THE "CLINIC" MEDICAL-DOSIMETRIC DATABASE OF MAYAK PRODUCTION ASSOCIATION WORKERS: STRUCTURE, CHARACTERISTICS AND PROSPECTS OF UTILIZATION

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***Abstract*—To study early (deterministic) and long-term effects of radiation exposure, the "Clinic" medical-dosimetric database for the Mayak Production Association worker cohort has been established at the Southern Urals Biophysics Institute (SUBI). This paper describes the principles of organization, structure and prospects of future utilization of this database. Health Phys. 94(5):449–458; 2008**

Key words: exposure, occupational; exposure, radiation; health effects; nuclear workers

INTRODUCTION

DURING RECENT decades findings of the studies on effects of exposure to ionizing radiation on human health have been widely published. These are mainly from four sources: Japanese survivors of the atomic bombings of Hiroshima and Nagasaki; patients exposed to radiation for medical purposes (radiation diagnostics and therapy); nuclear workers occupationally exposed to chronic radiation; and populations living in the areas contaminated with radionuclides as a result of accidents at the Chernobyl power station and Mayak Production Association (Mayak PA).

Each of these sources has limitations in terms of using the findings from study of these cohorts to develop and refine radiation safety and radiation protection standards and to solve problems in radiation medicine. In particular, the atomic bomb survivors were exposed to acute external radiation at a high dose rate, whereas occupational exposures at nuclear facilities have generally arisen over a much longer period. Use of the findings of the Japanese population studies involves models to extrapolate from high doses to low doses, and from single (acute) or high dose rate exposure to prolonged (chronic) or low dose rate exposure. However, all extrapolation models have uncertainties and have been the subject of debate over many years. Individuals therapeutically exposed to radiation are often cancer patients who received significant fractionated and localized irradiation at high dose rate along with other types of treatment (chemotherapy). Studies of nuclear worker cohorts in countries such as U.S., Canada, UK, and France do not at present provide sufficient information to estimate dose-response relationships precisely, mainly due to the fact that the overwhelming majority of these workers were exposed to low doses of radiation. It is clear that the data available on populations exposed to low doses, low dose rates, and prolonged exposure, especially from internal alpha exposure from incorporated ^{239}Pu, are insufficient at present to provide precise risk estimates.

The cohort of Mayak workers has high potential to provide such information. Mayak PA was the first Russian nuclear enterprise and is located in the Southern Urals in Russia. It was put into operation in June 1948 and included all the plants necessary for weapons-grade plutonium production: namely, reactors, a radiochemical plant, a plutonium production plant, and auxiliary plants. Due to a lack of experience in operating such an enterprise and the short period allowed by the government to produce weapons-grade plutonium, the majority of Mayak personnel who worked during the start-up phase and in the early period of operations (1948–1958) were chronically exposed to high doses of external and/or internal ionizing radiation.

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Practically from the very first days of the nuclear weapons production program, special medical institutions for both practical public health (Medical-Sanitary Department No. 71, now the Central Medical-Sanitary Unit No. 71) and research [Branch No. 1 of Biophysics Institute, now the Southern Urals Biophysics Institute (SUBI)] were established with the main aim of organizing medical provision for personnel working at Mayak and for the population of Ozyorsk (the city where Mayak PA is sited).

From the first days of Mayak operation, the special system of personnel medical observation included an obligatory pre-employment medical examination and routine medical examinations of all the workers based on a common standard program. These examinations were conducted once every three months during 1948–1954, once every six months during 1955–1960 and annually starting from 1960. In addition, workers underwent a more detailed examination at a specialized hospital (the SUBI Clinic) once every 3–5 y. After quitting their job at Mayak, if the former worker stayed in Ozyorsk, he/she was examined at the same specialized medical hospital based on the same standard program. This system of medical observation of Mayak personnel health allowed a unique archive of primary medical data to be accumulated.

As a consequence of the long-term and careful storage of the medical follow-up data, a unique medical-dosimetric database entitled "Clinic" for the cohort of Mayak workers chronically exposed to radiation has been established at SUBI.

It should be noted that individual dosimetry of external gamma exposure was introduced at each workplace after Mayak PA was put into operation (Khokhryakov et al. 2000b; Vasilenko et al. 2001; Anspaugh et al. 2002; Khokhryakov et al. 2002; Romanov et al. 2002). Monitoring for internal exposure from incorporated ^{239}Pu was introduced at Mayak PA during the 1960's (Khokhryakov et al. 2000a and b, 2001, 2002, 2006; Suslova et al. 2000; Romanov et al. 2002, 2003). Monitoring for internal exposure was performed on individuals working in the areas where the potential for internal exposure existed, whether or not the potential was high or low.

