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ASSESSMENT OF LOW INTENSIVITIES γ -IRRADIATION CHRONIC INFLUENCE ON THE STATE OF THIOL-DISULPHIDE EXCHANGE IN THE SMALL INTESTINE OF RATS

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Abstract

Today considerable attention is paid to the effects of ionizing radiation.chronic exposure in low doses and intensity to humans and other bio-objects. The changes in the structural characteristics of the genome, nuclear, microsomal, mitochondrial, plasma membranes, cell proliferation, and the processes underlying radioresistance / radiosensitivity caused by irradiation have been experimentally studied. prolonged exposure to ionizing rays in small doses gradually causes a decrease in the endogenous reserve of thiol-dependent systems, and their complete depletion, which negatively affects the body's resistance to adverse environmental factors. There is a possibility of disturbances in the synthesis of thiol disulfide high molecular weight components. **The objective:** to study the state of thiol disulfide, glutathione redox system and acetylcholinesterase activity in the small intestine of rats of different sexes and ages under physiological conditions and under conditions of prolonged γ -irradiation in a total dose of 0.75 and 1.0 Gy. **Results.** It has been established that in a small bowel of intact mature rats after prolonged total γ -irradiation with a dose of 1.0 Gy, there were quite significant changes in the content of thiol compounds in the tissues of the small intestine. It was found that the content of SH-groups of protein origin in the tissues of the small intestine decreased relative to the age of control group animals by 28.8% and at the

same time was lower than the value of males of the previous stage by 32.8%. The number of disulfide groups of protein origin in the small intestine of males three months after irradiation at a total dose of 1.0 Gy, relative to the same age control group animals, was 85.6% and at the same time was lower than the previous stage by 31.8%. **Conclusions:** 1. Under physiological conditions there are clear gender and age differences in the functional state of thiol-disulfide, glutathione redox system and acetylcholinesterase activity.

2. Prolonged total γ -irradiation in the total dose of 0.75 and 1.0 Gy causes quite stable and profound changes in the functional state of the systems under study.

3. The dependence of the detected changes on the time elapsed after radiation damage, the dose of γ -irradiation and the sex of the animals is clearly monitored.

4. Females have been shown to be more radioresistant than males.

Key words: long total γ -irradiation; thiol-disulfide; glutathione redox system; acetylcholinesterase activity; small intestine

Urgency. The study of an organism's adaptation to the action of adverse health factors and the likelihood of disease is one of the pressing problems of modern medical science. The urgency of this problem has increased significantly in the last decade and this is due to the sharp deterioration of the environmental situation both in the world and in Ukraine, due to man-made disasters and in particular one of the largest - the Chernobyl accident. Unfavorable social and living conditions due to the economic downturn, radionuclide contamination of large areas of Ukraine, lack of proper medical care have created the preconditions for the growth of the population's somatic pathology. Today, considerable attention is paid to the effects of ionizing radiation. Chronic exposure in low doses and intensity to humans and other bio-objects. The changes in the structural characteristics of the genome, nuclear, microsomal, mitochondrial, plasma membranes, cell proliferation, and the processes underlying radioresistance / radiosensitivity caused by irradiation have been experimentally studied. It has been established that radiation effects have a common molecular basis - DNA and its repair damage [1]. In the implementation of the damaging effect of γ -irradiation a significant role is played by the activation of lipid peroxidation processes [2, 3, 6]. In this regard, the maintenance of prooxidant-antioxidant homeostasis at a steady level plays a very important role in the life of irradiated organisms.

Today in medical science the issues of "critical" organs and tissues, "critical" cells and cellular structures, "critical" metabolic processes that form the primary response to any adverse factor, both external and internal environment, are widely discussed [4, 5, 7]. From

this point of view, such "critical" systems at the metabolic level include the processes underlying endogenous radioresistance and nonspecific resistance, which take an active part in the neutralization and utilization of excess oxygen-reactive intermediates formed after the action of γ - irradiation.

It is known that at the molecular level, the above systems are provided by redox transformations of high- and low-molecular-weight thiol compounds, which form the so-called thiol-disulfide system (TDS). In addition, it is proved that prolonged exposure to ionizing rays in small doses gradually causes a decrease in the endogenous reserve of thiol-dependent systems, and their complete depletion, which negatively affects the body's resistance to adverse environmental factors. There is a possibility of disturbances in the synthesis of TDS high molecular weight components.

