

Review

Acute Radiation Syndrome Survivors after Chernobyl Accident: History of Irradiation, Diagnostic Mistakes and Death Reasons in Long-term Period

David Belyi*, Alexander Kovalenko and Dimitry Bazyka

*State Institution "National Research Centre for Radiation Medicine of Ukrainian Academy of Medical Sciences",
Melnikov str. 53, 04050, Kiev, Ukraine*

Received 20 March 2013; revised 7 May 2013; accepted 10 May 2013

In 1986 it was officially stated that 237 patients got acute radiation syndrome (ARS) of different severity as a result of the Chernobyl accident but till 1989 this diagnosis was confirmed for 134 persons, including those 28 persons, who died within 11 to 96 days. Amongst 103 patients with unconfirmed ARS the main criteria for retrospective decline of diagnosis in 27 patients with typical clinical symptoms were incompleteness of early haematological data, and in 76 – the atypical character of haematological parameters recovery after their initial decrease. Of those individuals, 190 were living in the territory of Ukraine, and 19 persons in other republics of the former Soviet Union. Amongst Ukrainian residents 42 (24 ARS survivors and 18 non-ARS patients) have died till the end of 2012. The causes of death included oncological (16 patients from 22 with cancer and leukaemia diagnosed) and cardiovascular (14 patients) diseases, somatic diseases and infections (7 patients), accidents (5 cases). The localisation of cancer was rather different: kidney, colon, stomach, lung, lower jaw, thyroid gland, throat, prostate. Sudden cardiac death was the main reason of cardiovascular mortality whereas acute cerebrovascular disease ranked second and was followed by acute myocardial infarction and chronic heart failure.

Key words: Chernobyl accident; acute radiation syndrome; leukaemia; cancer

1. Introduction

Patients with a history of acute radiation syndrome (ARS) constitute a group of most heavily injured of those exposed to radiation effects as a result of Chernobyl Nuclear Power Plant (CNPP) accident. The health status of such patients is continuously monitored in Ukraine

by the National Research Centre for Radiation Medicine (NRCRM). Different phases of such research programs have been reported already¹⁻⁷. Two international projects – (1) Joint study project No 3 "Diagnosis and treatment of patients with acute radiation syndrome" (1991-1995); and (2) INCO-Copernicus project "Radiation over-exposed accident victims: evaluation of health consequences" (1998-1999) – have been completed and their results have already been published⁸⁻¹⁰.

However, the nature and spectrum of diseases developed in ARS survivors over a mid- and long-term period after radiation exposure is still under discussion. In particular, the role of radiation factor and its magnitude

*David Belyi, MD: State Institution "National Research Centre for Radiation Medicine of Ukrainian Academy of Medical Sciences"
Melnikov str. 53, 04050, Kiev, Ukraine
E-mail: dbelyi_2000@yahoo.com

in the late development of a somatic pathology in ARS survivors should be elucidated. Long-term effects on the cardiovascular system should be studied above all, as the indications exist about the relationship of the cardiovascular mortality with radiation exposure¹¹. An increase in the incidence and mortality from cardiovascular system diseases in a cleanup workers of the CNPP accident is also registered on an epidemiologic basis¹².

In 95% of ARS survivors, dyscirculatory impairments of cerebral haemodynamics were found during the first several years after the accident¹³. The further 20-year post-accidental monitoring at the NRCRM showed a high incidence of circulatory diseases. However, no correlation of the development of cardiovascular diseases in ARS survivors with the exposure dose or severity of ARS was found⁵. Meanwhile, a significant increase in the incidence of cerebral atherosclerosis and coronary heart disease (CHD) has been revealed in hibakusha with high exposure doses in a much later period after irradiation exposure¹⁴. Those facts mean that a lifetime analysis of the health status of ARS survivors should be carried out. It is such program of long-term studies what is planned at NRCRM.

The cohort of ARS survivors has shrunk substantially over 26 post-accidental years as compared with 1986, and it will continue to decrease. Some patients got lost for the follow-up. Nevertheless, the system of mortality registration in individuals with occupational pathologies implemented in Ukraine makes it possible to obtain data on the mortality of ARS survivors. This paper describes the initial group of patients with ARS diagnosed in 1986, and thus included in the high priority medical supervision cohort. The causes of death in the post-accidental period are also analyzed.

