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The Role of Radiobiology and Nuclear Medicine in Protection from the Effects of Ionizing Radiation (Domestic Experience)

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Abstract—This article presents the domestic experience in nuclear medicine, radiobiology, radiotoxicology, radiation protection, and health maintenance of nuclear industry workers and residents of the region of location of radiation hazardous facilities of the Russian Federation.

In addition, the authors address the history and stages in the establishment of nuclear medicine and radiobiology in Russia, as well as modern projects and the prospects of further development of healthcare provision for workers in the nuclear industry.

Keywords: nuclear medicine, radiobiology, radiotoxicology, radiation protection, radiation-hazardous objects, healthcare provision for workers in the nuclear industry.

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In Russia, systematic research in radiobiology, radiotoxicology, nuclear medicine, and radiation safety is considered to have begun on June 29, 1946 [1]. It was the day when the Council of Ministers of the Soviet Union issued a special Resolution to establish the first radiation laboratory as an autonomous research institution within the Academy of Medical Sciences, later renamed the Institute of Biophysics and currently known as the Burnazyan Federal Medical Biophysical Center of the Federal Medical Biological Agency State Research Center.

In February 1947, N.N. Anichkov, the President of the Academy of Medical Sciences, and G.M. Frank, the Director of this laboratory and corresponding member of the USSR Academy of Medical Sciences, presented a report on the proposed fields and plans of activity at the radiation laboratory, which was presented at the meeting of the Scientific and Technical Council (STC) of the First Main Directorate of the Council of Ministers of the USSR responsible for the

development and production of nuclear weapons in the Soviet Union. Active participants in the discussion were Academician I.V. Kurchatov, the Chairman of the Scientific and Technical Council and Scientific Director of the Soviet Nuclear Program, and the foremost scientists in this field: Academicians N.N. Semenov, Yu.B. Khariton, and I.K. Kikoin.

For the sake of historical objectivity, it should be noted that there was a generally little known and currently top secret Laboratory “B” established at the end of 1946 in the depths of the 9th Department of the People’s Commissariat for Internal Affairs in the Ural village of Sungul, with a staff of unescorted scientists taken from Gulag camps, interned German specialists, and free employees [2].

According to the available data, the work started at the radiation laboratory of the Institute of Biophysics has involved, since the 1950s, more than 30 institutes and laboratories of the Academy of Sciences, the Ministry of Health, the Ministry of Defense, and the Ministry of the Medium Machine-Building Industry, as well as chairs and laboratories of the Ministry of Higher Education. Their activities were coordinated by Task Group No. 1 of federal significance and Section No. 5 of the Science and Technology Council of the Ministry of the Medium Machine-Building Industry [3].

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Thus, the history of nuclear medicine and radiobiology in Russia is associated with the development of nuclear weapons and the establishment of the nuclear industry. At the origins of these sciences, there were outstanding scientists and healthcare coordinators such as Corresponding Member of the USSR Academy of Sciences G.M. Frank and Academicians of the Academy of Medical Sciences of the USSR A.A. Letavet, F.G. Krotkov, and E.I. Smirnov.

One of the top research trends in the field of nuclear medicine and radioepidemiology was the study of long-term radiation effects on the personnel and the population, including risk assessment for carcinogenic and genetic effects. This problem has been addressed by the establishment of medical dose registries (MDR), their social significance being determined by the unique combination of historical experience of Russian nuclear medicine and modern highly effective computer-based technologies.

The main dose registries are the following:

- The Regional Registry of persons exposed to radiation from the settlements in the Techa River basin.
- The Industry Registry of persons with occupational diseases.
- The Industry MDR of liquidators of the consequences of the Chernobyl accident and employees of the Ministry for Atomic Energy and Industry.
- Registry of acute radiation injuries in humans.
- Regional MDR of the personnel of the Siberian Chemical Combine (Seversk).
- Regional MDR of the personnel of the Mining and Chemical Combine (Zheleznogorsk).
- National Radiation and Epidemiological Chernobyl Registry (Obninsk).

The combined cohort formed on the basis of the Mayak Production Association Personnel Registry included approximately 57 000 workers with estimated external radiation doses; for some of them, the levels of exposure to incorporated plutonium were estimated. The study of long-term radiation effects in this cohort is the top priority due to the global degree of novelty of this resource.

The Burnazyan Federal Medical Biophysical Center of the Federal Medical Biological Agency of Russia has been keeping a registry and database on human acute radiation injuries that is unparalleled anywhere in the world [4, 5]. Based on these data, Russian and English versions of the Atlas on Human Acute Radiation Syndrome, the only one in the world, containing unique data on the clinical presentation and dosimetric characteristics of more than 150 people with acute radiation injuries, were published in 2016–2019 [6, 7].