The goal of this paper is to describe the principles of organization, structure, characteristics and perspectives of future utilization of the "Clinic" medical-dosimetric database for the Mayak worker cohort.

PRINCIPLES OF ORGANIZATION AND STRUCTURE OF THE "CLINIC" MEDICAL-DOSIMETRIC DATABASE

The creation of the "Clinic" medical-dosimetric database included several stages with specific tasks at each stage. The creation and organization of the "Clinic" medical-dosimetric database is shown schematically in Fig. 1.

At the first stage, the aims of the database creation were defined; the criteria for follow-up cohort identification were established; the availability and accessibility of the primary (basic) sources of information were checked; the structure of the database was developed; a manual for database content, coding, and data location in the database ("Code book") was prepared; unified forms ("Coding cards") to collect primary data were prepared; procedures for quality control to ensure completeness and accuracy of the data contained in the database were developed; and regulations for access to the primary data and to other data contained in the database were developed.

At the second stage, the primary information was searched, collected, and then extracted into the paper forms ("Coding cards"). Disease diagnoses and causes of death were coded in accordance with the International Classification of Diseases of the 9th revision (ICD-9), and quality control of the primary data was performed, including verification of diagnoses in accordance with the criteria used in general practice and with World Health Organization (WHO) criteria.

At the third stage, the primary data were double-entered into the electronic database, the information that had been entered was archived, and quality control of the database was performed.

It should be emphasized that quality control checks were an essential part of work during the creation and maintenance of the medical-dosimetric database and continue to be performed on a regular basis. In all quality control checks the acceptable limits of the differences and/or missing data were 5–10%.

CHARACTERISTICS OF THE "CLINIC" MEDICAL-DOSIMETRIC DATABASE

The cohort that is being followed up includes workers first employed at Mayak PA for any period of time at one of the main plants (nuclear reactors, radiochemical plant or plutonium production plant) during 1948–1982. The principles underlying the creation of the cohort have been described in detail earlier in both the Russian and Western literature (Koshurnikova et al. 1988, 1999). It should be emphasized that multiple quality control checks on the cohort identification showed that all the Mayak workers first employed at one of the main plants during 1948 through 1982 were included into cohort, and if there were several records on a worker's work history, they were correctly merged.

At present, the "Clinic" medical-dosimetric database contains complete medical and other data for 12,585 Mayak workers first employed at one of the main plants