2. Materials and methods

In the first days after CNPP accident, 499 patients with declared ARS were hospitalized. No clinical or laboratory signs confirming the diagnosis were found in the majority of them. In December 1986, it was officially stated that 237 patients got ARS of different severity as a result of the accident at the CNPP. Of those patients, 28 died within 11 to 96 days: 27 patients (20 patients with ARS grade 4 and 7 patients with ARS grade 3) died of extremely severe radiation-induced bone marrow failure and radiation lesions of skin, and one female patient with ARS grade 2 died of a concomitant disease on a background of recovered haematopoiesis¹⁵. Two more individuals died within the first day after the accident: one of them was buried under the ruins of the reactor, and the other died of fatal thermal burns in several hours after the explosion¹⁶. Of 237 patients with ARS, 118 were staying

on treatment in Moscow Clinical Hospital No. 6 and 119 in several hospitals in Kyiv.

Overdiagnosis of ARS was suggested back in 1986¹⁷. An analysis of source documents was made by the Institute of Biophysics (Moscow) with the participation of experts from NRCRM under the general guidance by prof. Angelina Gus'kova in the period from 1986 through 1989. Confirmation (exclusion) criteria were based on typical dynamics of hematological indices uppermost neutrophil granulocytes and thrombocytes during acute phase followed the irradiation, and clinical symptoms as well (Table 1)^{17, 18}.

Diagnosis of ARS was cancelled in 103 patients (10 patients treated in Moscow Clinical Hospital No. 6 and 93 patients treated in Ukrainian medical centres) due to incompliance of the clinical and laboratory data with radiation bone marrow syndrome or because of lack of medical data that would make it possible to confirm the diagnosis (Table 2). Thus, the number of patients with ARS reduced to 134 individuals. The rest of patients with unconfirmed diagnosis (ARS NC) were considered as definitely suffered from a radiation exposure, which, however, did not result in the development of classical radiation-induced bone marrow syndrome.

Taking in account that the majority of Chernobyl victims was living in Ukraine NRCRM have been established in Kyiv on October 1986. Starting from this date 190 patients residing in Ukraine have been under regular medical supervision and treatment in the clinic of NRCRM. During a first five-year period before a collapse of the USSR most of Ukrainians, two Russian and two Belarusian patients had been followed up also at Moscow Clinical Hospital No. 6 of the Institute of Biophysics. Therefore, data on first recovery period after ARS published by Kyiv and Moscow groups are almost identical. Since 1991 clinical analysis and treatment are performed by national centres.

Male patients prevailed among those exposed to irradiation: male patients comprised 89.3% of unconfirmed ARS diagnosis group, 92.7% of ARS grade 1 group, 96.0% of ARS grade 2 group, 100% of ARS grade 3 group and 95.2% of ARS grade 4 group (Table 3). The professional radiation anamnesis showed that among patients with confirmed ARS grade 1 to 4 there were 70 workers of the CNPP, 12 guardians of the plant (servicemen of the internal military forces of the Ministry of Internal Affairs of the USSR), 21 construction workers of the 5th and 6th new power blocks, 19 fire-fighters, 4 so-called "liquidators" (clean-up staff) and 6 individuals occasionally exposed to radioactive irradiation. Occupation of 2 died patients was unknown, therefore, such patients were not included in any of the aforementioned categories of injured persons¹⁸. The rectified data available now in the archives of CNPP and Chernobyl National Museum, make it possible to

