Leukemia and thyroid cancer in emergency workers of the Chernobyl accident: estimation of radiation risks (1986-1995)

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The work makes a direct epidemiological assessment of radiation risks in induction of leukemia and thyroid cancer in emergency workers after the Chernobyl accident. The Russian National Medical Dosimetric Registry has a compilation of data for 168 thousand emergency workers as of 01.01.1996. Analysis was performed of 48 leukemias and 47 thyroid cancers diagnosed and verified in emergency workers. The estimated radiation risks are: for leukemia - excess relative risk per Gy (ERR/Gy) is 4.30 (95% CI = 0.83, 7.75), excess absolute risk per 10^4 PY Gy (EAR/10^4 PY Gy) is 1.31 (95% CI = 0.23, 2.39); and for thyroid cancer - ERR/Gy is 5.31 (95% CI = 0.04, 10.58), EAR/10^4 PY Gy is 1.15 (95% CI = 0.08, 2.22).

Introduction

It is common knowledge that for low doses of ionizing radiation (0.2-0.3 Sv) estimates of radiation risks based on direct epidemiological studies are practically non-existent. Prediction of induction of malignant tumours by radiation in this range of doses is normally made by extrapolation of risk coefficients from the region of relatively high doses (1-2 Sv) to the region of low doses. Therefore, it is particularly important to establish radiation risk coefficients at low doses: the recommended coefficients and prediction models can then be tested for this range of doses.

In this sense, the data accumulated since the Chernobyl accident are of unique value. Indeed, during the first ten years of follow-up large amounts of epidemiological data have been collected characterizing health status of hundreds of thousands of people who received low doses. At the same time, there is limited number of studies in the literature on the estimation of the Chernobyl radiation risks and the question arises whether it is feasible to assess radiation risks by direct epidemiological studies at all.

In our earlier studies estimates were first made of excess relative risk for morbidity and mortality of emergency workers from malignant tumours and thyroid cancer incidence in children on the contaminated territory of the Bryansk region [1, 2]. It should be noted that the radiation risk coefficients obtained by direct epidemiological studies are in good agreement with the recommended models.

One of the first manifestations of the long term consequences of exposure to ionizing radiation for the health of the irradiated people is an increasing leukemia and thyroid cancer incidence rate. It is know that among radiation-induced malignant tumours leukemia and thyroid cancer have a short latent period (about 2-3 years for leukemia and 4-5 years for thyroid cancer). The time passed since the accident is enough for their induction.

This study deals with radiation-epidemiological analysis of thyroid cancer and leukemia incidence in emergency workers. The paper first presents estimates of radiation risks completed in 1986-1995 and compares them with predictions of models universally adopted in the world.

In our earlier studies, the cohort of emergency workers was described more than once [3-5]. We, therefore, dwell briefly on the cohort followed up in the framework of Russian National Medical Dosimetric Registry (RNMDR).

Materials and methods

As of 01.01.1996 the RNMDR database comprises medical and dosimetric information for 168 thousand emergency workers. In 1986, 77.7 thousand people were involved in remediation works, 58.7 thousand - in 1987 and 31.6 thousand - in 1988-1990. As is known more than 200 thousand of emergency workers from Russia took part in remediation activities in the 30-km zone of the Chernobyl NPP in 1986-1990. Therefore, ten years after the disaster unaccounted emergency workers continue to be entered in RNMDR. At present, RNMDR has a rigid hierarchy (in line with the Decree of the Russian Government): the national level of the registry is realized in Medical Radiological Research Centre in Obninsk, and 20 regional centres of the Registry are responsible for collection of data from annual check-ups across Russia which are then provided to the national level.

From the standpoint of dosimetric information about the emergency workers cohort, the Registry includes only official doses of external irradiation. The accuracy of determination of the external irradiation doses in emergency workers remains a very complicated issue. We estimate that the degree of uncertainty in calculating individual doses may be as high as a factor of 2.5-3.0.

