



State of Immunological Reactivity of Rat's Body after Exposure to Different Doses of γ -Radiation in a Long Period and their Offense of the 1st Generation

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Abstract

BACKGROUND: Recently, the problem of changes in immunological reactivity has become important with the growth of immunodeficiency states of a different nature. High radiosensitivity of the immune system, its stability in time and the irreversibility of some post-radiation changes can contribute to the development of long-term effects of radiation. One of the tasks of modern medicine and biology is to study the effect of chronic or fractionated ionizing effects on the body's immune system both in the early and late periods of irradiation and their 1st generation descendants. Therefore, it is necessary to study the long-term effects of sublethal and fractionated effects of γ -radiation on the immunological reactivity of the organism, non-specific phagocytic resistance, and their 1st generation descendants.

AIM: The aim of this study was to study the long-term effects of sublethal and fractionated effects of γ -radiation on the immunological reactivity of the organism, non-specific phagocytic resistance, and their 1st generation descendants.

METHODS: Seven series of experiments were performed on 105 white outbred sexually mature rats. 1-series intact (n = 15), 2nd series - (n = 15) irradiated with a sublethal dose of 6 Gr. (1 month), 3rd series - irradiated with a sublethal dose (3 months, n = 20), 4 - descendants 1 - generations after sublethal dose, 5 series - irradiated with a fractionated dose (1 month), 6 series - irradiated with a fractionated dose (3 months), and 7 - descendants of the 1st generation after fractionated γ -irradiation. Each series used 15 animals. Irradiation of animals 2-3-4 series was carried out on the Russian radiotherapy device "Agat-RM" γ -rays ⁶⁰Co, the dose of sublethal irradiation is 6 Gr. Irradiation of animals of 5-6-7 series was carried out on the Russian radiotherapy device "Agat-RM" with ⁶⁰Co-rays with topometric and dosimetric preparation of experimental animals, which facilitates the administration of a fractionated dose of 2 Gr. to animals 3 times within 3 weeks.

RESULTS: In the long-term period after fractionated γ -irradiation in the T-system of immunity, the following changes occur: Against the background of an increase in the total number of lymphocytes, there is a decrease in the pool of CD3+, CD4+ lymphocytes, immunoregulatory index, normalization of the lymphokine-producing ability of lymphocytes and a decrease in the pool of CD8+ lymphocytes. In the long-term period after fractionated γ -irradiation in the humoral link of immunity, an increase in the absolute amount of CD19+ by 3.5 times was noted, which significantly exceeded the indicators of both control and intact animals. The percentage of this pool of cells exceeded the data of intact ones by 1.7 times. In the studied time period, the antibody-producing ability in the spleen increased from 22 ± 1.3 to 45 ± 2.6, without reaching, however, the level of intact animals. At the same time, there was a significant decrease in the suppression index to 13% (p < 0.001) and the CIC concentration by 14 times (p < 0.001) in the blood serum. The indicators of F/n and NST-test were high by 1.43 and 2.46 times, respectively. Hence, in the long-term period after exposure to a fractionated dose of γ -radiation, the nonspecific phagocytic resistance of the organism is increased.

CONCLUSIONS: The tension in the humoral link of immunity is manifested by a decrease in the quantitative and qualitative indicators and an increase in the functional and metabolic activity of neutrophils.

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Introduction

The impact on the body, stress factors lead to a change in protective and adaptive mechanisms, disrupting the immune system, causing a post-stress immunodeficiency state [1], [2], [3]. Recently, the problem of changes in immunological reactivity has become important with the growth of immunodeficiency states of a different nature [4]. It is known that most

immunological processes unfold against the background of stress [5].

High radiosensitivity of the immune system, its stability in time and the irreversibility of some post-radiation changes can contribute to the development of long-term effects of radiation [2], [3], [6]. The role of the immune system in the development of distant radiation pathology under the influence of sublethal and fractionated doses of γ -radiation has not been sufficiently studied.