Table 1. Diagnostic criteria of ARS in different periods of its development

| Indices | ARS grade (severity) | | | |
|--|----------------------------------|---|---|---|
| | 1 (mild) | 2 (moderate) | 3 (severe) | 4 (very severe) |
| Range of absorbed dose (Gy) | 1-2 | 2-4 | 4-6 | 6-10 |
| Period of primary reaction | | | | |
| Vomiting | in 2 hours and later, single | in 1-2 hours, recurrent | in 30-60 min, multiple | in 5-20 min, intractable |
| Diarrhea | absent | absent | absent or probable | probable |
| Headache | short-term | moderate | moderate | intensive |
| Consciousness | clear | clear | clear | mental confusion |
| Body temperature | normal | subfebrile | subfebrile | high (38-39°C) |
| Skin and visible mucous membrane | normal | mild transitory hyperemia | moderate transitory hyperemia | apparent transitory hyperemia |
| Duration of primary reaction | Some hours | Up to 1 day | Up to 2 days | > 2-3 days |
| Latent period | | | | |
| Peripheral blood lymphocytes on 3-6 day ($\times 10^9 \text{ l}^{-1}$) | 1.0-0.6 | 0.5-0.3 | 0.2-0.1 | ≤ 0.1 |
| Peripheral blood leukocytes on 8-9 day ($\times 10^9 \text{ l}^{-1}$) | 4.0-3.0 | 2.9-2.0 | 1.9-0.5 | ≤ 0.5 |
| Diarrhea starting from 7-9 day | absent | absent | absent | apparent |
| Epilation, time of onset | invisible | may be on 15-20 day | in majority of patients on 10-15 day | in majority of patients on 7-10 day |
| Argranulocytosis onset (granulocytes $\leq 1.0 \times 10^9 \text{ l}^{-1}$) | absent or starts after 30 day | 20-30 day | 8-20 day | 6-8 day |
| Thrombocytes decrease below $40 \times 10^9 \text{ l}^{-1}$) | absent or starts after 25-28 day | 17-24 day | 10-16 day | before 10 day |
| Duration of latent period | 30 days | 15-25 days | 8-17 days | absent or $\leq 6-8$ days |
| Period of manifestation | | | | |
| Clinical syndromes | asthenia | infectious complication, hemorrhagic diathesis, epilation | infectious complication, hemorrhagic diathesis, epilation | intoxication, fever, gastrointestinal syndrome, hypotonia |
| Leukocytes count ($\times 10^9 \text{ l}^{-1}$) | 3.0-1.5 | 1.5-0.5 | 0.5-0.1 | < 0.5 or a patient dies earlier |
| Thrombocytes count ($\times 10^9 \text{ l}^{-1}$) | 100-60 | 50-30 | less than 30 | < 20 or a patient dies earlier |
| ESR ^a , mm h ⁻¹ | 10-25 | 25-40 | 40-80 | 60-80 |

Note: a – erythrocyte sedimentation rate

Table 2. Distribution of the patients subject to ARS grade before the diagnosis was confirmed and after this

| ARS grade | ARS was diagnosed in 1986 | | ARS was confirmed in 1989 | |
|-----------|---------------------------|---------------|---------------------------|---------------|
| | Russia, Moscow | Ukraine, Kyiv | Russia, Moscow | Ukraine, Kyiv |
| ARS NC | | | 10 | 93 |
| 1 | 31 | 100 | 23 | 18 |
| 2 | 46 | 13 | 44 | 6 |
| 3 | 21 | 5 | 21 | 1 |
| 4 | 20 | 1 | 20 | 1 |
| Total | 118 | 119 | 118 | 119 |

categorize all individuals injured during the Chernobyl disaster by their occupation as shown in Table 3.

The follow-up included regular full clinical examinations and laboratory check-ups for everyone. The check-up protocols included full blood count, biochemical tests (basic metabolic panel, chemical pathology and liver function tests), immunological profile (humoral and cellular indicators), thyroid tests (ultrasound and TSH, FT4), urinalysis, full physical examination, and various instrumental tests as necessary (electrocardiogram,

electroencephalogram, ophthalmological tests, gastro-duodenoscopy, chest X-ray, functional lung test etc. When necessary, patients were consulted by specialists (hematologist, endocrinologist, neuropathologist, ophthalmologist, pulmonologist, cardiologist, gastroenterologist, dermatologist, psychiatrist, urologist or gynecologist). Further, more complex diagnostic methods were applied under indications, including CT scans, biopsy, cardio-stress-ECG, colonoscopy, serological tests for specific causes, e.g. hepatitis A, B or C viruses,

Table 3. Distribution of the ARS and ARS NC patients by age, gender, professional and absorbed doses

