a quantitative indicator of radioactive contamination. According to the data [4], the maximal contamination with ^{137}Cs beyond the borders of the former USSR has not exceeded 185 kBq/m^2 (5 Ci/km^2). In Belarus the maximal density of ^{137}Cs fallout reached 59,200 kBq/m^2 (1600 Ci/km^2) [5] that is approximately 320 times higher than maximal contamination beyond the former USSR.

Tests [6] show that up to 23% of the total amount of the isotope ^{137}Cs released to the environment deposited on the territory of Belarus. This caused severe economic damage to Belarus, significant social and psychological tensions in affected regions of the country and an increase of the incidence in different diseases. For example, manifestation of additional thyroid cancers [7-17], cancers of stomach [17,18], lung [17,19], female breast cancers [17,20], leukemias [17, 21-24], nonmelanoma skin cancers [17,25] and other malignant neoplasms [17,26-27] have been registered in Belarus after the accident at the Chernobyl NPP.

Results of assessments [17-27] are in qualitative agreement with findings of authors [28] that could establish manifestation of additional thyroid, colon, and urinary bladder cancers in the Belarusian liquidators as well as of all malignant neoplasms combined together. An evident manifestation of the female breast cancers in women of the Gomel region was reported recently [29].

An increase in the incidence of thyroid cancers was also established in children of Ukraine and Russia affected by the Chernobyl accident [30,31]. In case of Russian liquidators radiation-induced thyroid cancers and leukemias as well as cancers of digestive and other systems were also found [32-34].

On top of malignant neoplasms a significant increase in the incidence in general somatic disease was found in affected populations of Belarus, Ukraine and Russia as well as in liquidators of these countries [35-42]. Data of the Belarusian, Ukrainian and Russian specialists [35-4] about link between the incidence in general somatic diseases coincide qualitatively with findings observed by survived inhabitants of Hiroshima and Nagasaki for which higher incidence in cerebrovascular and other somatic diseases in comparison with nonirradiated Japanese population was observed [43-46]. In case of atomic bomb survivors radiation-induced general somatic diseases gave the similar contribution to the additional mortality as radiation-induced cancers [45,46].

All these data indicate an incorrectness of conclusions made by some international organizations that only some increase of the incidence in thyroid cancers manifested in affected children of Belarus, Ukraine and Russia [47,48]. The radiological situation in contaminated regions of these countries as well as permanent worsening of health status of the Belarusian, Ukrainian and Russian emergency workers demonstrates very serious medical consequences of the Chernobyl accident. This requires scientific prognosis of radiological impact of the Chernobyl accident for population of affected countries for some long period of time. Such prognosis is important for elaborating of adequate protection measures to minimize health consequences of a long-term irradiation of populations affected at the Chernobyl accident. The present report forecasts radiation medical effects and is carried out on the basis of data on the incidence in malignant neoplasms established in Belarus before and after the Chernobyl accident. It was performed for the period 1986-2056.

Materials and Methods

Data of the Belarusian Cancer Registry of the Ministry of Health Care of the Republic of Belarus were used for forecasting of the Chernobyl medical effects [49-58] and statistical data on population numbers of the Belarusian regions as well as the entire country [59-62]. Monitoring of malignant neoplasms in Belarus began already in 1953 [58]. It is obligatory. All information about oncological patients goes to the Belarusian Cancer Registry from 11 oncological dispensaries and the N.N.Alexandrov Institute of Radiation Medicine and Oncological Disease of the Belarusian Ministry of Health Care. Since 1978 data on oncological diseases are collected in an electronic database. One can find the following information there about incidence and mortality ofoncological diseases: name and address of the patient, age, date, place where a case was diagnosed, ICD number of diagnosis, and diagnostic method (e.g. biopsy, autopsy, myelogram, immunohistochemical method used, etc.). These data are available for each oblast (region) of Belarus, the city Minsk (capital of Belarus) and for the entire country. There are 6 oblasts in Belarus: Brest, Gomel, Grodno, Minsk, Mogilev and Vitebsk.

Comparison of data of the Belarusian Cancer Registry with data established in other countries [63] demonstrates the high level of medical accounting of the incidence and mortality from oncological diseases in Belarus similar to the level reached in developed countries.

The forecast of medical effects of the Chernobyl accident described in the present report is based on the hypothesis of the equivalency of relative radiation risks of some cancers in different ethnic groups. The value of relative radiation risk can be determined with the formula:

$$RRR_i = \frac{R_i}{R_\Sigma}. \quad (1)$$

Here RRR_i - relative radiation risk of cancer in the i-th site, R_i - radiation

risk of this cancer, R_Σ -total radiation risk of some group of cancers, for example of the group of all solid cancers combined together.

The idea of equivalency of relative radiation risk of some cancer in different ethnic group can be described with the proportion:

$$\frac{R_i^A}{R_\Sigma^A} = \frac{R_i^B}{R_\Sigma^B}. \qquad (2)$$

Here upper indexes *A* and *B* refer to ethnic groups *A* and *B*.

The similar proportion can be written also for cancer in ***j'th*** site:

$$\frac{R_j^A}{R_\Sigma^A} = \frac{R_j^B}{R_\Sigma^B}. \qquad (3)$$

Division of the proportion (2) by proportion (3) gives:

$$\frac{R_i^A}{R_j^B} = \frac{R_i^B}{R_j^B}. \qquad (4)$$

According to the last proportion ratios of radiation risks of cancers in i-th and ***jth*** sites have to be the same in different ethnic groups.

The accuracy of this assumption was demonstrated in qualitative assessments of the incidence and mortality in malignant neoplasms in Belarus before and after the accident at the Chernobyl NPP [27].

It is evident that accuracy of the proportion (4) indicates automatically accuracy of proportions (2) and (3).

Assessments described in the present report were made on the basis of excessive absolute risks, EAR, because it characterizes impact of ionizing radiation more directly than excessive relative risk. The last value depends strongly on the background incidence in malignant neoplasms and can be different for different ethnic groups.

Time-averaged values of the excessive absolute risk were used in assessments. They were assessed on the basis of expression:

$$EAR^i = \frac{O^i_{m,k} - E^i_{m,k}}{\sum_m^k H_m^{i,Coll}} \quad (5)$$

.

Here $O^i_{m,k}$ and $E^i_{m,k}$ - numbers of observed and expected cancers in ***i-th*** site in the period ***m-k*** respectively, $H_m^{i,Coll}$ - collective equivalent dose of the ***i-th*** organ in a ***m*** year.

Additional incidences in malignant neoplasms and additional mortality from them were assessed in the present report for the period 1986-2056 for Belarus and other countries affected by the Chernobyl accident.

The following procedure of assessment was used for Belarus. Firstly on the basis of empiric data of the Belarusian Cancer Registry the spontaneous incidence in thyroid cancer in the period 1986-2004 was estimated. With help of the established data additional thyroid cancers manifested in the Belarusian population in 1986-2004 as a difference between observed and expected cases were estimated. Using these data and expression (5) the excessive absolute risk, EAR^*, of the incidence in thyroid cancers in Belarus was estimated. On the basis of this value and the collective equivalent dose of the thyroid gland irradiation assessed for 2005-2056 additional thyroid cancers in Belarus for this period 2005-2056 were then calculated. The following formula was used for such calculations:

$$N^{*}_{Th} = EAR^{*} \cdot \sum_{T=2005}^{T=2056} H_T^{Coll} \qquad (6)$$

.

Here H_T^{Coll} -collective equivalent doses of the thyroid gland irradiation of the Belarusian population in the year ***T*** as a result of the Chernobyl accident.

