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EDITORS’ FOREWORD

This Book of Abstracts comprises abstracts of papers contributed to the IIInd International Symposium “Chronic radiation exposure: possibilities of biological indication”, and a bibliographical index of works published by the scientists of the Urals Research Center for Radiation Medicine (URCRM) over the period 1962-1999.

The IIInd International Symposium is devoted to such essential issues of radiation biology as late medical-biological effects of chronic radiation exposure, pathophysiological mechanisms of stochastic (somatic and genetic) effects of radiation exposure in man (including effects of exposure to fetus and embryo), biological indication of radiation exposure and exposure doses, susceptibility to radiation-induced effects and biological indication of diseases associated with radiation exposure. Among different radiobiological aspects addressed by the Symposium the issue of small dose effects is paid a considerable attention.

The recent results of epidemiological studies based on the follow-up of cohorts exposed under different conditions (atomic bombardment in Japan, radiation incident on the banks of the Techa, environmental contamination due to Chernobyl accident and nuclear weapon tests, exposure of atomic industry workers, etc.) allow to gain a better insight into the nature of late health effects both in the exposed persons themselves and their offspring. The basic radiobiological dependences (risk coefficient, exposure dose threshold, type of dependence, etc.) governing induction of carcinogenic and non-cancer somatic effects are discussed.

A special focus is on oncogenic radiosensitivity. The issues addressed include molecular-biological and pathophysiological mechanisms of carcinogenic radiation effects and predisposition (including genetic) to them. Special attention is devoted to biological markers of susceptibility to radiation-induced diseases, and biological markers of post-radiational pathology. Indication of susceptibility to carcinogenic radiation effects based on biological markers is of great practical significance for identifying persons with increased risk for developing such conditions after exposure.

Biological indication and biological dosimetry are regarded as a promising line of research in radiobiology. The papers addressing different aspects of this issue discuss various approaches to biological dosimetry, interpretation of biodosimetry data, possibilities of radiation exposure indication at late times after exposure, and under the conditions of nonuniform irradiation. A considerable attention is paid to the influence of non-radiational factors (age, smoking, etc.) on the level of biological dose markers. Among many methods for biological indication of radiation exposure an important role is played by analysis of chromosome aberrations (particularly stable aberrations). A comparative analysis of efficiency of different methods for retrospective dosimetry is presented.

An important place in the contributed papers is occupied by immunological markers of radiation exposure and radiation-induced diseases. The mechanisms, the nature of immunity disorders and their role in the development of late somatic radiation effects are discussed.
A number of papers are devoted to the studies of adaptive response and genome instability induced by exposure to ionizing radiation. The radiobiological conditions of induction of such effects and the mechanisms of their development are considered.

The abstracts included in this book give an objective idea of the state of art in biological indication of radiation exposure, predisposition to stochastic effects and the most long-term effects, and of the place it occupies in radiation biology and medicine. It can be implied based on an appraisal of the current situation in this field of research that the prospects for biological indication and the theoretical basis for its development surpass significantly the current possibilities for its practical use.
DATABASE FOR A LIFE SPAN EPIDEMIOLOGICAL STUDY OF
CHERNOBYL ACCIDENT RECOVERY WORKERS (LIQUIDATORS):
RECOMMENDATIONS OF WORLD HEALTH ORGANIZATION EXPERTS
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The International Consultation on the development of a WHO Accident Recovery Workers ("Liquidator") Project which was held in St.Petersburg, Russia, 1994, recommended the establishment of two databases within the project framework. It was decided that one of the databases would include 125,000 liquidators (50,000 from the Russian Federation, 50,000 from Ukraine and 25,000 from Belarus) and be designed for a life span epidemiological study (LSES) of morbidity, disability and mortality in this group of population affected by the Chernobyl accident. The second clinical database on 5,000 liquidators would collect clinical information in order to analyse specific features of the signs and symptoms of diseases developing in liquidators and evaluate the treatment effectiveness. The standardised protocol, including recommendations for clinical monitoring of liquidators and epidemiological studies within the database, had been developed by WHO international experts in 1997 and it was implemented in the three countries. In 1998, WHO experts met in Kiev, Ukraine, and evaluated the progress of the establishment of the databases and provided recommendations for its further development. Liquidators for the LSES were selected from National Chernobyl Registries in line with the project protocol, and they included those residing in the non-contaminated territories of the Russian Federation and Ukraine and throughout Belarus. Specific requirements for the formation of epidemiological “Liquidator” project database (LPB) are as follows:

- To include in the LPB liquidators (men only) who participated in the clean-up operations in the Chernobyl area in 1986-1987.
- To carry out as specified in the Registration form the preliminary analysis of epidemiological indicators on oncological and non-oncological conditions, disability and morbidity.
- To carry out verification of diagnosis by experts at regional and central levels after finalizing the formation of the database from a quantity point of view.
- To develop a standardised software programme for the processing of epidemiological results taking into account the possibility of using ICD-9, ICD-10 and in the case of oncological pathology ICD-10-0.
- In addition to oncological diseases, to draw attention to the following pathological conditions: hypertensive disease, ischemic heart disease, liver diseases, diseases of nervous system and sense organs, diseases of blood and blood-forming organs, respiratory diseases, endocrine disorders.

- In order to study radiation risks it is recommended initially to divide all members of the study cohort included in the LDP into three groups: 0-50 mGy, 50-200 mGy, and more than 200 mGy.

- To continue the study of possible errors in official doses recorded on liquidators’ certificates and assess the average errors in dose groups.

- To implement from 1999 onwards the use of the Registration form for the collection of information on the liquidators included in the LPD. To implement this Registration form in the National Chernobyl Registries (NCR) and introduce a special code "PEI" in the NCR for liquidators selected for the LPD.

**LONG-TERM EFFECTS OF NUCLEAR TESTS AT THE SEMIPALATINSK TEST SITE ON THE ALTAI REGION POPULATION**

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The Altai Region is an administrative unit of the Russian Federation located in the south of Western Siberia and bordering in the south-west on the Semipalatinsk Test Site. Atmospheric nuclear tests were conducted at the STS from 1949 till 1962. Weather conditions in this region resulted in most radioactive products being transported towards the Altai Region. The greatest contribution to the radiation impact on the population was made by the first nuclear test of August 29, 1949. As a result of the fallout from this test, effective doses ($E$) in certain settlements in the south-west of the Altai Region exceeded 1 Sv.

In order to study health effects, a register containing data on 39179 individuals exposed in 1949, was compiled. In view of the fact that the register was compiled retrospectively, by present the vital status has been determined for 15862 individuals. Besides, the register includes external and internal control groups comprising totally 7514 individuals.

This cohort was used for epidemiological studies of mortality from various causes and prevalence of various diseases among the exposed population. Analysis of mortality among men indicated that in different age-at-exposure groups mortality risk increases at different times since exposure. Mortality rate from malignant neoplasm had a linear relationship with dose. The study has detected increased mortality rates from malignant neoplasm of some sites. Study of prevalence of different diseases among survivors revealed high risk for a number of diseases and classes of diseases.
LATE RADIATION EFFECTS IN POPULATION EXPOSED IN THE TECHA RIVERSIDE VILLAGES
(CARCINOGENIC EFFECTS)

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The development of carcinogenic effects is the principal consequence of exposure to small and medium doses of radiation. The discharges of radioactive wastes from the Mayak Industrial Association into the river Techa in the period 1949-1956 led to overexposures of 30 thousand people living on the banks of the river. The exposure of residents resulted from both external and internal radiation, the latter being due to consumption of river water and incorporation of primarily ${}^{89}\text{Sr}$, ${}^{90}\text{Sr}$ and ${}^{137}\text{Cs}$. The doses accumulated in soft tissues of exposed persons ranged from 0 to 1.18 Gy (mean dose = 0.084): 0-2.16 Gy to red bone marrow (mean dose = 0.34 Gy), 0-3.86 Gy to bone surfaces (mean dose = 0.60 Gy). The dose values listed above could result in an increased carcinogenic risk.

The first studies conducted in 1960 showed the death rate from gastric and esophageal cancer among exposed residents to be increased for the first 9 years of exposure. According to the results of a 29-year follow-up, risk of death from gastric cancer was 1.5, and from cancer of uterine cervix 2.1 calculated per 10 000 person-years (data published by M.M. Saurov et al.) The most manifest was an increase in leukemia risk values. Based on studies conducted by different researchers in different years, from the study of 1972 addressing 23 cases of leukemia, to the one of 1997 discussing 66 cases of leukemia, the estimated excess absolute risk values were comparable making up 0.8-0.9 per 10 000 person-years, and the excess relative risk was estimated to be 1.2-3.2 per Gy.

It was necessary to verify the data resulting from the studies conducted in earlier years since in a number of cases the analysis of effects had not taken into account migration, a characteristic feature of exposed population, and excess cases of solid cancers and leukemias had been correlated with the only dose estimates available, i.e., doses accumulated in bone tissue. Over the recent four years the efforts of the research group were aimed at enhancing the information in the URCRM data base and improving its quality. A dynamic follow-up of exposed persons based on the registry encompasses to date a 45-year period since the onset of exposure. During this period documentary data on cases and causes of death were collected. The Techa River cohort was extended to include persons who had received low doses because they came to live in the villages on the Techa after the radiation conditions in the locality had improved. An analysis of mortality data for that group has yielded more correct data on the basic rates of cancer. A more correct estimation of doses to red bone marrow and a few other organs was made. The preliminary leukemia risk assessment using
more accurate data listed above yielded the excess relative risk equal to (3.0-4.4) per Gy. Risk of solid cancers assessed on the basis of a relative model is characterized by a higher uncertainty and, according to preliminary estimations, is equal to 0.41 per 1 Gy. To obtain more accurate and reliable carcinogenic risk values will necessitate tracking exposed people who have migrated from the catchment area.

THYROID CANCER INCIDENCE AMONG PEOPLE WHO LIVED IN OZYORSK (CHELYABINSK-65) AS CHILDREN

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The city of Ozyorsk (former Chelyabinsk-65) is located near the Mayak complex, the first Russian nuclear facility, which became operational in 1948. Especially during the early years of Mayak’s operation, when the filtration of nuclear releases was imperfect, the population of the city was exposed to radiation from radioactive atmospheric emissions. The highest radiation doses to the public came from the radioactive iodine in the radioactive releases. Because of the well-known strong association between thyroid cancer and radiation exposure (UNSCEAR, 1994, Karaglou et al, 1996), we conducted a study under NIH contracts N01-CP-51025 and N01-CP-81034 to evaluated thyroid cancer incidence among Ozyorsk residents.

Thyroid cancer incidence was determined using our registry of children who once lived in Ozyorsk. This registry includes all individuals who were born in Ozyorsk after 1948 or moved to Ozyorsk after 1948 before they were age 15 years. To identify thyroid cancer cases, we selected approximately 19,500 individuals who are still living in Ozyorsk. Data on thyroid cancers have been obtained from medical institutions of Ozyorsk and from the regional medical institutions in Chelyabinsk. Twenty-nine cases of thyroid cancer (22 women, 7 men) were ascertained: More than half of the cases were diagnosed under the age of 40 years; the mean age was 36 years for females and 39 years for males. Using Russian national incidence data to calculate the expected number of thyroid cancers, preliminary analysis suggests that thyroid cancer incidence in the study cohort is three times higher than in the general population. No thyroid cancers were diagnosed under the age of 20, however only 0.3 would have been expected. The findings from this study are limited, because thyroid cancer national incidence rates are not available for all years or all ages and because currently we do not have data on radiation doses received by the population of Ozyorsk. These preliminary results, however, do indicate the importance of continuing epidemiological studies of exposed children and of estimating radiation doses.
HEALTH EFFECTS FROM NUCLEAR TESTING THE SEMIPALATINSK TEST SITE IN THE SEMIPALATINSK OBLAST
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Background:
The population near the Semipalatinsk test site was exposed to chronic radiation from nuclear weapons tests. Major contributions of the overall exposure derived from the first test in August 1949 and one in 1953.

Objective:
The objective is to evaluate the possible health effects of the radiation exposure due to the nuclear tests. Of main interest are malignancies, their occurrence in time and in relation to radiation exposure.

Material and Methods:
Data were taken from the archives of the KRIRME, which collects information on the health status of some 20,000 persons since the 1960s. Half of them are considered to be exposed, whereas the other half are considered to be less or not exposed. Two different study designs were employed. First, a series of cross-sectional studies in five year intervals were conducted. Second, two cohorts have been established and will be the basis for future cohort analysis. A nested case-control study on leukaemias is conducted among the exposed cohort.

Results:
The cross-sectional studies reveal an increased incidence of all solid cancers in the exposed areas. Preliminary results from the nested case-control study on leukaemias indicate a dose-response relationship. Results will be presented in detail at the conference.

STOCHASTIC EFFECTS OF ENVIRONMENTAL RADIATION EXPOSURE IN POPULATIONS LIVING NEAR THE MAYAK INDUSTRIAL ASSOCIATION - CANCER MORBIDITY
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The “Mayak” Industrial Association, located in the South Ural Mountains began operation in 1948 and was the first Russian site for the production and separation of plutonium. During the early days of operation, technological failures resulted in the release of large amounts of waste into the Techa River. Residents who lived on the banks of the Techa and Iset Rivers were exposed to varying levels of radioactivity. The objective of this study is to assess stochastic (carcinogenic) effects in populations exposed to offsite releases of radioactive materials from the “Mayak” nuclear facility located in the South Ural Mountains in Russia. Subjects of the present study are those individuals who lived during the period January 1950 through December 1960 in any of the exposed villages along the Techa River in Chelyabinsk Oblast. Death certificates and cancer incidence data have been routinely collected in the past from a four-rayon catchment area of Chelyabinsk Oblast. The registry assembled and maintained by the Urals Research Center for Radiation Medicine for the past 40 years is the basis for identifying study subjects for this project. Specific study aims for the study of cancer morbidity among members of the Techa River cohort are to: a) evaluate the incidence of cancer among current and former residents of Chelyabinsk Oblast who are in the exposed Techa River Cohort; b) integrate results from the dose-reconstruction study to estimate doses for risk assessment; and c) develop a structure for maintaining continued follow-up of the cohort for cancer incidence. In the earlier part of our collaborative effort, the focus has been to enhance the cancer morbidity registry by updating it with cancer cases diagnosed through 1997, to conduct a series of validation procedures to ensure completeness and accuracy of the registry, and to reduce the numbers of subjects lost to follow-up. A feasibility study to determine cancer morbidity in migrants from the catchment area is underway. Our preliminary analyses of cancer morbidity underscore the importance of examining both cancer mortality and cancer morbidity in conducting a comprehensive analysis of the occurrence of cancer in this important cohort.

**BONE TUMORS IN “MAYAK” WORKERS**

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Bone tumor risks were evaluated in 11,000 workers who started working at the “Mayak” Production Association in 1948 –1958 and who were exposed to both internally deposited plutonium and to external gamma radiation. Comparisons with Russian and US general population rates indicate excess risk, especially among those monitored for plutonium and among female workers. Comparisons within the “Mayak” worker cohort, which evaluate the role of plutonium body burden with adjustment for cumulative external dose, indicate excess risk among workers with burdens estimated to exceed 7.4 kBq and among workers in the plutonium plant who did not have routine plutonium monitoring data based on urine. In addition, analyses
treating the estimated plutonium body burden as a continuous variable indicate increasing risk with increasing burden (p < 0.001). Because of limitations in current plutonium dosimetry, no attempt was made to quantify bone tumor risks from plutonium in terms of organ dose, and risk from external dose could not be reliably evaluated.

INCIDENCE OF PREGNANCY AND LABOR COMPLICATIONS IN WOMEN EXPOSED TO CHRONIC RADIATION
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The focus of the study was on a retrospective analysis of the course of pregnancy and labor in women exposed to chronic radiation as a result of contamination of the river Techa with wastes from a radiochemical facility. In all, 1,897 labor histories were analyzed for a period 5-23 years since the onset of radiation exposure. The study group comprised 1,213 labor histories of women exposed to gamma- and internal radiation mainly due to $^{90}$Sr and $^{137}$Cs. The comparison group included labor histories of women who were resident in the villages of the same administrative rayons but were not exposed to the radiation. The study group was divided into subgroups depending on dose at labor. The incidence of obstetric complications was assessed taking into account parental dose to gonads (1-38 cSv), doses to maternal soft tissues (1-80 cSv), fetal doses. It was revealed as a result of the study that the incidence of impending abortion and premature labor, toxicosis of pregnancy and premature rupture of the amnion was statistically higher for women included in the study group. No differences were noted between the study and control groups with respect to other parameters. Nephropathy, anemia, abundant amniotic fluid, scant amniotic fluid, abnormal presentation, hemorrhage are revealed with equal frequency in the study and control groups. The multifactorial analysis was used to study the dependence of the incidence of obstetric complications on radiation exposure and non-radiational factors: the puerperant’s age, her occupation, number and numerical order of prior pregnancies and labors, presence of extragenital pathology, gynecological history.

ESTABLISHMENT OF A SYSTEM FOR FOLLOWING-UP A COHORT OF CHRONICALLY EXPOSED PERSONS
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The focus of the study was on the design of the follow-up of a population exposed due to radioactive environmental contamination in the Urals region resulting from releases from the Mayak Industrial Association. Epidemiologic studies conducted earlier showed an increased risk of leukemia, and a tendency towards an increased cancer death rate which stresses the necessity of a long-term prospective follow-up of the population with the purpose to assess the risk of late effects of radiation exposure.
For this reason the solution of methodological problems associated with a retrospective collection of information and development of an effective system for tracking cohort members is of essential importance. An organized information flow and document turnover serve as a fundamental basis for the follow-up system. The most important links of the system are as follows: medical examination and interviewing exposed residents; reviewing tax books kept at the village administrations; sending queries to the address bureaus; retrieving information from the ZAGS archives; collection of information on cancer cases among the followed-up population based on medical records stored at the regional oncology dispensary and at the pathological archives. The paper discusses the design and ways to improve the efficacy of individual links of the system. The process of follow-up of the exposed population is ensured by a unified computerized data base incorporating a software designed to exclusively serve the above-listed objectives. The study can serve as a methodological basis for a further development and improvement of the software ensuring operation of the UR-CRM’s Data Base.

CERTAIN CHARACTERISTICS OF LEUKEMIA CASES AMONG PERSONS EXPOSED IN THE TECHA RIVERSIDE VILLAGES
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Leucosogenic effect is one of the prominent stochastic consequences of exposure to ionizing radiation. In the period 1953 through 1997, 83 cases of leukemia were registered among members of the Techa River Cohort. The establishment, since 1967, of specialized hematological services at the URCRM clinic (head Doctor: V.A. Fomin, hematologists: N.E. Chudinova, R.G. Degtyaryova) contributed to a fairly complete registration of leukemia cases, good verification of diagnoses and a timely medical assistance to patients. Of additional importance is the fact that hematological care has been provided both for exposed and unexposed residents of the four rayons in the Chelyabinsk Oblast which allows to compare some characteristics of leukemia in exposed and unexposed patients.

The largest proportion of leukemia (46%) among exposed residents of the Techa riverside was diagnosed in the period from 1970 through 1979 while for unexposed people the distribution of newly established leukemia cases was uniform: 5-7 cases per year. It was noted that a higher percentage of myeloid (48%) and chronic lymphatic (42%) leukemias, and a lower percentage of undifferentiated leukemias (10%) was registered among exposed patients as compared to unexposed patients of the same age groups (45%, 35% and 10%, respectively). All exposed patients diagnosed with acute myeloid leukemia and acute undifferentiated leukemia died within the first year of the establishment of diagnosis. Life expectancy for exposed patients with chronic myeloid leukemia was 4 years, the maximum being 13 years. In one case which was followed-up for a long period of time (patient K., systemic number 63 645, cumulative dose to red bone marrow = 1.6 Gy) the preliminary diagnosis of
chronic myeloleukemia was made based on the detection of Ph or Ph-like chromosome, despite absence of clinical manifestation of the disease.

ANALYSIS OF SOME RISK FACTORS AMONG TECHA RIVER COHORT WOMEN WITH BREAST CANCER
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Breast cancer is known to be a hormone dependent cancer. On the other hand, it has been established that radiation exposure is an external environmental factor contributing to the increase of breast cancer among women atomic bomb survivors, as well as among women of Massachusetts and Nova Scotia tuberculosis fluoroscopy studies and Rochester series of post-partum mastitis patients. That’s why we have decided to carry out a study aimed at analysis of breast cancer cases among women exposed to radiation in the Techa riverside settlements, Southern Urals. The source of radiation exposure was releases of radioactive wastes by the Mayak Industrial Association into the Techa river during 1949 - 1956. The number of exposed women in the Techa River Cohort is 17,798. The radiation exposure dose to the soft tissues, including breast tissue, was conditioned by external irradiation from the river and internal irradiation due to Cs-137 incorporation. Dose to the soft tissues ranged from 0 up to 1.177 Gy, with mean dose 0.085 Gy. The cancer register of the Urals Research Center for Radiation Medicine (URCRM) contains 79 records of breast cancer cases which were registered over the period 1950-1996 and occurred among women exposed at the Techa riverside villages in Chelyabinsk and Kurgan Regions.

In the previous study of breast cancer cases performed using cohort approach, the excess relative risk (ERR) of breast cancer at exposure of 1 Gy was assessed, the ERR value is equal to 0.40 (95% confidence intervals: -0.50; 2.13, p=0.48). Also it was shown that age at the beginning of exposure is a modifier of exposure, and those who were under 10 at start of exposure have the highest risk compare to other age at exposure groups.