The problem of scientific development of the methods and ways to protect the population in areas of radiological emergencies had always attracted great attention. There are numerous publications devoted to

the vast experience accumulated in Russia [3, 8]. Examples are the book *Major Radiation Accidents: Consequences and Protective Measures* translated into English and Japanese [9] and the fundamental work *Nuclear medicine: A Guide for Medical Researchers and Healthcare Organizers*, in four volumes, edited by Academician L.A. Il'in [10].

It is known that the clinic of the Burnazyan Federal Medical Biophysical Center for many reasons has a vast experience in diagnostics, treatment, and medical rehabilitation of patients with acute radiation sickness [10, vol. 2]. Based on this experience, the classification of various radiation injuries caused by both external and internal radiation exposure, as well as the principles of biodosimetry and cytogenetic methods, were developed for the first time in world practice; in addition, effective treatment regimens for bone marrow syndrome and local radiation injuries were proposed [6, 11].

Nowadays, one of the actively developing innovative trends is the treatment of local radiation injuries using mesenchymal stem cells in combination with microsurgical techniques. Very encouraging experimental results have been obtained: the treatment procedure developed at the Burnazyan Federal Medical Biophysical Center accelerates wound surface healing by two or more times. More detailed information on this subject can be found in the joint article of specialists from the Burnazyan Federal Medical Biophysical Center of Federal Medical Biological Agency and the Institute for Radiation Protection and Nuclear Safety of France published in the international peer-reviewed journal "Cells" in September 2020 [12].

In recent years, studies of the molecular, biochemical, and genetic mechanisms of radiation injuries and recovery after radiation exposure have become a top priority, because scientists have focused their efforts on investigation of the role of DNA and its repair pathways as one of the key elements of living systems. Radiobiologists have studied the molecular and cell death mechanisms in irradiated cells. These studies are of great interest both for the formation of the conceptual basis of pathogenesis of radiation injuries and for the development of appropriate methods and techniques for prevention and treatment of radiation injuries [13–16].

At present, radiation safety assurance for the personnel and the population requires new highly sensitive technologies of biodosimetry that would surpass the conventional cytogenetic tests. The currently developed technologies for biodosimetry of radiation effects provides for an increase in the threshold of sensitivity to 30–50 mGy, which is extremely important for dose recovery, both in the personnel and as a result of radiation accidents [17–20].

Large-scale experiments in radiotoxicology were performed by Russian medical scientists with the participation of physicists–dosimetrists. The radiotoxi-

cology of the main biologically significant radionuclides, plutonium-239, polonium-210, cesium-137, strontium-90, iodine-131, etc., has been studied in detail [21–23]. The doses damaging the critical organs and red bone marrow were estimated, and radioprotective agents have been developed [24].

Radiopharmaceuticals as a basis of nuclear medicine and drugs for preventing incorporation of radioactive substances and stimulating their removal from the body were proposed and put into practice as a result of radiotoxicology research. In 1972, Professor N.N. Suvorov and his coworkers synthesized a chemical compound from the group of biological amines [25]. The dosage forms of this compound were tested in different military contingents, including the crews of two nuclear submarines after combat alert duty. This radioprotective agent was officially named indralin, and its solid oral form as tablets was designated as B-190 after A.I. Burnazyan. The scale of pre-clinical and clinical experimental studies of radioprotectants is comparable with the scale of modern research in the field of treatment of the new coronavirus infection. It is no coincidence that many people draw an analogy between COVID and radiation: both enemies are invisible and both pose a serious threat to people's life and health. At present, B-190 is a standard drug for prevention and immediate administration in case of gamma and gamma–neutron radiation exposure at the facilities of the Rosatom State Nuclear Energy Corporation, the Ministry of Defense, the Ministry of Emergency Situations, and other institutions. B-190 is also included in the emergency first aid kit of Rosatom personnel. The domestically produced agent Betaleukin is also recommended as an emergency radioprotectant administered within 2–3 hours after radiation exposure, and the original DNA-based drug deoxinate (derinate) is recommended for complex treatment of acute radiation sickness.

