IMMUNE STATUS OF THE MAYAK WORKERS EXPOSED OCCUPATIONALLY

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1. INTRODUCTION

Immune system is one of the most radiosensitive system of the body. Studies on its status when exposed occupationally are widely presented in the literature (Vetitnev AM, 1985; Vologodskaya IA, 1994; Oradovskaya IV et al., 1997, 2007; Tahaukhov RM et al., 2003; Rees G.S. et al., 2004; Voronova IA et al., 2005, 2007). However, the effect of protracted external gamma-rays and/or internal alpha radiation from incorporated plutonium on immune system has been studied insufficiently; and dose-effect relationship in most studies is not presented.

The objective of this research was to study the effect of protracted gamma-exposure and combined exposure (protracted external gamma-exposure and internal alpha radiation from incorporated plutonium) on immune status in Mayak workers.

The study cohort includes 100 Mayak workers first employed at one of the main facilities (Reactors, Radiochemical, Plutonium production) in 1948 – 1972 and 50 individuals never employed at the Mayak PA. All followed individuals were subdivided into 4 groups depending on type and dose of exposure. The first group (8 individuals) includes workers exposed to cumulative external gamma-dose from 0.5 Gy to 1.5 Gy; the second group (10 individuals) – workers exposed to cumulative external gamma-dose from 1.5 Gy to 3.0 Gy, the third group (82 individuals) – workers exposed to combined radiation (range of cumulative external gamma-doses from 0.7 Gy to 5.1 Gy and internal alpha-radiation from incorporated plutonium with Pu^{239} body burden from 0.3 kBq to 16.4 kBq). The fourth group (control, 50 individuals) includes persons of corresponding age and gender never exposed to ionizing radiation. Dose calculation was based on the dosimetry system MWDS-2008. An average age of followed individuals was 78.5±0.4 y.o. Groups did not differ in age statistically significantly. Patients who had malignant neoplasm, acute inflammatory process, and exacerbation of chronic diseases at the period of follow-up were not included into the study. Structures of chronic diseases in all study groups did not differ statistically significantly.

Current study was based on provisions of the Declaration of Helsinki developed by the World Medical Association. The project was approved by the Supervisory Board of Southern Urals State University. All respondents were asked to sign an informed consent concerning voluntary participation in the study, and и consent to processing of personal data.

2. METHODS

Immunoglobulins IgM, IgG, IgA, and IgE were studied using ELISA.

Concentration of different subpopulations of peripheral blood lymphocytes, such as T-lymphocytes (CD3+CD19–), T-helpers (CD3+CD+), T-cytotoxic lymphocytes (CD3+CD8+), B- lymphocytes (CD3–CD19+), natural killers (CD3–CD16+CD56+), T-NK-cells count (CD3+CD16+CD56+) was studied using flow cytometry.

Statistical analysis was based on correlation analysis (Spearman's method), and linear regression analysis. Statistical significance of regression parameters was assessed using Student's t-test; significance of regression itself was assessed by Fisher's ratio test [Draper et al., 1986]. Distribution analysis has shown that studied parameters did not follow a normal distribution. Evaluation of null hypothesis was based on distribution-free Mann-Whitney test. Level $p<0,05$ was considered as statistically significant.

3. RESULTS

Statistically significant decrease in concentration of immunoglobulin G and relative concentration of T-lymphocytes Gy (Table) was observed among individuals exposed to external gamma-rays only. Increased expression of immunoglobulins M and A was observed in persons exposed to external gamma-rays. As for expression of immunoglobulin E, increase was revealed in a group of workers exposed to cumulative gamma-dose less than 1.5 Gy only. There were decrease in absolute concentration of T-lymphocytes, and statistically significant increase in relative and absolute concentration of natural killers in a group of workers exposed to cumulative external gamma-dose more than 1.5 Gy in compare with control.

In addition, regression analysis has shown that relative concentration of T-helpers dependent on cumulative dose of external gamma-exposure was described by inverse linear function at whole studied dose range of external gamma-exposure (Fig. 1).