| Indices | ARS grade | | | | |
|---|---------------------|-------------|-------------|-------------|-------------|
| | ARS NC | 1 | 2 | 3 | 4 |
| Gender: f / m | 11 / 92 | 3 / 38 | 2 / 48 | 0 / 22 | 1 / 20 |
| Professional activity at the irradiation: | | | | | |
| • CNPP employers | 29 | 19 | 21 | 17 | 13 |
| • CNPP guardians | 2 | 8 | 3 | - | - |
| • builders | 6 | 3 | 15 | 3 | - |
| • fire-fighters | 34 | 6 | 7 | 1 | 6 |
| • clean-up staff | 12 | 1 | 3 | - | - |
| • occasionally irradiated persons | 20 | 4 | 1 | 1 | 2 |
| Age at the irradiation, years | n ^a =103 | n=41 | n=50 | n=22 | n=21 |
| M ± SD ^b | 36.4±10.4 | 34.1±8.5 | 37.9±13.5 | 37.4±13.5 | 31.8±9.2 |
| min – max | 18.4 - 60.3 | 17.6 - 56.3 | 17.9 - 79.3 | 20.4 - 72.6 | 23.2 - 53.6 |
| 95% CI ^c | 34.4 - 38.5 | 31.4 - 36.8 | 34.1 - 41.7 | 31.4 - 43.4 | 27.6 - 36.0 |
| Absorbed dose, Gy | n=18 | n=34 | n=44 | n=18 | n=18 |
| M ± SD | 0.4±0.3 | 1.0±0.6 | 2.4±0.9 | 5.1±1.5 | 9.9±2.2 |
| min – max | 0.1 - 1.0 | 0.1 - 3.3 | 0.5 - 4.9 | 2.9 - 8.2 | 6.4 - 13.7 |
| 95% CI | 0.2 - 0.5 | 0.8 - 1.2 | 2.1 - 2.7 | 4.4 - 5.8 | 8.8 - 11.0 |

Note: a – number of patients in the sample
b – mean ± standard deviation
c – confidence interval

Table 4. Death reasons in patients with ARS NC and ARS survivors in the post-accidental years

| ARS grade | Death reasons | | | | |
|-----------|-------------------------|---|--|-----------------------|-------|
| | Cardiovascular diseases | Oncological and oncohaematological diseases | Somatic, nervous and infectious diseases | Traumas and accidents | Total |
| ARS NC | 5 | 9 | 2 | 2 | 18 |
| 1 | 3 | 2 | 1 | 2 | 8 |
| 2 | 4 | 3 | 3 | 0 | 10 |
| 3 | 2 | 2 | 1 | 1 | 6 |
| Total | 14 | 16 | 7 | 5 | 42 |

bone marrow tests etc.

3. Results

The history of irradiation

The CNPP workers formed the biggest cohort of patients with ARS of different grade – 52.2%. The second biggest cohort (15.7%) comprised the builders of the 5th and 6th power units, and the third biggest cohort (14.9%) – fire fighters. Other injured included the guardians (8.2%), occasionally exposed persons (6.0%) and liquidators (3.0%), i.e., those persons who were sent by their enterprises to participate in accident rescue operations in the CNPP zone. Of 28 died persons, 20 were the workers of CNPP, 6 – fire fighters and 2 – occasionally exposed.

Amongst employers there was both the CNPP night shift and personnel arrived at the plant in the morning of April 26, 1986 after the reactor explosion. They took an active part in emergency and rescue operations into the plant shops and therefore were irradiated in high level doses.

The CNPP military guard watched the plant perimeter. The officers, who stood guard at the time of reactor

destroying, suffered from irradiation if their posts turned out on the way of nuclear fallout. Several persons had nausea and vomiting minutes-hours after the explosion and was substituted by another officers, who was undergone to high dose irradiation too.

Together with military guard builders were exposed to radiation due to radionuclides on the ground surface near mobile workers' locker rooms. Until the construction workers of night shift worked inside the premises of 5th and 6th reactors the exposure at the first hours after the accident was lower because of distance and wall shielding factors. However when the workers came back to their locker rooms early in the morning they were heavily exposed to the external irradiation and ground radiation sources (pieces of graphite and nuclear fuel) that led to combination of bone marrow syndrome with local skin radiation lesions of lower extremities.

The main task of fire fighters that reached the CNPP after fire alarm was to stop fire spreading along the roof of 4th reactor building directly to other plant shops. Six men, who extinguished the fire on the roof, got unviable general and local radiation damages. Several fire fighters spent on the roof less time and were far

from destroyed part of the roof. They survived mild and moderate ARS. ARS was incorrectly diagnosed in firemen who (a) was near their cars and controlled water supply for extinguishing the fire, (b) inspected the CNPP territory for seats of fire, (c) pumped out water from under the destroyed 4th reactor on May 6-8, 1986 and (d) distinguished a fire in the tunnel between 3rd and 4th block on May 22, 1986.

Cleanup staff is a name of voluminous cohort of people who were directed by their enterprises for emergency and rescue operations at the CNPP and 30 km radioactive zone. Professionally it was drivers, medical staff, engineers, servicemen and policemen.