The digestive system is one of the body's radiosensitive systems. Even under the influence of γ -irradiation small doses in the digestive tract there is a wide range of morphofunctional changes that lead to fluid loss, electrolytes, protein, digestive disorders, absorption of nutrients, excretion of endotoxins and exotoxins [6]. Of course, the combination of these disorders determines the role of the digestive tract in the adaptive reactions of the body as a whole.

One of the mechanisms of these changes at the molecular level can be caused by γ -irradiation, the gradual depletion of the body's antioxidant system. As a result, the generation of free radicals in organs and tissues increases uncontrollably, and not only lipid peroxidation but also proteins intensify. The latter is of particular importance, taking into account the participation of proteins in the structure of receptors, the functioning of enzyme systems, the regulation of the body's metabolism at organ and tissue levels.

Violation of neurohumoral regulation of small intestinal wall metabolism is not excluded under such conditions, as evidenced by studies of acetylcholinesterase (ACE) activity in the intestinal wall under γ -irradiation conditions [7].

The objective: to study the state of thiol disulfide, glutathione redox system and acetylcholinesterase activity in the small intestine of rats of different sexes and ages

under physiological conditions and under conditions of prolonged γ -irradiation in a total dose of 0.75 and 1.0 Gr.

Object of the study. Experimental studies were performed on 510 rats (Wistar line) of different ages and sexes. All animals were kept under standard conditions and on the standard diet at the vivarium of the Odessa National Medical University.

Groups of animals subjected to γ -irradiation were formed from healthy mature animals aged three months and weighted 180-200 g. The selection of animals was performed at a rate of 1 male per 4-5 females. For the experiment, females were selected so that they were at the same stage of the estrous cycle, which was determined using vaginal swabs.

Total γ -irradiation was performed on the basis of the X-ray therapeutic department of the Odessa Regional Oncology Center, using the gamma therapeutic unit "AGAT-R" №83 (isotope ^{60}Co). To irradiate the animals, they were placed in specially made organic glass cages. Irradiation was performed at 9 o'clock in the morning. To obtain a total dose of 0.75 Gy irradiation was performed under the following technical conditions: dose rate 107 rad / min, the distance from the source to the field was 75 cm, field size 20 • 20 cm, single dose 0.15 Gy, exposure 8 seconds, the number of repetitions-5, every 72 hours. To obtain a total dose of 1.0 Gy irradiation dose rate was 107 rad / min, distance from source to field - 75 cm, field size - 20 • 20 cm, single dose 0.1 Gy, exposure 6 seconds, number of repetitions -10, every 72 hours. Dosimetric control was performed by the dosimetry service of the Regional Oncology Dispensary (Odessa, Ukraine). Animals were removed from the experiment under ether anesthesia by rapid decapitation.

Results obtained and their discussion. It has been established that in a small bowel of intact mature rats after prolonged total γ -irradiation with a dose of 1.0 Gy, there were quite significant changes in the content of thiol compounds in the tissues of the small intestine (Table 1).

As shown in Table 1, on the 12th day after the end of radiation, the content of protein sulfhydryl groups in the small intestine of male rats decreased compared to similar values of intact animals by 15.3%. At the same time, the content of protein disulfide groups in the small intestine of irradiated males did not differ from the indicators in control group. In parallel, there was an increase in the number of low molecular weight sulfhydryl groups by 35.6% compared with intact animals, while the content of disulfide groups of non-protein origin did not differ from the latter. As a result of such changes, the thiol-disulfide ratio of macromolecular compounds decreased relative to that of intact animals by 11.3%. With regard to low molecular weight thiol compounds, the ratio of sulfhydryl to disulfide groups in this case exceeded the indicators of age control by 72.4%. These facts allow us to believe that the detected changes are obviously due to the occurrence of radiation-induced confirmatory changes that prevent the interaction of SS - groups with the molecules of the corresponding substrates needed for their recovery.