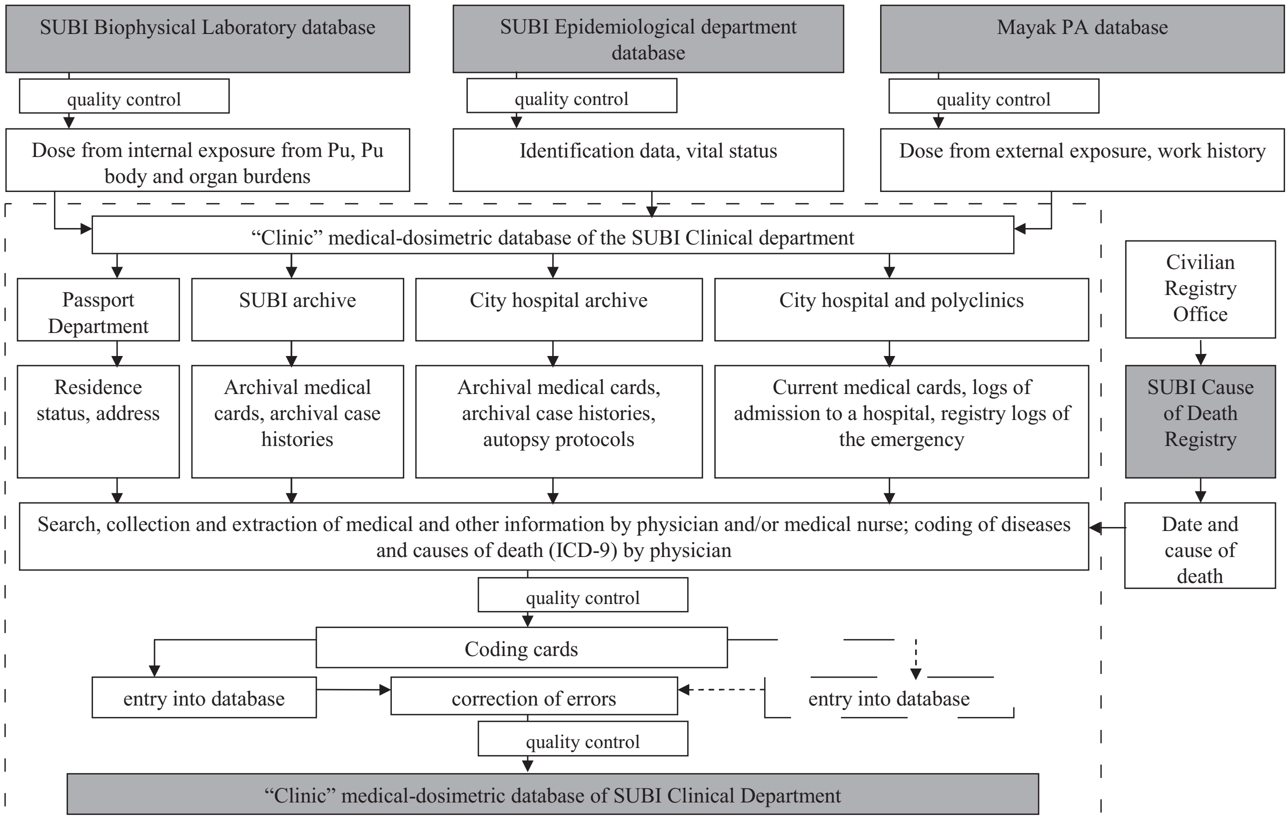

Fig 1. Collection of the primary data.

during 1948–1958.[§] Females make up 28.7% of the cohort.

The structure of the "Clinic" medical-dosimetric database and of the basic data currently contained in the database is shown in Fig. 2. As can be seen from Fig. 2, the "Clinic" medical-dosimetric database includes the following information: identification and passport data, work history and exposure dose, medical history, vital status, Ozyorsk residence, data on initial health at the pre-employment examination, clinical data for the whole follow-up period, and data on reproductive function and family. The main characteristics of the primary data contained in the "Clinic" medical-dosimetric database are described in detail below.

Work history

A work history including information on the dates of starting and ceasing employment at Mayak PA, the place of employment (plant, department, working place) and occupation is available for each member of the cohort. The sources of primary information on the work history were the worker's personal card and personal file from the Mayak Personnel Department and its archive. The overwhelming majority of workers (85.8%) had their permanent workplace at one of the main plants (nuclear reactors, radiochemical plant, or plutonium production plant). Only 14.2% changed workplaces by moving from one plant to another, i.e., had a so-called "mixed" work history.

The average durations of permanent employment at the nuclear reactors, radiochemical plant and plutonium production plant were about 14, 11, and 13.5 y, respectively.

While checking work history records for a 10% random sample of workers (1,258 individuals), it was determined that records on work history were incorrectly linked for 1 (0.08%) worker, who was employed during two different time periods at different plants, and records on employment (e.g., dates of moving from one plant to another) were incorrectly transcribed for 5 (0.4%) workers.

Dosimetry data

This paper is not focused on the description of algorithms and methods of external and internal dose calculation for Mayak PA workers as a number of dedicated dosimetry papers addressed these questions. These dosimetry papers are mainly based on the findings from the Russian Federation-United States of America

[§] All of the descriptive data are given here and subsequently are for the cohort of workers first employed at Mayak during 1948–1958.