Sum of additional thyroid cancers assessed for periods 1984-2004 and 2005-2056 gives then total number of additional thyroid cancers that have to be expected in Belarus in 1986-2056. Using this value as well as our hypothesis about equivalency relative radiation risks express with the proportion (2) additional incidence of cancers other than thyroid cancers was estimated for Belarus for the period 1986-2056. On the basis of these data and empiric ratios between incidence and mortality rates amounts of additional fatal cancers in Belarus in the period 1986-2056 was assessed.

The number of additional fatal cases from general somatic diseases was also assessed in the present report for Belarus for the period 1986-2056. In this case it was assumed simply that this number is equal to number of fatal malignant neoplasms that can be manifested in Belarus in the period 1986-2056.

Similar assessments were carried out also for other countries of the world affected by the Chernobyl accident. However, the accuracy of estimations performed for other countries is much lesser than for Belarus. These estimations were carried out on the basis of the proportion:

$$\frac{N_i^{Oth}}{N_i^{Bel}} = \frac{Q_0^{Oth}}{Q_0^{Bel}}, \qquad (7)$$

where N_i^{Oth} and N_i^{Bel} are number of some additional effects in the period 1986-2056, for example, number of additional solid cancers in other countries and in Belarus; Q_0^{Oth} and Q_0^{Bel} amounts of the isotope ^{137}Cs deposited in other countries and in Belarus as a result of the Chernobyl accident.

The last expression is based on direct transferring of radiation risks assessed for Belarus to other countries of the world. This contradicts our hypothesis that only relative radiation risks estimated on the basis of the expression (1) can be transferred from one ethnic group to other. Secondly, using of the expression (7) means that collective doses of irradiation depend only on the amount of deposited radioactive substances. This is an evident underestimation of collective doses in case of Western European countries because it is well known that collective doses depend not only on the amount of deposited radionuclides but also on population density that in countries of the West Europe is significantly higher than in Belarus.

Results

Radiation Doses.

The Chernobyl accident additional external and internal irradiation of affected populations. This irradiation is characterized by a significant difference in doses absorbed by different body organs.

Table 1. Thyroid exposure doses in Belarus [64]

Region	Collective Dose, 10^3 person-Gy				Population Dose, Gy/person			
	Age Groups							
	0-6	7-14	15-17	> 17	0-6	7-14	15-17	> 17
Brest	35.0	15.6	3.6	46.5	0.19	0.08	0.06	0.05
Vitebsk	0.5	0.2	0.1	0.9	<0.01	<0.01	<0.01	<0.01
Gomel	96.6	43.0	10.7	151.0	0.50	0.21	0.15	0.12
Grodno	16.4	7.3	1.7	24.0	0.12	0.05	0.04	0.03
Minsk*	23.0	10.1	2.5	32.7	0.06	0.03	0.02	0.02
Mogilev	9.9	4.3	1.1	16.3	0.07	0.03	0.02	0.02
Belarus	181.4	80.5	19.7	271.4	0.15	0.07	0.05	0.04

* Doses are calculated for the city Minsk and Minsk region.

Such conclusion can be drawn by comparison doses of the thyroid gland and the whole body irradiation in Belarus.

Doses of thyroid gland irradiation for populations of Belarus regions are given in Table 1.

The total collective dose of the thyroid irradiation of Belarusian population as a result of the Chernobyl NPP accident amounts to 553 thousand person-grey [56]. This is approximately ten times higher than the collective dose of the whole body irradiation of the Belarusian population [65].

Table 2 shows doses of the whole body irradiation of rural inhabitants of areas affected at the Chernobyl accident. It is known that doses of the whole body irradiation of urban inhabitants are lower by some factors than doses of rural inhabitants who were exposed to the same level of radioactive contamination. Hence data shown in Table 2 represent highest population doses of the whole body irradiation of people that live in areas of Belarus contaminated by ^{137}Cs to the level ≤ 1,480 kBq/m^2.

Table 2. Annual population exposure doses of the whole body in the population of the rural areas in Belarus as a result of the Chernobyl NPP accident (mSv/year) [66]

Year	Level of radioactive pollution, kBq/m^2 (*Cu/km^2*)					
	3.7 (*0.1*)	37 (*1*)	37-185 (*1-5*)	185-555 (*5-15*)	555-1,480 (*15-40*)	1,480 (*40*)
1986	0.0972	0.9719	2.896	8.339	23.62	51.22
1987	0.0468	0.4681	1.395	4.016	11.37	24.67
1988	0.0296	0.2957	0.8812	2.537	7.186	15.58
1989	0.0181	0.1806	0.5382	1.549	4.388	9.517
1990	0.0104	0.1042	0.3104	0.8938	2.531	5.490
1991	0.0089	0.0885	0.2639	0.7597	2.152	4.666
1992	0.0079	0.0772	0.2302	0.6628	1.877	4.071
1993	0.0069	0.0686	0.2043	0.5883	1.666	3.614
1994	0.0062	0.0621	0.1849	0.5324	1.508	3.270
1995	0.0057	0.0570	0.1698	0.4890	1.385	-
1996	0.0053	0.0531	0.1583	0.4556	1.290	-
1997	0.0049	0.0495	0.1475	0.4247	1.203	-
1998	0.0047	0.0469	0.1397	0.4021	1.139	-
1999	0.0044	0.0443	0.1319	0.3799	1.076	-
2000	0.0043	0.0425	0.1267	0.3647	1.033	-
2001	0.0041	0.0405	0.1206	0.3472	0.983	-
1986-2001	0.2651	2.651	7.899	22.74	64.41	122.1

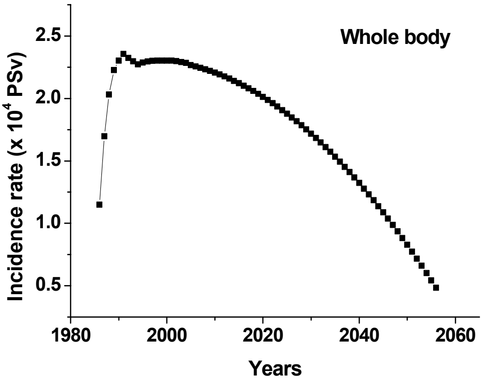
As can be seen from data of Table 2, population doses of the whole body irradiation of rural inhabitants of Belarus are in a range from some fractions of millisievert to hundred of millisievert.

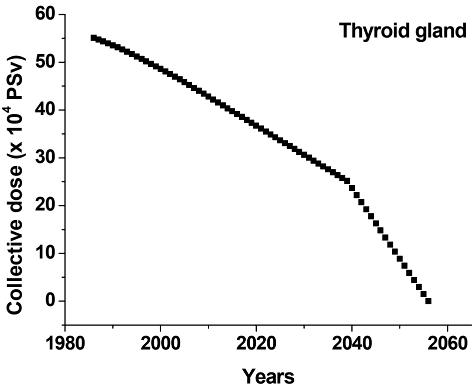
Assessment on the basis of these data shows that doses of the whole body irradiation of rural inhabitants in areas with the contamination level by the isotope ^{137}Cs in the range of 555-1,480 kBq/m^2 (15-40 Ci/km^2) reached approximately 60 mSv in the period 1986-1995. Using more advanced method of estimation Russian specialists assessed for the period 1986-1995 the same population dose of the whole body irradiation for Russian rural inhabitants in areas with the same contamination level by the isotope ^{137}Cs in the range of 555-1,480 kBq/m^2 [67]. This equality proves accuracy of doses given in Table 2. It is known that irradiation doses of the most irradiated fraction of irradiated group of people are approximately 3-5 times higher than the mean arithmetic value. This means that some fraction of the Belarusian population which resided in 1986-1995 in a territory with a contamination level by the isotop ^{137}Cs in the range of 555-1,480 kBq/m^2 (15-40 Ci/km^2) could receive doses of the whole body irradiation in the order of 180-300 mSv.