To study some radiation and non-radiation risk factors among 79 breast cancer cases, "case-control" approach and logistic regression models have been used. For each breast cancer case five controls were picked out from exposed women of the Techa River Cohort who have not developed breast cancer. Criteria of control selection were the follows: period (year of birth in the same 5-year period as the corresponding case); ethnicity; arrival on the Techa (before and after 1952); and also attained age (alive and not lost to follow-up at the age of diagnosis of the corresponding case). The following factors were taking into account as risk factors of nonradiation nature: a) menstrual function (age at menarche and age at menopause); b) age at first full-term pregnancy; c) number of labors; d) family history in relation to cancer in next-of-kin, including breast cancer cases; e) presence of benign neoplasms of breast. Dose accumulated in the soft tissues at the year of diagnosis or death from breast cancer considered to be radiation risk factor.
CHILDHOOD THYROID CANCER EPIDEMIOLOGY IN CHELYABINSK OBLAST
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The study was aimed at a retrospective analysis of surgical treatment for thyroid cancer (RC) in 93 children aged 4-17 years, in the period from 1976 through 1998. Of that number 24 were boys and 69 girls. Lents-Bauer index was 1:2.9.

Age composition was as follows: 3 children aged 3-7 years (pre-school age), 12 children aged 8-11 years (early school-age), 78 children aged 12-17 years (senior schoolchildren). In 15 cases (16.1%) children were hospitalized a year or later after the neoplasm in the thyroid had been detected.

Only in 54 cases (58%) hospital admission can be considered as timely, i.e. at stages I and IA of the disease. Reginal metastases were revealed in 36 children (38.7%), of which boys made up 33.3% and girls 66.7% (ratio 1:2). The most common cancer types were: papillary - 83.9%, follicular - 11.8%, medullar - 3.2%, non-differentiated cancer - 1.1%. In 77.4% of cases carcinoma developed in the otherwise intact thyroid tissue. At the time of the disease most of the children, 53.8%, were resident in the forest-steppe, and 26.9% in the steppe zones. Of this number 83.9% lived in towns of the Chelyabinsk Oblast at the time of the disease: 32.3% in Chelyabinsk, 8.6% in Magnitogorsk, 7.5% in Zlatoust, 35.5% in other towns. Rural residents made up 16.1%. Incidence calculated per 100 thousand child population in the Chelyabinsk Oblast was 0.1 in 1976; 0.7 in 1997. The incidence in Chelyabinsk city has been and still is high: 1.2 in 1976 and 1.3 in 1997.

RISK ESTIMATE WITH RESPECT TO MAGNETIC FIELD, IONIZING RADIATION, TRITIUM, BERILLIUM AND ANOTHER FACTORS FOR THERMONUCLEAR REACTOR ITER
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The ITER-personnel can undergo an effect of various ionizing and non-ionizing radiation: magnetic field, dc and quasi-dc one provided by the plasma currents and by the currents through magnetic coils, and the pulsed field provided by the plasma oscillations; high frequency and microwave radiation because of a leakage from the plasma heating equipment; laser radiation from the equipment for the plasma diagnostics; electrical and magnetic field of industrial frequency from a high voltage equipment; cyclotron radiation {microwave radiation at a frequency higher then 100 GHz) emerging from magneto- bremsstrahlung of separate electrons, metallic and carbonic dust and so on.

A non-specific effect on an alive organism is realized though the development of various non-specific reactions of the organism: stress, accommodation, activation. The recovery from the stress should provide the enrichment with an informational
flow. The curing effect is probably in this. However, at high intensity of an informational flow, i.e. at a high rate of the information transfer some fluctuations resulting in a stress after normal states emerge.

In according to publication of ICRP, the acceptable risk of death is adopted to be equal $100 \cdot 10^{-6}$ year$^{-1}$. More general idea and value is risk of illness. Risk of illness is much more risk of death. In this value it may be distinguish portion for magnetic field, ionizing radiation, berillium, tritium and another factors. In according to preliminary estimates, the risk of illness from magnetic field is about $(2-4) \cdot 10000 \cdot 10^{-6}$ year$^{-1}$.m$^3$.$\mu$g$^{-1}$ (for content in air). Qn the basis of experimental biological data on the frequency of experimental biological data on the frequency of leukoses, mammary gland tumors, malignant tumors, total frequency of tumors the risk of developing newgrowths at chronical priming of rats with tritium oxide, HTO, was estimated. Estimating the risk of leukoses induction by three doses 6.4 Gy, 3.25 Gy and 1.63 Gy, the risk of tritium leukemia is equal $350 \cdot 10^{-6}$cGy$^{-1}$. When all the dose data are taken into account, it equals $555 \cdot 10^{-6}$ cGy$^{-1}$. The coworkers from the Institute of Biophysics have also estimated the risk of mammal gland tumor development, equal $1400 \cdot 10^{-6}$cGy$^{-1}$ for the whole range of doses and $1070 \cdot 10^{-6}$ cGy$^{-1}$ for the mentioned three doses. The malignant tumors of mammal glands are about 13% of the total amount of tumors in these organs. Hence, the risk of malignant tumor emergence in mammal glands under continuous tritium oxide, HTO, entry is estimated to be near $10^{-4}$ that is in a good agreement with the materials of United Nations Scientific Committee on the Effects of Atomic Radiation. Estimating the risk of death for rats after chronical tritium oxide incorporation from all the malignant tumors in the calculation by the mentioned three doses the value $725 \cdot 10^{-6}$ cGy$^{-1}$ was obtained. The whole studied range of doses is estimated as $930 \cdot 10^{-6}$cGy$^{-1}$. This important number, as we consider it to be, for the ITER safety is needed to be precised later on in order no country - ITER - Project participant - has doubts about the risk estimate for the personnel and population.

**THYROID CANCER EPIDEMIOLOGY IN CHELYABINSK OBLAST**

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The study involved a retrospective analysis of the results of surgical operations on 3 671 patients with thyroid cancer (TC) over the period 1969 through 1998. The incidence of TC was observed to have been increasing steadily. Thus, it was estimated to be 0.49 in 1969, 3.49 in 1985, and 5.60 in 1995, per 100 000 population. The incidence estimated per 100 000 child population was 0.1 in 1976, and 0.7 in 1997. TC incidence among adults and children resident in Chelyabinsk city has been and still is high: 1.2 in 1976, 1.3 in 1997.

Incidence rate was found to be different for different geographical zones. In the wooded-steppe zone (slightly endemic for goiter) the rate is higher than in the mountainous-steppe zone (the zone of medium endemicity) and in the steppe zone (to-
tally unendemic). A high rate of the disease was registered in large industrial cities (Chelyabinsk, Magnitogorsk, Zlatoust): over 60%. For rural residents the rate is 11%. It has been noted that the incidence of TC increases with decreasing rate of endemic goiter.

For the Chelyabinsk Oblast, as a whole, the rates for women are significantly higher than those for men (ratio: 11.7:1). The respective ratio for children and teenagers was 3.8:1.

The morphological types of thyroid tumors registered in different geographical zones were noted to differ but slightly. Papillary carcinoma was found to be the prevalent type (74.4%).

In 72.6% of cases cancer developed in an otherwise intact thyroid tissue, and only in 27.4% it was combined with a pathological condition other than cancer.

No increase in the incidence of TC was observed among the residents of the East-Urals Radioactive Trace (EURT) and in the Techa riverside villages.

**FEDERAL PROGRAM ON SOCIAL AND MEDICAL REHABILITATION OF THE ALTAI REGION POPULATION EXPOSED TO RADIOACTIVE Fallout FROM NUCLEAR TESTS AT THE SEMIPALATINSK TEST SITE**

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The Altai Region is situated in the north-west of the Semipalatinsk Test Site (STS) where atmospheric nuclear tests were conducted from 1949 to 1962. Weather conditions in this region resulted in most radioactive products being transported towards Altai Region. The residents were unaware of the possible impact of the nuclear tests at the STS, no protection and rehabilitation measures were taken. The greatest contribution to population doses arised from the first nuclear test of August 29, 1949. As a result of fallout from this test, effective doses in certain settlements of Altai Region exceeded 1 Sv.

The social and rehabilitation measures aimed at maximum reduction of probable negative health effects of STS and compensation for the detriment are implemented within the scope of STS / Altai Federal Program. They were based on the exposure dose depending on which the population is divided into 2 categories: 1) individuals exposed to a total effective dose greater than 25 cSv as well as their children and grand-children; 2) individuals exposed to effective dose greater than 5 cSv but less 25 cSv as well as their children and grand-children. According to the concept all individuals assigned to the categories have been subject to medical follow-up and rehabilitation.

The new scientific approaches for planning optimal and direct measures on social, medical protection and rehabilitation are currently under development and proceed from a principal possibility of a reliable projection of effects of exposure and their prevention so as to preserve the health of the population of exposed territories.
HEALTH EFFECTS FROM THE NUCLEAR TESTS AT SEMIPALATINSK TEST SITE IN THE ALTAI REGION
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Background

The population in the Altai region was exposed to radiation from nuclear weapon tests at the Semipalatinsk test site. Major contributions of the overall exposure derived from the first test in August 1949.

Objective

The objective is to evaluate the possible health effects of the radiation exposure due to the nuclear tests. Of main interest are malignancies, their occurrence in time and in relation to radiation exposure.

Materials and Methods

Data were taken from the register at IRMEP, which started in 1992 and retrospectively collects information on the health status of approximately 50,000 persons. More than 39,000 persons are included into the exposed group, and two control groups of almost 11,000 have been established. It is aimed to conduct a cohort analysis. Due to not yet complete data collection, a nested case-control study on stomach cancer is conducted among groups, for which the follow-up is completed.

Results

Preliminary results from the nested case-control study on stomach cancer indicate a dose-response relationship, whereas there are differences between age groups. Results will be presented in detail at the conference.

RECENT FINDINGS ON CANCER AND NONCANCER RISKS IN THE ATOMIC BOMB SURVIVORS
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I will review the results of recent analyses of mortality and incidence analyses in the atomic bomb survivors. This will include a discussion of our findings of an association between radiation exposure and the risk of mortality for various noncancer diseases and a brief outline of the results for an updated analysis of cancer incidence that extends the previous analyses with seven additional years of follow-up. The noncancer risks are relatively small (rates are increased by about 10\% at doses of 1 Sv) and the shape of the response function for doses less than 0.5 Sv it unclear. However, because noncancer diseases account for about 75\% of all deaths, the lifetime excess risk of noncancer mortality could be comparable to that for seen for solid cancers. The discussion of the cancer incidence results will outline the basic finds, discuss the
age-time patterns that are seen these data, and describe direct evidence for radiation effects in the low dose range (0.005 - 0.2 Sv).

THE EFFECTS OF RADIATION EXPOSURE IN THYROID TUMORIGENESIS
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External radiation exposure during childhood is the major known cause of thyroid cancer. Studies of survivors of the atomic bombings in Hiroshima and Nagasaki, as well as populations receiving radiotherapy for benign or malignant diseases have been the major source of information about radiation-associated thyroid cancer. These studies have demonstrated that: exposure to x-ray or gamma radiation at doses as low as 0.1 Gy can increase thyroid cancer risk; there is a strong trend for risk to decrease with increasing age at exposure; the elevated risk continues for at least forty years after exposure, and that the risk was not significantly elevated following adult exposure. Benign thyroid tumors and other benign thyroid diseases also have been linked to external radiation in epidemiologic investigations. The role of $^{131}$I in the development of thyroid tumors is much less well understood. Most epidemiologic studies in which individual $^{131}$I organ dose estimates are available are of adult patients who have received either relatively low diagnostic or extremely high therapeutic doses of $^{131}$I. From these studies, there is little evidence of a dose response, however, based on small numbers of cases increased risks have been reported following $^{131}$I treatment for hyperthyroidism. These findings need further confirmation and the effect of hyperthyroidism itself as opposed to the $^{131}$I treatment still needs to be resolved. Over the last few years, a sharp increase in the incidence of thyroid cancer has been reported among children exposed to radionuclides from the Chernobyl accident. Recent studies of children living in the vicinity of Chernobyl at the time of the accident suggest a dose-response relation between childhood thyroid cancer and estimated radiiodine exposure to the thyroid. The post-Chernobyl thyroid cancers appear to have certain unique features: a large number of them are an unusual histologic variant of papillary carcinoma; the cancers are more aggressive than usually observed, and they have a high frequency of the ret/PTC oncogene. New data are needed to improve our understanding of $^{131}$I.

THYROID DISEASE PREVALENCE AND FALLOUT EXPOSURE IN KAZAKSTAN
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This report describes a field study of thyroid cancer and thyroid nodule prevalence among village residents in northeastern Kazakhstan, exposed as children to radioactive fallout from nuclear weapons test explosions at the Semipalatinsk Test Site (STS) (1949-1962). From studies of A-bomb survivors and medically-exposed populations, the health effects of ionizing radiation are fairly well quantified, but effects of fallout exposure are less well understood. Childhood exposure to ionizing radiation is known to be a risk factor for subsequent thyroid cancer, and presence of thyroid nodules is a marker for such exposure. Both conditions are usually indolent and likely to be long undetected in the absence of special diagnostic efforts. Thus, thyroid disease prevalence was an appropriate subject for an initial investigation of this potentially informative population.

A team of 15 Kazakstani and 10 US investigators screened 3000 residents of 8 villages near the STS during August, 1998, using equipment and supplies previously air freighted to Semipalatinsk. Subjects were current residents 20 years of age or younger at the times of the major fallout events (in 1949, 1951, 1953, and 1956), who had either been present then or who had migrated from relatively unaffected areas after 1962. Selection of villages was based on accessibility and on reconstructed gamma-ray doses calculated by Russian and Kazakstani scientists. Screening was by ultrasound thyroid scan for nodules and fine-needle aspiration biopsy of suspicious nodules, with malignancy determined by cytopathology. Finger-stick blood samples were collected on absorbent paper and assayed later (in the U.S.) for level of thyroid stimulating hormone (TSH). Informed consent was obtained for study participation, biopsy, and phlebotomy.

Participation rates by potential subjects were high. Thyroid nodules, ranging from 0.2 to 8 cm in diameter, were detected in 896 participants of whom 484 were recommended for biopsy. Thirty-one malignant thyroid tumors (30 papillary and 1 other) were found in 28 participants (3 male and 25 female). Prevalence of nodules and of malignant tumors were significantly related to estimated gamma-ray dose (used here as an index of total fallout dose from all sources), whereas TSH level was not.

This study demonstrated the feasibility of a collaborative epidemiological study of radiation-related health risk in the population near the STS, and obtained direct evidence of an association between thyroid disease risk and fallout exposure.
THE PROMISE OF MOLECULAR EPIDEMIOLOGY IN DEFINING THE ASSOCIATION BETWEEN RADIATION AND CANCER
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Molecular epidemiology involves the inclusion in epidemiologic studies of biologic measurements made at a genetic and molecular level, and aims to improve the current knowledge of disease etiology and risk. One of the goals of molecular epidemiology studies of cancer is to determine the role of environmental and genetic factors in initiation and progression of malignancies and to use this knowledge to develop preventive strategies. While promising extraordinary opportunities for revolutionizing the practice of medicine and reducing risk, this approach will need to address and resolve many challenges, such as ensuring the reliability of interpretation of molecular testing and resolving associated ethical, legal, and social issues. Traditional epidemiologic approaches determined that exposure to ionizing radiation poses significantly increased risk of leukemia and several types of cancer. Such studies provided the basis for setting exposure standards to protect the public and the workforce from potentially adverse effects of ionizing radiation. These standards were set by using modeling approaches to extrapolate from the biological effects observed in high-dose radiation studies to predicted, but mostly unmeasurable, effects at low radiation doses.

It is anticipated that the addition of the molecular parameters to the population-based studies will allow determination of real rather than calculated risks. While such studies on radiogenic cancers are limited to only a few, currently considered candidate genes, the exponential growth of scientific knowledge promises great expansion of such studies in the near future. An overview of the type of genetic and molecular approaches of potential importance to such studies will be presented.

MOLECULAR-GENETIC APPROACHES IN HUMAN CANCER EPIDEMIOLOGY
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Cancer is a disease of cell genome and three group of genes play a key role in conversion of normal cells to malignant ones (protooncogenes, gene-suppressors of tumor growth and gene-regulators of cell cycle). Mutations in these genes or changes in their functional activity have been described in most of the tumors. The most im-
important peculiarity of the tumors is their molecular-genetic specificity, so each tumor possess its own scenario of tumor development and progression and this rules are typical for each group of enumerated genes. Thus tumors of the same histological types being monoclonal may distinguished in the functioning and structure of genetic elements that involve in control of cell proliferation. But irrespective of genetic pathways the final consequence was one and the same - uncontrolled proliferation of certain cell types.

Group of genes has been described modification of which were frequently found in different types of tumors (mutations in gene suppressor p53, activation of protooncogenes myc and ras), only in specific tumor types (mutations in genes BRCA1 and BRCA2 in ovarian and breast tumors), only in specific histological type of tumor (mutations in protooncogene ret in thyroid tumors), at different stages of tumor progression (activation of protooncogene myc in neuroblastomas). These only few examples really shows that wide spectra of molecular biology techniques have been developed that allow to identify point mutations and to control level of expression of certain genes in tumor tissue that may be important for tumor progression. These data can be used for early diagnosis, characteristic of disease stage and its prognosis. These approaches are widely utilized for the analysis of familiar hereditary cancers.

During last few years new technique of loss of heterozygocity (LOH) detection by amplification of microsatellites repeats are wide-spreeded. This approach permit to detect deletions in different regions of chromosomes and in addition to assume presence of putative violations in the DNA reparation system. The last ones may be the reason of the appearance of secondary mutations that are necessary for manifestation of complete oncogenicity of the cells. Lot of data have been published that allow to conclude that abovementioned principles concerning the role of point mutations and gene activation in tumor progression are similar for the deletion mutations also. This approach open a possibility to detect in human genome many sequences that may represent new tumor-suppressor genes. The origin and function of these sequences will be identified in near future.

The techniques that were described above can be used only on verified biological materials. It must be tumor samples that need to be microdissected for the isolation of pure population of tumor cells. In the case of so called professional cancers the important step is to select cohorts of corresponding patients and control of level of possible carcinogenic action. The most serious is the problem with the patients that were irradiated due to the two main reasons: absence of statistically verified data concerning the association of the frequency of tumor appearance and radiation (excluding thyroid cancer and some leucosis) and difficulties with the precise detection of radiation doses.

**GENOMIC INSTABILITY INDUCED BY LOW DOSE RADIATION**

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Purpose: To study the cell manifestation of genomic instability in the surviving progeny of irradiated cells cultured for 30 generations after low dose of gamma rays and after exposure in 10-km Chernobyl zone (chronic irradiation, summary dose ~ 0.1 Gy) have been studied.

Results: It was shown that in more than 20 generations after exposure in cultured cells nonlethal (sister chromatid exchanges - SCEs) and lethal (giant cells, cells with micronuclei) damage arise de novo. Also, in the descendants of irradiated cells radiosensitivity was increased and a lack of the adaptive response and appearance of the cells with high frequency of SCEs was registered. Potentially lethal damage recovery was found to lead to a decrease of MN formation in the progeny of irradiated cells.

Conclusions: It can be supposed that these disturbancies are the manifestations of genomic instability which were observed in the progeny of irradiated cells for more than 20 cell cycles after low dose irradiation with low level of DNA damage. The results permit to suggest that the specificity of the action of low dose radiation is the appearance of the effects in the late descendants of irradiated cells. The type of damage and mechanism of genomic instability induction are discussed.

ESTABLISHMENT OF RUSSIAN HUMAN RADIObIOLOGY TISSUE REPOSITORY

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Russian Human Radiobiology Tissue Repository is established at FIB-1 on the basis of archived tissue materials collected at autopsies of Mayak PA workers deceased in 1960s-1980s. The primary task of the Repository is preservation and cataloguing of unique radiobiology human tissues for the purpose of conducting studies utilizing modern techniques in molecular biology, cytogenetics, microdosimetry etc. Tissue materials at the Repository are represented by formalin-fixed soft and bone tissue samples, paraffin blocks as well as histology slides for about 600 repository registrants. So far inventory and characterization of tissue materials from 200 individuals has been carried out; in each case occupational history, dosimetric characteristics and detailed medical information including definition of diseases and causes of death according to ICD-9 are available. Practically all registrants were hired at Mayak PA during early period of its start-up and adjustment. 89% of them were employed at radiochemical plant or plutonium production plant, 11% - at industrial reactor sites. Values of accumulated external exposure dose exceeded 100cGy for 79% of registrants. Plutonium body burden was monitored for 77% of registrants, and in two thirds of the cases radionuclide body burden exceeded 1.5 kBq.

Ad hoc morphological examination ascertained adequate preservation of histological structures in tissues stored. Lung samples of 23 cases are being successfully utilized in joint U.S.-Russian studies to solve live issues related to plutonium micro-
dosimetry (formalin-fixed tissue samples) and to analysis of carcinogenesis mechanisms (paraffin blocks).

**ACTIVITY OF DROSOPHILA MELANOGASTER TRANSPOSSABLE ELEMENTS AFTER CHRONIC GAMMA IRRADIATION**

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The mobile genetic elements have an ability to increase the transposition rate in response to environmental stresses. This leads to genetic instability, which can appear in *Drosophila melanogaster* as hybrid dysgenesis syndrome.

The laboratory stocks of *Drosophila melanogaster* were chronically irradiated with $^{226}$Ra by dose rate of 0.17 sGy/h during whole life history. The dose rate per one generation of *Drosophila* was 60-80 sGy. It have been studied the rates of recessive lethal mutations and stock characteristics in P-M and H-E systems of hybrid dysgenesis: the rate of hybrid dysgenesis sterility induction and the frequency of activation of P and *hobo* defective copies in stocks with genetic markers sn$^w$ and h(w$^+$).

It is shown that the rates of recessive lethal mutations in *Drosophila melanogaster* irradiated stocks are not affected by chronic irradiation. While the characteristics of irradiated stocks in hybrid dysgenesis systems are affected. In P-M hybrid dysgenesis system the rate of dysgenic sterility and the frequency of sn$^w$ mutations increase after irradiation. In H-E hybrid dysgenesis system we observe an increase of dysgenic sterility and h(w$^+$) transposition rates as well as decrease of these characteristics in distinguish stocks.