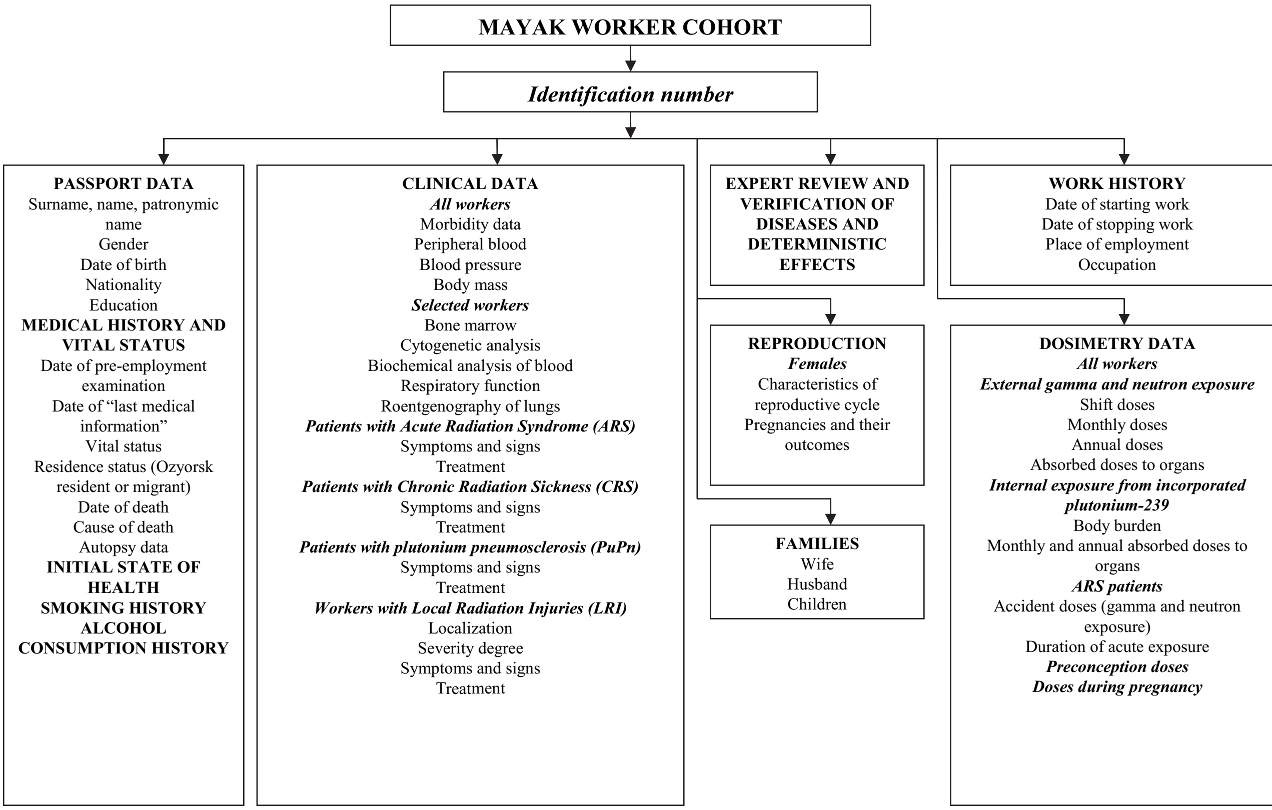

Fig. 2. Structure of the "Clinic" medical-dosimetric database.

(RF-US) project 2.4 "Development of the Improved Dosimetry System for Workers at Mayak Production Association" funded by the U.S. Department of Energy (DOE) (Bess et al. 2007; Krahenbuhl et al. 2002; Leggett et al. 2005; Smetanin et al. 2007a and b; Vasilenko et al. 2007a and b). It should be noted that the latest improved dose estimates based on the Mayak "Doses-2005" dosimetry system were used in this paper.

"Doses-2005" represents a significant improvement in the determination of absorbed organ dose from external radiation and plutonium intake for the original cohort of 18,831 Mayak workers. The methods of dose reconstruction of absorbed organ doses from external radiation uses: 1) archive records of measured dose and worker exposure history, 2) measured energy and directional response characteristics of historical Mayak film dosimeters, and 3) calculated dose conversion factors for Mayak study-defined exposure scenarios using Monte Carlo techniques. The methods of dose reconstruction for plutonium intake use two revised models developed from empirical data derived from bioassay and autopsy cases and/or updates from prevailing or emerging International Commission on Radiobiological Protection models. Other sources of potential significant exposure to workers such as from medical diagnostic x rays, ambient onsite external radiation, neutron radiation, intake of airborne effluent, and intake of nuclides other than plutonium were evaluated to determine their impact on the estimates.

External exposure. Annual external gamma doses were registered for 99.7% workers of the cohort (based on the Mayak "Doses-2005" dosimetry system). The average cumulated dose from external gamma exposure for the whole follow-up period was 0.91 $\pm$ 0.01 Gy (with a range of 0.0–5.92 Gy and a median of 0.58 Gy) for males and 0.65 $\pm$ 0.01 Gy (with a range of 0.0–8.12 Gy and a median of 0.38 Gy) for females in the cohort. The average annual dose was 0.11 $\pm$ 0.00 Gy (with a range of 0.0–2.68 Gy and a median of 0.05 Gy) for males and 0.09 $\pm$ 0.00 Gy (with a range of 0.0–1.49 Gy and a median of 0.04 Gy) for females in the cohort.

Internal exposure. ^{239}Pu body burden was measured in 30.4% of the cohort (based on the Mayak "Doses-2005" dosimetry system). The average ^{239}Pu body burden was 2.19 $\pm$ 0.15 kBq (with a range of 0.0–193.77 kBq and a median of 0.43 kBq) for males and 4.12 $\pm$ 0.67 kBq (with a range of 0.01–421.16 kBq and a median 0.38 kBq) for females in the cohort.

Workers who started employment at the main plants during 1948–1953 tended to receive higher external and internal exposures than did workers who started employment at the main plants during 1954–1958. Moreover, workers at the radiochemical plant received the highest average cumulative external gamma doses, and workers at the plutonium plant had the highest average ^{239}Pu body burden.

Other occupational exposures. It is known that 7,507 (59.7%) of the workers from the cohort were employed at locations elsewhere, e.g., in the nuclear, chemical, or building industry or in the military, before employment at Mayak PA. These workers are flagged in the "Clinic" database. Nine hundred and eighty-three of these workers were exposed to different chemical and other hazards, and 268 of these workers may have been exposed to radiation before employment at Mayak PA, e.g., during work at the experimental reactors or x-ray units. Workers with possible radiation exposure received at other workplaces before employment at Mayak PA are flagged in the database, although their doses will never be known.