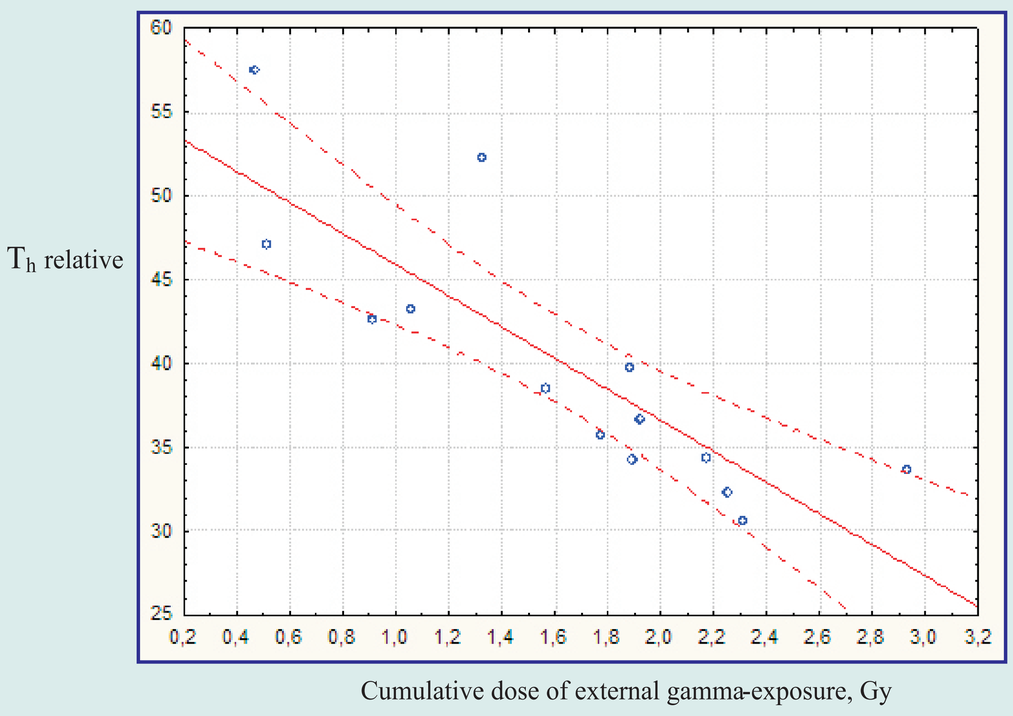

Figure 1. Relative concentration of T-helpers (dose range from 0.5 Gy to 3.0 Gy)

In this case the regression equation was as follows: $y = (55.183 \pm 3.097) - (9.290 \pm 1.743) * x$ (1)
where y – relative concentration of T-helpers (%),
x – cumulative dose of external gamma-rays (Gy).

Table – Characteristics of immune status among Mayak workers

Clusters of lymphocytes differentiation	Median				Lower quartile				Upper quartile			
	1	2	3	4	1	2	3	4	1	2	3	4
CD3+ relative %	71.0*	66.2*	72.2*	79.4	66.4	54.9	64.0	68.4	73.9	74.1	78.8	82.9
CD3+ absolute ,*10^6 cells per litre	1581.5	1127.0*	1373.0	1562.0	1115.5	858.0	1147.0	1150.0	1907.0	1419.0	1907.0	2021.0
CD4+ relative, %	47.10	35.1	42.3	41.6	43.0	33.7	35.7	31.5	55.0	38.6	47.7	46.9
CD4+absolute ,*10^6 cells per litre	1021.0	681.5	843.0	780.0	753.0	499.0	660.0	611.0	1199.5	849.0	1064.0	991.0
CD8+ relative,%	22.9	30.6	25.6	25.7	13.2	15.3	18.5	19.5	27.8	35.6	33.4	35.5
CD8+ absolute ,*10^6 cells per litre	486.0	442.5	530.5	508.5	182.0	384.0	364.0	302	667.0	658.0	731.0	825.0
CD3+16+56+ relative,%	2.2	2.9	2.6	1.5	0.9	1.6	0.9	0.794	4.4	5.4	4.5	2.5
CD3+16+56+ absolute ,*10^6 cells per litre	53.0	51.5	53.0*	31.0	10.0	27.0	18.0	12	115.0	128.0	97.0	56.0
CD3-16+56+ relative, %	12.7	16.9*	13.3*	9.4	9.5	13.7	8.6	6.9	17.6	23.1	20.5	13.8
CD3-16+56+ absolute ,*10^6 cells per litre	222.0	365.0*	276.0*	189.5	133.0	210.0	160.0	125	449.0	532.0	412.0	279.0
CD19+relative,%	10.3	7.8	7.4	7.4	7.8	4.6	5.6	5.784	12.2	9.2	9.8	9.7
CD19+ absolute ,*10^6 cells per litre	198.00	165.00	146.0	146.5	162.5	73.0	104.0	99.8	263.0	231.0	216.0	230.0
Ig M mg/l	1191.5*	1173.0*	968.0*	638.5	1098.5	909.0	713.0	528.0	1333.5	1756.0	1445.3	1015
Ig G mg/l	11335.0*	10295.0*	12697.0	13207.0	9172.5	8535.0	10610.0	10875.0	12785.0	12740.0	15180.0	18175
Ig A mg/l	3008.0*	3434.0*	3101*	1263.5	2259.0	2295.0	2266.0	747.0	3870.0	5910.0	4688.0	2992
Ig E IU/l	114.0*	42.5	50.1	44.6	76.6	17.2	23.8	23.9	321.6	76.8	103.3	76.4