**HEAT SHOCK RESPONSE AND ADAPTATION TO ADVERSE CONDITIONS**

M. Evgenev, O. Zatsepina, V. Molodtsov

All organisms, plants and animals, react to exposure to supra-optimal temperatures by inducing the synthesis of a group of proteins known as heat shock or stress proteins (hsp). The expression of hsp is the most convincing evidence of reaction of living organisms and cells on adverse changes of an environment and on a great variety of xenobiotic and biogenic factors. The synthesis of the most important inducible stress protein (in animals), hsp70, was marked in all known organisms. The modulation of the Hsp70 level in tissues and cells is observed in a course of various diseases, distrophy, Alzheimer's disease, breast cancer, trauma, cyrosis, intoxication and many other factors. Therefore the level of hsp is an important physiological indicator of the cellular response to certain injuring factors. Our investigation on various model organisms (such as different species of Leishmania, silk worms, Drosophila, lizards and mammals including humans) has demonstrated that all thermotolerant forms exhibit high constitutive level of hsp in their cells under normal physiological condi-
tions. Moreover desert forms are characterized by a peculiar interaction between HSF (heat shock transcription factor) which serves as a positive regulator and Ku-autoantigene which is probably negative regulator (CHBF) of the heat shock system. Our investigation of the heat shock response in ecologically different human population have shown that fibroblasts isolated from Turkmens (desert tribe) are able to synthesize hsp and other cellular proteins after severe heat shock while only trace synthesis of hsp was observed in the cells of a control group (Russians) after such a treatment. Besides, broad scale analysis of human populations has revealed significant individual polymorphism in terms of both constitutive synthesis of hsp70 and level of induction of hsps. Basing on the results of our extensive studies of heat shock response in various animal populations a model explaining the evolution of heat shock system in the desert animals is forwarded.

ГЕНЕТИЧЕСКИЕ ЭФФЕКТЫ ОБЛУЧЕНИЯ ЧЕЛОВЕКА.
ЭФФЕКТЫ ОБЛУЧЕНИЯ ЭМБРИОНА И ПЛОДА

RADIATION-INDUCED GERMLINE MUTATION
AT MINISATELLITE LOCKI
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Minisatellite loci provide the only currently available system for the efficient monitoring of germline mutation in humans and are capable in principle of detecting induced mutations in relatively small population samples. Previous studies have shown that acute doses of ionising radiation cause a significant increase in minisatellite mutation rate in experimentally irradiated mice. Minisatellite mutations were scored in the progeny CBA/H mice after acute paternal exposure to x-rays and chronic paternal exposure to gamma-irradiation and fission neutrons.

Our data suggest that mutation induction is only attributable to the spermatogonia stage of spermatogenesis, providing evidence for meiotic origin of minisatellite germline mutation in mice. For acute and chronic gamma-exposure the frequency of mutations increased linearly with radiation dosage from 0.5 Gy to 1 Gy, with a doubling dose of 0.33 Gy. At the same time, the fission neutrons are more effective than acute X-irradiation for the induction of minisatellite mutation. Finally, our results show that, in sharp contrast to previously used genetic systems, elevated germline mutation rates at minisatellite loci in mice can be detected in very small population samples and at relatively low radiation doses.

The frequency of minisatellite mutation was also studied among inhabiting rural areas of the Mogilev district of Belarus, which were heavily contaminated with radionuclides after the Chernobyl accident. The data showed a two-fold higher muta-
tion rate in exposed families compared with non-irradiated families from the United Kingdom. Within the Belarus cohort, mutation rate was significantly greater in families with higher parental radiation dose estimated for chronic external and internal exposure to caesium-137, consistent with radiation induction of germline mutation. The potential use of minisatellites in monitoring germline mutation in humans will be discussed.

**INTRA UTERINE EXPOSURE TO DIAGNOSTIC X-RAY AND RISK OF CHILDHOOD LEUKEMIA SUBTYPE**

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Leukemia is the most common malignancy among children. The incidence of childhood leukemia peaks at two to four years of age. Prenatal exposure to ionizing radiation has been associated with an increased risk for childhood leukemia, but the issue has been debated.

The aim of this study was to investigate the association between prenatal exposure to diagnostic x-ray (for different type of x-rays and x-ray during different parts of pregnancy) and the subsequent risk for childhood lymphatic and myeloid leukemia, in a population based setting. Cases in the study were all children born in Sweden and diagnosed with leukemia between 1973-1989 (578 with lymphatic leukemia and 74 with myeloid leukemia). An age and sex-matched control was randomly selected to each case. Children with Down’s syndrome were excluded. Exposure data was blindly extracted with regard to case or control status, from medical records. A total of 118 of the children with lymphatic leukemia and 111 of the controls were exposed to x-ray before birth, OR=1.08 (95% CI 0.82-1.44). Twenty of the children with myeloid leukemia and 12 of the matched controls were exposed to x-ray, OR=1.89 (95% CI of 0.84-4.24). Pelvimetry, but no other kinds of x-rays, was associated with a two-folded increase in risk for myeloid leukemia OR=1.98 (95% CI 0.67-5.81). After adjustments for confounding the risk estimate for myeloid leukemia, but not for lymphatic leukemia, increased even further, OR=6.42 (95% CI 0.89-46.20).

We conclude that the risk of lymphatic leukemia in children was not affected by x-ray performed in pregnancy during 1970’s and 1980’s in Sweden. However, there are indications of an association between myeloid leukemia and prenatal exposure of x-ray, but the attributable fraction is small.
DOSE-EFFECT AND FORMATION OF GENETIC ADAPTATION IN A SERIES OF SMALL MAMMAL GENERATIONS UNDER CHRONIC LOW-DOSE IRRADIATION
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Regularities of mutation process dynamics were studied for the first time in series of 1–22 small mammal generations (European bank vole – Clethrionomys glareolus, Schreber) under chronic low-intensity irradiation of natural populations. A significant rise in the frequency of different-type mutations (chromosome aberrations and polyploidy) in somatic cells as well as embryonal lethality within an alternation of no less than 12–22 animal generations was shown at reduced levels of radiation load that indicates higher genome radiosensitivity of somatic and germ cells of every subsequent animal generation as against the preceding generations and can be caused by accumulation of genetic load in chronically irradiated populations. The recorded effects were shown to be caused by low radiation doses (0,02–7,3 cGy at the absorbed dose rate 2–730 μGy/day). The form of dose-effect relationship for cytogenetic injuries in a series of chronically irradiated animal generations is better described by nonlinear functions. Higher radioresistance of the 21st–22nd irradiated animal generations revealed at additional acute gamma-irradiation (100–400 cGy) is indicative of genetic radioadaptation formation. Functioning of the repair system “adaptive response” was also revealed. So, the recorded mutagenesis levels in chronically irradiated populations after alternation of more than 20 animal generations result from proceedings oppositely directed processes – accumulation of mutations reducing adaptive capacity of individuals (genetic load) and formation of genetic radioadaptation. For lack of the latter, the recorded frequencies of cytogenetic injuries could be considerably higher by the 22nd animal generation.

INFLUENCE OF CHRONIC IRRADIATION IN LOW DOSES ON GENETIC STRUCTURES OF MICE
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The effect of chronic low-level gamma-radiation on genetic structures of mice on molecular and cell level was studied.

Chronic irradiation of CBA/lac male-mice was performed using the irradiation unit UOG-1 with a cesium-137 radiation source (dose rate was 30 μGy/hr). Animals
were irradiated during 20, 40 and 80 days up to total dose 1,44, 2,88 and 5,76 cGy accordingly.

For evaluation of genome damages of cells the following parameters were chosen: level of DNA-protein cross-links (DPC) in cells of thymus gland and lien, yield of abnormal sperm heads (ASH), micronuclei rate in normochrome erythrocytes (NCE) of peripheral blood of mice.

The results of the experiment testify to nonlinearity of dependence of formation DPC on dose (radiation time). The reliable increasing of DPC level on 20-th and 40-th days and recovery to control values by 80-th day of experiment was marked. Dynamics of changes DPC level in cells of thymus gland and liens is characterised by uniformity of type of a response on irradiation.

The cytogenetic investigations have shown, that the reliable increasing of ASH by 80-th day of irradiation was marked. Reliable changes of micronuclei rate of NCE was not registered during all the experiment.

Therefore for evaluation of genetic effects of a chronic radiation exposure in small doses by most adequate is the assessment of ASH. Use of DPC level as a biomarker is perspective, however, needs further investigations.

GENETIC CONSEQUENCES OF LOW DOZES IRRADIATION
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Researches of genetic consequences of irradiation in zone of Chernobyl Accident, executed by us on different objects, have revealed essential increase of levels of genetic variability. Significant elevation of levels of chromosomal aberrations, point mutations in humans, rodents, drosophila and plants very difficulty to explain by direct action of ionising radiation on genetic material.

In experiments on Drosophila melanogaster was revealed, that low dozes of irradiation (the saved doze was 0.7 Gy for generation) leads to significant increase of levels of genomic instability. Shown, that extent of alteration depends on genotype and epigenotype. Study of mechanisms of life span of chronic irradiated in low dozes mutant and wild stocks of Drosophila melanogaster has revealed the possible participation in regulation of radio-induced life span alteration the processes of apoptosis.

Executed researches have shown the ambiguity of phenotypic reaction of organisms on low dozes of chronic irradiation. Suggested, that influence of low dozes irradiation (including near the environmental) leads to destabilisation of genotype caused by induced transposing activity of mobile genetic elements.
THE FORECASTING OF DISTANT EFFECTS OF POPULATION'S EXPOSURE TO IRRADIATION: THE COMPUTATIONAL MODEL

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Making decision about actions in case of large-scale accident at a radiation dangerous object is usually based on estimation of expected effects which people directly exposed to irradiation can have. For the following generations possible distant effects are not taken into consideration, yet genetic effects are included into definition of non-stochastic effects. It happens because of difficulties in determination of risk coefficient of development men's unfavorable effects. Preliminary studies have showed that exposure to irradiation causes diminishing of amount of people who could reach the reproduction age. Decrease of this amount on 1-1.5% makes the population of extended reproduction go to population of limited reproduction. The creation of social conditions, leading to the increase of birth-rate and following corresponding amount increase of people who reach the reproduction age, could be the compensation of this damage. For the forecasting of the population size dynamics depending on damage compensation strategy the computational model is elaborated. By this program, depending on conditions of exposure to irradiation, possible variants of the demographic situation development in different, including small (about 300 persons) population size are modeled. The present program is possible to be used for appraisal and forecasting of distant effects of the Ural area population's exposure to irradiation.

POPULATION DYNAMICS AND INDECES OF SPECIES RADIOSENSITIVITY IN WOODLICE (CRUSTACEA, ISOPODA) UNDER CHRONIC IONIZING RADIATION

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Among soil invertebrates can be defined systematic groups, who’s life cycle give us a chance to reveal changes appearing in populations under radiation exposure. In nature such animals have the most close contact with contamination; some species accumulate metals in including radionuclides; large values LD\textsubscript{50/30} for adult individuals combine with high radiosensitivity of early ontogenetic stages within species. All these conditions were carried out for terrestrial isopods (woodlice).

Experiments with acute and chronic exposure were carried out with woodlice from various climatic zones. Species LD\textsubscript{50/30} was fluctuated within limits of 300-500 Gr. In reproduction period under prolonged \(\gamma\)-irradiation (total dose was 13-14 rentgen) and after acute exposure (0.5-3 Gr) the number of generations and the reproduction time were changed, the larvae number and the life duration were decreased. The age structure in micropopulations was changed only under prolonged exposure. The intensity death coefficient per day (\(K_x\)) for woodlice confirm this circumstance. \(K_x\)
was decrease with age in control and after acute doses, and under prolonged exposure $K_x$ was increased with age. In contrast to woodlice, collected in clean areas, for animals from 30-km Chernobyl Accident Zone (in May 1986 the dose was about 200 mR/h for $\gamma$-exposure) $K_x$ was increased with age both in the control and under prolonged exposure. In Chernobyl Zone the disturbance of age structure and reproduction time in woodlice micropopulations kept during 3-5 years after the accident, which caused to the changes in species composition and in species domination structure.

THE IMPACT OF RADIOACTIVE EXPOSURE OF RESIDENTS OF EAST URALS RADIOACTIVE TRACE ZONE (SVERDLOVSK OBLAST) ON THEIR DESCENDANTS’ HEALTH STATE

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Health state of descendants is one of the important criteria proving the danger of long-term residence of population in the center of radioactive accident, particularly in cases when the information concerning radio-ecological situation and exposure doses is insufficient and not reliable. In the existing centers the levels of radioactive exposure are, as a rule, characterized not only by the doze, but by a complex effect of radiation together with other damaging factors of non-radiational nature. That is why determining the role and character of influence of radiation factor over the descendants' health state has to be based on system analysis approach and evaluation of wide range of risk factors.

The influence of residence of population in the EURT zone over the health state of their children and grandchildren, was studied. The place of residence of ancestors during the time period just after the accident was considered as a part of complex of factors including medico-biological anamnesis, life style, chemical pollution of environment. Differences in strength and character of the fact of ancestors' residence at the territories with various levels of contamination over their descendants' health indices, were determined. Residence of parents and/or grandparents at the EURT territories with the highest contamination level proves to be a factor increasing the probability of the inherited birth defects, high respiratory incidence and decreased development rate in their descendants. Residence of parents and/or grandparents at the periphery of EURT causes mostly the stimulating effect on the development rate and doesn't significantly influence the incidence of their descendants. It is possible to improve the health potential of descendants of radioactively exposed population under the conditions of satisfactory radioactive situation by minimizing non-radiation risks.
INBORN ANOMALIES IN THE POSTERITY OF PEOPLE THAT POPULATE AREAS TO NUCLEAR WEAPON-RELATED FACILITIES

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It is one of the most actual problems of radiological medicine and epidemiology to study physical development and health in posterity of people that populate areas to nuclear weapon-related facilities. Authors has chosen the inborn anomalies frequency as an index of physical development and health because this index is considered to be one of the most informative.

Eight (8) thousand newborns from the population of the town of Sarov during 1968 – 1974 were in study. In the result of the study the inborn anomalies frequency and their distribution among the organism systems were evaluated.

It was found out that the frequencies of such anomalies as hip inborn dislocation, atrezia of gastric-intestinal system organs, gemangioms exceeded reliably the corresponded indices from Russian and foreign authors.

The amount of children with the inborn anomalies in the cohort of parents, lived in the town of Sarov for a long time (more than 3 years), exceeded reliably those in the cohort of parents, lived in Sarov from 1 to 3 years.

Cause-and-effect relationship between inborn anomalies in newborns and different hazardous influences, radiation included, is discussed.

THE CLINICO-GENETIC APPLIQUES TO THE ESTIMATION OF VARIABILITY RADIATION ‘S CHANGES OF BEHAVIOUR

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On the basis of 10 years work experience we put forward 3 theses.

1. The combination of influences of the low doses of radiation and the psychological stress leads up to phasic changes of the clinical status of victims: there are the unification of the psychophysiological indexes during first years after radiation’s incident and there is a bifurcational apparitions 5 – 7 years later that.

2. The descendants of the victims of stress-influences have a high frequency of symptoms of the dysembriogenesis. In fact, children of the East-Ural Radiation Tract’s citizen show these symptoms more often then children off the Chernobyl NPP Accident Consequences Cleaning up Participants. The plan of the clinical inspection of children had been developed. It allows to reveal somatic symptoms of the disembriogenesis, the disorders of the metabolism. All of the children to the deviant behaviour including drugs-addicted behaviour.

3. The psychological portraits of people who have gone through different social-ecological stresses (the participants of the radiation’s accident and the participants of the local wars including Chechen war) are authenticly distinguished from
one another by the electrophysiological symptoms. It leads us to the idea of the presence of specific things in the psychological effects of low doses radiation.

From our point of view two mechanisms are to be considered as a patogenetic foundation of the described bifurcational processes: the modificational variability and activation of recessive genes.

GENETIC EFFECTS UNDER CHRONIC ACTION OF RADIATION ON PLANT AND ANIMAL POPULATIONS

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Genetic effects have been studied in natural populations of plants on the territory of the East Ural Radioactive Track (EURT) since 1960 and in populations of plants and animals in the zone of the accident at the Chernobyl nuclear power plant since 1986. The main lines of the genetic research in both cases were similar: 1) study of the mutation process intensity in irradiated plant and animal populations in a dose rate-dependent manner and analysis of the dose-effect relationship for different types of genetic disturbances (point mutations, chromosome aberrations in mitosis and meiosis, reciprocal translocations and so on); 2) study of the mutation process dynamics in chronically irradiated plant populations in generations; 3) analysis of micro-evolutionary processes in irradiated populations of plants.

The work presents the data on the observed dose-effect relationship under the action of radiation on populations of Arabidopsis thaliana, Pinus sylvestris and some other plant species. Analysis of the mutation process dynamics in eight Arabidopsis populations in the zone of the Chernobyl disaster shows that although the level of embryo lethal mutations in the irradiated populations decreases with time in significantly exceeds the control level within six years after the accident. An increase in the frequency of reciprocal translocations with an increase in the dose rate of chronic irradiation was observed in spermatocytes of mouse-like rodents inhabiting the contaminated areas. The frequency of heterozygotes for recessive lethal mutations in mice decreased like in Arabidopsis with the time after the accident. A number of phenomena characteristic of chronically exposed populations are discussed: increased radioresistance (radioadaptation), appearance of abnormal karyotypes and selective markers.
A high sensitivity of the embryo to radiation exposure was shown by the works of Japanese authors studying prenatal effects of exposure to A-bomb (M. Otake, H. Kato, Y. Yoshimoto), and British authors investigating the consequences of exposure to X-rays in pregnant women for diagnostic purposes.

Radiation conditions observed in the Techa riverside villages after discharges of radioactive wastes into the river entailed population exposures due to external radiation and incorporation of radionuclides. A certain part of the population, namely, persons born at the time of maximum releases were exposed both in the antenatal and postnatal periods. An analysis of gonadal doses for members of the original Techa cohort estimated to date, and of fetal doses, showed that significant doses were received in utero only by those born between 1950 and 1956. Fetal doses for these persons ranged from 0 to 334 mSv, average dose being 20.6 mSv. In all, 3 897 people were exposed in the antenatal period.

The goal of the study was to assess both the carcinogenic embryotoxic effects that were registered over the 43-year follow-up, and the level and structure of mortality for the same period. Infant mortality was noted to be extremely high. This is evidenced by the fact that in the period 1950 through 1956, 386 (10%) out of total 3 897 antenatally exposed children died at the age under 1 year. The main causes of death were: 1/ diseases of the respiratory organs, 97 cases; 2/ infectious diseases, 81 case; 3/ 83 cases of perinatal pathology (intauterine hypoxia, asphyxia neonatorum, birth trauma, congenital infections, hemolytic disease, etc.). In 13 cases death was caused by congenital developmental defects. Because of high migration rate is was impossible to track all individuals exposed in utero. It is known, however, that among those who continued to live in the catchment area there were 12 deaths from solid cancer and 3 deaths from leukemia.

It is envisaged to study the dependence of the above-indicated pathology on fetal doses, and assess intrauterine exposure risk using a cohort and case-control approach.

ON EVALUATION OF GENETIC EFFECTS OF RADIATION EXPOSURE

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Analysis of radiation-related genetic risk is most often limited to the assessment of frequency of mutations in germline cells. A quantitative assessment of muta-
tions and their dependence on exposure dose lay the basis for classical radiation genetics. Current assessments of genetic radiation risks are mainly based on the extrapolation of experimental data. At the same time, direct studies in the offspring of exposed people are hampered by a large number of modifying factors of biological, medical and social nature. There exist laboratory methods applied for registering mutations in man (e.g., in spermatozoa), on one hand, and methods for registering hereditary diseases, chromosomal and mendelian, on the other hand. In radiation genetics there is a growing interest to studies of multi-factor diseases because of their high prevalence and the opportunity to obtain statistically more significant assessment of genetic radiation risk.

The laboratory methods for direct assessment of mutations do not allow to determine the extent of health damage inflicted on the offspring of exposed people since the mutations registered in germline cells do not all give rise to known hereditary diseases and pathologic manifestations. There exist various genetic immunological and physiological mechanisms oriented at elimination of mutations, mutant germline cells, as well as zygotes and emryos that have developed out of such cells.

The risk of birth of children with hereditary diseases is determined not only by increased rate of mutations but, to a significant degree, by a reduced efficiency of mechanisms involved in elimination of anomalous biological substrates. On the other hand, the effect of ionizing radiation can not only increase the output of mutations but it may, possibly, change the probability of their being developed into clinical entities. The effect of radiation exposure on a woman’s body under different exposure conditions has not been adequately investigated. However, changes observed in an ageing female organism, e.g., accumulation of peroxidation products which is, presumably, conducive to birth of children with Down’s syndrome, may also be induced by radiation exposure.

Based on the foregoing, two important, in terms of practical use, conclusions can be made. 1) The current epidemiological methods for estimating the genetic risk in exposed populations should be improved taking into account the information on a comprehensive effect of exposure on the status of different body systems in exposed persons, especially in mothers. In reality, the situation when only germline cells are exposed is inconceivable. Equally improbable is the assumption that exposure of, e.g., secretary glands, does not affect reproductive processes and the definitive fate of mutant cells. 2) More attention should be paid to qualitative characteristics of pathological manifestations characterizing late exposure effects, such as the structure and spectrum of hereditary diseases occurring under specific exposure conditions, the degree of severity of these manifestations (expression), sex ratio, etc. A detailed analysis of the entire complex of physiological and pathological manifestations accompanying radiation exposure will allow to gain, with sufficient substantiation, an insight into the mechanisms governing the origin of genetic disorders in the offspring of exposed population.

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IMPLICATIONS OF BIOLOGICAL MARKERS OF IRRADIATION, EXPOSURE DOSE, AND RADIATION-INDUCED EFFECTS FOR RADIATION MEDICINE
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There seems to be little doubt nowadays about a particular role played by the specific characteristics of the organism in the causation of post-radiational alterations detected at different levels of the development of the living matter (molecule, cell, organ system, organism, population). As a matter of fact, the likelihood of the development of stochastic, and even deterministic, effects at doses close to the threshold testifies to a significant role of the organism’s individual properties in the occurrence of radiation-induced effects. Individual characteristics were found to be of special importance in chronic exposure at a low dose range to which living organisms had been adapting themselves during the long period of evolution.