A characteristic feature of radiation exposure is the long-term preservation of damage in individual links of the immunity system and the long-term consequences and complications associated with it. The outcome of radiation injuries, the development of immediate and long-term consequences, depends on the state and sensitivity of the immune system to ionizing radiation. More often during this period, violations of the T-cell link are recorded, especially under the action of a sublethal dose of γ -radiation [1], [2], [3]. The appearance of disorders and imbalances in the humoral link of immunity and the long-term consequences and complications associated with it, is manifested by the acceleration of aging processes, the progression of chronic diseases of internal organs and the development of malignant neoplasms [2], [6].

Soon after sublethal irradiation, suppression occurs in all links of immunity, which is the basis for the formation of immunological deficiency [2], [7], [8]. Therefore, the use of immunological methods, a comprehensive study of the states of the cellular, humoral links of immunity, and non-specific phagocytic resistance of the organism of animals and humans are necessary as sensitive tests to assess the effectiveness of the aftereffect of sublethal and fractionated doses of γ -radiation of long-term consequences in the offspring of the 1st generation. With fractionated irradiation, the least biological effect is observed in comparison with a single irradiation in comparable doses. This phenomenon is explained by the development of restorative processes occurring in the body, which develop most intensively during the breaks between irradiation [8]. At the same time, the long-term effects of the action of ionizing radiation on blood cells in the dose range with fractionated radiation remain poorly understood [9], [10]. Consequently, one of the tasks of modern medicine and biology is to study the effect of chronic or fractionated ionizing effects on the body's immune system both in the early and late periods of irradiation and their 1st generation descendants [1], [2], [3], [11], [12].

Therefore, it is necessary to study the long-term effects of sublethal and fractionated effects of γ -radiation on the immunological reactivity of the organism, non-specific phagocytic resistance, and their 1st generation descendants.

Materials and Research Methods

Seven series of experiments were performed on 105 white outbred sexually mature rats. 1-series intact ($n = 15$), 2nd series - ($n = 15$) irradiated with a sublethal dose of 6 Gr. (1 month), 3rd series - irradiated with a sublethal dose (3 months, $n = 20$), 4 - descendants 1 - generations after sublethal dose, 5 series - irradiated

with a fractionated dose (1 month), 6 series - irradiated with a fractionated dose (3 months), and 7 - descendants of the 1st generation after fractionated γ -irradiation. Each series used 15 animals. Irradiation of animals 2-3-4 series was carried out on the Russian radiotherapy device "Agat-RM" γ -rays ^{60}Co , the dose of sublethal irradiation is 6 Gr. Irradiation of animals of 5-6-7 series was carried out on the Russian radiotherapy device "Agat-RM" with ^{60}Co -rays with topometric and dosimetric preparation of experimental animals, which facilitates the administration of a fractionated dose of 2 Gr. to animals 3 times within 3 weeks.

In peripheral blood, the total number of leukocytes and lymphocytes was determined. The state of the cellular link of immunity was assessed by the absolute and relative number of CD3+, CD4+, CD8+ and CD19+ cells with the corresponding monoclonal antibodies, the immunoregulatory index (IRI) was calculated by calculation IRI [13]. Determined the reaction of inhibition of migration of leukocytes (RIML on FGA) [14].

The state of humoral immunity was assessed by the number of B-lymphocytes (CD19+) - was determined with the corresponding monoclonal antibodies, by flow cytometry, the concentration of circulating immune complexes (CIC) - by the method [15], [16]. To study antibody-forming cells (AFC), we used the method of local hemolysis by Jerne and Nordin [17]. The suppression index (IS) was calculated as a percentage. The state of non-specific phagocytic resistance of the organism was assessed by the phagoactivity of polynuclear cells. The content of phagocytic polynuclear cells (neutrophils and pseudo-eosinophils) was investigated according to the method [18], [19]. Latex was used as a phagocytic material. Phagocytic indices (F/I) were considered the % of neutrophils entering phagocytosis of the total number of neutrophils. The indices of the mononuclear-phagocytic system were determined (NBT-test) [20], [21]. It is known that the weakening of the activity of phagocytosis caused by ionizing radiation forms a leukopenic form of phagocytic insufficiency, which develops as a result of slowing down the processes of proliferation and/or maturation of leukocytes [22], [23].

