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## STUDY OF THE CONSEQUENCES OF RADIATION ACCIDENTS

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# Immune Status of People with an Increased Chromosomal Aberration Level at Later Time Points After Chronic Radiation Exposure

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**Abstract**—Long after chronic radiation exposure mainly of red bone marrow (mean exposure dose was  $0.98 \pm 0.05$  Gy, individual dose range was 0.08–2.14 Gy), changes in the T-cell immunity such as a decrease in the relative number of CD3<sup>+</sup> lymphocytes and a decreased absolute number of CD4<sup>+</sup> cells, which did not depend on the maximum dose rate and the absorbed dose on red bone marrow and soft tissues, were observed in peripheral blood lymphocytes of individuals with increased levels of chromosomal aberrations (mainly dicentrics and translocations). The concomitant increase in the relative number of CD19<sup>+</sup> lymphocytes, which was mainly determined by the dose rate and absorbed dose on soft tissues, indicated a shift in the immunological balance in the direction of the humoral immune response.

**Keywords:** chronic irradiation, red bone marrow, chromosomal aberrations, immune status

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## INTRODUCTION

Chromosomal aberrations (CAs) are reliable biological markers of the effects of ionizing radiation, and their analysis under emergency human exposure is widely used for retrospective biological dosimetry. Residents of the coastal villages of the Techa River were exposed to chronic radiation, the dose of which has been verified for many years with various cytogenetic assays. The first studies, carried out 20 years after the onset of radiation exposure, made it possible to note a dose-dependent increase in the frequency of acentric fragments, as well as dicentrics and rings in peripheral blood lymphocytes (PBLs) [1]. In individuals exposed to chronic radiation in the dose range of red bone marrow (RBM) from 5 to 450 cGy, an elevated level of dicentrics in the PBL remained for 40 years after the exposure [2]. Later cytogenetic studies demonstrated not only the preservation of an elevated level of dicentrics but also a high level of translocations in the PBL. A linear dependence of their frequency on the dose of RBM was established in the group of people with predominantly internal exposure due to osteotropic <sup>90</sup>Sr [3]. It is important to note that at the same time a dose-dependent decrease in the functional activity of the T-cell immunity and indicators of natural cytotoxicity was noted in the inhabitants of the coastal villages of the Techa River (radiation doses on RBM ranged from 36.2 to 117.6 cGy) [4]. However, to date, the relationship between the frequency of CA in

the RBM and the functional state of the immune system in individuals exposed to chronic radiation has not been investigated.

The aim of this work was to study the characteristics of systemic immunity in individuals with an increased level of chromosomal aberrations in the long term after chronic radiation exposure, characterized by a wide range of doses of RBM irradiation.

## MATERIALS AND METHODS

A study of the characteristics of systemic immunity and the frequency of CA in 104 residents of coastal villages exposed to chronic radiation exposure was carried out 60–65 years after the discharge of liquid radioactive waste from the Mayak Production Association in the Techa River. The exposure was caused by exposure to external  $\gamma$ -radiation and the ingestion of radionuclides (mainly <sup>90</sup>Sr and <sup>137</sup>Cs) from river water and locally produced food. The main contribution to the formation of the absorbed dose of RBM irradiation was made by the osteotropic <sup>90</sup>Sr radionuclide. The maximum values of the dose to RBM reached 9 Gy. Doses to soft tissues (ST), which were analogues of doses to the thymus and peripheral organs of the immune system, mainly due to external exposure to  $\gamma$ -radiation and internal exposure due to incorporated <sup>137</sup>Cs, were significantly lower [4]. Thus, the radiation impact on the inhabitants of the coastal villages of the

**Table 1.** Dosimetric characteristics of the compared groups

| Group   | The dose rate to RBM (1951), Gy/year | The dose rate to ST (1951), Gy/year | Absorbed radiation dose to RBM, Gy | Absorbed radiation dose to ST, Gy |
|---|--------------------------------------|-------------------------------------|------------------------------------|-----------------------------------|
| Irradiated persons with an increased CA level, $n = 33$ | $0.28 \pm 0.03$<br>(0.07–0.78)*      | $0.04 \pm 0.01$<br>(0.01–0.26)      | $1.10 \pm 0.09$<br>(0.30–2.34)     | $0.08 \pm 0.02$<br>(0.01–0.49)    |
| Irradiated persons with normal CA level, $n = 71$       | $0.24 \pm 0.01$<br>(0–0.76)          | $0.02 \pm 0.01$<br>(0–0.26)         | $0.98 \pm 0.05$<br>(0.08–2.14)     | $0.07 \pm 0.01$<br>(0.01–0.50)    |

\* The range of individual dose values is specified.