Of 168 thousand emergency workers registered in RNMDR to date, 119 thousand (71%) have individual doses of external exposure. As is seen from Table 1 the highest radiation exposures for emergency workers occurred in 1986: more than 4.5% of 46575 people received the officially reported doses that exceeded the limit of 250 mGy.

For prediction of distant stochastic radiation effects it is necessary to account for age distribution of subjects (Table 2). It should be underlined that the mean age of emergency workers at the time when they worked in the 30-km zone was 33.5 years, which means that the average life span at radiation risk (after exposure) exceeds 25 years. Today (by 1 January 1996) the majority of emergency workers (31.7%) are between the ages of 40 to 44 years.

The primary goal of this study was to determine radiation risks of leukemia and thyroid cancer in the cohort of emergency workers. This was done based on the methods widely used in epidemiology. The derived coefficients of radiation risks were compared with the recommended values.

Table 1

Dose distribution for liquidators by year of arrival in zone

Year of	Number of	Dose, mGy					
Arrival	persons	0 - 49	50 - 99	100 - 149	150 - 199	200 - 249	> 250
1986	46575	18.2%	10.2%	10.1%	20.7%	36.3%	4.5%
1987	48077	24.0%	51.9%	9.7%	8.1%	5.8%	0.6%
1988-1990	24764	87.3%	9.7%	1.3%	0.7%	0.6%	0.4%
1986-1990	119416	34.5%	25.9%	8.1%	11.8%	17.5%	2.2%

Table 2

Age distribution for liquidators with an established external dose by year of arrival in zone

Year of	Age on 1th January 1996								
Arrival	< 30	30 - 34	35 - 39	40 - 44	45 - 49	50 - 54	55 - 59	60 - 64	> 65
1986	4.7%	13.8%	17.9%	22.0%	26.9%	8.6%	4.8%	0.9%	0.4%
1987	1.8%	7.9%	19.5%	36.6%	27.6%	4.9%	1.2%	0.3%	0.1%
1988-1990	1.6%	2.8%	29.1%	42.2%	20.7%	2.6%	0.7%	0.2%	0.1%
1986-1990	2.9%	9.3%	20.8%	31.7%	25.9%	5.9%	2.6%	0.5%	0.3%

Results and discussion

Leukemia incidence

The present analysis considers 48 cases of leukemia in emergency workers verified by the Medical Radiological Research Centre of RAMS and local health care establishments by 1 January 1994. Verification of leukemia is a complicated and lengthy procedure and, therefore, the study contains the analysis of incidence from 1986 to 1993 inclusive. By 1 January 1994 the RNMDR database contained medical and dosimetric information for 142 thousand emergency workers, among which 48 leukemias were reported.

Tables 3-6 show distribution of identified leukemias by some characteristics.

Our analysis of radiation risks accounts for all leukemia types (ICD-9 204.0-208.9). At the same time, it is common knowledge that chronic lymphocytic leukemia is not a radiation induced disease. The reason why all leukemia types were included in the study is because their number in 1986-1993 was few. Another important point to mention is comparison of observed and expected (including radiogenic) leukemias. The expected number of all leukemia types was calculated using a multiplicative prediction model in which coefficients were derived based on the Japanese cohort of atomic bomb survivors [6].

Table 3

Distribution of leukemia cases among EWs by date of entry in the Chernobyl zone

Date of entry (year)	Number of cases
1986	25 (52.1%)
1987	16 (33.3%)
1988	5 (10.4%)
1989	1 (2.1%)
1990	1 (2.1%)
Total	48 (100%)

Table 4

Distribution of leukemia cases among EWs by duration of stay in the Chernobyl zone

Duration of stay (months)	Number of cases
< 1	9 (18.8%)
1 - < 2	12 (25.0%)
2 - < 3	12 (25.0%)
3 - < 6	10 (20.8%)
6 - < 12	2 (4.2%)
12 +	3 (6.2%)
Total	48 (100%)