A number of processes which determined the probability of the development of radiation-induced changes (radiosensitivity, repair, genomic stability, genetic susceptibility, etc.), and the most likely endogenous factors influencing them (immune response, capacity for adaptive response shown by different systems and the body as a whole, etc.), have been currently identified. However, the insufficiency of our knowledge about the mechanisms of radiosensitivity (including carcinogenic), and the difficulty to perform analysis and use its results in each specific case, make it expedient to identify biologic markers of both radiation exposure proper and medical-biological effects associated with it.

The knowledge of individual characteristics influencing the development of radiation-induced changes is of great importance for defining the requirements which could be met by biological markers. Thus, exposure dose biomarkers should show the least dependence on the organism’s individual characteristics, and an ultimate degree of dose dependence. At the same time, compared to exposure dose, the input of the organism’s individual distinctions is of crucial importance for both markers of susceptibility to disease (cancer, leukemia) and radiation-induced effects.

Undeniably, biomarkers can be of different relevance (indication of radiation exposure, exposure dose, radiation-induced effects and predisposition to them) and specificity. The advantage that biomarkers present for radiation medicine can be attributed to the fact that, in addition to exposure dose, they take into account different specific characteristics of the organism thereby giving the physician a unique opportunity to make use of a unified parameter “created” by the organism as a result of an elaborate in-vivo interaction of genetic, immunologic, neuro-endocrine, etc., factors.
The detection of biomarkers of diseases associated with exposure to ionizing radiation, and the predisposition to them (including genetic one), allows to identify individuals with highest susceptibility to cancer, leukemia and other radiation effects, and ensure their early diagnosis. Biomarkers of radiation exposure and doses of radiation (particularly, those stable in time) are highly important for retrospective exposure dose reconstruction. Persistent post-radiational alterations represent reliable markers of doses formed over a long period of time, and a cumulative effect of radiation exposure. It should be noted that the study of the mechanisms and biomarkers of radiation-induced alterations allows to form a notion of an exposed vs an affected individual. The latter issue is of immense social and economic significance for the Urals region with its dozens of thousands of exposed residents.

CORRELATION OF PATTERNS OF EXPRESSION OF GENES ENCODING PRO-APOPTOTIC PROTEINS AND CYTOKINES WITH INDIVIDUAL RADIATION DOSE TO BELARUSIANS EXPOSED DURING THE CHERNOBYL CATASTROPHE

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Ionizing radiation is well known to not only to induce DNA breaks, leading to cell death, but also to modulate nuclear transcription factors and cytoplasmic proteins that may lead to altered gene expression resulting in apoptosis. Cytokine genes are implemented in pathological and protective processes triggered by exposure to IR. Accordingly, of the many genes affected by IR are those influencing cell proliferation, differentiation and death. Here, we examined the relationship between individual reconstructed IR dose and patterns of expression of genes encoding pro-apoptotic proteins and cytokines. Expression profiles were determined in mononuclear cells from peripheral blood of healthy subjects and patients with acute lymphocytic leukemia, all of whom were residents of Belarus in 1986. Subjects were administered an extensive questionnaire that was used to reconstruct individual dose based upon response and over 1 million available measurements of physical materials. The technique of microarray hybridization was employed to examine the expression of 268 pro-apoptotic and cytokine genes. RNA was isolated, reverse transcribed and amplified with specific primers on human gene filters. Phosphorimaging analysis was performed to amplify signals from each of the 268 genes encoding pro-apoptotic factors and cytokines. The most frequent mRNAs detected were for IL-6 and its receptor, TGF-beta, and FAS and FAS ligand. Other commonly expressed genes included those for IL-5, TNF-alpha, TNF receptor Type I and Type II, TGF-beta receptor Type I and Gp130. No apparent difference could be determined for gene expression in healthy individuals and leukemia cases. When a selected group of the most common-
ly expressed cytokines was compared to individual IR dose, a strong correlation was observed between dose to the bone surface (range of 0.1 to 20.0 mSv) and the percent samples expressing these genes \((r =0.75, \ p<0.001)\). Strong correlations were also found between the expression of pro-apoptotic and cytokine genes and total dose and dose to the bone marrow. Our findings raise the possibility that patterns of cytokine gene expression may develop in response to low level radiation exposure. Microarray hybridization is a potentially powerful tool for radiation epidemiology studies.

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**BLOOD COUNT AT INCORPORATION OF LESS TRANSPORTABLE CONNECTIONS OF PLUTONIUM**

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As is known blood count is the indicator acute and chronic external exposure. The changes in the system of a hemopoiesis at hit in an organism of radionuclides are defined by character of its allocation in organism and doses on critical organs.

In the present operation the pattern of peripheral blood represented at incorporation less transportable of connections plutonium - 239. The analysis of dynamic peripheral blood for 380 workers of plutonium production is carried. The periods of observation consist in 24-38 years. The metrics of erythrocytes were stable during all period. The thrombocytes and leucocytes changed in limits of boundaries of physiological norm.

At an incorporation less transportable of connections plutonium the greatest absorbed dose is on lungs and tracheobronchial lymphoglandulas.

Is parsed dose dependence of the leukogram on a dose critical organ. At an absorbed dose on lung 0,4 - 1,0 Gy and on tracheobronchial lymphoglandulas 10,1 - 60,0 Gy the stable lymphocytopenia since the first two-three years of operation and up to the extremity of observation is detected. At doses of the lower indicate show character of changes lymphocytes is various: from moderate lymphocytosis at dose on lymphoglandulas and lung 0,1 - 1,0 Gy and 0,01 - 0,05 Gy accordingly up to the proof expressed lymphopenia (40 - 50 % from starting level). The pathogenic mechanisms of the detected dependence dose - response on lymphocytes of peripheral blood are considered.

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**IMPROVED DOSIMETRY AND RISK ASSESSMENT**

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FOR PLUTONIUM-INDUCED LUNG DISEASE USING A MICRODOSIMETRIC APPROACH
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The risk of developing radiation-induced lung cancer is currently based on data from populations exposed either to relatively uniform, low-LET radiation, or from uranium miners exposed to radon and its progeny. Because inhaled alpha-emitting radionuclides (e.g., Pu, Am) produce nonuniform, chronic irradiation of the parenchymal region of the lung, a better scientific basis is needed for assessing the risk of developing radiation-induced disease from these radionuclides.

Scientists at FIB-1 and LRRI are collaborating in studying a population of workers from the Mayak Production Association, many who inhaled significant quantities of Pu and other alpha-emitting radionuclides during their careers. Fixed lung tissue samples are being used to determine the spatial distribution of Pu in human lung tissue with respect to specific lung structures, and to determine the effect of chronic tobacco-smoke exposure on the distribution of local Pu radiation dose.

Our initial results have shown that Pu particles were most often found associated with parenchymal and nonparenchymal scars, with other particles being found in organized lymphoid tissue or in the interstitium of the pulmonary parenchyma (respiratory bronchioles and alveolar region), and that there was an increased fraction of Pu particles associated with tissue scars in a smoker vs a nonsmoker. These preliminary results support the hypothesis that Pu particles are nonuniformly distributed in the parenchymal regions of the lung.

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ISOFERMENTS OF SERUM ALKALINE PHOSPHATASE (ALP) AS THE INDICATOR OF PLUTONIUM INCORPORATION
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Serum ALP has heterogeneous composition, its separate forms (isoferments) have expressed organ specificity. At normal and pathological condition usually distinguish the following isoferments: liver (normal and pathological), bone, intestinal, placental and with placental mobility. Therefore given research was used for medical supervision over the personnel of Prod. Assoc. “MAYAK”.

At the workers of plutonium production in comparison with the control the bone isoferment was discovered more frequently, thus was observed certain dose de-
pendence. However activity bone ALP in these cases was small, close that is observed in norm. In case of development of sarcoma (ossificationic) the expressed increase of serum bone ALP (at 5-10 of time) was marked.

The activity of liver normal isoferment at small incorporation of plutonium was close to the control, and at high plutonium incorporation - is increased in 2 times. At highest plutonium incorporation (> 90 kBq) frequently it was found out supplemental liver isoferment, having faster electrophoretic mobility - liver pathological ALP.

Intestinal ALP, meeting in norm only in 20 % of cases, at plutonium incorporation was manifested a little less often. Serum ALP with placental electrophoretic mobility , absent in norm, was revealed only at plutonium incorporation more than 15 kBq - in 16 % of cases.

The mechanisms of observable shifts, physiological importance and opportunities of their diagnostic use are discussed

COMBINATION OF THE ACTINIDE ANALYSIS DATA OF TWO HUMAN TISSUE ANALYSIS PROGRAMS: TRIUMPHS AND PROBLEMS
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The United States Transuranium and Uranium Registries (USTUR) and the Dosimetry Registry of the Mayak Industrial Association (DRMIA) are the two primary human tissue analytical programs known to the world. Each Registry has collected actinide element exposure information and analytical data from tissues collected at autopsy of occupationally-exposed workers in plutonium and uranium processing facilities. The two Registries have been collaborating to combine their data into a joint database for use in the study of uptake, retention, translocation, and excretion of actinide elements in humans. During the four-year collaborative research project, a number of similarities and differences in the methods used to collect the data were found. This report contains a discussion of the similarities and some of the major differences.

The methods for analyzing tissue samples used by the two Registries were quite different in the past; however, a series of sample exchanges with comparisons of the analytical results has shown the results to be in close agreement. One parameter used by both Registries that was not in agreement was the “residence time”, the time between exposure, or probable exposure, of a worker to the actinides and the death of the individual. Another difference between the Registries involved the methods used in calculation of skeletal actinide content on the basis of a limited number of bone samples collected at autopsy. An explanation of these differences with an evalu-
ation of their impacts, along with potential solutions will be presented. These differences, discovered during the collaborative project, did not preclude the use of the data, either separately or combined, to characterize the biokinetics of actinide elements in the human body.

**STATUS OF HEMOPOIETIC STEM CELL POOL IN CHRONIC GAMMA-IRRADIATION OF MICE**
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The focus of the study was on an analysis of the results of an experiment involving gamma-irradiation of CBA line mice for 270 days at the dose rate of 0.16 Gy/day until the total dose of 43.2 Gy had been reached. Using the exo-colonizing test the status of bone marrow and spleen CFU pool was evaluated. The spleen colonies were analyzed using histotogical sections. The number and volume of colonies was determined.

A dose-dependent decrease in the number of CFU was registered over a 180-day period. Minimum values of absolute CFU contents were noted in the spleen at day 90 and total dose of 14.4 Gy; and in the bone marrow at day 180 and total dose of 28.8 Gy. At day 270 (43.3 Gy) an absolute increase in CFU content by 79% was registered compared to the previous time period (180 days). During this period the absolute content of CFU in the spleen reached control values, and their concentration exceeded the control values 2.3-fold. The average size of the colonies was significantly lower than that in controls: 2.2 times lower in the spleen and 2.8 times lower in the bone marrow. The productivity of the splenic CFU correlated with that for controls. The productivity of bone marrow CFU accounted for 20% of values registered among animals of the same age. This allows to suggest that during the period of maximum inhibition of hemopoiesis (in the spleen at day 90, and in the bone marrow at day 180) the hemopoietic system was functioning in the mode of a search for a new stable status. The range of fluctuations of the mean-quadratic deviation of the values analyzed reaches 44-58%. It may be concluded based on the data of correlational analysis that the search for a hemopoietic system status adequate to the exposure is accompanied by the disappearance of some links between values characterizing the hemopoiesis status, and appearence of new links which are not obseved in controls. The paper discusses the changing trend in CFU differentiation under the conditions of a long-term irradiation.

**NEUROLOGIC SYNDROMES OF CHRONIC RADIATION EXPOSURE (DOSE – EFFECT)**

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The outcomes of the numerous clinical and experimental studies demonstrate that the radiation exposure results in essential changes at all the levels of structurally functional organization of the central nervous system (CNS): from the molecular processes to complex damages of functions of the higher nervous activity.

The clinical indicators of acute radiation exposure (nausea and vomiting) are described in the scientific literature.

The study of the nervous system condition in dynamics for 45 years of monitoring for 1090 workers exposed to occupational chronic ionizing radiation allowed to select clinical indicators of chronic external gamma-exposure: vascular hypotonia, weakness, microorganic changes of the CNS.

Frequency, terms of development, level of severity of symptoms have direct relation to exposure dose rate (p<0.001). Direct dependence of frequency of combination of the indicated symptoms from exposure dose rate is detected also (linear trend - $\chi^2=66.7$, p<0.001).

Organic changes of the CNS as a diffused micronecrotic changes in the myelin accompanied by glial proliferation with absence of any neurologic and somatic diseases and traumas are the clinical indicator of the high rate chronic external gamma-exposure (more than 2.5 Gy/year).

MITOTIC ACTIVITY OF BONE MARROW CELLS AS A MARKER OF CHRONIC RADIATION EXPOSURE

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It is well known that of all the cells of the human body proliferating hemopoietic cells show the highest radiosensitivity, and that ionizing radiation leads to a delay in the cell turnover. It has been determined that the tolerance of hemopoietic tissue to protracted exposure is higher than that to acute one. It was shown earlier (T.M. Fliedner et al., 1959) that in acute exposure the mitotic index can be regarded as a good biological dosimeter. To date, the possibilities for analyzing the proliferative activity of bone marrow cells for retrospective indication of chronic radiation exposure have not been adequately investigated.

A retrospective analysis of bone marrow preparations was made for 24 persons chronically exposed due to discharges of radioactive wastes from the Mayak facility into the river Techa. The cumulative dose of internal exposure (predominantly due to Sr-90) in bone marrow (BM) estimated for individuals under study was 0.05-1.55 Sv at the time of BM studies, and the dose rate to BM ranged from 0.6 to 158.0 cSv/year.
Individual doses were reconstructed based on the results of in-vivo measured body contents of Sr-90 and Cs-137 in WBC-9.1. The control group was composed of 6 un-exposed persons of similar age.

Bone marrow was obtained based on medical indications using a cytologic method 4-5 years after the onset of exposure. The most common changes in the peripheral blood observed in the study subjects were leukopenia, neutropenia, thrombocytopenia and a shift to the left of stab cells in the circulating blood. Fixation and staining of bone marrow preparations was done using conventional methods (May-Gruenwald, Romanovski-Giemza, 1968). The characteristics analyzed included differential cell ratio and proliferative activity (mitotic index) in the BM myeloid and erythroid series, as well as different mitosis-related pathologic changes in BM cells (chromosome fragments, chromosomal and cytoplasmatic bridges, polynuclear cells, giant cells, etc.). The dose and dose-rate dependence of proliferative activity in BM cells of the myeloid and erythroid cell series, as well as aberrations in the bone marrow cells, was analyzed.

ARABIDOPSIS THALIANA HEYNH. (L.) - AS A POSSIBLE TEST-OBJECT FOR BIOLOGICAL DOSIMETRY OF RADIATION CONTAMINATION OF THE ENVIRONMENT

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Arabidopsis thaliana is a well studied laboratory test - object for genetic research in plants. In particular, for determine the mutagenic activity of various chemical agents in Arabidopsis the embryo-test was developed by Muller which allows the mutagenic potential of an agent to be estimated already in the first generation. Arabidopsis thaliana is also widely used to estimate the genetic effects induced by ionizing radiation. Arabidopsis seeds have been found to be very radioresistant (LD$_{50}$ = 1000-1200Gy).

As our investigations in Chernobyl have shown, vegetating plants are quite sensitive to chronic radiation and can be used for monitoring of radioactive and chemical contamination of the environment. Long-term monitoring of the environmental mutagenic activity carried out by us in 6 populations of wild Arabidopsis in Strogino (Moscow) has demonstrated stable mutation levels characteristic for each population, in all the populations year by year not different from the control level. An increased frequency of embryo lethal mutations exceeding the control level more than three times was registered in one of the observed populations growing near a motorway.

The investigations in Chernobyl have shown that the levels of radioactive pollution forming the dose rate of 7-10 mR/h (γ-rays) result in a statistically significant increase in the frequency of embryo lethal mutations in Arabidopsis populations growing on the contaminated areas.
The obtained results allow us to recommend Arabidopsis thaliana as a test object for estimation of genetic consequences of environment contamination. The genetic effects of environmental contamination can be compared with the effect of acute irradiation of seeds (dose-effect curves are available in literature) and the pollution level can be expressed in the effects of acute irradiation. It will be good to obtain dose-effect curves for chronic irradiation of vegetating plants.

**BIOINDICATION OF MAN-MADE EFFECTS ON PINUS SYLVESTRIS TREE MICROP opulations GROWING AREA FROM THE LOCATING OF THE RADIOACTIVE WASTE TEMPORARY STORAGE AND WASTE PROCESSING ENTERPRISE**

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The cytogenetic damage research was carried out on reproductive (seeds) and vegetative (needles) plant organs of the *Pinus sylvestris* tree micropopulations. The micropopulations were chosen at the 30-km ChNPP zone and at location of the radioactive waste temporary storage and waste processing enterprise “Radon” (Sosnovy Bor, Leningrad region). The sampling sites are characterized by contrasting level of radiation. Results provides evidence on pronounced genotoxic influence presence in the investigated sites. In Sosnovy Bor region chemical toxicants make the significant contribution to pollution of the environment that was not observed in the 30-km ChNPP zone. The seeds collected in control and experimental population were compared by stability to acute \(\gamma\)-irradiation. The comparison has revealed the selection toward the increase of repair system action efficiency. The result of this was the increasing of average population radiostability. The presented results give evidence that the opinion widespread among the experts and officers of nature protection departments about the absence of additional pollution of the environment caused by the storage and utilization of moderate and low activity radioactive wastes is in disagreement with the reality.

**POPULATIONS OF WILD PLANTS AS BIOINDICATORS OF RADIOACTIVE CONTAMINATION**

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The work presents the results obtained using wild plants as test objects for studying remote genetic effects of radioactive contamination of the environment caused by the accidents at the plant "Mayak" in 1957 and at the Chernobyl nuclear
power plant in 1986 and by nuclear tests in the Semipalatinsk region. The test-
systems used in these studies were as follows: the frequency of chromosome aberr-
ations in mitosis and meiosis, the frequency of chlorophyll and embryo lethal muta-
tions, genetic polymorphism of loci encoding the synthesis of isoenzymes.

The main problems the genetic studies were focused on were the mutation pro-
cess intensity in a dose- and dose rate-dependent manner, mutation process dynamics,
analysis of microevolutionary processes in irradiated plant populations.

It has been found that the cytogenetic and genetic criteria for assessing the ra-
diation effects on plant populations are 1-2 orders of magnitude more sensitive than
the conventional radiobiological criteria. The dependence of genetic effects on the
dose of β-radiation is linear and is described by the equation of power function with
the index of <1. In the case of radioactive contamination of wide territories the chron-
ic action of ionizing radiation serves as an ecological factor changing the genetic
structure of natural populations. Upon prolonged exposure of plant populations to ra-
dioactive contamination they pass to a new and higher level of radioresistance.

MORPHOLOGICAL CHANGES IN THYROID GLAND OF MICE OF CBA
LINE UNDER A COMBINED INFLUENCE OF IONIZING RADIATION
AND TH(NO\textsubscript{3})\textsubscript{4}
O.V.Raskosha, O.V.Ermakova
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The main of a present investigation was the study of a combined influence of a
chronic gamma - irradiation and Th(NO\textsubscript{3})\textsubscript{4} in concentrations 0.03; 0.1 and 0.3 g per
kg of live weight during 60 days (1.4 cGy) and 90 days (4.3 cGy) on the structure of
thyroid gland of mice of CBA line. Th(NO\textsubscript{3})\textsubscript{4} entered through the mouth. All exper-
imental animals were containing on the standard ration of the vivarium conditions. A
quantitative morphometrical ways of tissue component analysis were using. The va-
 Validity of differences of average values compared on the Student’s criterion.

The disfunction of the stadying organ was observed after 30 days irradiating
and entering Th(NO\textsubscript{3})\textsubscript{4} of different concentrations. The activation of functions gland
was expressed in raising three-dimensional density and height follicular epithelium,
changing a form and sizes nucleus. On the other hand, increasing the diameters of
follicles in the experience show reduction of organ function activity. Proliferation fol-
licles of epithelium were noted. The activity of thyroid gland were decreased after
more long influence of ionizing radiating (90 days) and Th(NO\textsubscript{3})\textsubscript{4}. The most serious
morphological changes of gland were market using Th(NO3)4 in concentration 0.03
g per kg. The investigations in this domain is very important for interpretation partic-
ular feature of tissues biological reply to chronically combined (external and internal)
irradiation.

EFFECTS OF AN INTERNAL EXPOSURE FROM INCORPORAITION
OF PLUTONIUM-239 – OSTALGIC SYNDROME
M. Sumina

-43-
The plutonium - 239 a radioactive isotope, dangerous in professional conditions, is selectively put aside in an endosteum, irradiates radiosensitive frames of an osteal tissue, breaks processes of osteogenesis.

The outcomes of long-term overseeing by the persons in conditions of professional prolonged arrival in an organism of aerosols of plutonium - 239 have allowed to justify legitimacy of diagnostics and clinical manifestations of one of effects of an internal exposure- ostalgic of a syndrome.

Criterion of a substantiation of a syndrome:

1. Increase of frequency ostalgic of syndrome at a cumulative equivalent dose on osteal surfaces more than 0.6 Sv and year to a dose more than 0.03 Sv.
2. Increase of frequency of an osteodysplasia on materials of intravital histological study of an ileal bone of streets with ostalgic syndrome and contents of plutonium - 239 above marginal.
3. Increases of frequency of degenerative alteration of nervous filaments in tissue specimens at autopsy of the persons having at life ostalgic syndrome, at doses on osteal surfaces more than 100 Sv.

The correspondence of the clinical -morphological data in a range of the indicated doses can be considered as one of probable builders of a pathogeny ostalgic syndrome at an incorporation of radionuclides.