The domestic line of protective agents against incorporation of the most biologically significant radionuclides includes stable iodine (KI) at adult and pediatric doses to be used in case of exposure to iodine radionuclides; ferrocen-containing sorbent to be used for binding radioactive cesium in the gastrointestinal tract; and ion-exchange sorbents Adsobar and Polysurmin to be used for absorption of strontium radionuclides. The following complex-forming drugs are used to accelerate the removal of radioactive substances from the body: oxathiol used to prevent the incorporation of polonium-210 and pentacin-DTPA (diethylenetriamine-pentaacetic acid calcium trisodium salt) and zincacin (the zinc salt of this compound) used to stimulate the removal of radioactive isotopes of the rare earth elements, plutonium, and transplutonium elements.

Among different methods and ways to protect people against technogenic radiation exposure, the regulation (rationing) of radiation exposure of people and

strict abidance by the respective rules are exceptionally important. These studies were initiated by I.V. Kurchatov. In early 1949, he commissioned the Institute of Biophysics with developing and substantiating the tentative maximum permissible levels of radiation exposure for professional employees to fragmented radionuclides—uranium and plutonium fission products. In addition, Kurchatov conveyed the data on the properties of these radioactive substances, strictly secret at that time, to scientists of the Institute.

In 1952, the National Commission for Radiation Protection was established at the USSR Ministry of Health, with the main task to develop national radiation safety standards, the implementation of which was mandatory for all facilities using, producing, processing, storing, and transporting radioactive substances. In 1960, the first permissible levels were approved, followed by “Radiation Safety Standards” and “Basic Sanitary Rules for Radiation Protection.” Many years of experience in the radiation and hygienic support of works at all stages of the nuclear fuel cycle resulted in the development of “Sanitary Rules for Design of Nuclear Industry Enterprises and Facilities” and “Sanitary Rules for Design and Operation of Nuclear Power Plants.” At present, we have completed the preparation of a new regulatory document: “Safety Rules for Decommissioning of a NPP Power Unit.”

As a result of implementing these documents into practice, in strict adherence to operational discipline at the facilities of the Rosatom State Nuclear Energy Corporation, the average annual effective dose for personnel, according to the data of dosimetry monitoring, currently does not exceed the established radiation safety standards (the value of 2009): 20 mSv per year, being a fraction of this value (Fig. 5).

The experience in radiation and hygienic work in the period of establishment and operation of nuclear industry enterprises determined the demand of medical scientists for a three-zone system in the planning, construction, and maintenance of the respective facilities. The point at issue is the sequence of workers passing from the so-called dirty areas with radioactive contamination to the clean premises under continuous dosimetric control. This principle of protection against radiation has played a huge role in radiation safety assurance for nuclear industry workers.

As regards compliance with the above-mentioned regulations, the following fact can be presented: compared to 2000, the number of nuclear fuel cycle workers receiving an individual effective dose of 20 mSv/year has decreased to date from 547 people to single cases. We would like to note that there are 65 600 specialists under dosimetric control at the Rosatom State Corporation. Over the past 23 years, no cases of acute radiation sickness have been recorded among the corporation personnel, with only two confirmed cases of local radiation injuries in 2012.

Fig. 1. The founders of nuclear medicine and radiobiology: G.M. Frank, A.A. Letavet, F.G. Krotkov, and E.I. Smirnov.

Implementation of a science-based system of medical care and sanitary-hygienic regulation in the field of radiation safety resulted in rather low occupational morbidity compared to that in other industries, according to the data of the Departmental Registry of occupational diseases among the Rosatom personnel, and the contribution of diseases that can be associated with the radiation factor is only a few percent. These are single cases: for many years, ionizing radiation has been the cause of occupational (oncologic) diseases only among the employees involved in uranium mining.

In recent years, an ambitious “Breakthrough” program on the new-generation nuclear energy technologies and the new nuclear energy platform has been implemented at the initiative of the management of

the Rosatom State Nuclear Energy Corporation. It involves the development of a closed nuclear fuel cycle based on fast-neutron reactors with a new type of nuclear fuel: mixed uranium-plutonium nitride fuel. Having extensive experience in the studies on medical-hygienic and dosimetric support for the development of technologies and production of uranium-plutonium fuel and reprocessed uranium, the scientists and experts of the Burnazyan Federal Medical Biophysical Center have examined the radiation situation and have prepared the medical and technological requirements for radiation safety assurance for the personnel of the experimental demonstration complex established at one of the nuclear plants. The next stage will be substantiation of design solutions and requirements for radiation safety assurance in industrial implementation of the “Breakthrough” project for professional employees and local residents in the affected area.