Work is in progress within the SUBI Epidemiological Department to collate doses received after employment at Mayak, although it will not be possible to complete this work in the short-term. Not all workers with post-Mayak doses have been identified at present. However, these doses are generally much lower than those received at Mayak. At present work is in progress to create the branch medical-dosimetry registry of the RF nuclear industry workers, which will incorporate medical-dosimetry data for nuclear workers of enterprises such as Mayak PA in Ozyorsk, Siberian Chemical Combine in Seversk, Mining Chemical Combine in Zheleznogorsk, etc. (Takhauov et al. 2003; Trikman et al. 2006).

A small proportion of the workers in the cohort (about 100 or so) took part in the liquidation of the Chernobyl accident consequences during 1986–1988. However, it is not possible to identify these workers at present. While the doses that they received have large uncertainties, these doses are likely much lower in general than the doses received at Mayak.

Approximately 4,700 workers took part in the liquidation of the 1957 accident at Mayak PA. Doses received during liquidation of the consequences were measured and have been included in the Mayak occupational dose estimates (Mayak "Doses-2005" dosimetry system), although the workers involved in the liquidation of the accident at Mayak PA in 1957 have not been flagged in the "Clinic" medical-dosimetric database.

At present work is in progress at Mayak PA to estimate the contribution of diagnostic medical exposures to a worker's total exposure. It is clear that this contribution will be important, especially for workers employed during recent years. Information on diagnostic medical exposure is available practically for every worker. However, while it is anticipated that doses will be calculated, the amount of effort required means that doses will not be available for several years.

Vital status

The vital status of the workers is one of the most important characteristics of the database. The ascertainment of vital status, especially for workers employed at Mayak PA during the first decade of its operation and migrated from Ozyorsk, is a very complicated task and it has previously been described in detail (Koshurnikova et al. 1999). The SUBI Epidemiological Department is taking the lead in compiling data on both vital status and data on deaths amongst migrants. It is known that 46.8% of the cohort had died by 31 December 2000 and that 42.3% were alive at the time of this study. Vital status is unknown for 10.9% of the cohort. It should be emphasized that information on vital status is practically complete (99.97%) for Ozyorsk residents.

Residence status

Less than a half of the cohort (46.2%) were living in Ozyorsk as of the end of 2000 or had lived there up until their death, whereas about 52.9% had migrated from the city; information is being checked for the remaining 0.9% (118 individuals). Information on residence was based on primary data from the Passport Department of the Ozyorsk Internal Affairs Administration (address of residence, date of migration from Ozyorsk). It should be emphasized that for all those workers who migrated from Ozyorsk, their date of the "last medical information" is known. A random sample check showed that, for 93% of workers, this date coincides with their date of migration.

Date and cause of death

Cause of death is known for 95.7% of those cohort members who are known to have died.

In collecting information on mortality, sources of information such as medical cards and case histories, autopsy protocols, forensic medical examination protocols, and death certificates from the Civilian Registry Office were used. Causes of death were coded in accordance with ICD-9.

The autopsy rate in this cohort is high; namely, 33.8% of all deaths in the cohort and 61.7% of deaths among workers who died in Ozyorsk. Autopsy data allow causes of death to be identified reliably. However, quality control checks showed that the level of diagnostic verification for causes of death such as acute myocardial infarction and stroke was high even among workers for whom an autopsy was not performed. For example, data for a random sample of 90 workers recorded as having died from acute myocardial infarction were used for an expert review. Among the 36 individuals for whom an autopsy was performed, the diagnosis was confirmed in 100% of cases. Among the remaining 54 individuals for whom an autopsy was not performed, the diagnosis was confirmed for 53 (98.15%) individuals and not confirmed in 1 (1.85%) individual. As regards stroke, data for a random sample of 73 cases were used for an expert review. Among the 23 individuals for whom an autopsy was performed, the diagnosis of stroke was confirmed in 22 cases and was not confirmed in 1 (4.3%) individual. Among the remaining 50 individuals for whom an autopsy was not performed, the diagnosis was confirmed in 100% of cases.

Analyses of autopsy rates showed that the rate in females decreased with year of death, from more than 80% before 1980 down to about 25% in the 1990's. For males, the autopsy rate increased from 60–70% before 1970, up to around 80% during the 1970's–1980's and subsequently decreased to about 30%. Furthermore, for both males and females, autopsies were more frequent among workers with higher—rather than lower—gamma doses or ^{239}Pu body burdens.