Table 5

Distribution of leukemia cases among EWs by external irradiation dose

Dose (mGy)	Number of cases
< 50	12 (25.0%)
50 - 99	8 (16.7%)
100 - 149	6 (12.5%)
150 - 199	3 (6.2%)
200 - 249	7 (14.6%)
250 +	1 (2.1%)
No data	11 (22.9%)
Total	48 (100%)

Table 6

Distribution of leukemia cases among EWs by date of diagnosis

Date of diagnosis (year)	Number of cases
1986	1
1987	5
1988	5
1989	3
1990	6
1991	11
1992	9
1993	8
Total	48

As is seen in Table 3, 41 leukemias (83.4%) were observed in emergency workers of 1986-1987. Yet, the RNMDR database contains 116 thousand emergency workers of 1986-1987 which makes 81.7% of the whole database. That is why data of Table 3 do not permit drawing any unequivocal conclusions about 1986-1987 as risk factors. A deeper analysis is required to assess the relation of incidence in the irradiated cohort to that in a reference unexposed group. For this purpose, we calculated leukemia incidence for the male population of Russia standardized to the age distribution of emergency workers. This value accounts for expected number of cases. In the study we use the indicator widely used in epidemiological studies: SIR - ratio of observed and expected incidence*.

Table 7 summarizes SIR estimates for leukemias in emergency workers for two time intervals: 1986-1989 and 1990-1993. It should be emphasized that in both cases SIR is more than 100%, i.e. incidence of emergency workers is higher that of the control reference group. At the same time, this difference from the reference with the confidence level of 95% is statistically significant only in the 1990-1993 interval. It is also worth noting another point: the absence of

* Standardized incidence ratio (SIR) in the time interval [0, T] means the ratio of the number of newly detected cases in this interval (observed) to the number of expected ones in percent.

demonstrated radiation risk in the 1986-1989 period suggests that the assumptions in the prediction models regarding the latent period of 2-3 years in induction of radiogenic leukemia were correct.

As was mentioned above, the study of leukemia (all types) in the Japanese cohort of atomic bomb survivors was developed from a dynamic model of radiation risk and we used this model for our predictions [6]. Besides the predictions of the model, the main characteristics of the cohort of emergency workers were used: age and dose distribution and leukemia spontaneous incidence for Russia. Figure 1 shows data of the Chernobyl Registry on leukemia incidence in emergency workers and the corresponding prediction curve. What can be inferred from Figure 1? First, the prediction and actual data are in good agreement within error limits. Secondly, as follows from the prediction and can be clearly seen from the Registry data, the peak of radiogenic leukemia occurred 4-5 years after the accident with the attributable risk (AR) of 45-60% (AR = 1-1/SIR). This suggests that each second leukemia detected in emergency workers today is radiation induced. Though the proportion of radiogenic leukemias in emergency workers is expected to decrease steadily with time, continuation of studies this area is one of the priority tasks of RNMDR.

Table 7

SIR incidence of leukemia among EWs

Observation period years	Observed number of cases	Expected number of cases	SIR	95% confidence interval
1986-1989	14	12.3	113	62, 190
1990-1993	34	19.2	177	122, 247