Table 1

The content of sulfhydryl and disulfide groups in the small intestine of rats irradiated in a total dose of 1.0 Gy; $M \pm m$; $n = 10$; $\mu\text{mol} / \text{g}$

Experimental conditions			Protein			Non-protein		
Age	Term after exposure	Sex	SH-	SS-	TDS	SH-	SS-	TDS
3 ms	Control	M	4.51±0.22	0.69±0.03	6.54±0.33	0.37±0.02	0.10±0.005	2.9±0.15
		F	4.25±0.21	0.96±0.05	4.42±0.22	0.26±0.01	0.11±0.008	2.4±0.12
	12 th day	M	3.82±0.19* 84.7	0.66±0.033 96.7	5.8±0.29* 88.7	0.45±0.02* 121.3	0.09±0.005 92.2	5.0±0.30 172.4
		F	3.71±0.18* 87.3	1.54±0.08* 160.3	2.17±0.1* 49.1	0.35±0.017* 135.6	0.10±0.006 91.3	3.5±0.18 145.8
6 ms	Control	M	3.61±0.18	0.53±0.03	6.8±0.34	0.46±0.23	0.16±0.008	2.9±0.14
		F	3.95±0.20	0.90±0.05	4.38±0.22	0.48±0.024	0.13±0.0065	3.6±0.18
	3 ms	M	2.57±0.13* 71.2	0.45±0.02 85.6	5.7±0.28* 83.8	0.44±0.022 95.6	0.19±0.009 118.3	2.3±0.11 79.3
		F	3.2±0.16 82.2	1.27±0.06* 140.6	2.52±0.13 57.5	0.53±0.03 110.8	0.11±0.007 92.3	48.8±0.24 133.3
12 ms	Control	M	2.81±0.14	0.72±0.04	3.9±0.20	0.52±0.026	0.15±0.007	3.47±0.17
		F	3.20±0.16	1.09±0.05	2.9±0.15	0.68±0.03	0.13±0.006	5.23±0.26
	6 ms	M	1.79±0.11* 63.6	0.98±0.048* 135.8	1.82±0.09* 46.7	0.46±0.03* 88.4	0.2±0.009* 130.3	2.3±0.14* 66.3
		F	2.4±0.14* 75.4	1.08±0.05 99.3	2.22±0.11* 76.5	0.62±0.04 90.8	0.14±0.01 108.8	4.43±0.27* 84.7

Note: * $P < 0.05$ for one-year control

It should also be emphasized that such profound conformational changes in protein molecules lead to a decrease in their specific functional activity and even to its complete loss [7].

The response to prolonged γ -irradiation at a total dose of 1.0 Gy in females was somewhat different. Thus, in 12 days after γ -irradiation at a total dose of 1.0 Gy in the tissues of the small intestine of mature females there was a decrease in the content of protein sulfhydryl groups by 12.7% and these results were close to similar in males of the same age. Along with the indicated, at this stage of research in the small intestine of 3-month-old irradiated females, the content of protein disulfide groups increased sharply and equals 160.3% in relation to control. The detected changes in the ratio between protein sulfhydryl and disulfide groups caused a decrease in the redox potential of small intestinal tissue proteins of 3-month-old irradiated females by 50.9% compared with healthy females of the same age. At the same time, an increase in the content of non-protein sulfhydryl groups in the small intestine by 35.6% compared to the one-year control was observed, while the number of disulfide non-protein groups did not differ from the latter.

Thus, the changes in the protein sulfhydryl groups of small intestinal tissues in response to prolonged total γ -irradiation at a total dose of 1.0 Gy in males and females were

almost the same, while the shifts in the content of protein disulfide groups were significantly different.

The nature of the detected changes makes it possible to note that in radiation-affected females the activity of the high-molecular thiol-dependent link of the antioxidant system is higher than in males. The low molecular weight thiol disulfide system was also more active at this stage of the study. In this regard, the differences in the indicators of thiol-disulfide metabolism of small intestinal tissues of males irradiated at a dose of 1.0 Gy are also informative. The number of protein SS groups decreased 2.5 times, as a result of which the redox potential increased by 132%.

At the same time, in females changes in some indicators were the opposite. Thus, in females on the 12th day after irradiation at a dose of 1.0 Gy, compared with the animals irradiated at a dose of 0.75 Gy, the content of protein SH-groups increased by 17.0%, the level of protein SS-groups by 15.7%, which in turn caused a decrease in redox potential. Therefore, the differences in the changes in the thiol-disulfide system indicate a more intense course of thiol-disulfide metabolism reactions in females irradiated at a dose of 1.0 Gy compared to males. Attention should also be paid to the reaction of the number of non-protein SH- and SS-groups of small intestinal tissues of males and females on the 12th day after irradiation at doses of 1.0 and 0.75 Gy.