*– parameter statistically significantly differs from control (4)

Regression analysis has shown that relative concentration of T-lymphocytes dependent on cumulative dose of external gamma-exposure was described by inverse linear function at dose range from 1.5 Gy to 3.0 Gy (Fig. 2).

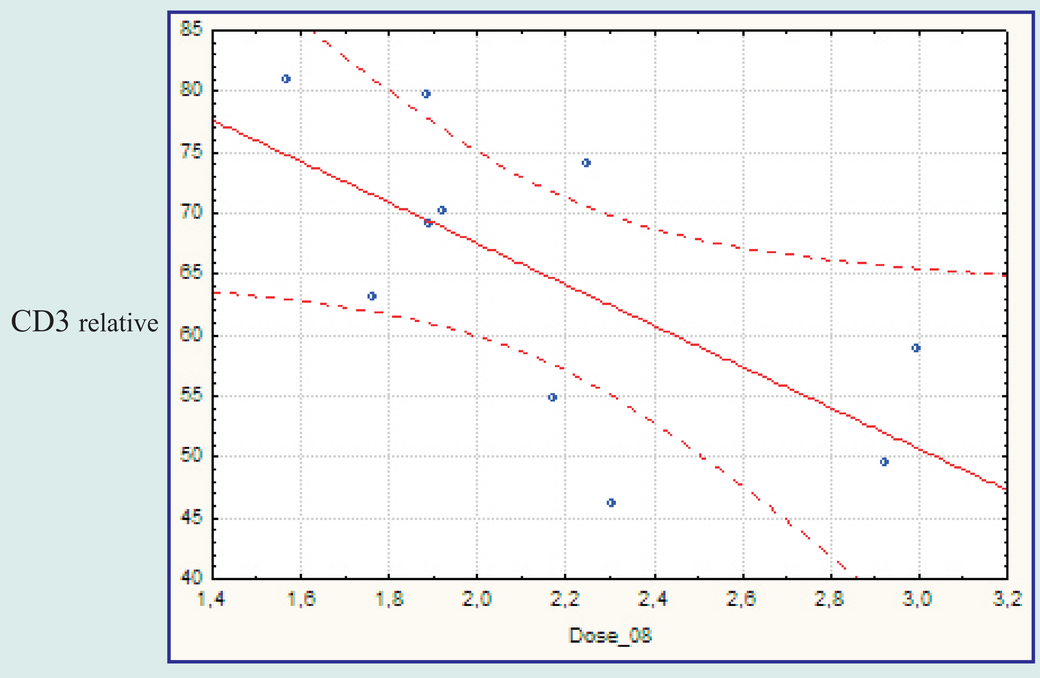

Figure 2. Relative concentration of T-lymphocytes (dose range from 1.5 Gy to 3.0 Gy)

The regression equation was as follows: $y = (101.19 \pm 15.18) - (16.85 \pm 6.86) * x$ (2)
where y – relative concentration of T-lymphocytes, %, x – cumulative dose of external gamma-exposure, Gy.