Techa River could be characterized as follows: radio-sensitive hematopoietic stem cells and bone marrow progenitor cells of lymphocytes received the highest doses, while mature hematopoietic and immunocompetent cells received a significantly lesser dose. The highest dose rates to RBM occurred during the period of liquid radioactive waste discharges in 1949–1956 directly into the Techa River. The maximum values of the dose rate were observed in October 1951 due to a massive emergency discharge. The dose absorbed by RBM was formed mainly by 1961. In subsequent years, the dose rate decreased sharply, and since 1985 its values have not exceed acceptable levels for the Russian population [5].

The main study group consisted of 33 irradiated individuals who showed increased levels of unstable exchange type CAs (mainly dicentric chromosomes) and stable CAs (mainly reciprocal translocations) in the PBLs. The criteria for the formation of a group with an increased level of CA were determined considering the spontaneous frequency of dicentric chromosomes in unirradiated residents of the Ural region [3] and translocations in representatives of unirradiated populations [6]. The critical value of unstable chromosome aberrations of the exchange type for the formation of a group of people with increased CA levels was 2.5 per 1000 cells, and that of translocations, 14.0 per 1000 cells. The study group consisted mainly of women ( $n = 25$ , 75.8%) 63–79 years of age (the mean age at the time of the survey was  $69.9 \pm 0.8$  years).

The comparison group was also formed from irradiated inhabitants of the coastal villages of the Techa River, the CA frequency in which did not exceed the standard values in the long term. The group was comparable with the main study group for the achieved age at the time of the survey (mean age was  $71.1 \pm 1.1$  years, age range: 59–83 years) and gender (81.7% of women). The comparison group included 71 residents of the coastal villages of the Techa River, who lived in similar social and economic conditions with representatives of the main group and received similar medical care.

Individual doses to ST, which are equivalent to doses to the thymus and peripheral organs of the immune system, as well as doses to RBM, were calculated using the dosimetric system of the Techa River

TRDS-2009 [5]. As can be seen from Table 1, the mean values of dose rate and the absorbed dose to RBM and ST in irradiated individuals with elevated levels of CA and in individuals with their normal level did not differ statistically significantly. The average values of the maximum dose rate and absorbed dose to RBM significantly exceeded those to ST, since they were largely due to  $^{90}\text{Sr}$  incorporation in bone tissue. The individual absorbed doses to RBM varied widely and included small, intermediate, and high values, while the doses to ST were mainly small. The maximum values of the dose rate to RBM reached 0.78 Gy and of the absorbed dose, 2.34 Gy; to soft tissues, 0.26 Gy and 0.5 Gy, respectively.

Chromosome preparations were obtained from a 52-hour culture of lymphocytes stimulated by phytohemagglutinin [7]. Standard cytogenetic techniques were used to assess the incidence of CA in the PBL: colchicine treatment of the T-lymphocyte culture for 2 hours, hypotension, and 3-fold cell fixation. The frequency of unstable chromosome aberrations (dicentrics) was assessed with 2% Giemsa dye chromosome staining. To assess the frequency of translocations, we used whole-chromosome probes (Metasystems, Germany) for 1, 2, and 12 chromosome pairs, or 1, 4, and 8 chromosome pairs. The study protocol included the main stages of in situ fluorescence hybridization, denaturation, and hybridization [8]. Metaphase chromosomes were analyzed by light and luminescence microscopy using an Axio Imager microscope (Carl Zeiss, Germany). From 100 to 500 metaphase cells were analyzed to estimate the frequency of unstable CAs, and from 500 to 3000, to estimate the frequency of translocations.