Methods for conducting experiments on animals were in accordance with the requirements of the Geneva Convention (1990) and the Declaration of Helsinki [24].

In series 4 and 5, experimental animals underwent a course of phytocomposition on intact animals; the effect of phytopreparations on the state of AOD and LPO was determined. Animals were removed from the experiment by euthanasia with ether anesthesia with incomplete decapitalization. Statistical processing of the results was carried out using the statistical software package SPSS version 20.0 for Windows (license of NJC MUA). When studying two or more groups, the type of data distribution was determined for each group. The distribution was also

carried out graphically using quantile diagrams. To describe quantitative data with a normal distribution, the arithmetic mean (am.) and standard deviation (sv.) were used. The difference between the groups was calculated using the Student's t-test.

Results

The indices of T-cell, humoral links of immunity and nonspecific phagocytic resistance of the organism were studied in irradiated animals in the near and distant period and their descendants of the 1st generation after general exposure to γ -radiation in a sublethal and fractionated dose (Tables 1 and 2).

To study the immediate effects of sublethal γ -radiation on the T-system of immunity, we performed 1 and 2 series of experiments on adult white outbred rats of both sexes.

In the near term, there is a significant decrease in the total number of leukocytes by 1.29 times, while the absolute and relative number of lymphocytes increased by 1.57 and 1.38 times, respectively. There was a decrease in the absolute and relative content of the subpopulation CD3+, CD4+, CD8+ lymphocytes, which led to a significant decrease in IRI by 1.81 times. Acute radiation manifestation also affected a decrease in the lymphokine-producing ability of leukocytes. RIML at FGA increased by 25%.

Analysis of the experimental material showed that under the action of sublethal γ -irradiation at a dose of 6 Gr. (Table 1), a decrease in both quantitative and qualitative indicators of the T-system of immunity is observed soon, which characterizes the development of an immunodeficiency state.

Table 1 shows that in the immediate period after ionizing exposure at a dose of 6 Gr. in the humoral link of immunity, an increase in the total number of

lymphocytes is associated with an increase in the absolute and relative number of CD19+ lymphocytes (by 1.83 and 1.85 times, respectively). Dysfunction of the humoral immunity of an irradiated organism is manifested in a 2.73-fold decrease in the amount of AFC in the spleen and an increase in the IS by 63 \pm 1.5%. The concentration of CIC in the blood serum is significantly reduced by 2.5 times.

Hence, in the immediate period after exposure to a sublethal dose of γ -radiation, dysfunction is noted in the humoral link of immunity, which manifests itself in a decrease in its qualitative indicator - a low amount of AFC in the spleen, an increase in the IS and a decrease in the concentration of CIC in the blood serum.

In the immediate period after exposure to a sublethal dose of γ -radiation, there were also changes in the non-specific phagocytic resistance of the organism. There was a tendency to a decrease in phagocytosis, these manifestations did not cause a significant change in the phagocytic number (F/n), and only the NBT-test indicator significantly increased by 4.75 times.

Analysis of the factual material shows that in the next period of radiation injury at a dose of 6 Gr, there is an increase in the functional and metabolic activity of neutrophils, which was accompanied by an increase in the NBT test by 61%.

From which it follows that the data obtained allow us to conclude that in the immediate period after sublethal irradiation at a dose of 6 Gr, the functional and metabolic activity of neutrophils increases. Our results are consistent with the data obtained [7].

Of the many factors that negatively affect human health, ionizing radiation occupies a special place, since even a single exposure to it can cause irreversible changes in the body.