The maximal individual doses of the whole body irradiation of rural inhabitants in Belarus could reach 1,500 mSv [66]. The thyroid doses in Belarus were even higher. According to estimation [68], they exceeded in some cases 60 Gy.

The exposure of thyroid gland of Belarusian population as a result of the Chernobyl accident ended practically in July 1986 because of a total decay of the isotope ^{131}I, which made the main contribution to thyroid doses. Since that time, continuous decrease of the collective dose of the thyroid gland exposure of the population of Belarus has been taking place. It was caused by the population mortality due to different reasons. The left part of Fig.1 shows the dynamics of the change of the collective equivalent dose of the thyroid gland irradiation in Belarus in 1986-2056.

Fig.1. Collective doses of the thyroid gland and the whole body irradiation of the Belarusian population in 1986-2056 as a result of the Chernobyl accident





The data shown in the left panel of Fig.1 were estimated in the present report on the basis of data presented in Table 1 by considering population mortality of the Belarusian population [60-62]. It is understandable that death of people caused by irradiated thyroid gland after the ending of irradiation causes a reduction of the collective doses of the thyroid gland irradiation.

The following simple method was used to assess a decrease of the collective equivalent dose of the thyroid gland irradiation. Firstly, it was assumed that people in Belarus die only after reaching the age 70 years. Secondly, it was supposed that the decrease of the collective equivalent dose of the thyroid gland irradiation as a result of death of irradiated people began only after practically full decay of the isotope ^{131}I or beginning from 1 August 1986. According to data given in the statistical handbook [60] 97,276 persons died in Belarus in 1986. There are no published data on monthly mortality rate in Belarus. Therefore it was assumed in the present report (the third assumption) that the mortality rate in Belarus is constant during a year. This gives the mean mortality rate equal to 8,106 persons per month for Belarus in 1986. The total number of persons that died in August - December of 1986 is then equal to 40,532 persons. Multiplication of this value with the mean population thyroid dose of adults taken from the last column and last row of Table 1 (0.04Gy) gives the fraction of the collective equivalent dose of the thyroid gland irradiation lost in August-September 1986 as a result of the death of 40,532 persons in this period. It is equal to 1,622 grey-persons. It has to be subtracted from the collective equivalent dose of the thyroid gland irradiation that was delivered to the Belarusian population as a result of the Chernobyl accident.

This procedure was performed in the present report for the period 1986 - 2056. By this assessment real data on numbers of people that died in 1986-2004 were used for the period 1986-2004. For the period 2005 - 2056 it was assumed that annual mortality of the Belarusian population has to be the same as in 2003. It was equal to 143,200 cases [60].

Approximately 7 millions 300 thousand persons older than 17 years lived in Belarus at the time of the Chernobyl accident [59]. The mean population dose of the thyroid gland irradiation of this subpopulation was approximately 0.04 Gy according to data given in Table 1. This dose was used by assessment of the decrease of the collective equivalent dose of the thyroid gland irradiation for the period in which this subpopulation (7 million 300 thousand person) has to die. After death of these subpopulation persons those who were younger than 17 years at the time of the Chernobyl accident will die. They received higher doses of the thyroid gland irradiation than persons that were at the age higher than 17 years at the

Chernobyl accident. This was taken also into account by estimation of the decrease in the collective equivalent dose of the thyroid gland irradiation in the period 1986-2056.

The right part of Fig. 1 shows the dynamics of the collective equivalent dose in the population of Belarus in 1986-2056 estimated also by taking into account the processes of natural mortality and birth in Belarus. In this case long-term effects of chronic irradiation of the whole body that decreases with time were also taken into account. The assessment method of the collective equivalent dose dynamic of the whole body irradiation is demonstrated here by estimation of the whole body irradiation in 2001. Let us consider the subpopulation that lives in areas contaminated by the isotope ^{137}Cs to the level 37 kBq/m^2. Let us assume that ***N*** persons died in these areas in 2001. According to data presented in Table 2, the population dose of the whole body irradiation accumulated in 1986-2001 by rural inhabitants of areas contaminated with ^{137}Cs to the level 37 kBq/m^2 is approximately 2.6105 mSv. Death of ***N*** persons that lived since the Chernobyl accident in these areas the fraction of the collective equivalent dose of the whole body irradiation equal to 2.6105****N*** P-mSv is lost. The population dose of the whole body irradiation accumulated by rural inhabitants of areas contaminated with ^{137}Cs to the level 37 kBq/m^2 was in 2001 approximately 0.0405 mSv per person (Table 2). Multiplication of this value with total number of rural inhabitants lived in 2001 in areas contaminated with ^{137}Cs to the level 37 kBq/m^2 gives the value of the collective equivalent dose delivered to this subpopulation in 2001. The difference between lost and delivered collective doses determines “real” collective dose of the whole body irradiation accumulated by subpopulation considered in this example.

The above-described procedure was used in the present report by assessment of the change with time of collective equivalent dose for the total population of Belarus. By this assessment collective equivalent doses of the whole body irradiation accumulated annually by the mixed Belarusian population (urban and rural) populations determined in the report [65] were used.

According to estimated data loss of accumulated doses of the whole body irradiation as a result of the effects of death prevails delivering of irradiation doses since 2000. Starting from this time a slight decrease of the collective equivalent dose of the whole body of the Belarusian population begins. The maximal value of the collective equivalent dose of the whole body irradiation in accordance with data of present report was reached in 1999. It was approximately $2.3 \cdot 10^4$ PSv. This value corresponds to the mean arithmetic population dose estimated for the whole country equal to approximately 2.3 mSv per person. Such dose of the whole body irradiation is delivered in Belarus due to the background irradiation during approximately 2 years (excluding contribution of radon).

Data represented in the Fig. 1 are estimated for the period of time 70 years after the Chernobyl NPP accident. This period is chosen because the average life expectance in Belarus is approximately 70 years. This means that at the end of this period, there will be almost nobody left in Belarus who could have received a radiation exposure of the thyroid at the moment of the Chernobyl NPP accident.

Incidence in malignant neoplasms as a Result of the Chernobyl NPP Accident

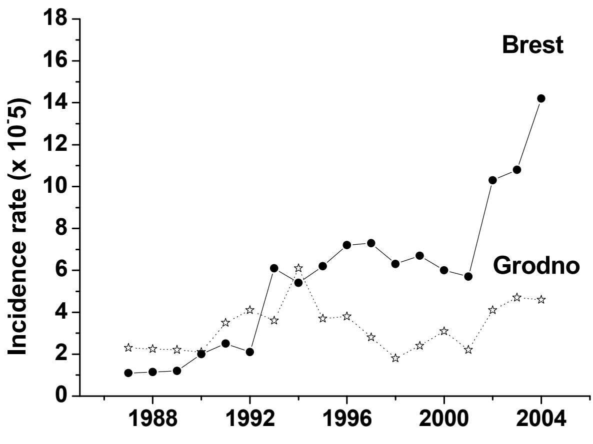
Estimations on the basis of procedures described in the previous section gave collective equivalent doses of the thyroid gland and the whole body irradiation averaged for the period 1986-2056 are approximately $34.5 \cdot 10^4$ and $1.77 \cdot 10^4$ man-sievert. As can be estimated from these data the collective dose of the thyroid gland irradiation of the Belarusian population exceeds by a factor 19.5 the collective equivalent dose of the whole body irradiation. One needs to notice here that this difference has to be much higher in case of children than in case of adolescents and adults. The reason for this difference between children from one side and adolescents and adults from other side arises from a significant difference in doses of the thyroid gland irradiation of these subpopulations of Belarus. Just opposite situation arises in case of the whole body irradiation. It can be assumed approximately that doses of the whole body irradiation of children, adolescents and adults are practically the same.