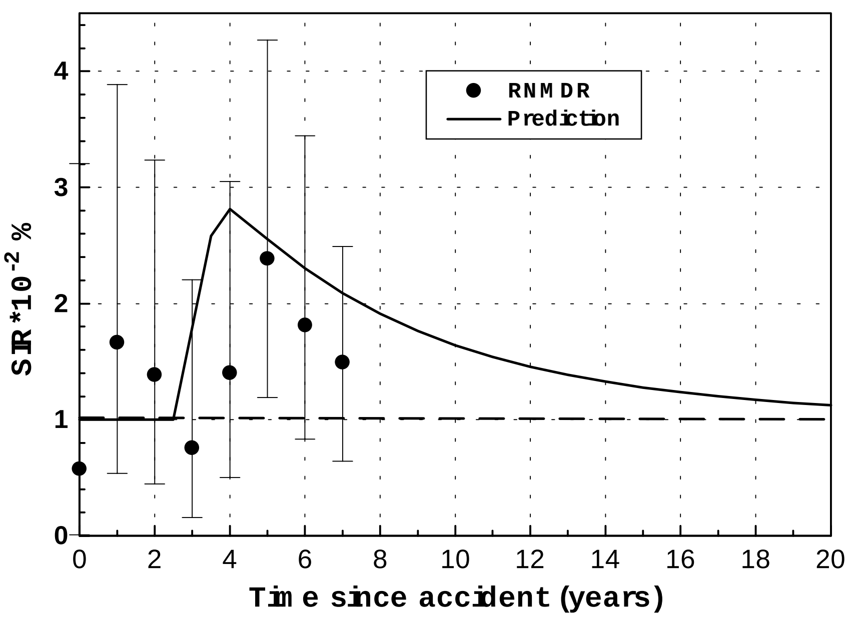

Fig. 1. Actual data and prediction of the dynamics of standard (leukemia) incidence ratio (SIR) in the emergency workers cohort.

Thyroid cancer incidence

By 1 January 1995 RNMDR included 47 thyroid cancers in emergency workers. These were diagnosed at various times since exposure: the time interval between entry into the 30-km zone and detection ranged from 1 to 8 years.

The hystologic types of the tumour were: 42.8% of patients had follicular cancer, 33.3% - papillar cancer, in 14.3% cases the tumour was some kind of carcinoma. Table 8 presents main epidemiological data on incidence. Overall, 28 thyroid cancers were detected in the emergency workers of 1986, 15 - in emergency workers of 1987 and 4 - those of 1988-1990.

Table 8 shows the standardized incidence ratios (SIR) for the observation period of 1986-1990 which is within the latent period for thyroid cancer and those for the post-latent period of 1991-1994. It should be noted that during 1986-1990 SIR does not differ significantly from 100% for all groups of emergency workers of 1986, 1987, 1988-1990. At the same time, in the post-latent period SIR by far exceeds 100% (except 1988-1990 emergency workers) and hence it reflects increased incidence, as compared to the control group. As a control group we took the male population of Russia standardized by age.

As is seen from Table 8, the groups of increased radiation risk are emergency workers of 1986 (SIR = 670%) and 1987 (SIR = 590%). Of the 1986 emergency workers, the highest risk is observed in those who worked in the 30-km zone in April-July.

To confirm the hypothesis about possible additional exposure of the emergency workers of April-May 1986 to iodine radionuclides we estimated accumulated SIR by months (Figure 2). It can be seen that the risk of thyroid cancer is the highest for the emergency workers involved in the recovery operations in June 1986. The risk for those working in April-May and July appeared to be almost identical. Therefore, at this point no definitive conclusion can be made about the effect of iodine radionuclides. On the other hand, though the external radiation doses in April-December 1986 were approximately the same (see Table 8), the risk of thyroid cancer increased noticeably by the end of 1986 (Figure 2).

Let us now move to prediction of occurrence of thyroid cancer in emergency workers. Figure 3 shows the observed incidence rate for emergency workers per 100 thousand people and the expected incidence rate (radiogenic plus spontaneous cancers). For calculation of spontaneous incidence we used statistical data for the Russian Federation [7]. As was said above, a considerable discrepancy between the observed and expected values is observed 4-5 years since the disaster.