Changes in the B-system of immunity, apparently, are also due to the presence of an internal cell defect due to a violation of the subpopulation composition of B-lymphocytes, due to damage to

Table 1: Influence of ionizing radiation at a dose of 6 Gr on the immune system of the body in the offspring of the 1st generation

Indicators	Study groups			
	1. Intact (n = 15)	2. Irradiated (30 days)	3. Irradiated + 90 days (n = 20)	1 descendants
Leukocytes in 1 μ l	6520 \pm 150	5022 \pm 255**	6112 \pm 125	7100 \pm 112 ⁰
Lymphocytes in 1 μ l.	1. 2800 \pm 113	1. 4400 \pm 150*	1. 3455 \pm 640	4111 \pm 99.8*
	2. 40 \pm 3.6	2. 54 \pm 1.2*	2. 56 \pm 2.0*	57 \pm 1.2*
CD3+	1. 1457 \pm 84	1. 415 \pm 18**	1. 1060 \pm 310	875 \pm 20.0*
	2. 32 \pm 2.2	2. 15 \pm 1.0*	2. 31 \pm 2.30	22.0 \pm 0.75 ⁰
CD4+	1. 698 \pm 85.9	1. 229 \pm 13.0**	1. 846 \pm 25.5	415 \pm 17.4 ⁰
	2. 21.2 \pm 1.9	2. 7.0 \pm 0.5*	2. 24 \pm 1.50	9.3 \pm 0.57 ⁰
CD8+	1. 488 \pm 2.2	1. 183 \pm 24.5**	1. 313 \pm 30.2*	475 \pm 17.4 ⁰
	2. 10.8 \pm 0.6	2. 4.0 \pm 0.5*	2. 8.0 \pm 1.70	13.0 \pm 0.47 ⁰
IRI	1.96 \pm 0.16	1.1 \pm 0.15*	2.7 \pm 0.15*	0.7 \pm 0.05 ⁰
RIML	0.8 \pm 0.06	1.2 \pm 0.03*	0.77 \pm 0.02	0.62 \pm 0.02*
CD19+in 1 ml/l	1. 318 \pm 16.5	584.3 \pm 15.8*	1. 619 \pm 16.3**	1. 792 \pm 26.3 ⁰
	2. 7.0 \pm 2.1	13.0 \pm 1.4*	2. 15 \pm 1.7**	2. 21.0 \pm 0.86*
AFC _s %	52 \pm 4.9	19 \pm 1.2**	40 \pm 2.3 ⁰	45 \pm 1.5
IS (index suppression in %)	-	63 \pm 1.5	23 \pm 1.40	13 \pm 2.2
CIC (g/l)	1.3 \pm 0.03	0.5 \pm 0.01*	0.2 \pm 0.01** ⁰	0.011 \pm 0.001** ⁰⁰
Phagocytosis %	36.0 \pm 2.4	33.4 \pm 2.4	53.6 \pm 1.6**	47 \pm 0.9 ⁰
P/n	1.6 \pm 0.23	1.7 \pm 0.2	2.6 \pm 0.2*	2.3 \pm 0.05*
NBT-test	4.7 \pm 1.6	7.6 \pm 0.4 ⁰	11.3 \pm 0.8**	6.0 \pm 0.47 ⁰

1.: Abs. n., 2.: Relative in %, *Reliability to the control (p<0.05). **Reliability (p < 0.001). ⁰Reliably to group 2 (p < 0.05). IRI: Immunoregulatory index, CIC: Circulating immune complexes.

hematopoietic stem cells and a mismatch in intersystem interactions.

In the long-term period after fractionated γ -radiation, both in the early and late periods, there is a depression in the humoral link of immunity.

In series 3 - a long-term period after exposure to a sublethal dose of γ -radiation in the T-system of immunity, there is a normalization of the number of leukocytes, lymphocytes, a subpopulation of CD3+ lymphocytes, an increase in the absolute and relative content of a subpopulation of CD4+ lymphocytes, and a decrease in the absolute and relative content of a subpopulation of CD8+ lymphocytes, which caused an increase in 1.35 times the IRI. By this period, the functional ability of the cellular link of immunity has been restored.