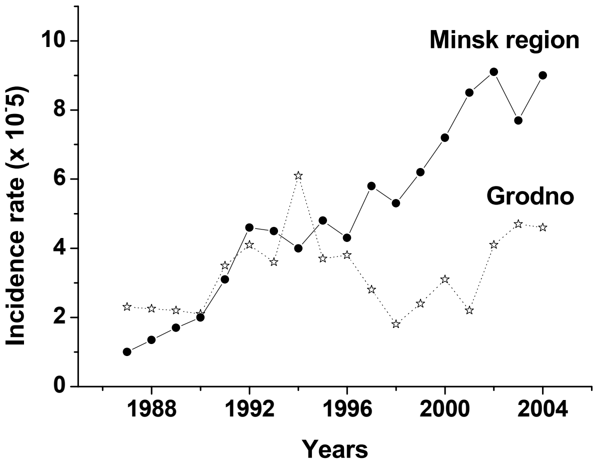
Very high doses of the thyroid radiation exposure in case of children explain why radiation-induced thyroid cancer in the children of Belarus appeared as the first effect of the Chernobyl accident [1].

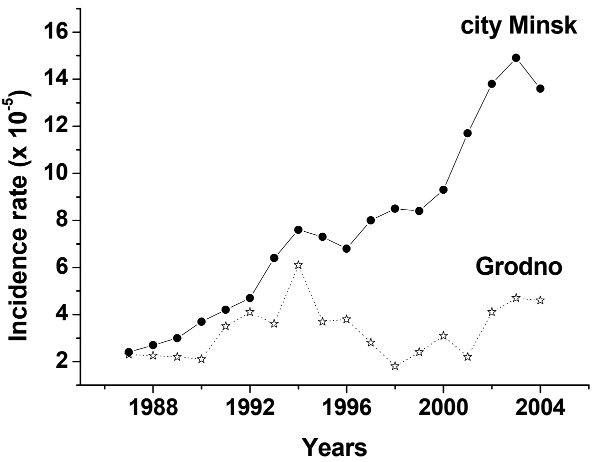
Data of the Belarusian Cancer Registry [50-58] show however that an increase in the incidence in thyroid cancers in Belarus after the Chernobyl accident occurred not only in children but in other age groups of population too. This resulted in significant increase of the incidence in thyroid cancers in all regions of Belarus. It was especially high in the Gomel, Brest and Mogilev regions that had highest levels of contamination with the isotope ^{131}I [69]. This indicates existence of some correlation between the level of ^{131}I deposition and level of additional thyroid cancers morbidity. The lowest increase in the incidence in thyroid cancers occurred in the Grodno region that is one of the cleanest regions of Belarus in respect of contamination with the isotope ^{131}I. Fig.2 demonstrates the incidence in thyroid cancers in different regions of Belarus in comparison with the Grodno region.

As can be seen from Fig.2 the incidence in thyroid cancers in populations of all Belarusian regions began to increase immediately after the Chernobyl accident. It was practically the same in different regions up to 1994. Then it begins to differ radically. In case of the Grodno region the incidence in thyroid cancers became in 1995-2001 close to the incidence registered immediately after the accident. However in case of other regions of Belarus the incidence in thyroid cancers continued to grow further. After 2000-2001 the incidence in thyroid cancers began to decrease (Gomel, Mogilev and Vitebsk regions, city Minsk) or remained practically constant (Minsk and Grodno regions). Only in case of the Brest region the increase in the incidence in thyroid cancers remained at least up to the end of 2004.

Fig.2. Incidence rates of thyroid cancers in regions of Belarus in 1987-2004




Minsk region
Grodno
Incidence rate (x 10-5)
Years
0
2
4
6
8
10
1988
1992
1996
2000
2004


city Minsk
Grodno
Incidence rate (x 10-5)
Years
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6
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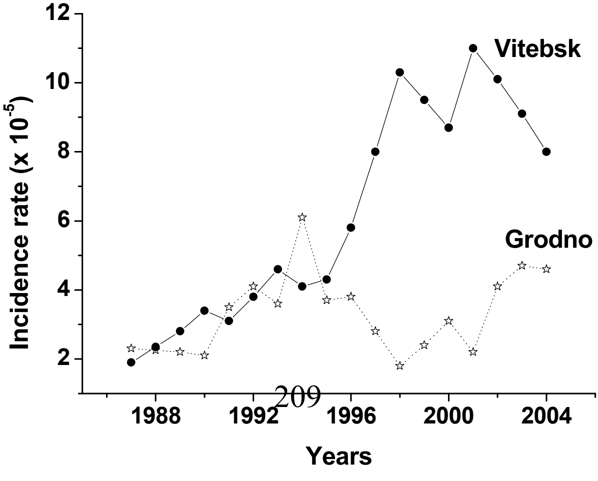
10
12
14
16
1988
1992
1996
2000
2004


Vitebsk
Grodno
Incidence rate (x 10-5)
Years
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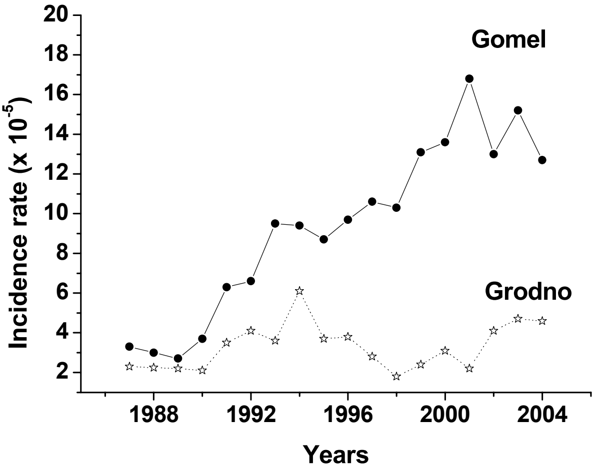
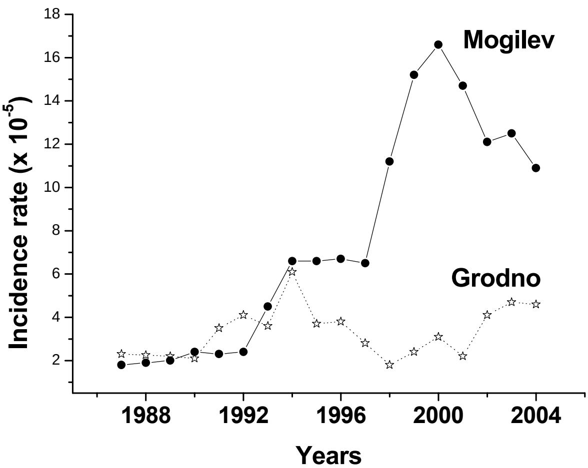
1988
1992
1996
2000
2004





It is clear, that any increase of the incidence in some cancer could be caused by two different reasons. Firstly, it can be a result of an improved screening of this cancer. Secondly, it can arise due to appearance of new carcinogen/carcinogens in the environment as well as a result of an increase in amounts of carcinogen/carcinogens that was/were in the environment before the increase in the incidence in this cancer. In the first case the incidence rate has to reach some higher value that has to remain constant later. In the second case, a decrease of the incidence will occur after some increase in the incidence in cancer. Data given in the present report show significant increase in the incidence in thyroid cancers in all regions of Belarus after the Chernobyl accident and the following decline. Such temporal pattern excludes the screening improvement as a main reason of observed increase in the incidence in thyroid cancers in Belarus after the accident at the Chernobyl NPP. It is clear that appearance of new carcinogen/carcinogens or increasing of their amount is responsible for observed change in the thyroid cancer incidence in Belarus after the Chernobyl accident.