Figure 4 presents the dynamics of SIR in 8 observation years for the 1986-1987 emergency workers. As is seen from Figure 4, the value of SIR for the time period corresponding to the latent period of 4 years remains practically constant: 220-260%. If we assume that during this period no induction of radiogenic cancers occurs, then the difference of the observed SIR from 100% accounts for the screening effect (better medical examination). This plot also gives an estimate of the expected input of radiogenic cancers to SIR under the assumption that the thyroid dose is only due to external exposure. It may be seen that the calculation model and risk coefficients [8, 9] account for only half of the real effect of the SIR increase after the latent period. If we exclude internal exposure of thyroid to iodine radionuclides, it can be inferred that either the model is not perfect or the external radiation dose is underestimated. Of course, it may be a combination of these, or other, factors.

Figure 5 shows SIR for the emergency workers of 1986 and 1987 separately depending on time since exposure. It is interesting to note that while for the emergency workers of 1986 SIR increases with statistical significance 4 years after the disaster, for the emergency workers of 1987 the SIR differs from 100% 5 years after the accident. This reaffirms the existence of the latent period in the induction of radiogenic thyroid cancers. In both cases (independent samples of 1986, 1987 emergency workers) it equals 4 years.

Estimation of radiation risks

As was stated above, the main goal of this study is not just an epidemiological analysis in terms of SIR, but also determination of radiation risk coefficients for leukemia and thyroid incidence in emergency workers. By this the following coefficients are meant: excess relative risk per Gy (ERR/Gy), excess absolute risk per 10^4 PY Gy (EAR/10^4 PY Gy) and attributable risk percent (AR%) at 1 Gy.

In estimation of radiation risk coefficients it has to be assumed that the increase in leukemia and thyroid cancer incidence is due to the dose factor only. At the same time, our calculations suggest that certain estimates of the dose relationship (using the epidemiological method of internal comparisons within cohorts) can be obtained only in the next 10-15 years. This requires about $2{\cdot}10^6$ PY of observations of the cohort (today this quantity is about 10^6 PY).

In a large-scale epidemiological study conducted some time ago to evaluate the radiation risk of thyroid incidence in children exposed to external radiation these coefficients were estimated to be: ERR/Gy = 7.7; EAR/10^4 PY Gy = 4.4; AR = 88% [10].

At the same time, there is only a limited number of works in literature dealing with estimation of radiation risks in induction of thyroid cancer after exposure to iodine radionuclides [11].

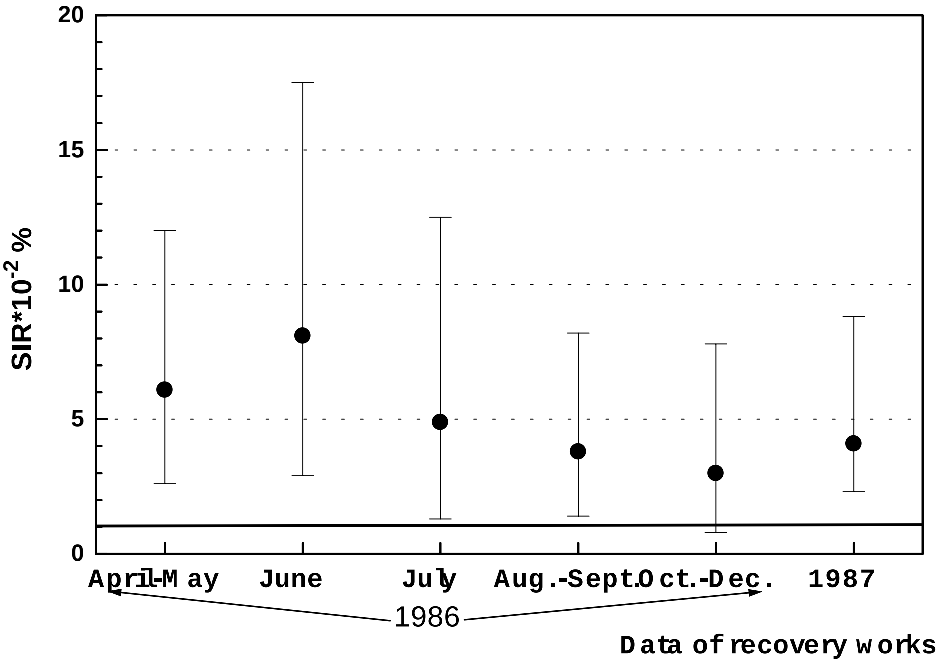

Fig. 2. Thyroid cancer incidence SIR among the emergency workers as a function of time of spent in the radiation exposure zone.