The study of systemic (innate and adaptive) immunity included determining the number of major populations and subpopulations of leukocytes in the blood, assessing the functional activity of neutrophils and blood monocytes, and determining the levels of serum cytokines and immunoglobulins of classes A, M, and G. The number of immunocompetent cells with phenotypes  $\text{CD}19^+$ ,  $\text{CD}3^+$ ,  $\text{CD}3^+\text{CD}4^+$ ,  $\text{CD}3^+\text{CD}8^+$ ,  $\text{CD}16^+\text{CD}56^+$ ,  $\text{CD}3^+\text{CD}16^+\text{CD}56^+$ , and  $\text{CD}95^+$  in the blood was determined by flow cytometry on a Navios flow cytometer (Beckman Coulter, United

**Table 2.** The frequencies of chromosomal aberrations of the exchange type in the compared groups

| Parameter                    | Irradiated persons with an increased CA level, $n = 33$ | Irradiated persons with normal CA level, $n = 71$ |
|------------------------------|---|---|
| Dicentric chromosomes, %     | 1.00 ± 0.13<br>(0–3.33)<br>$p < 0.0001^*$               | 0.02 ± 0.01<br>(0–0.20)                           |
| Reciprocal translocations, % | 1.43 ± 0.29<br>(0.1–2.4)                                | 0.77 ± 0.34<br>(0.1–1.2)                          |

\* Difference from comparison group.

States) using a standard panel of monoclonal antibodies against the corresponding CD-receptors of leukocytes (Beckman Coulter, United States). Assessment of the phagocytic and lysosomal activity of neutrophils and blood monocytes was carried out according to the method of I.S. Freidlin (1986) [9]. The NBT-test in the modification of A.N. Mayansky and M.K. Wicksmann (1979) was used to determine the intensity of the intracellular oxygen-dependent metabolism of these cells [10]. Evaluation of the cytokine concentration (IL-1 $\alpha$ , IL-1 $\beta$ , IL-1RA, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17, CSF-GM, CSF-G, TNF $\alpha$ , IFN $\alpha$ , IFN $\gamma$ ) and immunoglobulins of classes A, M, and G in the blood serum was performed by enzyme-linked immunosorbent assay in a solid-phase “sandwich” type on an automatic microplate ELISA Lazurite analyzer (DYNEX Technologies, United States) using commercial sets of monoclonal antibodies (VECTOR-BEST, Russia, and eBioscience, United States).

Statistical processing of primary data was carried out using the Microsoft Excel 2010 table editor, as well as the Statistica 10.0 package using nonparametric analysis methods. The study groups were compared by calculating the Mann–Whitney  $U$ -test. The null hypothesis of the absence of differences between the compared groups was rejected at  $p < 0.05$ , and the alternative hypothesis of the presence of statistically significant differences was accepted [11]. The Spearman nonparametric correlation analysis method was used to describe the relationship between immunity indicators and the values of the cumulative dose and dose rate to RBM and ST. The regression analysis method was used to assess the dependence of indicators characterizing the functional state of the immune system on the dose characteristics. The dependencies were approximated using a linear regression model.

## RESULTS

As already noted, the inhabitants of the coastal villages of the Tcha River exposed to chronic irradiation later showed an increased level of both stable CAs (primarily reciprocal translocations) and dicentric chromosomes [3]. As can be seen from Table 2, the mean frequency of dicentrics in the group of irradiated peo-

ple with increased CA levels was also significantly higher than that in the comparison group, while the mean value of reciprocal translocations in the PBL in individuals of the main study group was increased only slightly.

The study of the T-link of adaptive immunity revealed a decrease in the relative content of CD3<sup>+</sup> lymphocytes and the absolute number of CD4<sup>+</sup> cells in peripheral blood in irradiated individuals with elevated CA level (Table 3). The number of CD8<sup>+</sup> lymphocytes and the ratio of CD4<sup>+</sup> and CD8<sup>+</sup> cells did not differ from those in the comparison group. The number of lymphocytes expressing the “cell death” marker CD95 in people with elevated level of CA did not indicate a greater readiness for apoptosis in their lymphocytes compared with the comparison group. Although the mean content of CD19<sup>+</sup> lymphocytes in the main group was increased, the levels of serum immunoglobulins A, G, and M did not exceed these indicators in the comparison group.

As can be seen from Table 4, indicators characterizing the innate immunity functional state in irradiated people with increased CA levels corresponded to those in irradiated individuals with a level of rearrangement not exceeding normal values. Only a decrease in the total lysosomal activity of monocytes was noted in the main group. The cytokine status in irradiated people with increased CA levels did not differ from the comparison group (Table 5).