It is remarkable that the observed increase in thyroid cancers manifested at the same time when a constant decrease in the chemical pollution occurred in Belarus [70,71]. It began in Belarus in seventies of the last century as a result of a transfer from the use of hard fuel to natural gas for electricity and heat production. This caused a significant improvement in the environment of Belarus. Starvation of industry and agriculture at the beginning of eighties contributed also very significantly to the improvement of the environment in Belarus [70,71]. As a result of these processes the discharge of different pollutants into the environment of Belarus decreased by factors 2-3 in the period 1985-2004 [70,71].

It is clear that decrease in discharge of chemical pollutants into the environment of Belarus can not be responsible for the increase in the incidence in thyroid cancers observed in Belarus after the accident at the Chernobyl NPP. It is evident that radiation is the most probable factor that caused observed changes in the incidence in thyroid cancers in Belarus after the Chernobyl accident because this change could not result from the decrease in the amount of chemical pollutants. This hypothesis is supported also by geographical factor (higher increase by higher contamination with the isotope ^{131}I). There is only one finding that contradicts with the assumption that the increase in the thyroid cancers in Belarus after the accident at the Chernobyl NPP was caused by the impact of ionizing radiation. As can be seen from Fig.2 a very significant increase in the incidence in thyroid cancers occurred also in the Vitebsk region. However this region was practically not affected by the Chernobyl accident [69]. For example, deposition of ^{131}I in this region was much lower than in the Grodno region. Despite this difference the Vitebsk region demonstrated much higher increase in the incidence in thyroid cancers than the Grodno region. A question arises. If radiation were the origin of the observed increase in the thyroid cancers in Belarus after the Chernobyl accident why the incidence in thyroid cancers in the clean Vitebsk region is higher than in some contaminated regions of Belarus (Grodno and Minsk regions)?

There is a plausible answer to this important question. Probably the significant increase in thyroid cancers in the clean Vitebsk region could be a result of the migration of inhabitants of high-contaminated territories of Belarus.

The migration began soon after the accident at the Chernobyl accident. In first 10 years after the Chernobyl accident 842.6 thousand of the Belarusian citizens or 8.4% of the total population changed the places of their living in borders of Belarus [72].

The total number of people that changed their place of residence in borders of Belarus in 1986-2000 is 1,500,000 or 15% of the averaged population that was approximately 10 Million persons in this period [72].

The internal migration in Belarus from contaminated regions of Belarus was occurring partly as a result of an implementation of the State Program of minimization of the Chernobyl consequences. In the framework of the program about 135,000 persons were resettled from contaminated to clean territories [73]. Approximately 200,000 persons migrated from contaminated areas of Belarus without any assistance of the state [74].

Simultaneously with internal migration an intensive external migration began in Belarus after the accident at the Chernobyl NPP. As a result of it only in 1990-2000 675.1 thousand of the Belarusian citizens left the country for other states of the world [72]. This is 6.75% of the total population of Belarus.

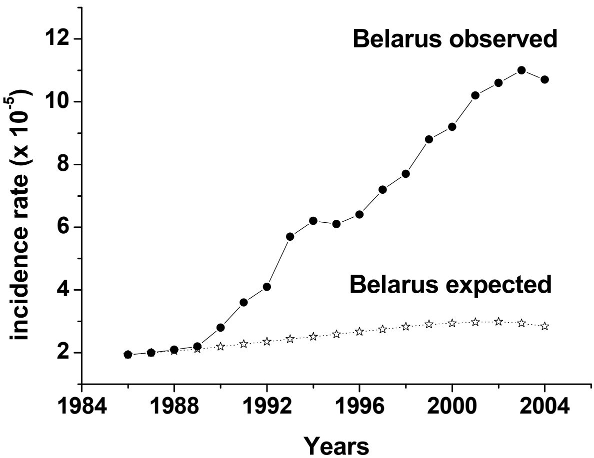
Significant fraction of people that emigrated from Belarus after the accident at the Chernobyl NPP lived on the territories affected by this accident. For example, approximately 130 thousand of persons of the Jewish nationality immigrated to Israel from contaminated areas of Belarus and Ukraine [75]. About 50% persons from this number lived before the emigration in high-contaminated territories of Belarus.

It is evident that internal migration influences significantly the possible correlation between incidence rates in different disease and levels of a radioactive contamination caused by the Chernobyl accident. The external migration decreases real manifestation of additional thyroid cancers in Belarus and as a result causes an underestimation of risk of additional thyroid cancers. The influence of internal migration can be excluded by considering the incidence in thyroid cancers in the entire country. In principle it is possible also to exclude the influence of the external migration. In order to achieve this goal one needs to assess the collective dose of the thyroid gland irradiation by considering the external migration. Such procedure was not performed in course of the present study. According to our assessment this can cause an incorrectness of estimated risk coefficients not higher than 10%. Such incorrectness is in frames of an incorrectness of the collective equivalent dose of the thyroid gland irradiation. Such conclusion can be drawn from comparison of different data sets on the collective equivalent dose of the thyroid gland irradiation of the Belarusian population [29,64,68]. Data presented in Fig.2 indicate that the incidence in thyroid cancers observed in the Grodno region can be used approximately as a spontaneous incidence in thyroid cancers in Belarus. It is clear that such method of the spontaneous incidence of thyroid cancer estimation has to overestimate real spontaneous morbidity in thyroid cancers. Such conclusion can be drawn because an evident manifestation of additional thyroid cancers occurred also in the Grodno region. Such conclusion can be done on the basis of data shown in Fig.2.

More correct assessment of the spontaneous incidence of thyroid cancers in the Grodno region and in other regions of Belarus as well as in the entire Belarus can be done by approximation of data observed in the Grodno region after the accident at the Chernobyl NPP. The left panel of Fig.3 shows result of the linear approximation of the incidence in thyroid cancers established in the Gomel region in 1987-1990, 1995-2004. Data registered in 1991-1994 in this region were not used for approximation of the expected incidence in thyroid cancers because as can be seen from Fig.2 in this period of time an additional increase in the incidence in thyroid cancer happened in the Grodno region.