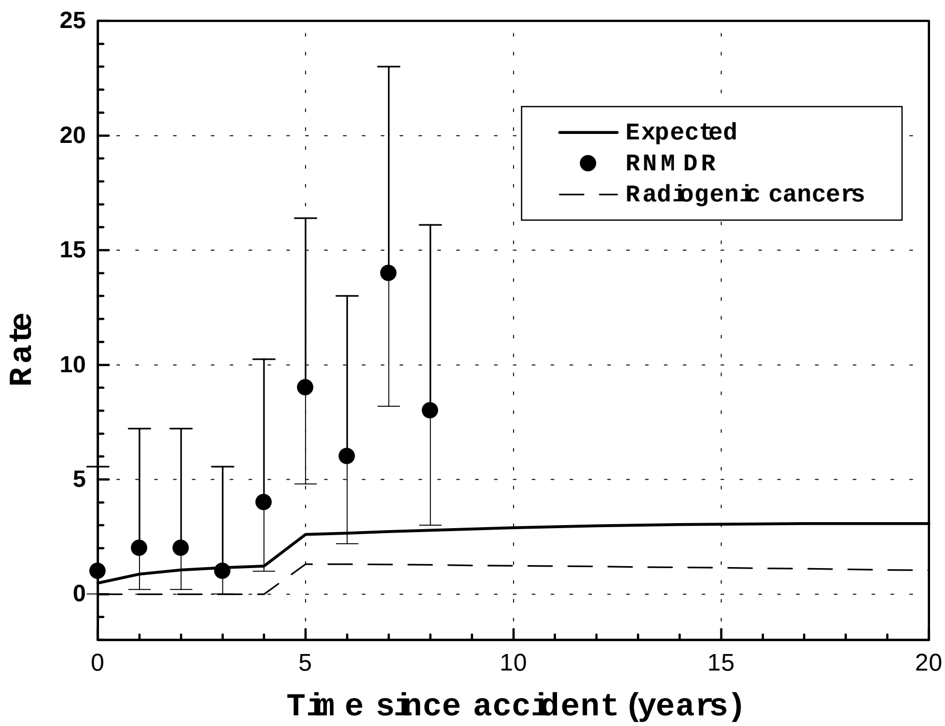

Fig. 3. Thyroid cancer incidence rate among emergency workers as a function of time since the accident.