The category "occasionally irradiated persons" included different people that could not be attributed to any afore-mentioned groups. These people never contact with radiation professionally and didn't take part in emergency and rescue operations at the CNPP, but they were exposed to irradiation nevertheless. For example, just before the accident, 3 engineers of Kharkov Turbine Works had been sent to CNPP in order to perform testing of a turbine manufactured at the said Turbine Works. During the accident, they were staying in close vicinity to the ruined reactor. Two of them died of ARS grade 4, whereas one of them survived ARS grade 3. A worker who operated with refrigerates in the NPP cafeteria survived ARS grade 2. ARS grade 1 developed in two women worked on their vegetable gardens that were on the way of nuclear fallout. Two men also survived ARS grade 1 because of they were at the plant in a mission. ARS NC was diagnosed in town Prypyat inhabitants who stayed closely to the CNPP.

Patients with ARS grade 1 to 3 and patients with unconfirmed ARS were actually of the same age group, while mean values of exposure doses differed significantly ($P < 0.001$).

The reasons of mistakable ARS

At diagnoses re-evaluation 45.5% of ARS diagnoses initially established haven't been confirmed. Analysis demonstrated that the main criteria for retrospective decline of diagnosis were incompleteness or atypical character of the early laboratory data.

The diagnosis of the ARS in 27 of 93 patients was declined due to the incompleteness of early laboratory investigation data. Peripheral blood counts in such patients within first 40 to 60 days after exposure were either absent or insufficient for estimation of the severity of bone marrow failure. Owing to different objective emergency family or work circumstances, patients were beyond medical supervision during the period of a possible manifestation of the disease. They usually have asked medical care after resolving personal problems during a recovery period when it was impossible to

establish diagnosis using haematological criteria. Accounting for the lack of laboratory data, diagnosis of ARS was made in 1986 on the basis of (1) a confirmation of a formal fact of staying in the zone of high irradiation in the initial period and (2) a history of a primary reaction with clinical symptoms described^{16, 17, 19}. Exposure doses in 4 of those 27 patients were determined within the subsequent months by chromosome aberrations assay and were equal to 0.2, 0.3, 0.8 and 1.0 Gy.

Another group of patients with unconfirmed ARS comprised 76 individuals. Haematological data were not uniform in that group. In particular, blood counts were within the normal values in 2 patients during the first 60 days after exposure, whereas 4 patients showed the signs of transient anaemia, 1 patient had lymphocytopenia and 3 patients – lymphocytopenia in combination with transient anaemia. Nevertheless, those 10 patients had symptoms of the primary reaction, including vomiting in 5 patients; and moderate radiation burns of feet were diagnosed in one patient. Somatic pathologies that would explain the observed changes in the blood analyses were found in none of the patients during their staying at the hospital.

Dynamics of neutrophilic granulocytes and platelets in the peripheral blood of the other 66 of 76 injured persons was not typical for the bone marrow syndrome such as a gradual or sharp, depending on the exposure dose, decrease down to the minimum level followed with an increase corresponding to a recovery of the blood count level. Differences between the haematological characteristics of those patients included the different extent of granulocytopenia and thrombocytopenia and the number of cases of the decrease in granulocyte and platelet levels beyond the lower limit of the physiological range. Following the exposure, granulocyte levels in the peripheral blood decreased beyond the lower limits in 51 patients and platelet levels in 61 patients. During the first 10 days after exposure, lymphocyte counts were reduced in 51 patients. Eventual nonrecurring reduction of either granulocyte or platelet levels was observed in 4 patients only, and granulocytopenia was combined with lymphocytopenia and erythrocytopenia in one of such patients. Nonrecurring granulocytopenia and thrombocytopenia was observed in 3 patients in combination with lymphocytopenia and erythrocytopenia. In other patients with ARS NC from 2 to 29 (5 on average) episodes of granulocytopenia and 2 to 16 (4 on average) episodes of thrombocytopenia were observed in the period from 5 to 60 days after exposure.

One can assent to an opinion that diagnostic mistakes were related to lack of knowledge and experience²⁰. Indeed, short sporadic episodes of cytopenia were frequently taken as the manifestations of bone marrow failure in patients with a history of stay in high radiation fields in a close vicinity to the ruined 4th reactor. However,

one should also account for that none of the injured persons of this initial accident period were provided by individual dosimeters designed for high levels of irradiation, and no information was available for health care staff about a possible patient doses calculated on the basis of route lists (such calculations were made substantially later). Therefore, physicians followed a conservative strategy: they would rather make a mistake and diagnose more severe condition than miss a diagnosis of a real disease.