In the context of further improvement of the medical and sanitary support for nuclear industry workers, the following scientific and practical trends are the top priorities:

- Improvement and development of new medical and sanitary technologies for radiation safety assurance.
- Completion of a unified system of radiation and hygienic response and medical aspects of protecting people in case of radiation accidents.
- Further search and development of the methods and techniques for prevention and treatment of human radiation pathology, including innovative biomedical technologies.
- Improvement of the techniques for studying the long-term consequences of radiation exposure of the personnel of radiation hazardous facilities and the population.
- Implementation by specialists of the Federal Medical Biological Agency of Russia of international cooperation in the field of nuclear detection, situational response, and countering nuclear terrorism [26]; this new scientific trend is the biomedical nuclear forensic science.

Fig. 2. L.A. Il'in, Academician of the Russian Academy of Sciences, Honorary President of the Burnazyan Federal Medical Biophysical Center of the Federal Medical Biological Agency State Research Center of Russia, with an edition of *Radiation Accidents*.

Fig. 3. The domestic pharmacological protective agents used in the event of gamma and gamma-neutron radiation exposure.

Fig. 4. The dynamics of radiation doses received by the personnel of the Rosatom State Nuclear Energy Corporation, 2009–2018.

Fig. 5. The dynamics of occupational morbidity of employees of the Rosatom State Corporation.

• Gradual transition to the prophylactic trend with respect to detection of occupational and socially significant diseases responsible for the main labor losses in the nuclear industry.

One of the most important trends in the field of protecting people from the effects of radioactive substances is research and development of personal protective equipment. In the initial period of establishment of the nuclear industry, when the concentration of radioactive aerosols in the air of working areas was, in most cases, hundreds to thousands of times above the standard values, the most important challenge was designing respiratory personal protective equipment. One of the successful solutions of this problem was the famous disposable respirator ShB-1 Lepestok made in

the late 1950s of the so-called Petryanov filter fabric (named after the outstanding Russian scientist, Academician I.V. Petryanov-Sokolov). The efficiency of these respirators at low breathing resistance was up to 99%. This work was awarded the Lenin Prize [27].

By early 2019, the production of ShB-1 Lepestok had reached six billion pieces, and it is successfully used in many industries. Figure 7 shows self-contained atmospheric protective ensemble suits for work with radioactive substances, including supplied-air models, designed with the participation of specialists from the Institute of Biophysics. Responding to the requests of our time, the Burnazyan Federal Medical Biophysical Center in cooperation with the Gamaleya Research Institute of Epidemiology and Microbiology

Fig. 6. The authors of the ShB-1 respirator Lepestok-200: S.N. Shatsky, I.V. Petryanov-Sokolov, S.M. Gorodinsky, and P.I. Basmanov.

Fig. 7. The personal protective equipment against ionizing radiation, bacteria, and viruses.

of the Russian Ministry of Health developed a technology for radiation treatment of overalls used in the work with the coronavirus infection, with the purpose of its repeated use in case of emergency.

Addressing the problem of radiation accidents, we should note that in the USSR there were altogether 352 radiation accidents at civilian institutions and at the facilities of the Ministry of the Medium Machine-Building Industry, the Ministry of Nuclear Energy and Industry, and the Ministry of Defense, according

to the Registry of the Burnazyan Federal Medical Biophysical Center (Table 1). The total number of incidents was 748; among them, acute radiation sickness (ARS) of various severity was established in 352 people, with 70 recorded fatal outcomes. The maximum number of ARS cases (134) occurred as a result of the Chernobyl accident. Here we refer to two contingents: witnesses to the accident and firefighters. There were no established ARS cases among the so-called liquidators, i.e., the contingent involved in emergency work

Table 1. Registry of radiation accidents and incidents in the USSR and Russia, 1949–2016

Type of incident	Number of incidents	Number of injured persons		
		Total	ARS	Dead
Incidents with radiation sources	90	154	45	15
X-ray machines and accelerators	43	52	—	—
Reactor incidents and loss of control over the critical mass of the fissile material (excluding Chernobyl 1986)	33	82	73	13
Chernobyl accident 1986	1	134	134	28
Accidents with local radiation injuries (LRI) at Mayak Production Association (1949–1956)	168	168	—	—
Nuclear submarine accidents and nuclear test emergencies	5	141	93	12
Other incidents	12	17	7	2
Total	352	748	352	70

at the Chernobyl nuclear power plant and in the 30-km area, or among the population living in the zones of radioactive contamination [4, 5].