Regression and correlation analysis of the dependence of established changes in systemic immunity in irradiated people with increased CA levels on the dose and dose rate to RBM, as well as to the thymus and peripheral immunogenetic organs (soft tissues), did not reveal a statistically significant contingency for the relative content of CD3<sup>+</sup> lymphocytes, the absolute number of CD4<sup>+</sup> lymphocytes, and the total lysosomal activity of monocytes (Table 6). However, even in the long term after radiation exposure, there was a moderate tendency toward an increase in the content of CD19<sup>+</sup> lymphocytes in peripheral blood with an increase in radiation exposure levels. The most pronounced dependence of this indicator was observed on

**Table 3.** Mean ( $M \pm m$ ) values of adaptive immunity parameters in individuals of compared groups

| Parameter  | Irradiated persons with an increased CA level, $n = 33$ | Irradiated persons with normal CA level, $n = 71$ | $p$   |
|--|---|---|-------|
| T-link of immunity                                 |   |   |       |
| CD3 <sup>+</sup> lymphocytes, %                    | 68.44 ± 1.33  | 79.02 ± 1.30                                      | 0.001 |
| CD3 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L  | 1.28 ± 0.09   | 1.45 ± 0.07                                       |       |
| CD4 <sup>+</sup> lymphocytes, %                    | 41.63 ± 1.31  | 42.90 ± 1.07                                      |       |
| CD4 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L  | 0.75 ± 0.05   | 0.90 ± 0.05                                       | 0.028 |
| CD8 <sup>+</sup> lymphocytes, %                    | 23.33 ± 1.29  | 22.37 ± 1.10                                      |       |
| CD8 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L  | 0.45 ± 0.05   | 0.47 ± 0.03                                       |       |
| CD4/CD8  | 1.99 ± 0.18   | 2.27 ± 0.13                                       |       |
| CD95 <sup>+</sup> lymphocytes, %                   | 3.18 ± 1.13   | 3.45 ± 0.61                                       |       |
| CD95 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L | 0.062 ± 0.018   | 0.080 ± 0.013                                     |       |
| B-link of immunity                                 |   |   |       |
| CD19 <sup>+</sup> lymphocytes, %                   | 12.20 ± 0.90  | 10.04 ± 0.63                                      | 0.028 |
| CD19 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L | 0.22 ± 0.02   | 0.21 ± 0.02                                       |       |
| Ig A, g/L  | 2.34 ± 0.20   | 2.30 ± 0.17                                       |       |
| IgG, g/L   | 13.79 ± 1.58  | 15.98 ± 1.39                                      |       |
| IgM, g/L   | 1.61 ± 0.21   | 1.38 ± 0.12                                       |       |

the dose rate to RBM and ST during the period of maximum discharges of radioactive waste in the Techa River (1951). A positive correlation was observed between the number of CD19<sup>+</sup> lymphocytes in the peripheral blood and the absorbed dose to the thymus and peripheral organs of the immune system (data not shown). A decrease in the total lysosomal activity of peripheral blood monocytes was not associated with either the dose rate or the absorbed dose to RBM and ST.

## DISCUSSION

This study of the functional state of the immune system, which included an analysis of the main parameters of adaptive and innate immunity, in people with an increased CA level in the long term after chronic radiation exposure did not reveal significant differences. A certain decrease in the number of T lymphocytes (mainly due to a subpopulation of CD4<sup>+</sup> lymphocytes), apparently, was caused by an increased CA frequency. However, this relationship is not unambiguous, since no relationship was found between the absolute number of CD4<sup>+</sup> lymphocytes and the exposure dose. It was previously shown that the frequency of CA (dicentric chromosomes and reciprocal translocations) in residents of the coastal villages of the Techa River even in the long term has a fairly clear dependence on the irradiation dose to RBM [3, 4].

Indeed, it is difficult to imagine that a decrease in the absolute number of CD4<sup>+</sup> lymphocytes in periph-

eral blood is associated with such a prolonged preservation of CA in the PBL. An increase in the frequency of stable chromosomal aberrations (mainly translocations) was observed only in eight individuals in the main group, which was 24.2% of the total number of examined irradiated participants with an increased CA level. Most of the people included in the main study group (75.8%) had an increased level of unstable exchange type CAs (mainly dicentric chromosomes). It is well known that they are not able to survive in the organism for a long time after irradiation, since the half-life of lymphocytes containing dicentric chromosomes, according to various authors, varies from 130 days to three years [12].