Morbidity data

At present morbidity data have been collected for 11,868 (94.3%) out of 12,585 workers in the cohort. Morbidity data have been collected up to 31 December 2000 for those who were alive and living in Ozyorsk as of that time, up to the date of death for those who died in Ozyorsk, and up to the date of the "last medical information" for those who migrated from Ozyorsk. The sources of information on morbidity were archive and current medical cards, case histories, logs of admission to hospital, and emergency registry logs. All diseases were coded in accordance with ICD-9 and entered into the "Clinic" medical-dosimetry database.

It should be noted that it was impossible to collect medical data for 717 (5.7%) workers owing to a lack of any medical documents.

One of the most important tasks while creating a database is the review and verification of the health data by experts. Expert review provides as complete detection as possible of all missing, for any reason, health effects on the one hand and verification of the health effects previously determined on the other hand. While creating the "Clinic" medical-dosimetric database, an expert review was performed based on re-analysis of clinical-laboratory, functional, and other medical data contained in the primary medical documents by a group of four highly-qualified experts. The expert review was made based on agreed and specified diagnostic criteria in accordance with WHO recommendations or other normative documents (Guskova and Baysogolov 1971; WHO 1990; Okladnikova 2001; Okladnikova and Guskova 2001; Selidovkin et al. 2001; Veretshagin and Varakin 2001; Chobanian et al. 2003; Gafarov and Blaginina 2005). It should be noted that the experts were not provided with the dosimetry information (type of exposure and radiation doses) when performing an expert review of deterministic effects. Thus, the expert review of deterministic effects resulted in "historical" and "expert" diagnoses that are contained in the "Clinic" medical-dosimetric database. "Historical" diagnosis is the health effect previously diagnosed by a physician during direct observation of a patient. "Expert" diagnosis is the verified "historical" health effect or health effect diagnosed for the first time during the expert review but obligatorily attributed to the calendar period of the clinical manifestations.

For example, to identify all cases of Acute Radiation Syndrome (ARS) and verify the "historical" diagnosis, information about radiation accidents/incidents at Mayak PA during the first years of its operation (1948–1968) with indications of the accident/incident date and the main characteristics, together with a list of workers involved in the accident/incident, was requested from the Mayak Radiation Safety Department. The sources of this information were Acts of Investigations of radiation accidents/incidents kept in the Mayak PA archive. Retrospective analysis of the primary data was performed based on the diagnostic criteria for ARS developed by A.K. Guskova and G.D. Baysogolov (Guskova and Baysogolov 1971; Selidovkin et al. 2001). During the retrospective review of ARS cases, the "historical" diagnosis was verified for 52 workers. However, the diagnosis was not confirmed for 18 workers, for whom mild ARS had previously been diagnosed. The involvement of these workers in radiation accidents/incidents was the main reason for their hospitalization in a specialized clinic. Intensive detailed examination led to the identification of unstable slight deviations in their health (e.g., unstable changes in the morphological composition of peripheral blood; subjective symptoms, such as appetite loss, nausea, headache, dizziness, sleep disorder, sleeplessness, etc.; as well as signs of hypotension, tachycardia and light neurological disorders). Verification of the "historical" diagnosis was impossible for 5 individuals owing to a lack of or incomplete primary clinical-laboratory data (e.g., medical cards or case histories had been lost).

Another example is the expert review and verification of the quality of diagnoses of circulatory diseases based on random samples of diagnoses, stratified by such parameters as sex and calendar period. Expert review involved a re-analysis of the medical data by highly qualified experts. For example, three cardiologists and one physician of high qualification reviewed and verified diagnosis of acute myocardial infarction. The expert review included three successive stages. At the first preparatory stage, organizational tasks (random sampling, invitation of experts, development of the forms for expert review and verification based on the diagnostic criteria recommended by WHO, search and preparation of the primary medical information contained in the archival medical documents) were undertaken. At the second stage, each expert independently of the others analyzed all of the available medical documents and filled in an expert form. The experts were provided with medical cards and case histories containing detailed primary data on the patient's examinations and tests (laboratory, functional, radiological, and other instrumental tests). The third and final stage of the expert review was a joint (collective) discussion of each case by the expert group, in order to decide whether the original diagnosis could be verified.

For example, during the expert review of 90 cases of acute myocardial infarction, there was only one case that the experts did not confirm, i.e., the diagnosis of acute myocardial infarction was verified in 98.8% of cases in the sample. In a separate review of 77 cases of stroke, the original diagnosis was confirmed in 70 (90.9%) cases, not confirmed in 4 (5.2%) cases, and a conclusion was impossible in 3 (3.9%) cases owing to incomplete medical documentation.