Fig.3. Incidence rates of thyroid cancers in the population of the Grodno region (left panel) and in Belarus (right panel) after the Chernobyl accident

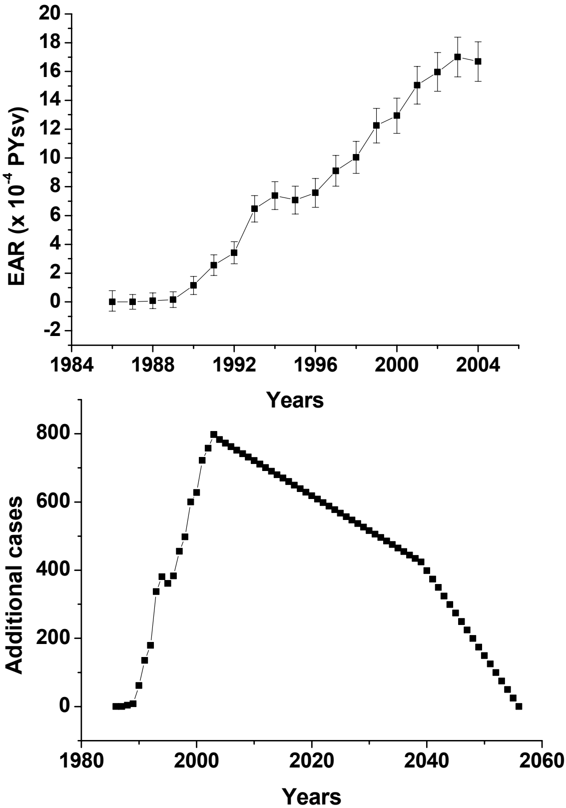
Bars in the curve presented in the left panel of Fig.4 denote



95% confidential intervals of the excessive absolute risk.

The approximation demonstrated in the left panel of Fig.4 was carried out by considering the incidence in thyroid cancers as a function of the fraction of persons at the age 60 years and older. Such method of analysis was proposed in the report [65]. It is more correct than approximation of the incidence as a function of time because it takes into account the change in the age distribution of population.

Fig.4. Excessive absolute risk (left panel) and numbers of additional thyroid cancers in Belarus in 1986-2056 (right panel)



The following expression was established by this approximation:

$$IR_{\exp} = 27.6151 \cdot f_T, \qquad (8)$$

$$R^2 = 0.1792,$$

$$P = 0.1703$$

Here $IR_{\exp}$ - expected incidence rate in population with fraction of persons at the age 60 years and older at some time T and f_T - fraction of persons at the age 60 years and older at time T.

As it is shown in [65], the use of the fraction of elderly people in the analysis of the cancer morbidity allows taking into account the change in the age distributions of analyzed populations.

As can be seen from the (8) the statistical power of the linear regression on the basis of data established in the Grodno region in 1987 - 1990, 1995 – 2004 is quite low. The reason for it is using of data that demonstrate an evident manifestation of additional thyroid cancers in 1995 – 2004 also in the Grodno region. This means that expression (8) gives an overestimation of the incidence in thyroid cancers. As a result, using of this expression for assessment of the spontaneous incidence in thyroid cancers in regions of Belarus after the accident at the Chernobyl NPP has to underestimate the real numbers of additional thyroid cancers.

The right panel of Fig.3 presents registered incidences in thyroid cancers in the entire Belarus as well as expected incidences estimated by using expression (6) and fractions of old persons in the entire Belarus calculated for the period 1986-2004.

The empirical equation (8) was used in the present report for assessment of additional thyroid cancers manifested in Belarus in 1986 – 2004 on the basis of data [49 - 58] and data on collective equivalent dose of the thyroid gland irradiation as a result of the Chernobyl accident. Results of this assessment are shown in Fig.4. Here the left panel of Fig.4 presents values of the excessive absolute risk and the right panel of it gives numbers of additional thyroid cancers that can be expected in Belarus in 1986-2056 as a result of the Chernobyl accident.

The calculations we made show that the EAR increases practically linearly in the period of 1989-2002 and then stabilises after 2002. The arithmetic mean value of EAR calculated by using expressions (4-6) for 2003 and 2004 years is approximately 16,85 cases per 10^4 man-sievert-years. We used this figure as well as the collective dose of the thyroid gland irradiation of the population of Belarus (calculated by considering the mortality of the Belarusian population) to evaluate the number of the radiation-induced thyroid cancers in 1986-2056. Such estimation assumes the constancy of the excessive absolute risk of the incidence in thyroid cancers in the period 2005-2056.

The calculations made in such a way provide 31,400 additional thyroid cancers in Belarus in 1986-2056 as a result of the Chernobyl NPP accident. Apparently, this number has to be viewed as a certain maximal amount as it is derived from the assumption that in the period of 2005-2056 the EAR remains constant and at 16,85 cases per 10^4 man-sievert-years. Verification of the correctness of this assumption will be possible in several years when the new data about the morbidity of thyroid cancer in Belarusian population will be received.

It is clear that the number of the additional thyroid cancers, calculated by using the assumption that the EAR in the period 2005-2056 remains constant at 16,85 cases per 10^4 man-sievert-years, can not exceed the real number of the additional thyroid carcinoma more than by factor 2. Such conclusion is based on the fact that the number of the radiation-induced thyroid carcinoma occurred in 1986-2004 is according to assessment carried in the present report is about 7,000 cases. Let us assume that the incidence in thyroid cancers in Belarus will decrease to spontaneous level beginning from 2005 and that this decrease will be finished in 2020 or during 15 years. Let us assume that in this case the number of additional thyroid cancers will form some symmetric bell-shaped curve. In accordance with this assumption the same number of additional thyroid cancers or approximately 7,000 cases has to manifest in the period 2005-2020. The last allows us to assess the full number of the radiation-induced cancers in 1986-2056 as a result of the Chernobyl accident, which is 14,000 cases. This number can be considered as a minimal possible amount of radiation-induced thyroid cancers, which will appear in Belarus as a result of the Chernobyl accident.

The abovementioned maximal number of thyroid cancers (31,400 cases) can be used for estimating the number of non-thyroid solid cancers. According to the data determined as a result of monitoring the inhabitants of Hiroshima and Nagasaki who experienced the atomic bombardment, the excess absolute risk of all solid cancers established for the period of 1958-1987 constituted 29,7 cases per 10^4 man-sievert-years [60]. The meaning EAR of the thyroid cancer in this population of Hiroshima and Nagasaki constituted 1,6 cases per 10^4 man-sievert-years [76]. As it follows from these figure, the total number of radiation-induced solid cancers in case if the radiation doses of all organs and tissues are approximately equal, as it happened with the inhabitants of Hiroshima and Nagasaki, exceeds 18,56 times the number of radiation-induced thyroid cancers. It can be assumed that the same ratio between excessive absolute risks of thyroid cancers and all solid cancers exists also in case of radiation-induced solid cancers caused in Belarus as a result of the Chernobyl accident (hypothesis about an equivalency of relative radiation risks determined by proportion (2) of this report). Such assumption allows us to determine the maximal amount of all the solid cancers of radioactive origin for a hypothetical case when the collective dose of the whole body radiation exposure can equal the collective dose of thyroid radiation exposure. It was mentioned above that for the population of Belarus, the collective dose of the thyroid constituted 553,000 person-gray. The calculations show that the total number of all the solid cancers of the radioactive origin will be 582,784 cases, if the collective doses of the whole body and thyroid radiation exposure equal 553,000 person-gray.

The number of cancers equalling 582,784 cases is derived by multiplying the maximal number of radiation-induced thyroid cancers (31,400 cases), which we estimated for the period of 1986-2056, by the multiplier 18,56. The number of excess solid cancers other than the thyroid cancers would equal 551,384 cases. However, as it was shown above, the collective dose of the whole body was about 19,5 times less than the collective dose of the thyroid. The division of the number 551,384 by the factor 19,5 gives the number of 28,276 cases of radiation-induced solid cancers other than the thyroid cancers, which shall appear in Belarus in 1986-2056. It should thus be expected that, as a result of the Chernobyl NPP accident in Belarus in the period of 1986-2056, approximately an additional 28,000 non-thyroid solid cancers will be registered.