Consequently, in the long-term period after sublethal γ -irradiation in the T-system of immunity there is a normalization of the number of leukocytes, a subpopulation of CD3+ lymphocytes, lymphokine-producing ability of leukocytes, an increase in the number of a subpopulation of lymphocytes with helper and a decrease in the number of a subpopulation of lymphocytes with suppressive activity.

In the long-term period after sublethal γ -irradiation, the number of leukocytes and lymphocytes in the peripheral blood normalizes in the humoral link of immunity. There is a further significant increase in the absolute and relative numbers of CD19+ lymphocytes by 2.49 and 3.0 times, respectively, the number of AFC in the spleen increases by 2.73 times, reaching the lower level of the control indicator, while the IS decreases by 4.84 times in comparison with the control group from $63 \pm 1.5\%$ to $13 \pm 1.2\%$. At the same time, there is a further (2.5 times) decrease in the concentration of CIC in the blood serum.

As you can see, in the long-term period after acute radiation exposure in the offspring of the 1st generation, there is a tension in the humoral link of immunity, which manifests itself in an increase in the number of CD19+ lymphocyte subpopulations, low antibody production in the spleen, the concentration of CIC in the blood serum and an increase in the IS.

Certain changes also occur on the part of nonspecific phagocytic resistance of the organism. In the long-term period after exposure to a sublethal dose of γ -radiation, an increase in the phagocytic number was noted by 1.63 times, phagocytosis and the NBT test by 1.47 and 2.4 times, respectively.

These changes indicate that in the long-term period after exposure to a sublethal dose of γ -radiation in the offspring of the 1st generation, an increase in nonspecific phagocytic resistance of the organism is observed. To study the immunological reactivity of the organism after exposure to a sublethal dose of γ -radiation in the offspring of the 1st generation, we performed a 4-series of experiments. In series 4 - after sublethal irradiation in the offspring of the 1st generation, leukocytosis, lymphocytosis, a decrease in the absolute and relative content of CD3+ and CD4+ lymphocytes, and the IRI are noted in the peripheral blood. The absolute number of CD8+ lymphocyte subpopulation corresponds to the data of the control group. The relative content of the CD8+ subpopulation of lymphocytes remains high, significantly exceeding the control groups. The lymphokine-producing ability of leukocytes increases.

Thus, in irradiated animals with a sublethal dose of γ -radiation and their 1st generation descendants in the T-system of immunity against the background of leukolymphocytosis, there is a decrease in the number of CD3+ and CD4+ lymphocytes and an increase in the lymphokine-producing ability of leukocytes.

Certain changes are observed in the humoral link of the immune system in the offspring of the 1st generation. The number of subpopulations of CD19+ lymphocytes in peripheral blood increases to control levels. A decrease in the number of AFCs in the spleen to $40 \pm 2.3\%$ is accompanied by a decrease in the IS by 1.6 times and the concentration of CIC in the blood serum by 6.5 times. It should be noted that, despite the tendency to an increase in antibody production in the spleen, the decrease in the IS and CIC concentration in the blood serum do not reach the level of control values and remain significantly low. In the offspring of

Table 2: State of the immune system with fractionated γ -irradiation in the offspring of the 1st generation