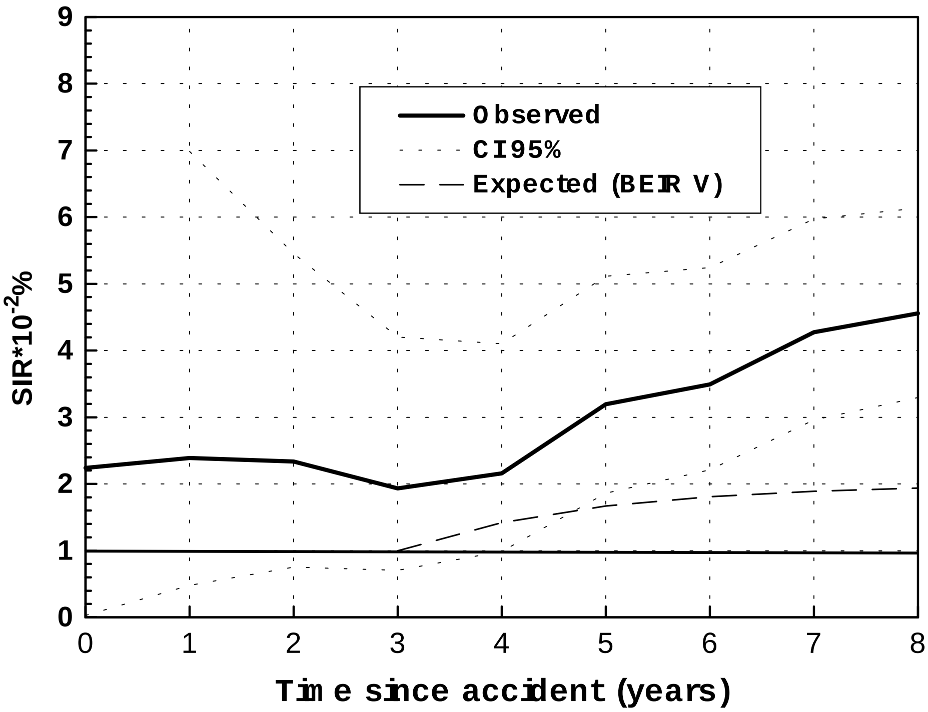

Fig. 4. Dynamics of thyroid cancer incidence SIR among emergency workers (who worked in 1986 or 1987).

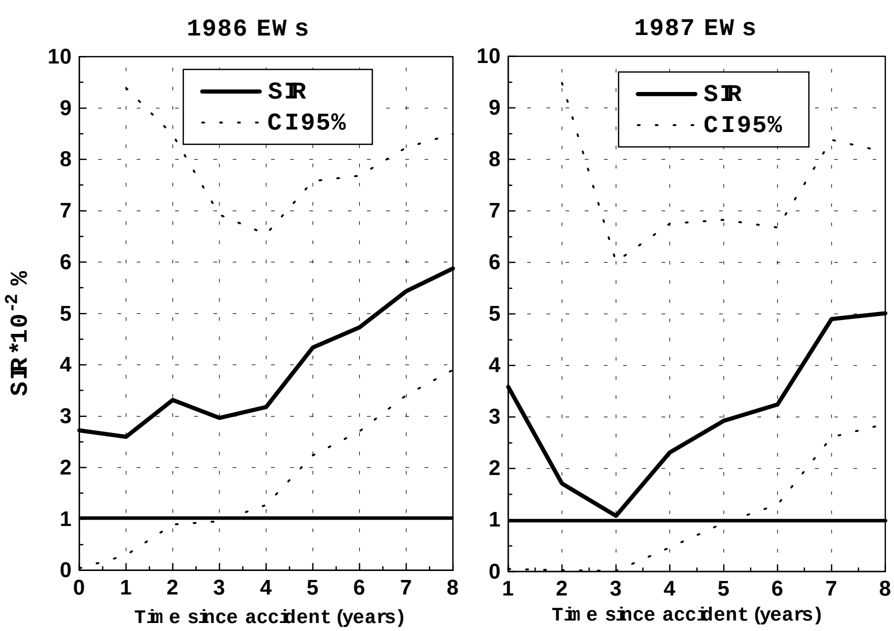

Fig. 5. Dynamics of thyroid cancer incidence SIR among emergency workers (1986 and 1987 workers separately).

As leukemia and thyroid cancer is a rare diseases and the time of follow-up of the emergency workers cohort is relatively short, an external control group was used for estimation of radiation risks as an unexposed group.

To estimate excess absolute risk normalized to unit dose the ratio was used:

$$EAR = \frac{O - E \times \alpha}{PY \times D},$$

where
O is observed number of cases;
E is expected number of cases obtained with data of national medical statistics;
α is coefficient allowing for the screening effect;
PY is person-years of observation;
D is external radiation dose [Gy].
Excess relative risk per 1 Gy is calculated with the formula:

$$ERR = \frac{EAR \times PY}{E \times \alpha}.$$

The attributable risk at 1 Gy dose was obtained from the ratio:

$$AR = \frac{ERR}{1 + ERR} \cdot 100\%.$$

The confidence interval were calculated using the method of linearization of the function of random variables.