The revealed features of the T-link of immunity cannot be explained by the current doses to RBM and ST, which in the last 30 years do not exceed the permissible exposure levels for the Russian population. Immunity changes in individuals with an increased frequency of unstable CAs in PBLs, described in the current study, as well as in persons with increased frequency of mutations in the T cell receptor gene [13] may be a consequence of the development of genome instability in bone marrow T-cell progenitors in the period of maximum radiation exposure. It is known that radiation-induced instability of the genome of irradiated stem cells can manifest itself not only in the form of an increased frequency of CA and gene mutations in daughter cells (lymphocytes), but also their increased death in the long term [14]. In specific con-

**Table 4.** Mean ( $M \pm m$ ) values of innate immunity parameters in individuals of compared groups

| Parameter   | Irradiated persons with an increased CA level, $n = 33$ | Irradiated persons with normal CA level, $n = 71$ | $p$   |  |
|---|---|---|-------|--|
| Neutrophilic granulocytes   |   |   |       |  |
| Neutrophils, %  | 55.77 $\pm$ 1.73  | 52.66 $\pm$ 1.32                                  | 0.005 |  |
| Neutrophils, $\times 10^9/L$  | 3.19 $\pm$ 0.19   | 3.18 $\pm$ 0.14                                   |       |  |
| APN, %  | 4.43 $\pm$ 0.57   | 4.25 $\pm$ 0.39                                   |       |  |
| IPN, conventional units   | 9.23 $\pm$ 1.71   | 9.72 $\pm$ 1.21                                   |       |  |
| Phagocytic number, conventional units   | 1.91 $\pm$ 0.19   | 2.30 $\pm$ 0.22                                   |       |  |
| Spontaneous NBT-test of neutrophils, %  | 51.33 $\pm$ 2.20  | 55.14 $\pm$ 1.70                                  |       |  |
| Induced NBT-test of neutrophils, %  | 49.87 $\pm$ 2.53  | 51.59 $\pm$ 1.37                                  |       |  |
| TLAN, conventional units  | 13.09 $\pm$ 1.15  | 14.07 $\pm$ 0.83                                  |       |  |
| Monocytes   |   |   |       |  |
| Monocytes, %  | 5.43 $\pm$ 0.59   | 6.43 $\pm$ 0.36                                   |       |  |
| Monocytes, $\times 10^9/L$  | 0.30 $\pm$ 0.04   | 0.38 $\pm$ 0.02                                   |       |  |
| APM, %  | 5.77 $\pm$ 0.78   | 4.82 $\pm$ 0.46                                   |       |  |
| IPM, conventional units   | 11.77 $\pm$ 2.12  | 10.29 $\pm$ 1.26                                  |       |  |
| Phagocytic number, conventional units   | 1.79 $\pm$ 0.17   | 2.13 $\pm$ 0.17                                   |       |  |
| Spontaneous NBT-test of monocytes, %  | 54.57 $\pm$ 1.72  | 53.68 $\pm$ 1.72                                  |       |  |
| Induced NBT-test of monocytes, %  | 54.73 $\pm$ 2.59  | 53.56 $\pm$ 1.35                                  |       |  |
| TLAM, conventional units  | 0.85 $\pm$ 0.12   | 1.22 $\pm$ 0.10                                   |       |  |
| Cytotoxic cells   |   |   |       |  |
| CD3 <sup>-</sup> CD16 <sup>+</sup> CD56 <sup>+</sup> lymphocytes, %               | 15.82 $\pm$ 1.21  | 16.77 $\pm$ 1.00                                  |       |  |
| CD3 <sup>-</sup> CD16 <sup>+</sup> CD56 <sup>+</sup> lymphocytes, $\times 10^9/L$ | 0.302 $\pm$ 0.032                                       | 0.361 $\pm$ 0.030                                 |       |  |
| CD3 <sup>+</sup> CD16 <sup>+</sup> CD56 <sup>+</sup> lymphocytes, %               | 5.77 $\pm$ 0.72   | 5.52 $\pm$ 0.50                                   |       |  |
| CD3 <sup>+</sup> CD16 <sup>+</sup> CD56 <sup>+</sup> lymphocytes, $\times 10^9/L$ | 0.115 $\pm$ 0.019                                       | 0.118 $\pm$ 0.012                                 |       |  |

APN (APM)—the activity of phagocytosis of neutrophils (monocytes); IPN (IPM)—the intensity of phagocytosis of neutrophils (monocytes); NBT test—a test with nitro blue tetrazolium; TLAN (TLAM)—total lysosomal activity of neutrophils (monocytes).