The use of the minimal number of radiation-induced thyroid cancers (14,000 cases) for the similar estimations allows us to estimate the minimal number of the possible radiation-induced non-thyroid solid cancers in Belarus in 1986-2056 as approximately 12,600 cancers.

According to [77], a lifetime risk of radiation-induced leukemias in the population of Hiroshima and Nagasaki which experienced the atomic bombardment, will constitute around 1,1% per sievert, and the lifetime radiation-induced risk of all solid cancers about 10,9% per sievert. The calculations based on these numbers for survived inhabitants of Hiroshima and Nagasaki show that contribution of solid cancers in the total mortality from radiation-induced malignant neoplasm's in this subpopulation is approximately 90.8% of the total mortality caused as a result of radiation impact. Correspondingly, the contribution of leukemias to the mortality from all radiation-induced malignant neoplasms in case of atomic bomb survivors is about 9,2%.

Assessment on the basis of data of the Belarusian Cancer Registry shows that the ratio of mortality to morbidity in case of solid cancers is practically the same as the ratio of mortality to morbidity in case of leukaemia. This allows us to assume that contribution of radiation-induced solid cancers in case of survived inhabitants of Hiroshima and Nagasaki is approximately 90,8% to the morbidity from all radiation-induced malignant neoplasms observed by them. The contribution of radiation-induced leukaemia's to the total incidence of all radiation-induced cancers will be then equal to 9,2%. The assumption that the similar correlation in contributions of solid cancers and leukaemia's exists also in Belarus allows us to estimate the possible number of radiation-induced leukaemias in Belarus in 1986-2056. The use of maximal (28,276) and minimal (12,600) number of radiation-induced solid cancers, which should be expected in Belarus in 1986-2056, provides respectively numbers of possible radiation-induced leukaemia's as a result of the Chernobyl accident equal to approximately 2,854 and 1,272 cases.

The comparison of these numbers with estimations of the number of radiation-induced leukemia appeared already in Belarus in 1986-2004 [22-24], shows that the minimal number of radiation-induced leukemias mentioned above (1,272 cases) is visibly underestimated. It is approximately 2 times less then number of additional leukemias, which already occur in Belarus after Chernobyl NPP accident. The total number of radiation-induced leukemias, which appeared in Belarus in 1986-2004, is according to reports [22-24] approximately 2,300 cases. This means that using of the minimal number of radiation-induced solid cancers (12,600 cases) other than thyroid cancers does not allow correct assessment of the number of additional leukemias. On the contrary, using for this assessment the estimated number 28,276 of solid cancers other than thyroid cancers allows assessing correctly the number of leukemias manifested in Belarus after the Chernobyl accident. Therefore one can conclude that more probable is to expect in Belarus in 1986-2056 about 31,400 additional thyroid cancers, about 28,300 other solid cancers and approximately 2,854 leukemias.

Table 3 represents rounded data about numbers of solid cancers and leukemias, which have to appear in 1986-2056 in Belarus and all countries of the world including Belarus. Data estimated for Belarus were used by assessment of additional cancers and leukemias in other countries of the world excluding Belarus. Estimations for these countries were made on the basis of the proportion (7). Numbers received in this way were summed with numbers assessed for Belarus and results of this are in the third and fifth columns of Table 3.

Table 3. Incidence and mortality from solid cancers and leukemias expected in 1986-2056 as a result of the Chernobyl accident

Localization	Incidence		Mortality	
	Belarus	All countries (including Belarus)	Belarus	All countries (including Belarus)
Thyroid cancer	31400	137000	3140	13700
Other solid cancers	28300	123000	16400	71340
Leukemias	2800	12000	1880	8040
In total	62500	270000	21420	93080

One needs to notice here that by estimation of numbers of fatal malignant neoplasm's following ratios of mortality to incidence for Belarus and all the other countries of the world were used, 10% for thyroid cancers, 58% for solid cancers and 67% for leukemias. These values were estimated on the basis of data given in references [50-58].

The last expression is based on a direct transferring of radiation risks assessed for Belarus to other countries of the world. This contradicts to our hypothesis that only relative radiation risks estimated on the basis of the expression (2) can be transferred with assumptions. The first is an assumption about an equality, it was assumed that radiation risks in other countries are the same as in Belarus. Secondly, it was assumed that collective doses. The use of the expression (7) means that radiation risk established for the Belarusian population was transferred to other populations of the world. Another assumption used by estimation of possible medical effects caused by the Chernobyl accident in countries other than Belarus is that collective doses of population irradiation in these countries depends only on the amount of deposited radioactive substances. This is an evident underestimation of collective doses in case of Western Europe because it is well known that collective doses depend not only on the amount of deposited radionuclides but also on population density as well as on transfer coefficients along food chain and style of life of irradiated people.

Radiation risks

Data in the second column of Table 3 allow us to estimate the lifetime excessive absolute risks of radiation induced cancers and leukemias. They can be obtained by dividing of numbers of additional cancers by appropriate collective irradiation doses. Calculated values of excessive absolute risks are shown in Table 4.

Comparison of values in Table 4 with data established in [60,62] shows that additional risks of malignant neoplasm's of the Belarusian population are about ten times higher than risks of radiation-induced cancers established for inhabitants of Hiroshima and Nagasaki, who survived nuclear bombing. Such feature of radiation-induced malignant neoplasms caused as a result of the

Chernobyl accident was demonstrated for the first time in the report [27].

Table 4. Excessive absolute risks of solid cancers and leukemias for Belarus population, averaged for 1986 – 2056

Type of cancer	Thyroid gland	Other solid cancers	Leukemias
$EAR \cdot 10^4$ man-sievert-years	13	230	20

General somatic diseases

It is known at present that radiation-induced cancers are not the only effects of ionising radiation to the organism. Long-term observation of atomic bomb survivors gave reliable evidences that ionising radiation causes an increase in the incidence and mortality in different general somatic diseases [43-46]. Similar findings were established by studying of different groups of people irradiated as a result of the Chernobyl accident [35-42]. The contribution of general somatic diseases caused by the impact of ionizing radiation to the total mortality that can be caused as a result of the Chernobyl accident was estimated simply by assuming that is equal to contribution of additional malignant neoplasms. This assumption gives approximately 20,000 fatal cases from additional increase of mortality from general somatic disease in case of Belarus. The total number of additional fatal cases in all countries of the world including Belarus that can be caused as a result of additional incidence and mortality in general somatic diseases will be then approximately 90,000 cases.

Taking into account this assumption one can assess the total number of additional fatal cases from malignant neoplasms and general somatic diseases caused in 1986-2056 in Belarus equal to approximately 40,000 cases. In case of all countries of the world including Belarus the total number of additional fatal cases from all reason can be estimated equal to 180,000 cases. This means that medical consequences of the Chernobyl NPP accident can be compared with medical consequences of the atomic bombardment of Hiroshima.

Discussions.

A qualitative character of estimations carried out in the present report is evident. Such conclusion can be drawn especially in case of general somatic disease assessed for Belarus as well as in case of malignant neoplasms and general somatic diseases assessed for other countries affected by the Chernobyl accident.

Our assessment of possible medical effects in other countries of the world is based on transferring of radiation risks estimated for Belarus. Such transferring can cause very serious errors in estimation of additional incidence and mortality in these countries. Another problem in case of countries other than Belarus arises from using expression (8) that ignores the difference in population density and other important factors that strongly influence the value of the collective equivalent dose delivered to people as a result of the Chernobyl accident. All these problems do not allow to forecast the correct amount of additional fatal cancers and additional mortality from general somatic diseases in countries other than Belarus by using methods described in the present report. This is the reason of low accuracy of data estimated in the present report for all countries of the world affected at the Chernobyl accident. According to our assessment, the accuracy of additional cancers and leukemias presented in Table 3 can be approximately 50%. The accuracy of numbers of additional fatal cases arising from general somatic diseases caused by the Chernobyl accident is possibly about 100%.