A retrospective analysis of haematological parameters of patients with ARS NC showed substantial differences as compared with patients with ARS grade 1. Individual haemograms of patients with ARS NC did not comply with those typical for ARS supporting the absence of typical bone marrow failure syndrome. Meanwhile, episodes of reduced peripheral blood levels of granulocytes and platelets, minimum levels of granulocytopenia and thrombocytopenia, actual terms of their onset and lymphocytopenia in the first 10 days after exposure testified to the substantial radiation-induced haematological injury.

T. Fliedner and W. Nothdurft²¹⁾ believe that a single dose of 0.5 Gy or lower may induce a damage of the hematopoietic tissue in a certain region of the bone marrow. G. Gruzdiev²²⁾ shares their opinion having found that irradiation dose of 0.5 Gy may induce a reduction of the level of myeloid cells in the bone marrow down to 58% of the physiological level, and a reduction of the peripheral blood neutrophils down to subnormal values. HLA phenotype studies performed in ARS grade 1-2 in comparison with ARS NC with the similar known doses of exposure have suggested also possibility of association of atypical bone marrow changes with different subjects radiosensitivity²³⁾. Of course there still exist other uncertainties.

Thus, we can suggest that signs of radiation damage of hematopoietic tissue confirmed with haematological or dosimetric characteristics were observed in 73.8% of patients with unconfirmed ARS.

The reasons of death during long-term period

Only 209 individuals were still alive by the end of 1986, including 106 ARS survivors and 103 patients with unconfirmed ARS. Of those individuals, 190 were living in the territory of Ukraine, and the residual 19 persons – in other republics of the former Soviet Union.

For study of the late health effects of radiation exposure the identical criteria and approaches of the assessment of health data were used irrespectively of the results of the 1989-th re-evaluation of diagnoses.

During three years after CNPP disaster 190 patients residing in Ukraine underwent medical examination in NRCRM, but by the end of 2012, the actual number

of followed-up patients reduced to 118 (ARS NC–61, ARS grade 1–27, ARS grade 2–24, and ARS grade 3–6). Altogether, 42 patients, including 18 patients with unconfirmed ARS and 24 ARS survivors, died during 26 years after CNPP accident. Thirty individuals, including 20 patients with unconfirmed ARS and 10 ARS survivors, were lost for medical supervision.

Eighteen patients with ARS NC and 24 ARS survivors died during the period from 1987 to 2012. Oncological and oncohematological pathologies prevailed among the causes of those deaths (Table 4). Blood disorders included a case of hypoplasia of hematopoiesis (D61.9 according to International Classification of Diseases of 10th revision) in 1987, acute myelomonoblastic leukaemia (C92.5) in 1998, three cases of myelodysplastic syndrome (D46) in 1993, 1998 and 2002, and a case of polycythemia vera (D45) in 2011. Two patients died of stomach cancer (C16.8) in 2004 and 2005 and two of colon cancer (C18.9) in 2001 and 2005. Laryngeal cancer (C13.9) in 2001, prostate cancer (C61) in 2003, urinary bladder cancer (C67.8) in 2008, maxillary sinus cancer (C31.0) in 2010 and mandible malignant neurinoma (schwannoma) (C47) in 2004 caused the death in one patient each. One patient with unconfirmed ARS died of femoral soft tissue sarcoma (C49.2) in 1993.

Cardiovascular diseases placed the second (after oncological pathologies) prevailing cause of long-term mortality after exposure (Table 4). In the period from 1986 to 2012, sudden cardiac death was the cause of death of 9 persons (I46.1). Either essential hypertension (I10, I11) or/and coronary heart disease (I20.1, I25.0, I25.1) were diagnosed in all such died persons. Post-mortem examination of none of them showed any signs of myocardial infarction or another acute pathology that might be the cause of death. Fatal heart rhythm disorders could result in lethal outcome. Three more patients with underlying essential hypertension died of acute cerebrovascular disease (1991, 2006, 2008) (I61, I63). Chronic heart failure (I50.1) and acute myocardial infarction (I21) were the causes of death of one patient in 2007 and another in 2010 respectively.

We have found no correlation between the cases of oncological or cardiac death and dose of radiation exposure or ARS grade.