Relative concentration of T-cytotoxic lymphocytes statistically significantly decreased with raising dose of external gamma-exposure at the range of cumulative doses from 1.5 Gy to 3.0 Gy (Fig. 3).

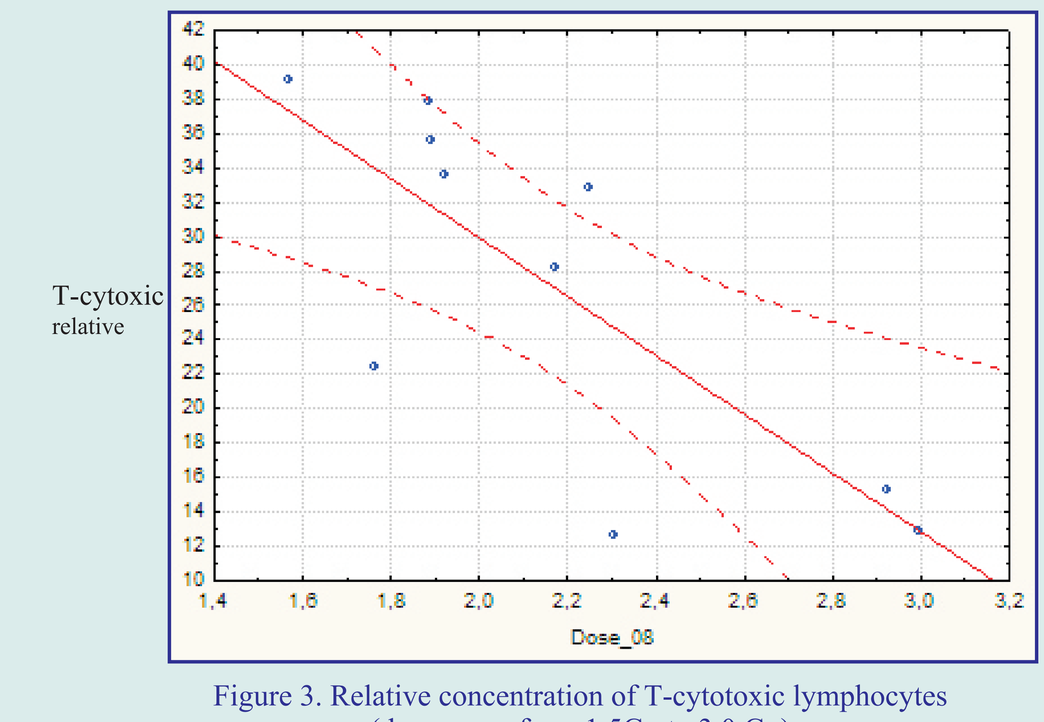

Figure 3. Relative concentration of T-cytotoxic lymphocytes (dose range from 1.5Gy to 3.0 Gy)

The regression equation was as follows: $y = (64.11 \pm 10.95) - (17.09 \pm 4.95) * x$ (3)
where y – relative concentration of T-cytotoxic lymphocytes (%), x – cumulative dose of external gamma-exposure, Gy.

Relative concentration of T-NK- lymphocytes was described by inverse linear function at dose range from 1.5 Gy to 3.0 Gy (Fig. 4).