Estimates of radiation risk coefficients were made for the cohort of the 1986-1987 emergency workers. This was because the latent period in leukemia and thyroid cancer induction have paired for the indicated cohort.

In estimation of radiation risk coefficients in the present study we introduced a parameter α accounting for the effect of in-depth screening of emergency workers. In line with the regula tions of the Ministry of Health Care of Russia the emergency workers are to undergo an in-depth medical examination on a yearly basis. This fact should be taken into account because as a control comparison group we used the male population of Russia standardized by age to the cohort of emergency workers.

For leukemia incidence the coefficient α = 1. Indeed, as is seen from Table 7, during the latent period (1986-1989) SIR = 113% and it does not differ with statistical significance from 100%.

For thyroid cancer incidence (Table 8) α = 2.6. This is because during the latent period (1986-1990) SIR = 260% (when no radiation induced cancers are expected), differs from 100% with statistical significance and reflects the effect of in-depth screening.

The indicated screening effect is well known from the literature. For example, the in-depth screening coefficient for the cohort of atomic bomb survivors (LSS) is: 2.4 for female and 3.5 for male population [10].

Tables 9, 10 present radiation risk estimates for the emergency workers cohort and their comparison with literature data by other cohorts.

As is seen from the tables, there is good agreement between the risk values obtained by us and coefficients published earlier in the literature. Further epidemiological study of the emergency workers cohort would permit deriving radiation risks from basic parameters: radiation dose, age at exposure and time since exposure.

Table 8

Table 9

Radiation risk of leukemia incidence among EWs (1986-1993 observation period)

Data source	EAR/10^4 PY Gy (95% CI)	ERR/Gy	AR (at 1 Gy) %
EWs	1.31 (0.23, 2.39)	4.30 (0.83, 7.75)	81
LSS cohort	2.38	7.8	88

Table 10

Radiation risk of thyroid cancer incidence among EWs (1986-1994 observation period)

Data source	EAR/10^4 PY Gy (95% CI)	ERR/Gy	AR (at 1 Gy) %
EWs	1.15 (0.08, 2.22)	5.31 (0.04, 10.58)	84
BEIR V	1.25	5.8	85

Conclusion

The results of the radiation-epidemiological studies on leukemia and thyroid incidence in the emergency workers of the Chernobyl accident are important from two aspects.

First, they provide objective evidence to the medical consequences of the Chernobyl disaster. Indeed, dozens and hundreds of Chernobyl studies have been published recently whose results are conflicting and groundless. In some works the consequences of the disaster are globally overestimated, which results in further spreading of the " Chernobyl syndrome" . Others, on the contrary, are biased to minimize both direct stochastic radiation effects and indirect effects related to psychoemotional aspects of the Chernobyl accident. For objective estimation it is necessary to rank all adverse factors and, primarily, estimate the number of radiation-induced diseases.

The second issue of importance is the application of the Chernobyl experience to determine radiation risk coefficients based on the analysis of medical consequences of the disaster. It should be emphasized that there is a unique possibility of epidemiological analysis of the first 10 years since the accident. As a result of many-years studies of the Japanese cohort of atomic bomb survivors, epidemiological material of several million person-years is available. The currently used models and radiation risk coefficients are mostly based on those studies. On the other hand, the amount of epidemiological data on the Chernobyl accident is comparable to the Japanese data even today (10 years after the disaster). Therefore, today's task is to adjust existing models and coefficients and create new ones based on the Chernobyl epidemiology. This is particularly important considering the range of low doses (to 0.5 Sv) and difficulty of obtaining reliable risk coefficients for these dose range. This is, in fact, the goal we pursued in this study, though the presented results are only preliminary and can be corrected in future based on information provided to the National Chernobyl Registry.

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