Other somatic pathology, in particular, pulmonary gangrene (J85.0), liver cirrhosis (K74) caused death in 1 patient (in 1987) and 2 patients (in 1995 and 1998), correspondingly. One patient with unconfirmed ARS died of encephalomyelitis with bulbar paralysis in 1988, and two ARS survivors (1995, 2004) and one patient with unconfirmed ARS (2006) died of tuberculosis (A15).

Injuries suffered in a traffic or other accidents were lethal in five persons (in 1986, 1995, 1995, 2002 and 2010).

Average age of died patients was 58.8 ± 13.7 years; on the date of death, the youngest had 26.3 years of age

(patient with ARS grade 1, sudden cardiac death), and the oldest – 87.3 years (patient with ARS grade 3). Nine patients died in the age below 50 years, and among the other patients, 13 individuals died in the age below 60.

Thus, the share of malignant tumours in the causes of long-term mortality was 23.8% (10 patients, average age: 61.4 ± 13.0 years), blood and hematopoietic tissue diseases – 14.3% (6 patients; average age 56.8 ± 6.8 years) and cardiovascular pathologies, including stroke, – 33.3% (14 patients; average age 61.9 ± 15.7 years).

Of 75991 victims of atomic bombing of Hiroshima enrolled in the program of the Life Span Study at the Radiation Effects Research Foundation, 28737 persons died during the period from 1950 to 1985¹⁴. The aforementioned diseases were the cause of death in 20.7% (5936 patients), 0.5% (146 patients) and 38.8% (11164 patients) of those patients, correspondingly. The period of follow-up of exposed people in Japan was twice as large as our period of follow-up, nevertheless, the relative numbers of patients died of malignant tumours and cardiovascular diseases were actually similar in both studies.

According to Y. Shimizu *et al.*²⁴, higher lethality rate caused by circulatory system diseases was observed in persons below 40 years of age on the date of exposure or in persons with exposure dose above 2 Gy according to dosimetric model DS86. A lack of significant correlation between cardiac death and exposure dose in our study may be explained, first, with a smaller number of deceased subjects because of a shorter follow-up period, and second, with a smaller group of examined patients as compared with the cohort exposed in Japan.

4. Conclusion

A study of the late health effects in the group of survivors after ARS diagnosed in 1986 was performed by the standardized criteria irrespectively of the results of the diagnoses re-evaluation in 1989. Analysis demonstrated that the main criteria for retrospective decline of diagnosis in 27 patients with typical clinical symptoms were incompleteness of early haematological data, and in 76 – the atypical character of haematological parameters recovery after their initial decrease. During the 1986-2012 follow-up period 42 of 190 patients deceased from the number of persons who followed up in NRCRM. The prevailing causes of death were malignant tumours, including oncohaematological pathology, and cardiovascular diseases. These data coincide with obtained in A-bomb survivors. No dose dependency of mortality and no difference between ARS and ARS NC were demonstrated at the study period.