Despite quite low accuracy of performed assessment data established in the report they indicate a very important peculiarity of additional medical effects manifested in Belarus and other countries after the Chernobyl accident. Data estimated in the present report undoubtedly demonstrate that radiation risk of thyroid cancers at least is higher than radiation risk established for atomic bomb survivors.

This is fully unexpected result because of a very significant difference in dose and dose rates of the thyroid gland irradiation of atomic bomb survivors and inhabitants of areas affected at the Chernobyl accident. In case of inhabitants of Hiroshima and Nagasaki doses of the whole body irradiation were equivalent to doses of the thyroid gland irradiation. The arithmetic mean dose of the whole body and consequently of the thyroid gland irradiation of survived inhabitants of Hiroshima and Nagasaki is approximately 0.2 Sv [78]. This is by factor 5 higher than the mean arithmetic dose of the thyroid gland irradiation of the Belarusian population (see Table 1). The main contribution to doses delivered to the whole body and consequently to the thyroid gland in case of inhabitants of Hiroshima and Nagasaki was made during 1 microsecond [79]. In case of population of Belarus irradiation of the thyroid gland lasted at least 3 months after explosion of the Chernobyl reactor or during approximately $7.9 \cdot 10^6$ seconds. Combining data on irradiation doses and duration of irradiation shows that dose rates of the thyroid gland irradiation in Belarus were approximately by factor $4 \cdot 10^{13}$ lower than dose rates of the thyroid gland irradiation of atomic bomb survivor.

The higher radiation risk of the incidence in thyroid cancers in Belarus ($EAR \approx 16.5/10^4$ PYSv) than in atomic bomb survivors ($EAR \approx 1.6/10^4$ PYSv) despite of such immense difference in irradiation dose rates gives the clear evidence that radiation risk at least in case of thyroid cancers does not decline with decrease of dose rate.

The similar difference in radiation risks between the Belarusian population and atomic bomb survivors was established also for stomach, lung, female breast, leukemia, non-melanoma and other malignant neoplasms [17-20,24-27]. Manifestation of additional malignant neoplasms other than thyroid cancers is caused by irradiation of the whole body. It was shown in previous section that doses of the whole body irradiation in Belarus were approximately by factor 20 less than doses of the thyroid gland irradiation. This means that dose rates of the whole body irradiation of the Belarusian population were ten times less than dose rates of the thyroid gland. Therefore, dose rates of the whole body irradiation in Belarus were lesser more than by factor 10^{14} than dose rates of the whole body irradiation of survived inhabitants of Hiroshima and Nagasaki.

Despite their qualitative character data estimated in this report as well as in reports [17-20,24-27] indicate that radiation risks of malignant neoplasms of the Belarusian population are at least notless than radiation risks observed by atomic bomb survivors.

Similar or higher than in case of atomic bomb survivors radiation risks of malignant neoplasms were also established in other groups of people experienced long-term irradiation at low dose rates.

For example, the excessive relative risk of mortality from solid cancers of Russian liquidators determined for the period 1991-2001 was estimated equal to 0.34/Gy [34]. This value can be converted to0.5 /Sv using equivalent absorbed dose instead the equivalent one. The last figure is by factor 1.7 higher than excessive relative risk of survived male inhabitants of Hiroshima and Nagasaki irradiated at the age 30 years. For this subgroup the excessive relative risk of mortality from all solid cancers equals 0.29/Sv [80]. Here one needs to notice that females contributed only 1% to the total number of Russian liquidators [33]. And this is a reason for comparison of data established for Russian liquidators with data established for male inhabitants of Hiroshima and Nagasaki.

The Russian liquidators as well as liquidators from other regions of the former USSR worked in the 30-km zone of the Chernobyl reactor approximately 1 month or during 3 Million of seconds. Thus dose rates of their irradiation were approximately $3 \cdot 10^{12}$ times less than dose rates of atomic bomb survivors irradiation.

The excessive relative risk of mortality from solid cancers of inhabitants of rural villages on the Techa River (Russia) proved to be approximately 0.92/Gy [81]. This value can be expressed as 1.3/Sv by using equivalent absorbed dose instead of absorbed dose. The last figure is by factor 3 higher than excessive relative risk of mortality from radiation-induced solid cancers established for atomic bomb survivors and equal to 0.42/Sv for sex-averaged population.

Reliable results indicating the absence of a decline in radiation risks with decrease of dose rates were established recently for population of the Semipalatinsk region (Kazachstan) irradiated chronically due to local fallout from Soviet atmospheric nuclear weapons testing [82]. The excess relative risk of mortality from solid cancers in case of the Semipalatinsk population is 1.77/Sv (95%CI from 1.35 to 2.27). This is by factor 4 higher than radiation risk of mortality from solid cancers in case of atomic bomb survivors (0.42/Sv [80]).

All these data show clearly that there is no decline in radiation risk of malignant neoplasms by decrease of dose and dose rates. Existing data show the opposite picture. Coefficients of radiation risk estimated for chronically irradiated populations are higher by some factors than coefficients of radiation risk established for atomic bomb survivors. This means that chronic irradiation is more dangerous than acute. The last conclusion relates however only to such range of doses and dose rates that do not induce deterministic effects.

In light of discussed data it is clear that radiation risks established for atomic bomb survivors are not relevant for normal populations exposed to long-term irradiation at low doses and low dose rates. Using them for assessments of medical consequences of populations affected at the Chernobyl accident and similar population will underestimate real effects of irradiation. Such underestimation will be much higher if forecast of possible medical effects of long-term irradiation at low dose and low dose rates is performed by using radiation risks established for survived inhabitants of Hiroshima and Nagasaki together with using the DDREF factor suggested by the International Commission on Radiological Protection (ICRP) [83]. According to ICPR radiation risk of chronic irradiation at low doses and low dose rates has to be divided by some factor because it is lower than radiation risk of acute irradiation.

This recommendation as well as data established by observing of atomic bomb survivors was used some years after the accident at the Chernobyl NPP by group of prominent Soviet specialists [84]. According to data estimated in the report [84] one had to expect 91 additional thyroid cancers in the period 1990-2020 in Belarus: 39 in children and 52 in adults. As it was shown in the present report the full number of additional thyroid cancers that manifested in Belarus in 1986-2004 is approximately 7,000 cases or by factor 77!!! Higher than it was forecasted by authors [84] for the period 1990-2020. The history of modern science does not know any such confusion with scientific forecasting.

It is evident that some reliable forecasting can be performed only on the basis of medical data established in ethnic group that were affected at some radiological accident. The present report demonstrates using of this method for establishing of Chernobyl consequences for Belarus.

Conclusions.

The analysis of the incidence in malignant neoplasms in Belarus shows that the accident at the Chernobyl NPP will lead to an additional mortality of about 40,000 people in Belarus in the period of 1986-2056. This figure includes additional mortality caused by additional malignant neoplasms and additional general somatic diseases. The total mortality from all diseases in all countries of the world including Belarus as a result of the Chernobyl accident can be approximately 180,000 cases. These data indicate that the Chernobyl accident is a real catastrophe comparable with natural accidents like tsunami in 2004 or with consequences of the atomic bombardment of Hiroshima and Nagasaki.

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