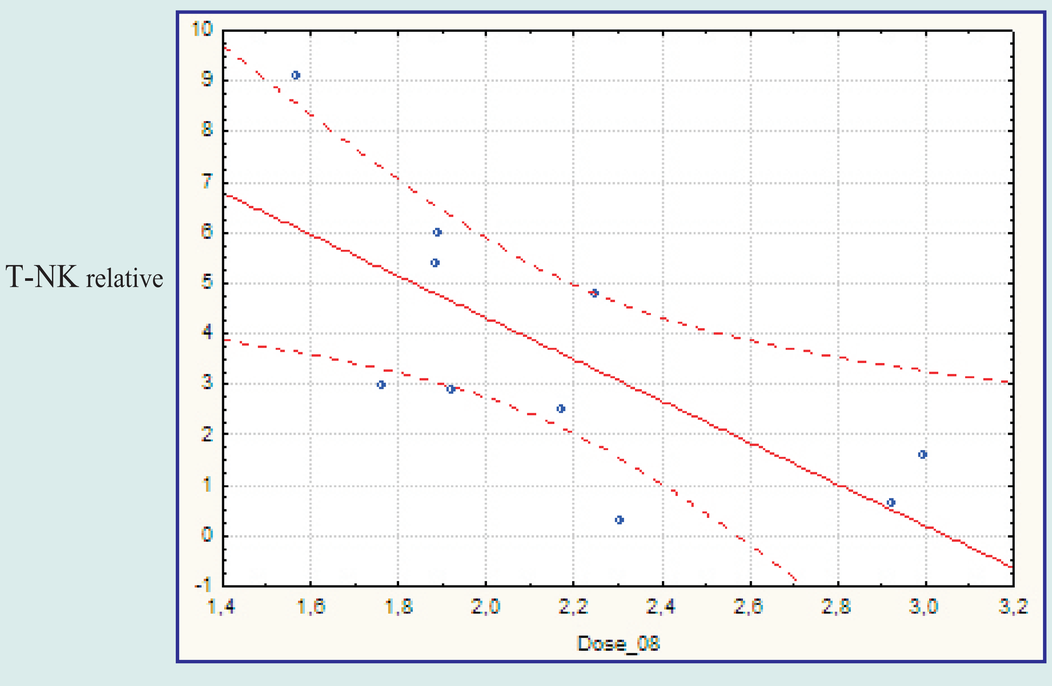

Figure 4. Relative concentration of T-NK- lymphocytes (dose range from 1.5Gy to 3.0 Gy)

The regression equation was as follows: $y=(12.55 \pm 3.14) - (4.12 \pm 1.42) * x$ (4)
where y – relative concentration of T-NK- lymphocytes,%, x – cumulative dose of external gamma-exposure, Gy.

Found regression dependencies (1) – (5) were statistically significant ($p<0,05$).

Due to combined exposure to external gamma-rays and internal alpha-radiation from incorporated Pu^{239} concentration of immunoglobulins M and A in blood serum of Mayak workers, absolute count of T-NK cells, and absolute and relative concentration of natural killers statistically significantly increased, meanwhile relative concentration of T-lymphocytes in compare with control statistically significantly decreased. However, no statistically significant relation of blood components in followed individuals to plutonium body burden was revealed.

4. DISCUSSION

Findings (i.e. decreased relative concentration of T-lymphocytes in all study groups) were consistent with the results of analysis for concentration of T-lymphocytes in workers of reactors facility of Seversk nuclear power plant (Tahaukhov et al., 2005).

Decreased concentration of T-cytotoxic lymphocytes was observed among residents of TMI region [McKinnon et al., 1989].

Decreased expression of CD4 lymphocytes was also revealed by authors in a cohort of a-bomb survivors, Hiroshima and Nagasaki residents, after 42 – 46 years from the date of acute exposure (dose greater that 1.5 Гр) (Kusunoki et al. 1998; 1999).

Increased relative concentration of NK (CD16+) in workers of plutonium production facility of Seversk nuclear plant power (40 – 62 y.o.), who had Pu^{239} body burden from 0.019 to 0.481 kBq and more, in comparison with workers not exposed to plutonium aerosols was revealed (Tahaukhov RM et al., 2003; Voronova et al., 2007). These findings are compatible to the results of the current study, which has shown increased relative concentration of natural killers in groups of workers exposed to external cumulative gamma-dose more than 1.5 Gy (group 2), and combined exposure (group 3).

According to Japanese studies in a-bomb survivors, direct relationship between concentration of IgM and dose was found (Fujiwara et al., 1994, Akiyama et al. 1995). However, no statistically significant relation between this parameter and dose (internal and external) was found in the current study.

At the same time, results on concentration of IgG, IgA, and IgE accord well with data from other studies (Fujiwara et al. 1994; Akiyama et al. 1995; Ovcharova et al., 2006; Akleev and Ovcharova, 2007; Oradovskaya et al., 2007).

Thus, the conducted analysis has shown that protracted external gamma-exposure and internal alpha radiation from incorporated plutonium cause changes in different components of immune system. These changes may play an important role in pathogenesis of long-term effects. To confirm preliminary findings further research is required.