**Table 5.** Mean ( $M \pm m$ ) serum cytokine levels in individuals of the compared groups

| Parameter             | Irradiated persons with an increased CA level, $n = 33$ | Irradiated persons with normal CA level, $n = 71$ |
|-----------------------|---|---|
| IL-1 $\alpha$ , pg/mL | 0.83 $\pm$ 0.28   | 1.19 $\pm$ 0.13                                   |
| IL-1 $\beta$ , pg/mL  | 40.81 $\pm$ 12.09                                       | 34.52 $\pm$ 8.77                                  |
| IL-1RA, pg/mL         | 133.24 $\pm$ 71.21                                      | 415.41 $\pm$ 134.33                               |
| IL-2, pg/mL           | 12.87 $\pm$ 4.11  | 9.90 $\pm$ 1.28                                   |
| IL-4, pg/mL           | 4.76 $\pm$ 0.96   | 5.92 $\pm$ 0.95                                   |
| IL-6, pg/mL           | 18.78 $\pm$ 10.35                                       | 12.34 $\pm$ 6.40                                  |
| IL-8, pg/mL           | 4.78 $\pm$ 1.30   | 14.37 $\pm$ 8.18                                  |
| IL-10, pg/mL          | 9.67 $\pm$ 1.37   | 10.89 $\pm$ 1.98                                  |
| IL-17, pg/mL          | 4.17 $\pm$ 0.79   | 3.57 $\pm$ 0.54                                   |
| CSF-GM, pg/mL         | 3.44 $\pm$ 0.61   | 3.99 $\pm$ 1.90                                   |
| CSF-G, pg/mL          | 7.37 $\pm$ 2.23   | 9.83 $\pm$ 1.42                                   |
| TNF $\alpha$ , pg/mL  | 5.33 $\pm$ 0.55   | 4.89 $\pm$ 0.44                                   |
| IFN $\alpha$ , pg/mL  | 6.32 $\pm$ 1.65   | 6.75 $\pm$ 1.23                                   |
| IFN $\gamma$ , pg/mL  | 17.68 $\pm$ 3.71  | 16.76 $\pm$ 2.50                                  |

**Table 6.** Correlation coefficients between immunity indices, which significantly differed in irradiated people with increased CA levels from those in the comparison group, and dosimetric characteristics

| Parameter   | The dose rate to RBM (1951), Gy/year | The dose rate to ST (1951), Gy/year | Absorbed radiation dose to RBM, Gy | Absorbed radiation dose to ST, Gy |
|---|--------------------------------------|-------------------------------------|------------------------------------|-----------------------------------|
| CD3 <sup>+</sup> lymphocytes, %                   | 0.02                                 | −0.11                               | 0.07                               | −0.08                             |
| CD4 <sup>+</sup> lymphocytes, ×10 <sup>9</sup> /L | −0.1                                 | −0.15                               | −0.11                              | −0.10                             |
| CD19 <sup>+</sup> lymphocytes, %                  | 0.37                                 | 0.47                                | 0.19                               | 0.45                              |
| TLAM, conventional units                          | 0.21                                 | 0.15                                | 0.12                               | 0.15                              |

ditions of uneven exposure of residents of the coastal villages of the Techa River, when large doses to RBM occurred, radiosensitive stem cells were, of course, critical targets.

Another mechanism of detected changes in immunity may be due to dysregulation of the immune response after chronic exposure to ionizing radiation. Thus, a violation of cell-mediated immunity (a decrease in the number of naive CD4<sup>+</sup> lymphocytes), observed simultaneously with an increase in the functional activity of the B-link of the immune system, in survivors of the atomic bombing in Japan, suggested that radiation exposure may induce a shift in the balance towards the Th2-response [15]. The results of the present study also indicate a shift in the immunological balance in chronically irradiated individuals with increased CA levels in lymphocytes towards a humoral immune response.

### CONCLUSIONS

In the conditions of chronic irradiation of residents of the coastal villages of the Techa River, when the absorbed doses to RBM reached high values, people with an increased CA level in the PBL demonstrated some alterations in systemic immunity in the long term after the onset of radiation exposure. The changes affected mainly adaptive immunity (a decrease in the relative content of CD3<sup>+</sup> lymphocytes and the absolute number of CD4<sup>+</sup> lymphocytes, an increase in the number of CD19<sup>+</sup> cells in peripheral blood) and indicated a shift in the immune response in irradiated individuals with increased CA levels towards the humoral immunity. The results of previous studies in Japan demonstrated similar changes in systemic immunity after acute high-dose exposure of people due to the atomic bombings of the cities of Hiroshima and Nagasaki [15].

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