TO THE PROBLEM OF THE BIOMARKER’S DEVELOPMENT FOR THE VALUATION OF RADIOSENSITIVITY OF THE VASCULAR ENDOTHELIUM (ELECTRON MICROSCOPY STUDY OF THE MYOCARDIAL CAPILLARIES ENDOTHELIUM OF RATS)

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Institute of Experimental Medicine, RAMS, Saint Petersburg, Russia

The analysis of the after-effects of the Cernobyl’s nuclear power plant accident has discovered the lack of correspondence between the vascular pathology revealed and the usual meanings on the strong vascular radioresistance. This report will shows the facts that certify the special cellular effects existence which might lie in the basis of the remote vascular pathology progress after irradiation with low doses and to use that as the biomarkers for evaluation of this pathology.

The material obtained from the rats myocardial capillaries endothelium, that has been irradiate with the X-rays at doses 0.5; 2.25 and 4.5 Gy respectively, was analyzed. It shows that even at the dose of 0.5 Gy in the population of the endotheliocytes appears special strong potential changes that looks like long-term raising of the cells’ come-out with the signs of irreversible ultrastructural damage: oedematous degeneration, plasmolemma’s rupture, total disintegration of intracellular structure,
wide intracellular lysis. This effects has no dose dependence and kept during the most part of the animal life span. The gradual decreasing of the thickness of the endothelial surface is occurring as the result of this changes.

Thus, it may be stated that in the slowly renewed vascular endothelium, observed the ultrastructural damage are more adequate markers of the radiosensitivity than a traditionally studied chromosomal aberrations. Furthermore, it seems to be interested to study a biopsy materials and processing the constant cell lines of the endothelium cells.

ANALYSIS OF EFFECTS OF DOSE RATE AND ACCUMULATED DOSE ON HEMOPOIESIS AND IMMUNITY PARAMETERS IN CHRONIC γ-IRRADIATION

Urals Research Center for Radiation Medicine, Chelyabinsk, Russia

The study was conducted on male CBA-line mice. The age of the animals at the time of experiment was 90 days, body weight 24-26 g. The animals were exposed to chronic irradiation in the EKO-77 complex at dose rates: 0, 1, 4, 6 and 16 cGy/day. Hematological and immunological studies were performed at days 30, 90, 180, 270, 360 and 540 of exposure at cumulative doses ranging from 0.3 to 57.6 Gy.

The effects of chronic irradiation on hemopoiesis were assessed based on the following criteria: cellularity of bone marrow, thymus, spleen; number of colony-forming units (CFU) in the spleen, hemopoietic tissues (bone marrow, spleen); total peripheral blood leucocyte count; analysis of myelograms and leucograms.

Evaluation of immunity status involved relative and absolute counts of neutrophils, lymphocytes, and the main populations of lymphocytes (T-, B-cells, large lymphocytes containing granules) in the peripheral blood; antibody-forming cells in the spleen; peroxydase activity of neutrophils in the peripheral blood.

The effects of dose rates and absorbed doses on hemopoiesis and immunity characteristics were assessed using the multi-factor linear anaysis of conjugation signs in the total despersion model.

Most parameters were significantly influenced by both absorbed dose and dose rate though some of them were found to be influenced by only dose rate or only absorbed dose.

INFLUENCE OF CHRONIC RADIATION EXPOSURE ON THE FREQUENCY OF SOMATIC MUTATIONS IN RESIDENTS OF THE SOUTH URALS REGION

A.V. Akleyev, G.A. Veremeyeva
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The frequency of somatic mutations was evaluated for residents of the Techa riverside (Chelyabinsk region, Russia) who were exposed to chronic, mostly internal,
and mostly external radiation. In all, 165 individuals were examined, 35 of them comprised a comparison group. The mean dose to red bone marrow was $121.5 \pm 6.6$ cSv. GP assay and analysis of TCR-mutant lymphocytes were used in the study. An increase in the frequency of TCR-mutant lymphocytes with dose of both chronic external and internal radiation exposure. No changes in the levels of mutant erythrocytes with dose have been noted. No linear dependence between both types of somatic mutations and dose has been traced.

HEMATOPOIESIS UNDER CHRONIC LOW DAILY DOSE GAMMA IRRADIATION: EARLY PHASES OF EVOLVING MYELODYSPLASTIC DISEASE IN CANINES
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Low daily doses of sufficiently intense ionizing irradiation over an extended period can induce a spectrum of late-arising diseases of which cancer is a major component. To develop quantitative relationships between chronic radiation exposure, specifically in terms of dose-rate, total dose, and time, and the induction patterns of the major health risks of concern (e.g., sepsis, aplastic anemia, fibrosis, cancer, etc.), long-term, near-continuous gamma irradiation studies (at daily dose rates ranging from 3-263 mGy day$^{-1}$ 22 h day$^{-1}$) were carried out using a large (canine) animal model.

Results of this work indicated that chronic whole-body gamma ray irradiation at daily dose-rates of 75 mGy day$^{-1}$ and above, survival times were relatively short; less than 300 days when exposures were initiated at ~ 400 d of age. The dominant cause of death in these short-lived, irradiated animals was aplastic anemia (AA) that was often complicated in the terminal phase with septicemia. The frequency of fatal sepsis increased dramatically from ~11% incidence at 75 mGy day$^{-1}$ to 100% incidence at the high dose-rate of a 263 mGy per day$^{-1}$. By contrast, at daily exposure rates below 75 mGy day$^{-1}$ (38 to 3 mGy day$^{-1}$), survival times were greatly extended (beyond 300 days) for the majority of the exposed animals (>1800 days). Late arising cancers contributed significantly to the death of these relatively long-lived animals. Myeloproliferative diseases (MPD), mainly myeloid leukemias, were the dominant cancers seen at dose rates ranging from 75 to 18.8 mGy day$^{-1}$. When these daily exposures were carried out continuously, i.e., from approximately ~400 days of age to death, the incidence of MPD was quite high, ranging from 42% at 75 mGy day$^{-1}$ to 16% at the lower dose-rate of 18.8 mGy day$^{-1}$. However, when the daily dose-rate was reduced to still lower dose-rates, i.e., 7.5 or 3 mGy per day$^{-1}$, or the exposure was discontinued, the incidence of MPD declined significantly (e.g., to 1% incidence under continuous exposure, or to 0-12% when daily exposures at dose-rates of 38-75 mGy day were discontinued once preset total doses had accumulated [at 4.5-30 Gy]). These MPD induction frequencies under specific dose-rate and total-dose exposure

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conditions are considered to be significant, as the incidence of spontaneous MPD in the dog is exceedingly low (less than 0.02%).

The induction and progression of these survival-compromising, late-arising hematopathologies appear to be driven to a large extent by degree of hematopoietic suppression that occurs early during the exposure phase, and, in turn, by the capacity of hematopoietic system to repair, restore and to accommodate under chronic radiation stress. The upper limit of this accommodative capacity expressed by the individual is determined mainly by radiological and temporal exposure conditions, but also in part by genetic background of the responding animal. During very early phases of exposure, marked differences in hematopoietic proficiency were observed and were prognostic for the major types of evolving hematopoietic disease (e.g., AA versus MPD). The hematopoietic capacity of MPD-prone animals, in contrast to AA-prone animals, was substantial, although clearly aberrant both in terms of the capacity to sustain injury, as well as for subsequent reparative functions. Myeloid lineage progenitors characteristically acquired increased radioresistance, modified cellular and molecular repair functions, and altered cell-cycle and clonal properties. Additional differences were noted between the AA- and MPD+ response phenotypes, but all tended to highlight a progressive “loss” or “gain” of function at various levels of hematopoietic tissue organization. Whereas the MPD phenotype was generally associated with a “gain-in-function”, the AA phenotype was associated with a “loss-in-function”. The more notable of these changes included: AA-associated reductions in blood levels of superoxide dimutase; AA-associated elevation in the net scorable cytogenetic damage; MPD-prone increases in select types of nonrandom chromosomal lesions, such as the 1q+ lesion; AA-associated structural rearrangements of the retinoblastoma (Rb) tumor-suppressor gene; MPD-associated structural changes (rearrangements and point mutations) within the N-Ras protooncogene.

We addressed the possibility that a radioprotective effect could be exerted by periodic pharmacologic intervention with various types of immunomodulating agents. This concept has been validated, in part, by demonstrating that by treating periodically, chronically irradiated, MPD-prone animals with low concentrations of a bacterial lipopolysaccharide (LPS) survival under chronic irradiation could be significantly extended. Presumably this LPS-induced survival extension has an underlying hematopoietic mechanism that is tied to extended progenitorial damage capacity, repair, and possibility self-renewal functions. These presumptive mechanism(s) are currently under investigation, as are a continuing search for alternative chemopreventive agents that might limit late-arising diseases and enhance survival.

**USE OF CYTOGENETIC AND MOLECULAR BIOMARKERS FOR RADIATION DOSE ASSESSMENT**
W.F. Blakely¹, P.G.S. Prasanna¹, S.B. Melnov², C.J.C. Hamel¹, S.J. Zullo³,
Chromosome-aberration-based bioassays are the conventionally accepted approach to assessing radiation doses in cases of accidental and occupational overexposures. However, cases involving prior exposures and studies of large cohorts confound conventional analytical approaches and require alternative methodologies. To meet this challenge, we are developing semiautomated delivery platforms for cytogenetic methods and identifying new molecular biomarkers that leverage analytical polymerase chain reaction (PCR) technologies. Our objective is to establish a system of rapid, high-throughput procedures that are precise and practical in a variety of radiation exposure scenarios.

The need to score large numbers of metaphase spreads is a major limiting factor of cytological procedures. Typically, thousands of spreads from mitogen-stimulated lymphocytes of peripheral blood samples must be examined to obtain a statistically significant score of chromosome aberrations. Detection of chromosome aberrations in interphase cells rather than metaphase spreads would make it easier to score the appropriate number of aberrations in cells. The premature chromosome condensation (PCC) procedure induces rapid formation of chromosome-like condensation of chromatin from interphase nuclei, eliminating the need for mitogen stimulation and significantly reducing analysis time. We modified the procedure by adding an enzymatic treatment to enhance the chemically mediated condensation and to consistently produce higher PCC yields in G0 lymphocytes. Using whole-chromosome fluorescence in situ hybridization (FISH) to visualize chromosome number 1, cells containing radiation-induced aberrations are readily identified as containing more than two chromosome domains. To date, our studies using a modified PCC-FISH assay have achieved a meaningful dose-response encompassing a range of 0 to 7.5 Gy in cells exposed to gamma rays and allowed to repair for 24 hours prior to analysis.

Radiation-induced DNA mutations may be useful dose assessment biomarkers. A specific 4,977-bp deletion in human mitochondrial DNA (mtDNA) is known to accumulate naturally with age. A recent study by Kubota et al. (Radiat. Res. 148: 395, 1997) used a nested PCR method and showed that ionizing radiation induces the same mtDNA deletion. We developed an in situ PCR method to detect cytologically this “common” 4977-bp mitochondria DNA deletion (mtDNA4977) in human cells. Using human peripheral blood lymphocytes in an in vitro model system, we demonstrated a dose-dependent (0.5, 1, 2 Gy) increase in the incidence of ⁶⁰Co gamma-
irradiated cells containing the deletion after a 4-day postirradiation incubation with or without mitogen treatment.

We will also report on studies using a powerful quantitative PCR procedure that can record PCR product accumulation during amplification. Measuring molecular biomarkers in this way makes feasible retrospective dose reconstruction studies from DNA-containing tissue registries, enabling studies that cannot be carried out using cytogenetic methods.

ЦИТОГЕНЕТИЧЕСКИЕ ПОДХОДЫ В РЕТРОСПЕКТИВНОЙ БИОЛОГИЧЕСКОЙ ДОЗИМЕТРИИ

RETROSPECTIVE BIOLOGICAL DOSIMETRY: KEY PARAMETERS AFFECTING RELIABILITY OF DOSE ESTIMATES

T. Straume
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Several parameters, both biological and physical, can substantially influence radiation biodosimetry results. These include “natural” variations in the biodosimeter background signal within the study population, stability of the radiation-induced signal with time after exposure, exposure environments that are more complex than those involving controlled laboratory studies, distribution of both quantity and quality of radiation within the body, calibration of the biodosimeter, and limits of detection.

In the case of cytogenetic biodosimetry, it has been observed that exchange-type chromosome aberrations (reciprocal translocations and dicentrics) may be used to reconstruct radiation dose after acute, uniform whole-body exposure (albeit within certain dose ranges). The stability of cells with reciprocal translocations should make the use of those aberrations useful in retrospective biodosimetry. However, additional data are required to validate reciprocal translocation biodosimetry (i.e., translocations detected using fluorescence in-situ hybridization, FISH) for the protracted and complex exposure conditions that are relevant to most population studies. In contrast, the instability of cells with dicentrics, and the apparent interindividual variability in stability, make the use of those aberrations increasingly uncertain with time after exposure. Of concern also for FISH studies are the observations that staining and scoring criteria seem to be inconsistent among laboratories, and that calibration curves have received inadequate attention. Also, the number of aberrations scored per individual is often insufficient. In the case of electron paramagnetic resonance (EPR) dosimetry, results from laboratory studies also appear promising. However, as with FISH dosimetry, EPR has significant uncertainties and limitations associated with applications to populations involving exposure scenarios more complex than those in controlled laboratory studies. EPR also requires tooth samples, which may be difficult to obtain.
These and related issues will be discussed along with recommendations aimed at improving the validation of FISH and EPR for retrospective dosimetry.

**CHROMOSOME ABERRATIONS IN THE LATENT PERIOD OF CHRONIC RADIATION SICKNESS CAUSED BY EXTERNAL GAMMA-EXPOSURE**  
N.D.Okladnikova, L.E.Burak  
Branch # 1 of the State Research Center, Institute of Biophysics, Ozyorsk, Russia

Since 1965 chromosome analysis of the lymphocytes of peripheral blood is used at the first Russian atomic complex as indicator of chronic exposure. Large groups of personnel (more than 1000 individuals) in the different terms from the beginning till the end of contact with gamma-exposure sources were examined. Formation of the main chronic exposure dose is related to 1949-1956. In 15 years after exposure, in the total dose of 1.0 Gy-9.0 Gy frequency of chromosome aberrations in peripheral blood lymphocytes from 8 to 10 times exceeded spontaneous level, in 25 years – 6-10 times and in 35-40 years – 4-5 times. In the structure of aberration types changes of stable type prevail (70-89%). At the last stage of observations a tendency to increase of the number of aberrations with increase of the total exposure dose, was observed. Maximum value of this parameter is achieved for individuals whose exposure dose was more than 6.0 Gy. No pathological cell clones were discovered except for Ph, chromosome in the case of chronic myeloleukemia (total exposure dose 1.9 – 3.4 Gy). For patients with malignant tumors of different localization (106 individuals) no specific chromosome aberrations were detected.

Cytogenetic studies demonstrated that chromosome aberrations in the peripheral blood lymphocytes are the group indicator in the latent periods after chronic external exposure, however it is not a individual biological dosimeter. The conclusion goes along with the data obtained in the joint studies with the FISH method with professor M. Bauchinger (Germany) and professor N. Nakamura (Japan).

**INTERPRETATION OF RESULTS OF FISH ASSAYS WHEN ZERO OR ONLY A FEW TRANSLOCATIONS ARE OBSERVED**  
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2 Urals Research Center for Radiation Medicine, Chelyabinsk, Russia  
3 Battelle Pacific Northwest National Laboratory, Richland, WA, USA

A method for reconstructing dose is scoring of stable chromosome translocations by FISH. We have examined results for 40 residents of the upper Techa Riverside (Bauchinger et al. Intl. J. Radiat. Biol. 73:605-612; 1998; plus unpublished data). On the basis of \( a \) translocations observed in \( n \) cells, dose \( D \) is calculated as...
\[ D = \frac{\frac{\alpha}{2.05 \cdot 0.19 \cdot (1-0.19)n} - c}{\alpha} \] ,

where the numbers are from the Lucas equation to extend results to the whole genome, \( c \) for this population is 0.0057±0.0010 and \( \alpha \) is 0.030±0.007 Gy\(^{-1}\). Unfortunately, the most frequent value of \( a \) is 0 and only 4 values are >3. Thus, especially for the cases of 0 scored translocations, it is useful to define the 95% confidence limits of dose. This can be done with the binomial distribution, where the probability, \( \Pr\{a|n\} \), of observing \( a \) translocations in \( n \) cells is

\[
\Pr\{a | n\} = \frac{n!}{a!(n-a)!} p^a (1-p)^{(n-a)}. 
\]

Values of \( p \) (and corresponding values of dose) were calculated so that

\[
\sum_{i=0}^{a} \Pr\{i | n\} = 0.025 \text{ or } 0.975.
\]

For example, for one resident 0 translocations were found in 201 cells scored; the upper 95% confidence limit on dose is 1.73 Gy. For another resident with 0 translocations in 763 cells, an upper limit of 0.32 Gy is derived.

* - Performed under the auspices of the U.S. Department of Energy, the U.S. Environmental Protection Agency, the U.S. National Aeronautics and Space Administration, and the Ministry of Health of the Russian Federation

**REVEALATION OF RELATIONSHIPS BETWEEN ACUTE RESPIRATORY DISEASES MORBIDITY IN CHILDREN, MICRONUCLEUS TEST INDEXES AND FACTORS OF ENVIRONMENT WITH HELP OF LOGIC AND STATISTIC METHODS**

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The revealing of the prepathology cytogenic changes connected with failure of human adaptation possibilities under unfavourable factors of environment is the very important problem. The determination of the number of micronuclei of blood lymphocyte stimulated by phytohemagglutinin (spontaneous level) allows to estimate as
the effects of various genotoxic factors and adaptation potential of organism. The micronucleus test includes also the changes of micronuclei number under 2 regimes of irradiation in vitro - 1) 1 Gr; 2) 0.05 Gr and after 5 hours - 1 Gr. To analyse the relationships between the indexes of micronucleus test the various indexes of children's health and enviroment factors we investigate the 117 children from 3 kindergardens with different enviromental conditions in Zhukovsky town in Moscow region. The methods of correlation analysis and pattern recognition (Statistically Weighted Syndromes) were used. The recognition algorithm is formed by the analysis of empirical data table. Selection of optimal sets of informative variables provides a maximum of true predictions. As a result the set of factors was found which allows to carry out the prepathology diagnostics and to prognose the adaptation failure. The algorithm also allows to determine the group of children with high risk of acute respiratory diseases. We have to note the high significance of unfavourable environment factors for the acute disease level. It was detected that the acute morbidity of children and absence of adaptive response in micronuclei test depend on the level of sanitary and ecological well-being of the environment, while the functional state of organizm systems is connected with the factors of risk in family. Thus a possibility for monitoring of the children at an individual level was obtained.

CELL NUCLEI PATHOMORPHOSIS AND CHROMOSOME ABERRATIONS IN HUMAN LYMPHOCYTES AFTER IRRADIATION
V.Y.Kravtsov, R.F.Fedortseva, E.K.Monosova, N.M.Yartseva and A.M.Nikiforov
All-Russian Centre of Emergency and Radiation Medicine, EMERCOM of Russia, S-Petersburg, Russia

To check positive correlation between parameters “frequency of cells with abnormal nuclei” and “frequency of metaphases with dicentrics and rings” we have been conducted experiment with in vitro irradiation and cultivation of human lymphocytes. After an X-irradiation and cultivation during 72 h with cyt B (after completion of 1-th postirradiation mitosis), frequencies were studied of the appearance of binuclear lymphocytes with nuclear pathomorphosis (the “tailed” nuclei, internuclear bridges and dumb-bell-shaped nuclei). Linear-square dose dependencies have been established for all studied forms of nuclear anomalies. Parallel measurements of frequencies of chromosome aberrations (dicentrics and rings) have been performed in the same cultures in 51 h (1-th mitosis) after the PHA-stimulation. Using the method of calculation of the frequency of cells with investigated nuclei pathomorphosis we have managed to predict the frequency of metaphases with dicentrics and rings. The dose-response curve for metaphases with dicentrics and rings predicted theoretically described as $Y=0.026 +0.042D + 0.018 D^2$, while experimental one - as $Y=0.003 +0.047D + 0.018 D^2$.

In our opinion, the investigated types of nuclear anomalies are form due to mitotic divisions of cells with dicentrics and centric rings. So, method of abnormal nucleai may be used for biologic indication of radiation exposure.
THE CYTOGENETIC EFFECTS OBSERVED IN NUCLEAR WORKERS AFTER CHRONICAL RADIATION EXPOSURE
T.G.Semionova¹, O.I.Potetnya¹, N.N.Shepel¹, A.V.Sevan`kaev², G.N.Gasteva²

¹ Medical Radiological Research Center, RAMS, Obninsk, Russia
² State Research Center of RF – Institute of Biophysics, Moscow, Russia

The cytogenetic study of 53 nuclear workers exposed to ionizing radiation over extended period (mainly during 25 or more years) was carried out. The workers were divided in two groups. The first group consists of 26 persons with chronic radiation sickness following exposure to external radiation only. The second group consists 27 patients with the same diagnosis as the result of the exposure to both external and internal radiation of $^{239}$Pu. $13,750$ and $13,400$ metaphases were scored for these groups respectively.

The chromosome aberration frequency observed in the first group ranged from 0.4 to 4.6%. The average frequency was 2.3% that is twofold excess over spontaneous level. The frequency of chromosome aberration observed in the second group ranged from 0.2 to 12.6%. The average value not only was threefold excess over spontaneous level but significantly differed from the similar parameter of the first group. Almost all subjects demonstrated essential excess of chromosome type aberrations over chromatid type (5:1). Exchange chromosome aberrations such as dicentrics, centric rings and anomalous monocentric predominate in the aberration spectrum. Statistically significant difference of average frequency of dicentrics for the first group (0.7 per 100 cells) in comparison with the second one (1.4 per 100 cells) was found. These rates exceed spontaneous level by 5 and 10 times respectively.

Thus, persons with chronic radiation sickness represent a group of high risk for development of delayed radiation effects, in particular, carcinogenic effect, therefore they should be under permanent follow-up.