Indicators	Study groups			
	1. Intact (n = 15)	2 - Irradiated + 1 month (n = 20)	2. Irradiated + 90 days (n = 20)	1 descendants
Leukocytes in 1 μ l	6520 \pm 150	6200 \pm 290.4	6690 \pm 145	5700 \pm 150 ⁰
Lymphocytes in 1 μ l	1. 2800 \pm 113	1. 3125 \pm 105*	1. 4116 \pm 50.8*	2900 \pm 124 ⁰
	2. 40 \pm 3.6	2. 53.5 \pm 1.4**	2. 32.3 \pm 4.40 ⁰	51 \pm 1.3 ⁰
CD3+	1. 1457 \pm 84	1. 3426 \pm 27.2**	1. 1376 \pm 36.7	832 \pm 29.4 ⁰
	2. 32 \pm 2.2	2. 30.0 \pm 1.0	2. 12.3 \pm 0.7 ⁰	29 \pm 1.1
CD4+	1. 698 \pm 85.9	1. 584 \pm 45.3	1. 1066 \pm 31.9 ⁰	528 \pm 83*
	2. 21.2 \pm 1.9	2. 22.2 \pm 0.9	2. 25 \pm 4.1	18 \pm 0.8 ⁰
CD8+	1. 488 \pm 22	1. 96.6 \pm 11.4**	1. 308 \pm 20.3 ⁰	324 \pm 19*
	2. 10.8 \pm 0.6	2. 4.3 \pm 0.5**	2. 7.3 \pm 1.4 ⁰	12 \pm 0.7 ⁰
IRI	1.96 \pm 0.16	6.0 \pm 0.39**	3.4 \pm 0.41 ⁰	1.62 \pm 0.22
RIML %	0.8 \pm 0.06	0.62 \pm 0.06**	0.81 \pm 0.040	0.54 \pm 0.02 ⁰
CD19+in 1 μ l	1. 318 \pm 16.5	1. 145.0 \pm 9.9**	1. 514 \pm 42 ⁰	165 \pm 17.7 ⁰
	2. 7.0 \pm 2.1	2. 14.2 \pm 1.0 **	2. 12.3 \pm 0.7*	4.8 \pm 0.9 ⁰
AFC in %	52 \pm 4.9	22 \pm 1.3 **	45 \pm 2.60	48 \pm 2.5
IS (ind. suppression in %)*	-	57.6 \pm 1.2*	13 \pm 0.38	11.5 \pm 0.23
CIC (g/l)	1.3 \pm 0.03	0.7 \pm 0.01**	0.05 \pm 0.001 ⁰	0.007 \pm -0.0008 ⁰
Phagocytosis	36.0 \pm 2.4	70 \pm 2.6**	52 \pm 0.8*	29 \pm 1.5 ⁰
F/n	1.6 \pm 0.23	3.3 \pm 0.05 **	2.3 \pm 0.1*	2.6 \pm 0.17*
NBT-test	4.7 \pm 1.6	12.0 \pm 0.72**	11.6 \pm 3.9*	17 \pm 0.4 ⁰

1.: Abs. μ , 2.: Relative in %, *Reliability to the control (p<0.05). **Reliability (p < 0.001). ⁰Reliably to group 2 (p<0.05). IRI: Immunoregulatory index, CIC: Circulating immune complexes.

irradiated animals of the 1st generation, the activity in the humoral link of immunity is manifested in an increase in the number of CD19+ lymphocytes. The number of the latter is statistically increased in comparison with the control group by 1.5 times. In the blood serum, there is a significant decrease in CIC, the antibody-producing ability of the spleen corresponds to the control value.

Summarizing the data obtained, it can be stated that in the long-term period, the irradiated animals show depression, while the descendants of irradiated animals of the 1st generation show the activation of the humoral link of immunity.

In the descendants of the 1st generation, after exposure to a sublethal dose of γ -radiation, the following changes appear in the humoral link of immunity: an increase in the absolute and relative number of CD19+ lymphocyte subpopulations by 2.49 and 3.0 times, respectively. The formation of AFC in the spleen is normalized, while the IS was $13 \pm 2.2\%$ the concentration of CIC in the blood serum is reduced.

Hence, in the humoral link of immunity in the descendants of the 1st generation after exposure to a sublethal dose of γ -radiation, there is an increase in quantitative and normalization of qualitative indicators.

In the long-term period - after sublethal γ -irradiation, the phagocytosis index, phagocytic number and NBT test significantly increase by 1.7, 1.5 times, respectively, which indicates an increase in the functional capacity of the non-specific phagocytic link of immunity.