In addition to cases currently registered as circulatory disease, a random sample of records of other clinical outcomes was reviewed to check for missing or not identified circulatory diseases. For this type of expert review, random samples of workers over 40 y old who were never diagnosed with a particular form of circulatory disease were selected from the "Clinic" database. They consisted of 99 individuals never diagnosed with acute myocardial infarction, of whom 50 were alive and 49 had died (with an autopsy performed for 17 of the deceased individuals) and 106 individuals never diagnosed with stroke, of whom 2 had unknown vital status, 42 were alive and 62 had died (with an autopsy performed for 21 of the deceased individuals). To perform this expert review, archival and current medical cards as well as case histories including autopsy protocols were collected. The review showed that acute myocardial infarction was seen at autopsy in 2 (2.0%) out of the 99 randomly selected workers, whereas all of the other workers in this sample (98.0%) did not have registered clinical symptoms and signs typical for acute myocardial infarction. Of the 106 workers in whose medical documents stroke was not mentioned, 1 (0.9%) new case of stroke was diagnosed at autopsy, while archival medical cards were found and data on stroke diagnosis were entered into the morbidity data for 2 (1.9%) workers whose registered cause of death was stroke.

In all quality control checks of the completeness of clinical records contained in the "Clinic" medical-dosimetric database, the percentage of missing data was less than the lowest acceptable level of 5%. The findings indicate that information about health effects contained in the database is complete enough to enable detailed health studies to be undertaken.

Clinical, laboratory and functional data

It is known that the hematopoietic system is one of the most radiosensitive systems (Thoma and Wald 1959; Guskova and Baysogolov 1971; Baranov et al. 1995; Wald 1998; Friesecke et al. 1999; Gusev et al. 2001; Selidovkin et al. 2001). Because of this, data from peripheral blood and bone marrow tests have been entered into the database for the whole follow-up period for, respectively, 11,861 (94.25%) and 1,790 (14.22%) of the Mayak workers. The average number of peripheral blood and bone marrow tests per worker during the whole follow-up period was about 43.9 and 1.7, respectively.

Peripheral blood tests were included into the standard program of examination and were obligatorily performed for each Mayak nuclear worker irrespective of place of employment and exposure dose. Bone marrow examinations were predominately performed for Mayak workers exposed to acute radiation (during radiation accident/incident) or chronic radiation in high doses to examine bone marrow hemapoiesis.

Due to the fact that the methods of peripheral blood and bone marrow tests changed during the follow-up period, procedures to standardize methods were developed and were used in creating the "Clinic" medical-dosimetric database.

It should be noted that the test performed before occupational exposure to radiation, i.e., estimation of a worker's initial state of the hematopoetic system, is very important for analysis of peripheral blood indices. In the "Clinic" medical-dosimetric database, information on the initial state of peripheral blood indices is available for 11,380 (90.4%) workers in the cohort.

On the other hand, examination of respiratory function, which is very important for the diagnosis of occupational pneumosclerosis, was not performed at the pre-employment medical examination (before work at Mayak), so we do not have data on the initial state of respiratory function among workers of the cohort. The respiratory function examination was included into the expanded medical examination standard in the late 1950's for workers exposed to ^{239}Pu aerosols and was performed only once every 5 y at a hospital with the necessary expertise/equipment. At present the "Clinic" medical-dosimetry database contains data from respiratory function examinations for 1,950 (15.5%) individuals, with an average of 3.1 examinations per worker over the whole follow-up period.

The standard examination for Mayak workers included obligatory fluorography of the lungs of all workers without exception, and roentgenography of the lungs of workers exposed to ^{239}Pu aerosols, conducted once every 3 y independently of the presence or absence of lung disease or deterministic effect (occupational pneumosclerosis). It should be emphasized that fluorography was obligatory at the pre-employment medical examination (before work at Mayak). In contrast, roentgenography was performed at the pre-employment medical examination only if indicated by the corresponding worker's complaints.

At present, the "Clinic" medical-dosimetric database contains data on roentgenography of lungs for 537 individuals, with an average of 38.3 examinations per worker during the whole follow-up period. Work to collect these data is in progress.

It should be noted that Mayak nuclear workers, independently of the plant they worked on and levels of their exposure, were examined based on the same standard program including the strictly defined set of clinical, functional and laboratory tests up to the present time, to the date of death or to the date of migration from Ozyorsk. However, a small portion of Mayak nuclear workers, mostly those chronically exposed to radiation at doses of more than 0.5 Gy per year, was also examined with additional tests (for example, bone marrow examination, cytogenetic examination, respiratory function examination, etc.).

Risk factors

At present the proportion of workers for whom information on risk factors has been collected is 94.7% for smoking, 94.7% for alcohol, 89.9% for blood pressure, and 75.4% for body mass index. Data on initial health status were collected for about 94% of the workers in the cohort. All of the available medical documents and interviews of workers based on a specially developed standard questionnaire were used to collect information on risk factors and on initial health status.