RETROSPECTIVE BIOLOGICAL INDICATION OF LOW DOSES IRRADIATION
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All-Russian Center of Radiation Medicine Emercom of Russia, St.Petersburg, Russia

Unstable chromosomal aberrations in peripheral blood lymphocytes of 300 clean-up workers 6-12 years after the accident were investigated. Clean-up workers were divided into 5 groups in accordance with radiation doses picked out from the official documents: $>5$Gy, $5>10$Gy, $10>20$Gy, $20>25$Gy, unknown doses.

Control group consisted of 48 persons of the similar age and health status with no radiation history. The yield of chromosomal aberrations, including radiation
markers (dicentrics and rings) slightly but not significantly increased with the increasing of absorbed doses and significantly exceeded the control level (p< 0.001):

<table>
<thead>
<tr>
<th>Dose (cGy)</th>
<th>Number of persons</th>
<th>Aberrant cells (%)</th>
<th>Dicentrics (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;5</td>
<td>50</td>
<td>2.38±0.30</td>
<td>0.13±0.05</td>
</tr>
<tr>
<td>5&gt;10</td>
<td>41</td>
<td>2.52±0.34</td>
<td>0.16±0.06</td>
</tr>
<tr>
<td>10&gt;20</td>
<td>50</td>
<td>2.72±0.42</td>
<td>0.19±0.06</td>
</tr>
<tr>
<td>20&gt;25</td>
<td>82</td>
<td>2.91±0.28</td>
<td>0.35±0.06</td>
</tr>
<tr>
<td>Unknown</td>
<td>107</td>
<td>2.47±0.21</td>
<td>0.26±0.04</td>
</tr>
<tr>
<td>Control</td>
<td>48</td>
<td>2.04±0.26</td>
<td>0.03±0.02</td>
</tr>
</tbody>
</table>

Data of questionnaires such as duration and character of works at Chernobyl nuclear power station, illnesses, life style and so on were analysed. The only factor which was found to be responsible for the increased level of radiation markers in clean-up workers was the participation in recovery works. It seems important to emphasize, that even in a remote period clean-up workers significantly differ from the control group mostly by radiation-specific type of chromosomal aberrations.

Thus, dicentrics could be used as a simple method of biological indication in a wide range of low doses long period after radiation exposure.

**CYTOGENETIC ANALYSES IN LYMPHOCYTES OF RADIOLOGISTS OCCUPATIONALLY EXPOSED TO CHRONIC LOW LEVEL IONIZING RADIATION**

T.Kharchenko, N.Slozina, E.Neronova, A.Nikiforov
All Russian Center of Emergency and Radiation Medicine Emercom of Russia, St.Petersburg, Russia

Chromosomal analyses were performed in blood lymphocytes of 6 radiologists who turned to All Russian Center of Emergency and Radiation Medicine for decision of expert questions and medical care. All investigated people had health problems (including persistent leukopenia in two cases and cataract in two other). We revealed a significantly elevated level of chromosomally aberrant cells in the radiologists (3.75%±0.79 compared with 1.56%±0.22 in the control group). This was mainly due to increased levels of dicentrics and rings (0.92%±0.3 vs 0.04%±0.02) and chromatid exchanges (0.17%±0.11 vs 0.00%±0.03). It is possible that unexpected high level of radiation markers at the same time with the real health disturbances may be explained by presence of documentary non-fixed overexposure.

The radiologists as one of the most occupationally exposed to ionizing radiation cohort have a great risk of developing radiation-induced diseases. It seems to be expedient using cytogenetical monitoring in this cohort for improving the control about radiation safety and health.
CYTOGENETIC EXAMINATION OF THE POPULATION OF MUSLYUMOVO

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During 1993-1994 cytogenetic examinations were performed in a group of 136 persons from the settlement Muslyumovo located on the Techa River at a distance of 78 km from the plutonium-producing plant Mayak in the Chelyabinsk Region. The results of the Cytogenetic examination involving the analysis of unstable chromosome aberrations were compared with the results of examination of a control group composed of inhabitants from a non-contaminated region (30 persons).

It was found that frequency of aberrations of the chromosome type, namely dicentrics and centric rings, in the inhabitants of Muslyumovo considerably exceeded (5-10 fold) that in the control group. The highest level of disturbances (9-10 times higher than in the control group) was recorded in persons born before 1949 (the beginning of discharging of radioactive products into the Techa River) or in the period of the highest pollution of the Techa River by radionuclides (1949-1953). In 10 inhabitants of Muslyumovo blood cells with multiple chromosome aberrations were detected.

The results obtained suggest a long-term preservation of a portion of cells with unstable chromosome aberrations in the blood of people who received sufficiently high doses of irradiation due to environmental pollution by radioactive products. It is also necessary to take into consideration the effect of incorporated radionuclides ($^{90}$Sr – $^{90}$Y) still remaining in the organisms of the examined people on the level of chromosome aberrations.

THE ESTIMATION OF LIFE-TIME PERIOD OF LYMPHOCYTES THAT CONTAIN UNSTABLE ABERRATIONS BASED ON THE STUDY OF GROUP OF PERSONS WITH HIGH DOSES FOR THE IMPROVEMENT OF PAST EXPOSURE BIOSIMETRY

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The aim of the work was the study of the possibility to apply the cytogenetic characteristics to biosimetry in a long time for past irradiation. The investigation was carry out on peripheral blood lymphocytes of patients cohort from 6-th Hospital of Institute of Biophysics (Moscow) by conventional cytogenetic method. A group of
Chernobyl liquidators consisted of 10 male persons aged 24 – 48 years at the moment of irradiation in 1986. All of them were subjected to acute radiation exposure in high doses as the result they demonstrated the acute radiation syndrome of varying severity. Data analysis displayed the Poisson distribution of dicentrics in cells. This certifies that the patients irradiation was close to the uniform whole body irradiation. The cytogenetic dose assessment was done basing on yield of dicentrics observed. The doses estimated ranged from 0.7 to 8.7 Gy. The first blood samples were taken from 1 to 49 days after the irradiation and the last ones were collected in 11 years. For each patient from 4 to 9 blood samples were made. 500 metaphases were analysed in each sample in generally. The time dependence of the yield of dicentrics and dicentrics plus rings was obtained and fitted by the next function \( Y_0 \exp(-t/T) \), where \( Y_0 \) initial yields of aberrations, \( t \) - time since irradiation, \( T \) - parameter. It was estimated that \( T \) ranged from 0.6±0.04 to 8.5±1.86 years. However there was no good fitting by the single exponent function in the range \( t > 6 \) year. That is why further study is expected.

**TEST ON CHROMOSOME ABBERRATIONS IN LYMPHOCYTES OF PERIPHERAL BLOOD FOR PLUTONIUM-239 BIOINDICATION**

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Plutonium-239 alpha-particles induce multiple damages in the cell DNA. Process of reparation of these damages is very complex and is not that efficient than in the case of rare ionizing radiation. In the experiment the cytogenetic effect of plutonium-239 is demonstrated (Dolphin G.W. et.al., 1970; Brandon W.F. et al., 1974). Not many clinical cytogenetic studies were conducted (Hempelmann S.H. et.al, Tawn E.I. et.al, 1985; Okladnikova N.D. et.al, 1994, 1996).

The purpose of this work is to make an assessment of chromosome aberrations being a bioindicator of plutonium-239 in the human body. Routine method of the two-days peripheral blood lymphocyte culture was used. The assessment of total number of chromosome type aberrations, number of stable and non-stable aberrations for 100 metaphases was made. 344 individuals were examined: 194 individuals – workers of plutonium plant and 150 individuals – control group. Personnel of the plant had the occupational contact with aerosols of plutonium-239 compounds with low transportability, for which the lung is the most exposed organ. Plutonium-239 body burden varied within 0.37 to 22.2 kBk. Number of chromosome type aberrations for 100 cells for those individuals who had plutonium body burden, 10 times exceeded spontaneous level and correlated with the amount of deposited radionuclide. For quantitative assessment of this dependence the phenomenological model was offered: 

\[
N = N_0 + a \ln \left( \frac{q}{q_0} \right),
\]

where \( N \) – is the total number of chromosome aberrations for 100 cells; \( N_0 \) - the number of chromosome aberrations for 100 cells in the
control group; $q$- radionuclide body burden (kBk); $q_0$ - threshold value of the nuclide body burden (kBk). Biophysical meaning of the $\alpha$ parameter is the number of chromosome aberrations at $q$ that $e$ times exceed the threshold ($q_0$). Similar dependence of the number of chromosome aberrations from absorbed lung dose was detected. Threshold burden of radionuclide ($q_0$) was 0.26 kBk, lung threshold dose ($D_0$) - 4 cGy (80 cSv). Thus, chromosome aberrations in lymphocytes of peripheral blood are the indicator of plutonium-239 incorporation.

SUITABILITY OF FISHPAINTING FOR ROUTINE DOSE RECONSTRUCTION OF ACCIDENTAL HUMAN RADIATION EXPOSURE

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The FISH technique with composite whole chromosome-specific DNA probes, named FISH-painting, is presently considered the most reliable method to detect structural (so-called “stable”) chromosome aberrations. FISH-painting provides uniform labelling of the entire length of the chromosomes corresponding to the chosen DNA probes. This technique may be used to help for dose reconstruction of overexposure of humans to ionising radiation and needs to be further validated for this purpose. Several laboratories are thus working towards establishing biological dosimetry using FISH even if the technique is still not fully standardised and validated as a “biomarker”. The main objective of this presentation is to discuss the suitability of a triple-colour FISH-painting (chromosomes 2 + 4 + 12) for routine dose assessment. Several points will be discussed according to the data obtained: (1) the reliability and limitations in case of accidental low dose or suspicion of exposure; (2) the establishment of a translocation background level, i.e. about 31,000 cells scored and a background frequency estimated at 2.4 translocations per cell; (3) the establishment of reference calibration curves after irradiation in vitro ($^{60}$Co, 0.1 Gy.min$^{-1}$, 0.5 Gy.min$^{-1}$, 1 Gy.min$^{-1}$); (4) dose assessment of cases of human accidental irradiation at high dose exposures ($^{192}$Ir, $^{137}$Cs); (5) dose reconstruction of non-human primates (Macaca mulatta, rhesus monkeys) subjected to total body irradiation some years before the FISH analysis. A calibration dose-effect relationship was established previously in the laboratory (in vitro, rhesus blood, $^{60}$Co, 0.5 Gy.min$^{-1}$) and used as reference for the dose reconstruction. The results obtained have shown that the chromosomal non-complete translocations seems to be less persistent than the complete ones.

Each study point will be presented and discussed according to the present views on this subject in the literature. A present state of art of the suitability of FISH-painting for routine dose reconstruction will be given and perspectives proposed.
The question of significance of immune disorders in induction of long-term sequelae of radiation exposure is still controversial. The objective of the present study was to assess immunity status in Mayak PA veterans at the time of realization of severe deterministic and neoplastic sequelae of occupational exposure and to determine relationship between incidence of immune disorders and accumulated dose of external exposure. 3 groups of individuals (108 persons) subjected to chronic radiation exposure were formed; mean dose values in these groups amounted to 119.4±3.5; 235.2±10.4 и 368.8±7.4 cSv. The majority of them were exposed to alpha-irradiation from incorporated Pu-239 in addition to external gamma-irradiation (Pu body burden up to 40 nCi). Control group included 54 Mayak PA workers for whom mean dose value amounted to 9.5±0.4 cSv. Content of leukocytes, lymphocyte populations and subpopulations (using monoclonal antibodies), level of Ig G, M, A in blood serum, complement activity and functional activity of leukocytes (NBN-test, latex phagocytosis, reaction of braking of leukocyte migration) were studied. Mean values for content of leukocytes, lymphocytes, and neutrophiles for persons from all groups didn’t differ from normal values. Exception was T-lymphocytes. Their content for persons from basic groups was 20% lower than in control group. It is necessary to stress that leukopenia cases in basic groups were detected 2.2 times more frequently than in control. Quantity of T-helpers in persons from all groups tended to decrease, and quantity of T-suppressers - to increase, that is why the ratio T-h/T-s was 1.2-1.4 times lower than normal. Mean values of Ig level in Mayak PA veterans were within norm, however number of persons with statistically significant deviations of Ig G and M from norm was 2.4 times greater in basic groups. No principal differences in fagocytic and cytotoxic function of leukocytes, complement activity were detected in basic groups as compared with control group. At the present stage of the study no direct dependency of immune disorders on chronic exposure dose was revealed.
IMMUNOLOGIC INVESTIGATIONS ON PERSONS WHO ARTICIPATED IN LIQUIDATION OF RADIATION ACCIDENTS AND IN NUCLEAR WEAPONS TESTS IN TIME REMOTE FROM THE ACTION OF RADIATION


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Results are presented of immunologic inspection of a group of persons who participated in liquidation of aftereffects of various radiation accidents (Kyshtym, Chernobyl, in atomic submarines) and in nuclear testing at Semipalatinsk, North, Totsk proving grounds. The investigation was performed 10-40 years later than the person had been subjected to radiation.

Both in the liquidators and the participants of nuclear tests even in remote period after the action of the ionizing radiation were revealed alterations in the humoral nonspecific protection, changes in the content of immunoglobulins in the blood serum, humoral and cellular autoimmune shifts, considerable increase in content of viral antigens in the respiratory tract, and release of respiratory viruses from the body. The increased sensitivity of lymphocytes to viral antigens was observed. In the half of men who tested the nuclear weapons on Novaya Zemlya an enhanced content in blood of the tumor necrosis alpha-factor was detected. The difference in the immunologic distortions was revealed depending on unsimilar radiation situations and on the time elapsed since the action of the ionizing radiation.

Certain distortions observed may be due to the elderly age of the persons under inspection and to accompanying deseases. However the lack of some of these distortions in the control groups does not allow to exclude that they originate from combined action of the ionizing radiation and non-radiation factors (stress, unfavorable environmental factors etc).

The role of humoral and cellular autoimmune distortions in the morbidity of people after prolonged time from the action of the ionising radiation was demonstrated.

The leading place among the different radiation pathology that potentially threat to the health of a recovery workers (RW) of the Chernobyl’s nuclear power plant (CNPP) accident (1986) taken by the thyroid gland (TG) injuries. The thyroid gland is the critical organ for iodine radionuclides, which isotopes was polluted at the moment of catastrophe.

Appearance of a antibodies to the thyreoglobuline (AbTG) and the thyreoper-oksidaza (AbTPO) might be use as a one of early laboratory marker of the autoimmune processes at the thyroid tissue.

We have conducted investigetions for estimation of Ab contents to tissue antigens in the blood serum of RW. The blood serum of the 83 male recovery workers who worked on the CNPP at 1986-1987 using the ELISA method was studied. The AbTG was established in the 17 persons (20.5%), AbTPO — in the 6 persons (7.2%). The middle concentration of the AbTG in the group of the recovery workers is 79.34 ± 11.89, AbTPO — 21.40 ± 0.25 ME/ml; and donors (n22) has — 54.70 ± 5.20 and 17.89 ± 1.10 ME/ml respectively. In fact the rate of subclinical carriage was significantly higher (p<0.05) among recovery workers than among the donors, basically for the content of Ab in the range 100-150 ME/ml. Among the recovery workers with clinically confirmed autoimmune thyroiditis frequency rate of Ab was found at 67% of cases.

The 70% of recovery workers with confirmed antibodies carriage has been working at the accident zone in the spring-summer of the 1986, e.g. in so called “iodine period”.

It is concluded that evaluation of the Ab in the group of recovery workers could be used as the marker of thyroid autoimmune pathology progressing, which could certify the initial indications of the unstochastic effects of the low doze radiation upon the thyroid gland.

IMMUNOLOGICAL METHODS OF TREATMENT AND PREVENTION OF RADIATION INJURIES
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Purpose of our report - to demonstrate the efficacy of immunoprophylaxis and treatment of secondary pancytopenic immunodeficienice in acute radiation disease.

Analysis of published reports has shown at least three approaches to immunotropic prevention and therapy of acute radiation disease: 1) ex-ogenic (natural and synthetic) immunostimulants; 2) endogenous immunostimulants and 3) substitute therapy. All these treatments improve the resistance of immune system to postradiation infection. In addition, there are three extraimmune therapies: 1) antibiotics, anti-
viral and anti-fungal agents; 2) vitamins and 3) aseptic regiment. All these treatment decrease the bacterial contamination of an irradiated organism.

Cooperation between clinical radiation medicine and immunology promotes better understanding of problems in prevention and treatment of acute radiation disease.

MECHANISMS OF APOPTOSIS CELLS OF IMMUNE SYSTEM CELLS AT CHERNOBYL’S ACCIDENT LIQUIDATORS
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It is known that radiation exposure causes deleterious effect on the immune system. Even low doses of radiation induce apoptosis. The investigators suggest that it is possible relationship between synthesis and production of cytokines and apoptotic process. With the purpose to determine correlation between expression of Fas-antigen and synthesis of cytokines after low doses irradiation the Chernobyl’s accident liquidators were investigated. In consequence of the study increasing of Fas-antigen was revealed. This increasing correlated with changing in synthesis and production of cytokines. In this group was discovered increasing of the cell number synthesied interleukine-1β (IL-1 β), interleukine-4 (IL-4) and tumor necrosis factor-α (TNF-α). The number of cell producing tumor necrosis factor-α, promoting apoptosis, were increased. To prove the radiation low dosescontribution in forming of immune disturbensis reveald in liquidators the experiments by irradiation PBL of healthy persons in vitro were held. Cells were X-irradiated by 12,5, 25 and 50 cGy. In this experiments was obtained increasing of cell expression apoptotic marker Fas-antigen after irradiation in all doses. Also was discovered increasing of the cell number synthesied TNF-α. The number of cell producting TNF-α, promoting apoptosis, were increased. Correlation between number of cells expressing Fas-antigen and number of cells with intracellular and surface forms of TNF-α was obtained in the Chernobyl’s accident liquidators and in experiments. Obtained data allowed to suggest the including of TNF- signal pathway as additional mechanism of immune cell apoptosis after irradiation and corroborated the theory of low doses influence on disturbences in immune sistem of liquidators.

These data allow to consider the apoptosis as cell mechanism included in pathogenesis of diseases, wich can be showed later long time after irradiation.

THE IMMUNLOGIC MONITORING OF THE PEOPLE AFFECTED WITH THE FACTORS NUCLEAR INDUSTRY
The laboratory and immunologic-examination of large group of people exposed to the factors of nuclear industry was carried out three times. Two contingents were investigated – nuclear combine’s workers (1 gr) and population of territory adjoining to this combine (2 gr). The primary examination of the 1 group of person revealed a decreased number, with increased per cent of CD3+ cells and decreased number of CD8+, CD16+ cells, B-lymphocytes and phagocytic activity. Immunological state of 2 group people was characterized by increased number of lymphocytes and more intensely decreased of CD8+ number and, as a result, increased ratio CD4+/CD8+. In the course of immunological monitoring some tendencies were displayed. The per cents of CD8+, CD16+ cells, B-lymphocytes and phagocytic activity were higher and per cent of CD3+ cells, and ration CD4+/CD8+ – lower in secondary examination in comparison to the results of the primary examination.

**SIGNIFICANCE OF IMMUNOLOGICAL MARKERS FOR INDICATION OF RADIATION EXPOSURE**

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At late times (43-48 years after exposure) a proportion of residents exposed to chronic radiation in riverside villages on the Techa (the range of cumulative exposure doses to bone marrow: 7-4 766 mSv) were noted to have an increased frequency of stable chromosome aberrations (mostly translocations) and somatic mutations in peripheral blood TCR. No linear dependence was traced between the frequency of somatic mutations and the cumulative dose to bone marrow for the entire exposed population group. The frequency of chromosome aberrations was significantly higher in subjects exposed at the dose of over 200 cSv. The presence of a significant inter-individual variability in the frequency of translocations and somatic mutations in subjects with comparable exposure doses can testify to a considerable effect exerted on their level by the organism’s individual characteristics (radiosensitivity and specific features of repair of post-radiational injury).

The input of exogenous and endogenous factors influencing most fundamentally the frequency of somatic mutations and translocations has been evaluated based on a systemic analysis, which allowed to draw the following conclusions about their level: - the patients’ physiological parameters such as gender, age and ethnicity, viewed as a whole, do not influence significantly the frequency of somatic mutations, while the level of stable chromosome aberrations is, to a large extent, determined by the gender and ethnicity of exposed subjects;
- frequency of somatic mutations increases with cumulative dose and age at onset of exposure;
- frequency of chromosome aberrations and somatic mutations is only slightly influenced by immunity parameters;
- there exist associative links between the level of chromosome aberrations, somatic mutations and the presence of certain HLA-antigen.

БИОФИЗИЧЕСКИЕ ПОДХОДЫ В ИНДИКАЦИИ ЗАБОЛЕВАНИЙ

LASER METHODS IN ONCOLOGY DISEASE DIAGNOSTICS
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There are two tasks in tumor diagnostics. The first is the discovery of the malignant or benign tumor, which is reliably performed through clinical morphological methods. The main hindrance with these is their duration. The second, more important, task is the establishment of whether the process of malignant growth exists in the organism in general. The latter is connected to the formation of a heightened oncology risk group in the screening investigation of the given contingent. Laser methods can be applied for both these tasks.

Changes in morphology and partial macromolecular tissue structures in the malignization process involve small-scale surface changes and changes in the absorption properties of the sub-cell structure, which is reflected in changes in their diffuse reflecting characteristics. Measuring the spectral reflection coefficient of normal and tumor tissues with the aid of an automated optical-acoustic spectrophotometer enabled their differences to be shown, depending on how pronounced the lesion. On the basis of these investigations a spectrophotometric attachment to the Quartz-32G gastroscop was developed, recommended for application by the New Technology Committee of the Russian Health Ministry.