The above results suggest that the high phagocytic capacity of neutrophils and macrophages indicates the inclusion of adaptive mechanisms in the long-term period of irradiation. In the offspring of the 1st generation of irradiated animals, in comparison with the 2nd group, a significant decrease in phagocytosis and NBT test is noted. But in comparison with the indices of the intact group, phagocytosis and phagocytic number are significantly higher by 1.3 and 1.4 times, respectively. The functional-metabolic activity of neutrophils is 22% higher than the data of an intact organism, while in the long-term period after irradiation, not only the functional-metabolic activity of neutrophils increases, but also an increase in the functional activity of leukocytes. The high activity of the nonspecific phagocytic link of immunity is also preserved in the trained descendants of the 1st generation, but in a less pronounced form.

A large volume of clinical and experimental research has been devoted to the problems of high doses of ionizing radiation. It has been shown that high doses of radiation can destroy not only cells, but also damage tissues and organs, ultimately leading to the death of the whole organism. [1], [2]. At the same time, according to the literature, the influence of fractionated γ -radiation on the immune system of the body in the long-term period and in the descendants of the

1st generation has not been sufficiently studied.

To compensate for this problem, we performed 5, 6, and 7 series of experiments. Table 2 shows that in the early period after exposure to fractionated γ -radiation in the T-system of immunity there is an increase in the absolute and relative number of lymphocytes, where an increase in the number of CD3+ lymphocytes and a stable number of CD4+ lymphocytes play a significant role in this, which is also reflected in high rates IRI, since in this period the absolute number of the CD8+ lymphocyte subpopulation decreases by 5 times, and there is a significant decrease in RIML on PHA, which indicates an increase in the lymphokine-producing ability of leukocytes.

Hence, under the action of a fractionated dose of γ -radiation in the next period in the T-system of immunity, the quantitative indicators decrease and the qualitative indicators increase.

The results of the effect of fractionated γ -radiation on the humoral link of immunity in the near and long term are presented in Table 2. From the presented digital material, it can be seen that the state of humoral immunity a month after fractionated irradiation presented the following picture: the relative number of CD20+ lymphocytes increased by 2 times, while its absolute indicator decreased by the same number of times. During this period, the concentration of CIC in the blood serum significantly decreased from 1.3 ± 0.03 g/l to 0.7 ± 0.01 g/l ($p < 0.001$), the amount of AFC in the spleen decreased 2.3 times compared with the control indicators. IS increased to $57.6 \pm 1.2\%$.

Consequently, in the near term, in the humoral link of immunity under the action of a fractionated dose, there is a decrease in the qualitative indicator, which is manifested in a decrease in the number of AFCs in the spleen, the concentration of CIC in the blood serum and an increase in the IS.

Thus, under the action of a fractionated dose of γ -radiation in the next period in the humoral link of immunity, there is an increase in the quantitative and a decrease in the qualitative indicator.

In the immediate period after exposure to a fractionated dose of γ -radiation, there is a significant 2.1-fold increase in the phagocytic number (F/n), an increase in the functional-metabolic activity of neutrophils, which was accompanied by an increase in the NBT test by 155% and phagocytosis by 1.94 times.

Hence, the data obtained allow us to conclude that in the immediate period after fractionated exposure, the nonspecific phagocytic resistance of the organism increases in white rats.

Analysis of the above material shows that in the long-term period after fractionated γ -irradiation in the T-system of immunity, the following changes occur: Against the background of an increase in the total number of lymphocytes, there is a decrease in the