For factors such as alcohol and smoking, a quality control check was performed based on comparison of data from different sources (medical documents, interviews) for 251 workers randomly sampled from the cohort. The comparison of data on smoking showed no discrepancy in smoking status (smoker, non-smoker) and in numbers of cigarettes smoked, i.e., non-smokers were reported to be non-smokers and smokers were reported to be smokers. In 4.65% of cases there were differences between different data sources in the date of starting smoking and in the date of stopping smoking. The comparison of data on alcohol consumption for individuals who were reported in medical documents to be either a non-drinker or a moderate drinker showed good agreement (94.9%). However, 60% of those persons who were diagnosed with chronic alcoholism concealed the fact of alcohol abuse during interviews and usually said that they drank "little," "seldom," or "in moderate amounts." Nevertheless, the percentage of individuals diagnosed with chromic alcoholism in the random sample of 251 individuals was only about 3.6%.

Reproductive outcome

In contrast to other cohorts of nuclear workers, a substantial proportion of the workers at Mayak PA were female. Despite the fact that work on the creation and maintenance of the "Clinic" medical-dosimetric database has been already carried out for about 10 y, data on reproductive outcome in Mayak female workers have only been collected during the past 2 y. Up until now, data on age-specific reproductive data (age at menarche, age at start of sexual life, age at marriage, age at menopause), number of pregnancies and their outcomes (delivery, spontaneous abortion, medical abortion), and information about husband and children, etc., have been collected for only 1,490 (41.3%) of the female workers in the cohort. Collection of the primary data is in progress. We are also planning to collect information about families of male Mayak workers.

It should be noted that the structure of the "Clinic" medical-dosimetric database is constantly changed in accordance with the introduction of new sections of data to address new scientific tasks. At present, work is in progress on extension of the database structure and expansion of the primary data in the database by expansion of the cohort, extension of the follow-up period and entry of new data sets (e.g., information about family, biochemical tests, cytogenetic tests, etc.).

UTILIZATION OF THE "CLINIC" MEDICAL-DOSIMETRIC DATABASE

The primary data currently contained in the "Clinic" medical-dosimetric database allow several different research projects to be conducted to study the effects of ionizing radiation on humans; for example:

- deterministic radiation effects such as ARS, chronic radiation sickness (CRS) and plutonium pneumosclerosis (PuPn) (State Contract No 11.324.02.0 with RF Federal Medical-Biological Agency; Grant No R01-OH007866 with U.S. National Institute of Occupational Safety and Health; Contract No NRC-04-98040 with U.S. National Regulatory Commission);
- mortality and morbidity from non-cancer diseases among individuals exposed to external and/or internal radiation [State Contract No 11.309.06.0 with RF Federal Medical-Biological Agency; Contract No FP6-516478 with European Commission on Southern Urals Radiation Risk Research (SOUL)];
- radiation risk and contribution of non-radiation factors to cancer development (State Contract No 11.324.02.0 with RF Federal Medical-Biological Agency; Contract No DW020008 with U.S. Lovelace Respiratory Research Institute);
- detection of molecular markers of radiation-induced lung cancer (Grant No RBO-20305-OZ-02 with U.S. DOE);
- reproductive health of Mayak workers (State Contract No 11.311.06.0 with RF Federal Medical-Biological Agency; Grant No R01-OH007866 with U.S. National Institute of Occupational Safety and Health);
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and many more.

At present, limited access to the "Clinic" medical-dosimetric database via the Internet is being developed for Russian and foreign researchers interested in using the data to verify specific hypotheses concerning health effects of occupational exposure to ionizing radiation. This work is being conducted in the framework of Grant No R01-OH007866 with the U.S. National Institute of Occupational Safety and Health.

CONCLUSION

At present, the "Clinic" medical-dosimetric database 1) is a constantly operating system of collecting, documenting, organizing, checking and archiving personal data, and 2) provides a basis to study the effects of ionizing radiation on human health.

Primary data contained in the "Clinic" medical-dosimetric database will allow us to study the:

- early deterministic effects of occupational exposure, including dose-response and dose-time-response dependences, dose thresholds and their uncertainties;
- radiation risk for cancer and non-cancer diseases and impact on life expectancy;
- contribution of radiation and non-radiation factors to cancer and non-cancer effects;
- reproductive health of individuals exposed to external and/or internal exposures;
- genetic effects of radiation;
- clinical and molecular-genetic mechanisms of early, intermediate and late radiation effects including mechanisms of radiation-induced cancer;
- role of individual radiosensitivity in response to exposure to ionizing radiation; and
- principles of diagnosis of occupational and occupation-specific diseases including criteria for establishing the relation between diseases and occupational exposure; etc.

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