Spectral-luminiscent medical diagnostic methods have two directions. The first is the spectroscopy of cell structure fluorescence. Before the appearance of lasers it was established that the fluorescence spectra of normal and tumor tissues differs. The application of fluorescent spectrometer lasers with high spectral excitation capacity increased the speed and quality of achieving spectra and raised the level of reliability of these diagnostic methods. The second direction is related to the investigation of exogenous photosensitizers. This diagnostic direction is close to photodynamic tumor therapy. Namely spectral-luminescent methods allow one to determine the concentration of photosensitizer in the tissues and according to luminiscence intensity distribution to accurately define the tumor spread, optimize the irradiation procedure and
control treatment efficiency. Many technical systems for luminiscent diagnostics in photodynamic therapy have already been created.

One of the most important indicators of the state of a tissue is its micro-circulation function. The presence of a pathological process leads to changes in blood supply structure and dynamics. These changes can be fixed by the laser capillary blood analyzer LAKK-G.

A serious shortcoming of general tumor and pre-tumor screening methods is the lack of efficient objective pre-clinical diagnostics. To achieve express oncology disease diagnostics a method has been developed of multi-parameter molecular analysis of blood plasma with the use of the laser spectroscopy correlation method, based on the effect of dynamic light diffusion of the tested sample of biological liquid. A problem-oriented program-apparatus complex was formed – the Blood Analyzer Laser (APK LAK), distinguished by its express and high automation of the measurement process, excluding the influence of the operator on the analysis result and providing an objective conclusion.

APK LAK can be used for screening investigation with the aim of forming oncology risk groups and for operative estimates on the efficiency of applied resources and methods of anti-tumor treatment, as well as a subsequent monitoring of patient health.

Laser methods do not substitute all other methods but they do considerably widen the possibilities of medical diagnostics.

DIFFERENTIAL POSSIBILITIES OF LASER CORRELATION SPECTROSCOPY (LCS) METHOD IN LATE CANCER RADIATION EFFECTS IN MAN
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The issue of stochastic effects of radiation exposure (mostly leukemia and cancer), and early detection of malignant tumors, as a key aspect of that issue, is of crucial importance to the population of the Southern Urals where 3 major radiation accidents occurred in the 1950s and 1960s. Given the large number of exposed population, screening is considered to be the most expedient method to organize medical observation of exposed persons.

As was shown by the results of medical examinations performed for 1 390 residents of the Techa riverside villages, laser correlation spectrometry (LCS) of blood plasma has proved to be a highly effective screening method for early (pre-clinical) detection of malignant neoplasms and pre-cancerous conditions. It was established that LC-spectra of blood plasma in persons with cancer and pre-cancer could easily be differentiated, particularly over the high-frequency range of the spectrum, from non-cancer conditions.
As a result of the study a diagnostic algorithm has been developed which allows to conduct computer-based classification of LC blood plasma spectra as a component of the system for monitoring health status in exposed population.

BIOPHYSICAL FUNDAMENTALS OF A SYSTEM FOR MONITORING THE LEVEL OF HEALTH-SAFEGUARDING PROCESSES IN THE POPULATION LIVING IN ENVIRONMENTALLY ANOMALOUS ZONES

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Currently, two approaches predominate in monitoring the health of populations exposed to man-made and natural accidents:

1. Clinical-laboratory screening of population aimed at diagnosing initial stages in the manifestation of different diseases;
2. Detection of etiognomic markers of pathologic conditions (infectious, exogenous, endogenous, cytological, etc.).

The first approach, in spite of the practical difficulties involved in the organization of comprehensive clinical-laboratory examinations, and the high labor intensity it necessitates, prevails over the second one since identification of strictly etiognomic factors of certain pathological processes requires the application of a large number of sophisticated molecular-biophysical methods which sometimes cannot be utilized in express-mode monitoring studies.

The methodological complex we are proposing has been tested by the above-indicated research groups. It has been developed to meet the requirements of express studies to be used in monitoring large populations. The concept of this multi-parameter study is based on the belief that an indispensable condition for registering a certain pathological trace consists primarily in deadaptation of systems responsible for processes regulating the key health-safeguarding mechanisms (sanogenetic mechanisms) which include: a) mechanisms regulating metabolic processes and humoral
immunity; b) mechanisms regulating CNS sensomotor functions; c) mechanisms regulating respiratory, cardio-vascular functions; d) mechanisms regulating deintoxication processes. In keeping with the notions outlined, the corresponding computerized methods were incorporated into the biophysical complex:

1) laser-correlational spectroscopy of biological liquids which allows to monitor the balance in the metabolic system and humoral immunity;
2) an automatic complex for registering alterations in the sensomotor systems of the CNS;
3) a computerized cardio-rhythmographic apparatus allowing to detect the degree of dysbalance in the regulation of the cardio-vascular system;
4) a computerized spectrometer for detecting the main regulatory processes ensuring pulmonary gas exchange;
5) skin bilirubinometer detecting changes in the blood bilirubin level.

All these methods are based on the use of miniature devices ensuring collection of information under various conditions of operation, and of portable personal computers (note-books). The results of examinations are processed by a unified software which ensures registration of the level of alterations that are detected using a 4-score system. The software not only enables analysis of parameter values (which is highly significant for compiling the corresponding populational risk group registries), it gives the competent recommendations. The complex which is easy to handle, non-invasive, and ensures a high rate of analysis, is characterized by a high operational capability (no less than 100 complete identifications per day) which reduces considerably the costs of monitoring.

Specific results obtained by monitoring the population living both on the East-Urals Radiation Trace and on other territories exposed to environmental anomalies will be presented.

**EXPERIMENTAL BASIS OF THE LASER-CORRELATIONAL SPECTROSCOPY METHOD FOR PROGNOSTICATING LATE EFFECTS OF CHRONIC \( \gamma \)-IRRADIATION**

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Animals used in the experiment were CBA-line mice aged 80-90 days bred and maintained on a standard ration in the vivarium of the URCRM. To evaluate the role of individual characteristics of homeostasis in the development of late effects of chronic exposure to radiation, blood was collected and laser-correlation spectrum (LCS) of blood plasma was determined for each animal before the experiment was started. The animals were exposed to external \( \gamma \)-irradiation in the EKO-77 complex at dose rates 1, 4, 6, 16 \( \text{cGy/day} \). Based on a comparison of LCS findings with the animal’s life span it became possible to identify a group of animals whose LCS was of bi-modal shape, with the
Ist peak representing particles measuring 20 nm, and the input of such particles in light scattering being no higher than 20%. Life expectancy for such animals was longer in all dose groups than life expectancy for all the remainder animals.

Besides, it was possible to identify the specific features of LCS which allow to sample groups of animals with a high and low probability of cancer development. Animals with a monomodal LCS spectrum and particle size mode of 100-200 nm are characterized by a lower frequency of tumor development. Animals whose LCS showed the input into light scattering of particles of $\leq 50$ nm to be not lower than 51%, manifested a higher incidence of neoplasm. In animals with different characteristics of LCS the incidence of cancer development did not differ from the average-for-group values.

**PLUTONIUM – 239 AND RESTRICTION OF CHANGE IN LUNG**

(CLINICAL STUDY)

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At inhalation of aerosols $^{239}$Pu an organ of a main deposition of a radionuclide are lung. In experiment the character of a disease of a pulmonary tissue in a wide range of doses of an internal exposure is investigated at arrival in an organism of connections $^{239}$Pu of the different class of transportability. The morphological basis of a defeat is made by an interalveolar sclerosis. The pneumosclerotic variation for group of the workers having on character of the professional activity contact to aerosols $^{239}$Pu are earlier circumscribed. The purpose of the present research was an estimate of dependence of metrics of the function of external respiration (FER), including vital capacity lung (VCL), the pulmonary diffusing capacity ($D_{co}$), bronchial permeability, with an absorbed dose on mild for staff plutonium of production. The outcomes of long-term clinic-function research for 1960 practically of healthy workers plutonium of production are parsed. At an amount accumulation of plutonium less admissible allowance (AA) is not detected of clinic-function changes of a bronchial-pulmonary means. Statistically significant lowering of a metric VCL is detected at an absorbed dose on mild $20,31 \pm 0,79$ cGy, lowering $D_{co} = 8,13 \pm 0,29$ cGy. The excava
tion of changes is shown at further accumulation of a dose. At an absorbed dose on mild 4,0 Gy and more syndrome restriction is combined with roentgenologic by changes appropriate to a pneumosclerosis. The metrics describing bronchial permeability do not correlate with an absorbed dose on mild. Their dependence on an index of smoking is placarded).

**HLA-B27 ANTIGEN - REACTIVE ARTHRITIS BIOMARKER**

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Immunological typing of 295 patients with arthritis was carried out. All the patients belonged to the Eastern Slavonic ethnic group. Of these 102 suffered from rheumatic arthritis (RA), 91 - from ankylosing spondyloarthritis (AS), and 102 - from reactive arthritis (ReA). Diagnosis was made on the basis of clinical and laboratory instrumental studies. The control group consisted of 305 healthy individuals all of whom were the residents of the Chelyabinsk region.

While carrying on comparative analysis of antigen occurrence we observed a decreased level of HLA-A19 in all three types of arthritis. Patients with ReA and AS were noted to have frequent occurrence of B27 and A2 while increase of B35 was characteristic for RA. Frequent occurrence of high immunogenic subloci of HLA system was observed in patients with ReA while the number of low immunogenic subloci was significantly decreased in them. Analysing the occurrence of haplotypes in patients with ReA it was found that AIB8, A2B5, AIOB27 occurred less frequently and A2B13, A19B14, A32B15 occurred significantly more frequently in patients with ReA compared with control subjects.

Analysing the occurrence of HLA antigens of A and B loci within the group of ReA patients it was found that HLA-B27 antigen occurred more frequently in enterocolitic type (81.25%) than in urogenital type (61.29%) when the disease was associated with oligoarthritis, sarcoileitis, ophthalmic disorder as well as Reiter triad, B27 occurred less frequently in cases of primary disease. Patients having HLA-B27 phenotype had a significantly increased ESR, increased number of leukocytes, fibrinogen, α2-globulins as well as T-lymphocytes.

The obtained findings can be used as a criterion to evaluate the course and prognosis of the disease.

**CAPABILITIES OF PSYCHOLOGICAL DIAGNOSTIC OF STRAINS OF CONDUCT FOR THE FACES WHICH HAVE TRANSFERRED EXTREME EVENT**

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The problems of biomedical, epidemiological and dosimetric aspects of the distant effects of irradiation doubtlessly are actual. However, on our view, it is necessary to muse of capabilities of diagnostic of psychological consequences of experience of an extreme situation, for example, operation of definite producing doses on mentality of the person.

The psychodiagnosis disposes different instruments for detection of individually - personal features of the person. But, on our view, only one method of application allows to reveal plutonic, subconscious processes happening in mentality of the per-
son, and also uncovers dynamic of these processes. It is the method of application L. Sondy.

Primitively enough to repute, that the human existence is stipulated only acquired both social, and biological factors, that the person is born " net leaf of a paper ". It is represented to expedient opposition state about an omnipotence of a medium in relation to the individual to an antithesis about personal selectivity of the individual in relation to the same medium, in which one it(he) will appear.

On what factors this selectivity depends? Is interquartile, from a constant, actual and as though diving through all human acts, operation, experience. Sondy has called such factors as radicals, i.e. native born impulses stipulating and maintaining human acts and conduct, rushing and desire, underlining thus their heritable nature.

So, after a psychodiagnosis of the liquidators of emergency on Chernobyl Crash has appeared, that most frequently meeting radicals in this group is a necessity in respect and recognizing on the part of other people and necessity " to be the man " in. From these items, on our view, the gear of violation of processes of acclimatization to new conditions for a sectional category of the people becomes more exhibited, the strains of conduct are explained, you see it is those necessities, which one are not satisfied neither significant social medium, nor company as a whole.

Therefore it seems, that basically it is possible to answer on problematic for doctor a problem: " Why one people which have survived extreme event, are characterized by psychogenic disorders, and other - is not present? " Is interquartile, the capabilities of a strain of mentality are connected to availability - absence of so-called "instigating" radicals, necessities, which one either are satisfied, or is not present.

THE ELECTROPHYCHOPHYSIOLOGICAL PHENOMENON AS A MARKER OF PREDISPOSITION OF A HUMAN BEING TO RADIATION EFFECTS
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To 10-ng term observation of the victims of low doses of radiation and the psychological stress have helped to formulate a concept of development of a new form of the patology – the informational disease. This informational disease based on phenomenon which we named as “electrophychophysiolodgycal phenomenon“ of the desadaptation (EPPP).

From our point of view discovered phenomenon has a fundamental apparition and can be used as a criterion of adaptation reactions both individual and populational levels. It is shown that bifurcational apparitions in the status of our patients take place 5-7 years after radiation’s influence. There are three groups of patients with different predispositions to sudden cordial death had appeared at that time.

The differences between the groups insert such indexes as : the level of physical work capacity, the predisposition to autoimmunity reactions, the degree of aterogenic changes of lipides, the kind of attitude to themaelf diseases, the type of social adaptation.
Believe that clinical differences between groups described about are based on individual reactivity which depends upon geno- and phenotypical characteristics of the people who have being observed.

THE MEDICAL HELP IN THE SPECILAZED CENTER FOR RADIATION MEDICINE
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The Urals Regional Center for Emergency Workers of the Chernobyl Accident & their children is the specialized medical Center for 10.000 people in Ural, who received radiation in Chernobyl, in the Eastern Ural, during nuclear testing.

There are three phases of the specilazed Center’s work with our patients & their children - the so called “aimfull disperserization”.

The first phase of our work is the screening investigation, which is performed in consultative & diagnostical departments.

The second phase of the Urals Regional Center’s work is the full investigation & treatment of people, who received radiation, in the clinical & physiotherapy departments of the Center or in some Urals medical Centers including Oncological, Endocrinological, Pulmonary ones.

The third phase of the Center’s work is the after-treatment rehabilitation, which is necessary & justified for 85,6% of our patients, some of them visited the Urals & Russian sanatories.

The resultes of the Urals Center’s work are:
- the level of the psychical disorders @ the level of the acute myocardial infarcts don’t increase last four years among the Emergency Workers.
- the level of mortality has been decreased since 1995 year among the Urals Emergency Workers.

TOPICAL PROBLEMS OF DIAGNOSTICS AND BIOINDICATION OF CHRONIC INTOXICATIONS CAUSED BY POISONINGS SUBSTANCES SUBJECT TO DISPOSAL
P.E. Shkodich, Y.V Alexandrov, N.A. Petrushova

The diagnostics of chronic intoxications by xenobiotics which are organic compounds of many formulations in the human body remains one of the most complex problems to be solved in occupational hygiene and pathology. This problem comes into importance in the case of a person’s contact with highly toxic substances and when employing individual protective devices(IPD). This raises the question of whether the IPD are reliable enough in service and advantageous for protection. Of
practical significance in this connection is the challenge how to obtain objective evidence on intake of potent poisoning substances (PPS) in the body.

Under conditions of chronic exposure to low doses (below the threshold of harmful effect) of poisoning substances (PS) the occurrence of clinical features of chronic intoxications is delayed for many years whereas clinical manifestations remain little specified. Recognition of preclinical stage of chronic intoxication is based on the use of specific (for particular PS) and highly sensitive diagnostic tests, i.e. biotest. Assessment of the body «contact» with PS of skin blistering action is possible on a basis of determination of metabolites (e.g. mustard gas) or change in activity of a number of enzymic systems (e.g. mustard gas, lewisite). The PS of skin blistering action having a well-marked irritating effect manifest exposure through clinically pronounced signs of skin and mucosa lesions (upper respiratory tract, eyes).

The resorption of organophosphorus compounds (OPC) in the body is accompanied by a marked anticholinesterase action which is recognized on a basis of a decrease in the activity of blood ChE. The results of examinations of workers engaged in handling of highly toxic OPC (DDVP, sarin, soman) show that determination of the overall activity of AChE and BuChE in the serum ChE is not always informative: a decrease in AChE activity is less sensitive and decrease in BuChE activity is less specific. The overall activity of BuChE is subject to a decrease under stress, physical load, overheating and in a number of general diseases.

The study on content of molecular forms (isoforms) with the use of electrophoresis in polyacrylamide gel (PAG), as well as of the constants of ChE inhibition in vitro with unspecific and specific ChE inhibitors has been performed. Proposed for laboratory diagnostics is a set of tests on determination of low level exposures to OPC in men.

**ROLE OF INDIVIDUAL STATUS OF THE NERVOUS SYSTEM IN THE DEVELOPMENT OF LATE EFFECTS FROM CHRONIC EXPOSURE TO \( \gamma \)-RADIATION**

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Two genetically heterogenic animal populations were used in the experiment: CBA-line mice and white non-pedigreed mice aged 80-90 days raised and maintained on a standard full-value ration at the vivarium of the experimental department of the Urals Research Center for Radiation Medicine. Animals were exposed to external \( \gamma \)-radiation in the EKO-77 complex at dose rates 1, 4, 6, 16 cGy/day. To evaluate the individual characteristics of nervous activity each animal was tested for behavioral reactions using the "open field" method: horizontal and vertical locomotor activity, emotional reactions, grooming, investigative activity. In addition, the passive evasion reflex was evaluated, and the adaptive strategy was determined using maximum loads.
As a result of comparisons between the individual characteristics of the nervous activity and the animal's life span, certain particularities of the nervous activity have been traced which allows to identify groups of animals with different rate of neoplasms among non-pedigreed and line mice, and groups with different life span among white non-pedigreed mice.

The following assumption can be made based on the data obtained: there exist individual genetic characteristics associated with definite behavioral reactions which determine a probable life expectancy and the probability of cancer development; it becomes possible based on individual behavioral reactions to identify groups of individuals different in terms of prognosticated probable life expectancy and rate of neoplasms.

АДАПТИВНЫЙ ОТВЕТ

ADAPTIVE RESPONSE IN RADIOBIOLOGY. SPREADING, INFLUENCE OF ECOLOGICAL AND SOCIAL FACTORS

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Institute of Biochemical Physics RAS, Moscow, Russia

The spontaneous level of lymphocytes with micronuclei and the manifestation of adaptive response (AR) have been determined (irradiation in the adaptive dose 0.05 Gy and 5 h after in challenged dose of 1.0 Gy). It was shown the decreasing of the amount of children and adults with AR and the increasing of radiosensitivity after adapting irradiation was observed in the people living on the regions contaminated with radionuclides after incident in Chernobyl. Perhaps, the chronic low dose irradiation results in the inhibition of AR induction in the part of population.

In Moscow the children with AR are rare (especially in some districts) in social bad-living children - the children of the chronic alcoholics parents and children-narcotists. The high pressing of genotoxic factors may be the reason of this phenomenon. AR is absent or amount of children with AR significantly decreases in the mentally deficient population and in this case in some groups the radiosensitivity after adapting dose increases. So, the absence of AR may not be connected with chromosome aberrations. AR ability depends on the level of spontaneous genomic damage and decreases after threshold level. The mechanisms of AR, conditions of its manifestation, its universality, genetic determination, the group of risk are discussed.
RESPONSE OF CELLS INDUCES DISPLACEMENT OF INTERPHASE CHROMOSOME PERICENTROMERIC LOCUSES
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Research Center for Medical Genetics Russian Academy of Medical Sciences, Moscow, Russia

Adaptive response (AR) is one of the fundamental cell reactions on low and high doses successive influence. It is proposed that low dose of radiation switch of cell in the condition of “ready” to reparation. A mechanism of this process is unclear. So far as a mechanism of DNA double strand break (DSB) reparation generally is connected with recombination events, we suppose that low doses of radiation stimulate rapprochement of chromosome homologous locuses in interphase nucleus. The normalized distances between nucleus center and 1q12 hybridization signals were investigated in G0 human lymphocytes using image analysis system and nonradioactive in situ hybridization. The 1q12 locuses disposed near nuclear membrane in normal cells. Under influence of X-radiation (160 kV) in the interval of 3-25 cGy (adaptive doses) 1q12 moves into internal nucleus region. The part of cells with displaced pericentromeric regions is in dependence on a period after exposure and increase between 0.5 and 5 hours. It should be emphasized that 5 hours after exposure is the time of completion of preparation to AR. The analogous effect of chromosome locuses displacement was observed earlier for cell transition from G0 to S phase. It is possible that chromosome displacement in G0 cells under low doses radiation is promote DSB reparation in the AR process. A pathology due to non-reparated DSB is not excluded if the displacement is absent.

DNA FATE IN CHILDREN LYMPHOCYTES WITH REPAIR-DEFICIENT DESEASES RESULTED AS RADIOADAPTIVE RESPONSE
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Radioadaptive response (RAR) is the increased cell resistance to gamma radiation (high doses) forming in cells pretreated by low doses of radiation. As a rule cytogenetic methods are used to study RAR but there are just a few articles concerning DNA fate caused by RAR (Kleczkovska, Althaus 1996).

The key-problem concerning RAR mechanisms being actively discussed is the participation of DNA repair in this cell protection forming.

We have investigated various repair-deficient cells isolated from the patients with hereditary diseases (Marfan and Elers-Danlos syndroms, homocystinurea) characterized earlier as repair-deficient syndroms. RAR level in Marfan syndrom lymphocytes was equal to the one in cells of normal donors, while in homocystenurea and Elers-Danlos syndrom cells RAR was absent. In human cells lines pretreated
with cadmium chloride in low concentrations adaptive response (AR) was observed while these cells were treated (after 3 hours) by the same mutagen in challenge concentration and AR level was equal to the one occurred in cells pretreated by gamma-radiation and challenged with cadmium chloride induced irreparable DNA damage. Thus these data show DNA repair and AR non-dependence in human cells.