pool of CD3+, CD4+ lymphocytes, IRI, normalization of the lymphokine-producing ability of lymphocytes and a decrease in the pool of CD8+ lymphocytes. This means that in the long-term period after exposure to a fractionated dose of γ -radiation in the T-system of immunity, there is a normalization of the lymphokine-producing ability of leukocytes and a decrease in the subpopulation of lymphocytes with suppressive activity. In the long-term period after fractionated γ -irradiation in the humoral link of immunity, an increase in the absolute amount of CD19+ by 3.5 times was noted, which significantly exceeded the indicators of both control and intact animals. The percentage of this pool of cells exceeded the data of intact ones by 1.7 times. In the studied time period, the antibody-producing ability in the spleen increased from 22 ± 1.3 to 45 ± 2.6 , without reaching; however, the level of intact animals. At the same time, there was a significant decrease in the IS to 13% ($p < 0.001$) and the CIC concentration by 14 times ($p < 0.001$) in the blood serum. Therefore, dysfunction in the humoral link of immunity after exposure to a fractionated dose of γ -radiation is manifested in a decrease in functional ability, which is manifested in the AFC indices in the spleen, the IS and the CIC concentration in the blood serum. In the long-term period after exposure to a fractionated dose of γ -radiation, a decrease in phagocytosis was noted, in comparison with the immediate period, remaining significantly high in comparison with the control indicator. The indicators of F/n and NST-test were high by 1.43 and 2.46 times, respectively. Hence, in the long-term period after exposure to a fractionated dose of γ -radiation, the non-specific phagocytic resistance of the organism is increased.

Discussion

The descendants of the 1st generation after fractionated exposure to γ -irradiation have a significantly reduced number of leukocytes in the peripheral blood. Against the background of leukopenia, there is an increase in the relative number of total lymphocytes. The relative content of the CD3+, CD4+, and CD8+ cell pool and the IRI were lower than the control levels. A significant decrease in RIML on PHA indicates a high functional activity of the T-system of immunity. Also, from the factual material it can be seen that in the descendants of the 1st generation, after fractionated exposure to γ -irradiation in the T-link of immunity, there is a decrease in total T-lymphocytes and lymphocytes with helper and suppressor activity. At the same time, there is a high functional capacity of leukocytes.

In the offspring of the 1st generation of irradiated animals after fractional exposure to

γ -irradiation, there is a tension in the humoral link of immunity, which is expressed in insufficient production of both the relative and absolute number of the CD19+ subpopulation of lymphocytes, which are significantly less than the compared values. This link is marked by the normalization of the quality indicator. The amount of AFC in the spleen corresponds to the baseline, a decrease in the IS from $57.6 \pm 1.3\%$ to $11.5 \pm 0.23\%$, and the concentration of CIC in the blood serum.

Thus, in the offspring of the 1st generation of irradiated animals after fractionated exposure to γ -irradiation, there is a tension in the humoral link of immunity.

In the descendants of the 1st generation, the effect of fractionated γ -radiation was manifested in a significant decrease in phagocytosis by 1.2 times compared with the intact group, and 1.8 times with the 2nd group. The decrease in phagocytosis was accompanied by a significant increase in the phagocytic number by 1.6 times. As in the second group, the values of the NBT-test were high. Its value significantly exceeded the control level by 3.6 times.

The results of the experimental study lead to the fact that in the long-term period in irradiated animals and their offspring of the first generation, the action of fractionated γ -radiation causes an increase in the functional-metabolic activity of neutrophils. Therefore, in the descendants of irradiated animals of the 1st generation, fractionated γ -radiation does not significantly affect the quantitative composition of the T-system of immunity, but it causes the activation of the lymphokine-producing ability of T-lymphocytes.

Based on the results of the factual material, it should be concluded that in the long-term period after fractionated γ -radiation, activation in the humoral link of immunity occurs, which manifests itself in an increase in the total number of lymphocytes, the pool of CD19+ cells and antibody production in the spleen. An increase in the phagocytic activity of leukocytes may, along with a protective effect, also play a role in feedback mechanisms. It is believed that activated phagocytes cause a significant suppression of T- and B-lymphocytic mechanisms of immunity.

Thus, in the long-term period after fractionated γ -irradiation, the indices of the nonspecific phagocytic factor reflect the high functional activity of neutrophils and other white blood cells.

Conclusions

The tension in the humoral link of immunity is manifested by a decrease in the quantitative and qualitative indicators and an increase in the functional and metabolic activity of neutrophils.

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