References

1. Bebeshko V G, et al. (1989) Rehabilitation of victims of acute radiation sickness. In: Medical aspects of the Chernobyl accident. p 267. IAEA, Vienna.
2. Bebeshko V, et al. (1995) Health effects of the Chernobyl accident. In: Teylor M ed. Proceedings of the Twentieth international symposium "Uranium and Nuclear Energy: 1995". pp. 67–73. The Uranium Institute, London.
3. Bebeshko V, Kovalenko A and Belyi D (1996) Long term follow-up of irradiated persons: rehabilitation process. In: Karaoglou A, Desmet G, Kelly GN and Menzel HG eds. The Radiological Consequences of the Chernobyl Accident. pp. 607–609. European Commission, Brussels.
4. Bebeshko VG, et al. (1999) Radiation cataracts in high dose liquidators who developed acute radiation syndrome. In: Junk AK, Kundiev Y, Vitte P and Worgul BV eds. Ocular radiation risk assessment in populations exposed to environmental radiation contamination. pp. 51–56. Kluwer Academic Publishers, Dordrecht.
5. Belyi DA, Bebeshko VG, Weiss M and Fliedner TM (2002) The cardiovascular system: observations in Chernobyl accident victims. In: Fliedner TM, Feinendegen LE and Hopewell JW eds. Chronic Irradiation: Tolerance and Failure in Complex Biological Systems. pp. 258–264. The British Institute of Radiology, London.
6. Bebeshko V, Belyi D, Kovalenko A and Gergel O (2002) Health consequences in the Chernobyl emergency workers surviving after confirmed acute radiation sickness. In: Follow-up of delayed health consequences of acute accidental radiation exposure. pp. 5–26. IAEA, Vienna.
7. Bebeshko VG, et al. (2003) Medical monitoring results of survivors with acute radiation syndrome after Chernobyl disaster. In: Shibata Y, Yamashita S, Watanabe M and Tomonaga M eds. Radiation and humankind. pp. 115–122. Elsevier, Amsterdam.
8. Gottlober P, et al. (2001) The outcome of local radiation injuries: 14 years of follow-up after the Chernobyl accident. J Radiat Res 155: 409–416.
9. Steinert M, et al (2003) Delayed effects of accidental cutaneous radiation exposure: fifteen years follow-up after the Chernobyl accident. J Am Acad Dermatol 49: 417–423.
10. Boehm BO, et al. (2009) Thyroid examination in highly radiation-exposed workers after the Chernobyl accident. Eur J Endocrinol 160: 625–630.
11. Preston DL, et al. (2003) Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and noncancer disease mortality: 1950–1997. J Radiat Res 160: 381–407.
12. Bebeshko VG, Bazyka DA and Buzunov V (2007) Chernobyl: current situation of non-cancer diseases. In: Shibata Y, Namba H, Suzuki K and Tomonaga M eds. Radiation Risk Perspectives: Proc. of the Second Nagasaki Symp. of Int. Consortium for Medical Care of Hibakusha and Radiation Life Science (Nagasaki) (International Congress Series, vol 1299). pp. 54–59. Elsevier, Nagasaki.
13. Gorban NG and Torubarov FS (1990) Cerebral hemodynamics in acute radiation disease in the victims of the accident at the Chernobyl nuclear power station. Med Radiol (Mosk) 35: 20–23 (In Russian)
14. Effects of A-bomb radiation on the human body (1995) Shigematsu I, Ito C, Kamada N, Akiyama M, Sasaki H and Harrison B eds. Bunkodo Co., Tokyo.
15. Gus'kova AK, et al. (1989) Acute effects of radiation exposure following the Chernobyl accident: immediate results of radiation sickness and outcome of treatment. In: Medical aspects of the Chernobyl accident. pp. 233–256. IAEA, Vienna.
16. Gus'kova AK, et al. (1987) Acute radiation effects in victims of the accident at the Chernobyl nuclear power station. Med Radiol

- (Mosk) 32: 3–18 (In Russian).
17. Mettler Jr FA, Gus'kova AK and Gusev I (2007) Health effects in those with acute radiation sickness from the Chernobyl accident. *Health Phys* 93: 462–469.
 18. Belyi DA, Khomenko VI and Bebesko VG (2009) Emergency preparedness of Research Center for Radiation Medicine and its hospital to admit and treat the patients with signs of acute radiation sickness. *Radiat Prot Dosimetry* 134: 159–163.
 19. Anno GH, Baum SJ, Withers HR and Young RW (1989) Symptomatology of acute radiation effects in humans after exposure to doses 0.5 - 30 Gy. *Health Phys.* 56: 821–838.
 20. Khalyavko IG and Boichuk RR (1992) Retrospective analysis of acute radiation sickness diagnosis: criteria and mistakes. In: Accident at the Chernobyl NPP: radiation monitoring, clinical problems, social and psychological aspects, demographic situation, low doses of ionizing radiation (Information bulletin, issue 2, vol 2). pp. 129–138. Kiev (In Russian).
 21. Fliedner TM and Nothdurft W (1986) Cytological indicators haematopoietic effects. In: *Biological indicators for radiation dose assessment*. pp. 123–152. MMV Medizin, Munich.
 22. Gruzdev GP (1988) Acute radiation bone marrow syndrome. *Medicine, Moscow* (In Russian).
 23. Minchenko J (1998) Genetic systems of blood. In: Kovalenko ON ed. *Acute radiation sickness*. pp. 76–84. Ivan Fedorov, Kyiv (In Ukrainian).
 24. Shimizu Y, Kato H, Schull WJ and Hoel DG (1992) Studies of the mortality of A-bomb survivors. 9. Mortality, 1950-85: Part 3. Non-cancer mortality based on the revised dose (DS86). *J Radiat Res* 130: 249–266.