One year after the events in Chernobyl, the Institute of Biophysics sent a fundamental report to the United Nations Scientific Committee on the Effects of Atomic Radiation, the world scientific authority most competent in this field. In the report to the UN General Assembly in 1988, the Committee assessed the information provided by the USSR as comprehensive and very valuable, considering it to be indebted to all authors for the willingness to share their experience and acknowledged their professional excellence and human compassion for such tragic circumstances [28].

Much attention has always been paid to the problem of scientific development of the methods and ways to protect the population in areas of radiological emergencies. It should be recalled that 19 years before the Chernobyl accident Soviet scientists, on the basis of their own experimental data and trials with volunteers, compiled the “Instructions on Iodine Prophylaxis in the Event of Radiation Accidents at Nuclear Plants,” which was approved by the USSR Ministry of Health; in 1970, the USSR Ministry of Health approved the unclassified “Temporary Guidelines for the Development of Measures to Protect the Population in the Event of Nuclear Reactor Accidents,” also prepared under supervision of the Institute of Biophysics [29].

In the framework of analysis of radiation accidents, the Chernobyl disaster takes a special place, primarily due to its scale. It will be recalled that this accident resulted in radioactive contamination of the territory of the European part of the USSR over an area of about 150 000 km² with about 6.2 million residents (within an isoline of 1 Ci/km²). In the shortest time possible, it was necessary to solve the problem of developing a scientifically grounded strategy for gov-

ernment actions to protect the population in these unprecedented and life-threatening circumstances. Within two weeks after the accident, the research team working at the emergency facility together with experts of the USSR State Committee for Hydrometeorology and the agro-industrial complex developed, under the scientific supervision of Academicians L.A. Il'in and Yu.A. Israel (for the first time in world practice), “Recommendations on the criteria for habitability, need of resettlement, and temporary displacement in the territory exposed to radioactive contamination as a result of the Chernobyl accident.” This document approved at the highest level on May 22, 1986, established the emergency regulations for radiation exposure of the population: 100 mSv in the first year after the accident (with a subsequent decrease in this value) and establishment of first zoning of the territories depending on the levels of gamma radiation in situ. In the areas with high levels of radioactive contamination (the zones of tight control), where radiation doses could be more than 100 mSv/year without taking restrictive measures, there were 273 000 people living in 789 settlements. According to the Recommendations, the following life activity restrictions were introduced in these zones: a ban on consumption of milk and local food products with their replacement by “clean” products, preferential stay of people in buildings rather than in open areas, etc. As a result, the radiation dose was reduced by three times compared to the established regulations. Radiation safety assurance for the population living in the zones of radioactive contamination required numerous calculations of the maximum permissible levels of internal radiation exposure (100 mSv of total exposure: the emergency temporary standard). In the same period, the guidelines for radiation and hygienic control in situ and at food production enterprises were developed.

The measures for protecting people, including the analysis of the radiation situation and radiation burden on the population of affected areas, allowed medical scientists to make a preliminary forecast of potential long-term consequences in the form of cancer incidence [3]. This prognosis indicated an extremely low probability of radiation-induced leukemia and solidary cancers, with the exception of expected increase in the number of malignant thyroid tumors among children. In the latter case, it was for administrative, organizational, and bureaucratic reasons, which played a negative role, preventing practical implementation of the methods and procedures of iodine prophylaxis and other recommendations developed long before the Chernobyl accident. The above-mentioned forecasts were confirmed by some foreign and domestic experts.

The Chernobyl accident raised a serious question about the fate of the population of Kiev, the capital of Ukraine, of three million people, as the Politburo of the Central Committee of Ukraine planned to evacuate the entire child population and, therefore, most adults to areas not affected by radiation on May 7, 1986. Yu.A. Israel and L.A. Il'in opposed this proposal at the Politburo meeting, relying on scientific data on the radiation situation and its forecast. As a result, this action with obvious grave socioeconomic consequences was halted and the validity of position of the scientists was later fully confirmed.

In conclusion, it should be noted that the Russian Academy of Sciences, for the first time in the history of our country, has dedicated a Scientific Session of the General Meeting to the anniversary date of a particular industry. The history of the Atomic Project demonstrates not the contribution of the Academy of Sciences to the development of the nuclear industry but rather its top priority for this epoch-making undertaking. The prophetic words of Academician I.P. Pavlov, the outstanding Russian physiologist, which he uttered more than 100 years ago in 1914, are more than ever resonant with the problems of today: "What we, Russians, particularly need now is the propaganda of science aspirations, the abundance of research tools, and the passion for scientific work. It is obvious that science is becoming the main leverage in the life of the people; neither independence nor, moreover, deserved position in the world can be retained without it."

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