THE COMPARISON OF ADAPTIVE RESPONSE AT $\gamma$-RADIATION AND TREATMENT WITH HEAVY METALS IN HUMAN CELLS

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Adaptive response (AR) — a form of cell protection against mutagens. AR is expressed in the formation of increased resistance to high doses of mutagens or radiation if cells pretreated with low doses of radiation or chemicals. AR is registrated on chromosome aberrations, cells viability, micronucleus test, DNA breaks (Wolff, 1996; Klezkovska et al.). There are only few publications about AR in the experiments with heavy metals which induced irreparable DNA damage. The goal of our work was the investigation of AR in human cells pretreated with low doses of $\gamma$-radiation or NiSO$_4$ and following treatment with high doses of radiation or NiSO$_4$. Cell viability was served as a criteria of AR. Kinetics of cell viability in pretreated with $\gamma$-radiation (0.1Gy) revealed their increased resistance. Similar resistance was formed if cells was irradiated by the same dose or treated with NiSO$_4$ ($10^{-7}$M, 20 hours) and following treated with NiSO$_4$ in concentrations $10^{-3}$-$10^{-5}$M at which cell viability was reduced till 50%. Authors were discussed possible mechanisms at the comparison of cell protection against $\gamma$-radiation and NiSO$_4$ in the condition of AR.
MRRC RAMS provides the large-scale dosimetical monitoring of accumulated doses in the population of Bryansk Region territories contaminated after the Chernobyl accident. ESR dosimetry of teeth enamel is one of the most appropriate methods for such monitoring. The Table presents mean accumulated doses estimates (for period from 1986 until 1995) obtained by ESR dosimetry in teeth enamel in comparison with modelling evaluations of the effective accumulated dose in the three contaminated rayons of Bryansk region and in one non-contaminated rayon of Kaluga region. The applied method of ESR dosimetry was approved by Russian Federal Bureau of Standards (GOST R 22.3.04-95, M., 1997). The modelling estimates were performed in accordance with Methodical Directions which had been aproved by Russian Ministry of Health ( MU 2.6.1. 579 - 96, M., 1996 ). Only those data were included which corresponded to the contaminated rayons where the number of ESR estimated individual doses exceeded 100 (N>100).

For ESR estimates of doses only the enamel of posterior teeth (position 4-8) were used in order to exclude the UV influence from the sun. The following dose correction factors have been used: correction for 65 mGy - as the value of initial intrinsic signal of the method, energy dependence correction factor 1.2. Correction for the accumulated natural background radiation during time of tooth existence was performed as well.

<table>
<thead>
<tr>
<th>District</th>
<th>N Number of individual ESR doses</th>
<th>Mean ESR dose in rayon, mGy</th>
<th>Uncert. of mean dose, MGy</th>
<th>Mean Cs-137 soil contamination, kBq m^-2</th>
<th>DS=DE+DI, mGy *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bryansk region</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gordeevsky district</td>
<td>226</td>
<td>29</td>
<td>4</td>
<td>444</td>
<td>34=20+14</td>
</tr>
<tr>
<td>Klintzovsky district</td>
<td>114</td>
<td>30</td>
<td>8</td>
<td>230</td>
<td>32=14+18</td>
</tr>
<tr>
<td>Zlynkovsky district</td>
<td>104</td>
<td>50</td>
<td>8</td>
<td>633</td>
<td>43=30+13</td>
</tr>
<tr>
<td>Kaluga region (not contaminated territories)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Borovsky district</td>
<td>64</td>
<td>&lt;1</td>
<td>4</td>
<td>&lt;4</td>
<td>-</td>
</tr>
</tbody>
</table>

* DS - total accumulated effective dose; DE - accumulated effective dose of external irradiation; DI - accumulated effective dose of internal irradiation.

As it follows from the presented data there was found sufficiently good agreement between the ESR-estimated doses and the doses calculated according to physical models. It should be noted that ESR dose correlated with the total accumulated effective dose but not with the doses of internal or external irradiation.
The statistical distributions of individual ESR doses are being discussed in the report.

**COMPARATIVE ANALYSIS OF METHODS USED IN EXTERNAL DOSE RECONSTRUCTION FOR THE TECHA RIVER POPULATION**

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Discharges of liquid waste into the Techa River during the period 1949 through 1956 were the major source of radioactive contamination of the river and its adjacent territories. The residents of the villages along the Techa were exposed to both external irradiation from contaminated river sediments and flood plane soils, and internal irradiation due to ingestion of radionuclides with river water. The main contributor to the internal exposure was $^{90}\text{Sr}$ which is accumulated in bone tissues and retained there for many years. A large number of $^{90}\text{Sr}$ measurements in the whole body, teeth and bones serve as the basis for the internal dose reconstruction. Absorbed doses due to external exposures were estimated based on gamma dose rate measurements along the riverside, and information about typical life patterns of the inhabitants of the villages. Such approach had a number of limitations resulting from random and systematic errors in dose estimates. Over the last few years, additional information on the releases and environmental contamination near the Techa River was derived from the archives. Also, the models describing radionuclide transport in the Techa river and gamma-fields near the river shorelines were developed. In addition, pilot studies addressed to the use of electron paramagnetic resonance (EPR), thermoluminescence dosimetry (TLD) and fluorescence in situ hybridisation (FISH) methods were performed for the Techa River area. The comparative analysis of these new data sets permits to evaluate the applicability of different retrospective dosimetry methods for external dose estimation and to outline further efforts in this direction.

**EXTERNAL GAMMA-DOSE RECONSTRUCTION IN THE UPPER TECHA RIVER: THE NEW RESULTS OF THERMOLUMINESCENCE INVESTIGATIONS**

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The data obtained by using quartz containing materials as natural thermoluminescent (TL) dosimeters for the external gamma-dose reconstruction are very important for the investigation of the consequences of radiation accidents as well as radioactive contamination of the populated areas. Pilot investigations showed the ad-
vantages of TL method for estimating the external doses from the complex and extensive radioactive source which was formed in period 1949-1956 along the Techa river valley. In this paper were analyzed the new results of TL measurements of brick samples from the village of Metlino where inhabitants received significant doses of external irradiation. The measurements of radionuclide contents in water, bottom sediments of the Techa river and Reservoir 10 near the TL sampling sites were carried out simultaneously with dose rate measurements. These data are used for a more correct description of the source geometry in the settlement, and reassessment of the exposure of population. It is shown that highest doses of about 4-5 Gy were determined on bricks collected from the walls of buildings exposed to the contaminated river shore line. The results presented in this paper are used to validate models developed for population's external dose calculations.

THE DENTAL ENAMEL MINISAMPLING METHOD FOR ESR DOSIMETRY

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The known at present methods of retrospective dosimetry - cytogenetic method of chromosomal aberrations in lymphocyte cultures of peripheral blood, ESR analysis of dental enamel, glycoforin test on erythrocytes and the others - for the first time make real possibility of objective determination of the personal dose, which has been accumulated for a long period of time.

ESR signals of tooth enamel dependence on afterexposure to irradiation time was studied by many authors and all of them mark the extremely stability of these signals.

However, difficulties in systematic sampling of material, caused by conducting the reconstruction of the doses with use only extractioned in the normal course of dental practice teeth, strictly limit large-scale application of the method. That is why the development of the minisampling dental enamel "in situ" method, avoiding extraction of the whole tooth with subsequent restoration of chewing function, allows considerably expand sphere of application of the ESR method.

At present the development of the minisampling dental enamel method and verification of agreement of the data with the results obtained within "traditional" method, which required extraction of the tooth, is being carried out by State Research Center of Institute of Biophysics together with the chair of orthopedic stomatology and implantology of Qualification Improvement Institute.

DOSE RECONSTRUCTION FOR WORKERS OF THE MAYAK PRODUCTION ASSOCIATION

P.Jacob¹, J.Vasilenko²
Estimates of individual gamma exposures of Mayak workers and of inhabitants of Ozyorsk were performed by three independent methods: enamel doses determined by EPR, bone marrow doses determined by FISH with a calibration curve for transmissible 2B translocations, and absorbed doses in air in front of the body derived from occupational film badge dosimetry and from an assessment of background radiation in Ozyorsk. Main characteristics of EPR retrospective dosimetry with enamel are explained. EPR analyses were performed for 24 inhabitants of Ozyorsk with no or with negligible occupational exposures (<10 mGy). According to the assessment of medical exposures and natural and anthropogenic background radiation in Ozyorsk, the average background dose for these persons was (60±6) mGy,. In full agreement, the EPR analyses gave an average value for the absorbed dose in enamel of (62±11) mGy. According to the FISH analyses, the average bone marrow dose in excess to the natural background of translocations in the calibration curve was (256±47) mGy. For 44 workers of Mayak a good correlation between enamel doses and results of occupational dosimetry was found. Disagreements for individual workers could be explained by characteristics of the photon fields at the working places. For the same workers there was only a weak correlation between the bone marrow dose determined by FISH and absorbed dose in air. The results indicate a decrease of the transmissible 2B translocations with time after exposure. The decrease shows a large individual variability. Comparison of FISH results with enamel dose confirms these observations.

REASSESSMENT OF EXTERNAL DOSES FOR THE TECHA RIVER RESIDENTS
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Radioactive releases into the Techa River in the 1950s caused external and internal exposure of the residents of the riverside villages. A more detailed analysis of additional information on the releases, environmental contamination, and population behavioral factors as well as a specifically developed model for radionuclide transport in the Techa River allowed to carry out a reassessment of external doses for that population. New estimates of external doses for Techa River residents are presented. The basic information used in dose reassessment was as follows: available data on external dose-rate measurements near the Techa River shoreline since the beginning of measurements; available data on modeled gamma dose rates in air near the Techa River shoreline before the beginning of measurements; additional data on external dose-rate measurements within residence areas on Techa River in the period of
releases and after them; available information for behavioral pattern of the Techa River residents. The new assessments of external doses are significantly (3-10 times) lower than the respective values estimated and published earlier. The main factors accounting for the decrease in dose values are discussed.

COMPARATIVE RATING OF EFFICIENCY VARIOUS METHODS RETROSPECTIVE DOSIMETRY AFTER SCALE RADIATION ACCIDENT
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SSC Russian Federation - "Institute of biophysics", Moscov, Russia

The experience shows, that instrumental dosimetry in case of large nuclear failure be not capable to give the settling information on individual doses of radiation received by the participants of liquidation of its consequences. Thus, each large failure is connected to necessity retrospective dosimetry.

On the basis of own experience of reconstruction of doses and analysis of results known from the literature, the authors consider, that by capable methods of reconstruction of doses, which do not surpass 0.5 Gy are only following: an output unstable chromosomal aberration, EPR-spectrometry of enamel of teeth and imitating modeling of activity of the liquidators. Irrespective of a basis of these methods: biological for first, physical for second and mathematical for third, all of them are as a matter of fact expert.

For all listed methods is characteristic elimination of the information on a dose of an irradiation of the liquidator. In the first case it is connected with elimination of crates of blood containing chromosomal damages, in second - to accumulation of an additional dose in a tooth in the post accident period, in third - that the participant of works forgets in due course important details of the work on liquidation of failure.

Told wholly concerns to reconstruction of doses of external scale - radiation. Second, on a level of influence on the liquidators is external бета-излучение on skin covers and хрусталик. In this case first two methods retrospective dosimetry are not applicable and the third method - imitating modeling becomes complicated with simultaneous increase of uncertainty in a rating of a dose, since in this case transition to a dose of external beta-radiation is made through the attitude $P_\beta/P_\gamma$ at known size D. However even in this case uncertainty in a rating of doses will be less, than in case of a rating of doses from incorporated radionuclides, which are much lower, than dose from bete-radiations.

In the report the results of application of existing methods retrospective dosimetry with reference to accident on ChNPP and comparative rating of their efficiency will be submitted.

DYNAMICS OF PLUTONIUM HUMAN EXCRETION AFTER THE DELAYED DTPA INJECTION
Z.Menshikh, V.Khokhrjakov, E.Lubchansky, N.Okladnikova
In connection with improvement of radiation conditions on «Mayak» PA the plutonium body burden at the personnel decreases, using of DTPA with the diagnostic purpose therefore can matter. On the basis of excretion measurings after the delayed introduction of DTPA (pentacini) to 22 workers in clinical conditions the influence of a preparation doze (D, g) on acceleration multipie of plutonium urine removing (Ka) is investigated. The power dependence kind is received: 
\[ Ka = 204 D^{0.79 \pm 0.12} \]
for the investigated area of dozes from 0.025g up to 0.25g. Extrapolation of the received expression for limits of area of supervision results leads to the overestimated results: so for example, with \( D = 1 \)g is received four-multiple understating in comparison with the literary data, that is connected, probably, to rather smaller relative plutonium pool volume, accessible for complex binding with DTPA.

Excretion dynamics within first two days and two next weeks was research. The empirical temporary dependence allows to calculate the meanings of plutonium urine excretion factors for an estimation of the radionuclide body burden on tests, collected in some time after chelate influence is received.

**APPLICATION OF EPR DOSE RECONSTRUCTION WITH TEETH TO SOUTHERN URALS POPULATION. ACHIEVEMENTS, PROBLEMS AND PERSPECTIVES**

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The method of EPR dose reconstruction in teeth is based on the measurements of the stable radiation-induced radicals in hydroxyapatite, which is a mineral component of all dental tissues (tooth enamel, dentin, and cementum). Technically, this method consists of teeth collection, sample preparation, EPR measurements, and calibration of EPR radiation response in dosimetric units. As it follows from the results of the latest international intercomparisons, doses in the range 150-200 mGy can be reconstructed precisely and reliably. The dose detection limit is about 50 mGy, and is likely to be brought down to 25 mGy. However, from our point of view, the main difficulty of applying the EPR dose reconstruction is correct interpretation of the obtained results. The latter is affected by specific conditions of the population exposure. The peculiarities of the Southern Urals case are: (i) a relatively long-term and low-rate irradiation; (ii) a considerable period (40-50 years) between the time of receiving the main portion of the dose and the dose reconstruction; (iii) substantial (often predominant) \(^{90}\)Sr dose contribution; (iv) various contributions to the total reconstructed dose (external, internal, background, medical etc.). The developed approaches to interpretation of the results of EPR dose reconstruction, which take into account the peculiarities listed above, will be discussed. Possible new directions and perspectives of EPR retrospective dosimetry applications will be also described.
THE INFLUENCE PLUTONIUM IN WORKERS
AT THE RADIOCHEMICAL PLANT

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The data were obtained on results of radiochemical analysis of soft tissue and bone samples taken at autopsy of workers of the radiochemical plant. It is shown that the health state and the grade of the pathological process have an effect upon distribution of systemic Pu at the long time after inhalation intake in workers. The skeleton to liver systemic ratio is 50,3 : 42,3 = 1,2 for the practically healthy people. As the health state worsens and the pathology becomes more sthenic that is accom-pained by the involving of the liver in the pathological process the fraction of the Pu deposition in liver decreases and the fraction in the skeleton increases in the same grade. The people with serious liver diseases (cancer, massive metastases in the liver, cirrhosis, alcoholism) have got the ratio the skeleton : the liver = 77,9 : 14,9 = 5,5. The scientific data on this problem are absent in references. On the base of the results of the multifactorial regression analysis it is shown that the intensity of Pu translocation from the liver to the skeleton occurs faster under pathological processes than under the normal life conditions. It should to be assumed that for persons with different heavy chronic diseases the skeleton and liver exposure doses may differ from the calculated ones if the doses are evaluated from the models that do not take into account the plutonium recycling in systemic organs under the pathological processes.

STUDY OF THE NATURE OF THE DOSE DISTRIBUTION IN THE RURAL INHABITANTS (CHERNOBYL EXPERIENCE)

A.M.Skryabin

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The dose distribution in the population is the result of multifactory interaction. Conceptually, a dose has a double nature: physical and humanitarian. The second one, reflecting the practical activity of the people, united in the socium, is not studied. The understanding of the processes of the dose formation and their modeling is impossible without studying the interrelationship between these two factors and the clarification of their roles. The two-factor statistical analysis of the parameters of the internal dose's distribution (WBC-measurements), i.e. the average dose (D) and the standard geometric deviation (βg-parameter), was conducted. The physical factor was formalized into the factor-sign "the density of the territory contamination with $^{137}$Cs ($\sigma$, Ci/km$^2$)" and the socio-humanitarian one was denominated through the number of the inhabitants in a settlement i.e. in the socium (N, person). Scales are taken in the interval breakdown: $\sigma$ - <5, 5-10,>10 Ci/km$^2$; N - <100, 100-500, >500 persons. As a result, the 3 x 3 –matrix of the distribution of average dose and average standard geometric deviation was received. The clear dependence of these distribution parameters on the N- and $\sigma$- factors is set up. In particular, D shows a direct dependence on...
σ and inverse dependence on N. βg – parameter shows a direct dependence on both of these factors. In other words, with the growth of the number of the inhabitants in a settlement D decreases, but with the increase of the density of the contamination D increases. The polar effect of the factors is evident. Thus, the greater number of the inhabitants and the density of contamination there are the greater variance of dose (βg – parameter) we have. The correlation of the N- and σ-factors in both cases is in favour of N, i.e. the humanitarian factor is dominant in the dose formation process.

**RECONSTRUCTION OF ⁹⁰Sr INTAKE FOR POPULATION LIVED ON THE TERRITORY OF EAST URALS RADIOACTIVE TRACE**

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The East Urals Radioactive Trace (EURT), resulted from a thermal explosion in a tank containing radioactive waste from nuclear fuel reprocessing cycle at the plutonium production complex Mayak 29 September 1957. The release of about 2 million curies to the atmosphere occurred. Considerable quantity of environmental ⁹⁰Sr examinations, bone- autopsy, and Whole Body Counter (WBC) ⁹⁰Sr measurements were performed at URCRM in the period 1958-1997. The available ⁹⁰Sr measurements in the food stuff samples and in the bone samples for the residents from the EURT were analyzed. That allowed to determine the methodological approaches to ⁹⁰Sr intake reconstruction both for residents of resettled and non evacuated villages. For non-evacuated settlements (Bagaryak, Boulzy, Yushkovo, Tat. Karabolka, Allaky) dietary intake was reconstructed in detail on the basis of analysis of ⁹⁰Sr content in local food stuffs. Calculated values of ⁹⁰Sr intakes were used for ⁹⁰Sr skeleton content estimations. For this purposes the calculated ⁹⁰Sr annual intakes were introduced to age-depend model for ⁹⁰Sr retention in human bone. The comparison of calculated ⁹⁰Sr bone concentrations and measured values allows to confirm that the calculation method is reliable for about 15% of adult population (the called critical group) with maximal level of intake. The average values of ⁹⁰Sr intake, characteristic of the other part of population, are lower by a factor of 3.5. For evacuated settlement there are no reliable data on ⁹⁰Sr content in rations. The analysis of WBC data is practically the only way to estimate ⁹⁰Sr intake level. ⁹⁰Sr intake was assumed as a acute intake, and strontium ingestion level was calculated according to the ⁹⁰Sr biokinetic model for residents evacuated within 7-14 days (Berdyanish, Satlykovo, Galikaev) and 250 days after explosion (Alabuga, Yugo-Konevo).

**EFFECTIVITY OF URGENT DTPA-THERAPY AT PLUTONIUM INTAKE THROUGH THE DAMAGED SKIN IN CONSEQUENCE OF CHEMICAL SKIN BURN**

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Intravenous injection of DTPA in one day after skin contamination by plutonium-239 nitrate and then during followed 30 days at decreasing dose of chelate allowed to remove 98% of resorbed radionuclide. The systemic measure of alpha-activity of contaminated skin, urine analysis, blood and plasma analysis allowed to observe the dynamics of the intake process and to evaluate the radionuclide fraction resorbed into the blood which was 4.1% from the initial deposition on the skin.

The kidneys clearance of plutonium at different stages of chelatotherapy changed from 3-4 ml/min to 110-190 ml/min. The high effectivity of the treatment is explained by effective chelate influence on plutonium removing at early phase after the radionuclide intake into the blood.

ASSESSMENT OF INTERNAL EXPOSURE IN THE TOOTH TISSUES DUE TO INCORPORATED $^{90}$Sr

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The retrospective EPR-dosimetry research in the tooth tissues of the Techa Riverside population has been conducted since 1993. The purpose of the investigations is reconstruction of cumulative doses of external radiation. However, the results obtained on tooth samples collected from the Techa riverside population represent doses accumulated due to several sources of irradiation. Along with doses from background and external exposure, the irradiation from incorporated $^{90}$Sr takes place in tooth tissues. In this study we calculated the tooth tissues dose coefficients for different teeth. The results can be used to assess doses from internal $^{90}$Sr exposure. For this purpose a Monte-Carlo method for statistical modeling was used. The dependence of dose coefficients on the geometrical sizes of tooth tissues was described. An essential influence of teeth sizes on the results of dose coefficient calculation was shown. The sizes of teeth from the investigated population were measured and their statistical parameters were analyzed. Taking into account these results the enamel and dentine dose coefficients and their variations for all teeth of denture were calculated for each tissues-sources. This work may have very important applications. The results obtained in this study allow to get more correct interpretation of dosimetric EPR-measurements.

DIETARY INTAKES OF $^{90}$Sr AMONG THE POPULATION OF THE EAST-URALS RADIATION TRACE OVER THE TOTAL PERIOD SINCE THE ACCIDENT
Estimation of the current and cumulative effective exposure doses for residents of the EURT area will require the use of data on the rates of dietary intakes of radionuclides for the overall time period since the accident. Levels of contamination of foodstuffs with $^{90}\text{Sr}$ have been determined systematically since 1960 in 6 populated areas located within 30-90 km of the epicenter of the blast (Allaki, Bulzi, Bagaryak, T. Karabolka, Shcherbakovo, Yushkovo). The specific activity of $^{90}\text{Sr}$ in milk for the period 1958-1959 was reconstructed based on data for the year 1960, and the dependences governing the decrease with time of $^{90}\text{Sr}$ content in milk after the fallout of the radionuclide in 1967 due to a down-wind transfer of activity from the shores of the Karachai Lake. Under these conditions, the specific activity of $^{90}\text{Sr}$ in milk was found to have decreased 2-fold during the pasturing period 3 years later, compared to that registered in 1967.

A decrease with time of specific activity of the radionuclide in milk which is the main pathway of $^{90}\text{Sr}$ intakes is described by an exponential dependence with a period of half-decrease ($T_{1/2 \text{ eff}}$) of about 10 years.

Four decades after the accident the estimated annual intake of $^{90}\text{Sr}$ with diet was 3.6 mBq/day at initial contamination density on the territory of 1 Bq/m$^2$. Compared with the first year after the accident the dietary intake of $^{90}\text{Sr}$ has decreased 150-fold as of now.