Thus, the concentration of low molecular weight SH groups in the tissues of the small intestine of females on the 12th day after irradiation at a dose of 1.0 Gy was 31.4% lower than in females irradiated at a dose of 0.75 Gy. No statistically significant differences were found in males of similar groups, but a tendency to decrease, in those irradiated at a dose of 1.0 Gy, was observed. As for disulfide groups of non-protein origin, their number in the small intestine of females irradiated at a dose of 1.0 Gy was 55.0%, and in males it was 41.2% lower than in animals irradiated at a dose of 0.75 Gy. Thus, based on the position that the content of non-protein SH-groups under conditions of prolonged γ -irradiation correlates well with radioresistance, these changes are one of the signs of noticeable depletion of non-protein thiol-dependent link of the antioxidant system.

The fact that the level of non-protein SH-groups in females increased significantly more than in males compared to controls, we can assume greater radioresistance of females to prolonged low-dose exposure.

This was confirmed by the results of a study of the state of the thiol disulfide system in the tissues of the small intestine of males and females three months after the end of γ -irradiation in a total dose of 1.0 Gy. It was found that the content of SH-groups of protein

origin in the tissues of the small intestine decreased relative to the age of control group animals by 28.8% and at the same time was lower than the value of males of the previous stage by 32.8%. The number of disulfide groups of protein origin in the small intestine of males three months after irradiation at a total dose of 1.0 Gy, relative to the same age control group animals, was 85.6% and at the same time was lower than the previous stage by 31.8%. At this stage of the study, the thiol-disulfide ratio was also experienced, the indicators of which in relation to the control equaled 83.8%, which was almost twice as high as similar values in males on the 12th day after radiation injury. The content of sulfhydryl groups of non-protein origin in the small intestine of males after three months action of total γ -irradiation in the total dose 1.0 Gy did not differ from the same age control and values on the 12th day after irradiation. On the contrary, at this time in the small intestine of males the content of disulfide groups of non-protein origin increased and the level of age-related control prevailed by 18.3%. The increase in the content of non-protein SS groups contributed to a decrease in the thiol-disulfide ratio compared to one-year-old intact males by 20.7%, and it was more than twice lower than the level on the 12th day after radiation injury in males.

Three months after prolonged total γ -irradiation at a total dose of 1.0 Gy in the small intestine of females, the content of sulfhydryl groups of protein origin was lower than the control by 17.8%. The detected shifts were significantly lower than in one-year-old irradiated males and outperformed the latter by 24.5%. The number of disulfide groups of protein origin in the small intestine of females in three months after radiation damage decreased relative to the previous term by 17.5%, but the level of control group animals was prevailed by 40.6%. The rather low level of sulfhydryl groups and high of disulfide ones contributed to the reduction of the redox potential compared to the control by 42.5%, but in comparison with the indicators of the previous term it increased quite significantly. In irradiated females of this age, the content of sulfhydryl groups in the small intestine was higher than the in control group by 10.8%, and disulfide did not differ from the latter. Redox potential outweighed the control by 33.3%.

Thus, prolonged total γ -irradiation at a dose of 1.0 Gy contributes to a fairly stable and significant changes in the thiol-disulfide system of the experimental animals small intestine and the detection of shifts is more significant in males.

The study of the state of the thiol disulfide system in the small intestine of males and females in three months after γ -irradiation at a total dose of 1.0 and 0.75 Gy revealed a number of features. The content of protein SH groups in males after irradiation at doses of 1.0 and 0.75 Gy did not differ, while the number of disulfide groups was almost twice as high in

males irradiated with 0.75 Gy. The redox potential in males three times after γ -irradiation in the total dose of 0.75 Gy was 1.8 times lower which is also important. The number of non-protein SH-groups in males in three months after γ -irradiation at a total dose of 1.0 Gy did not differ from the control group indexes, but, at the same time, was lower than males irradiated at a dose of 0.75 Gy, by 30.8%. It is noteworthy that the content of non-protein disulfide groups in the small intestine of males after γ -irradiation at a total dose of 1.0 and Gy was significantly lower than that in those irradiated at a dose of 0.75 Gy. The redox potential in males was slightly lower in three months after γ -irradiation at a total dose of 1.0 Gy. In females in three months after prolonged exposure to γ -irradiation at a total dose of 1.0 and 0.75 Gy, the content of protein SH-groups was 23.5% higher than in female rats irradiated at a dose of 0.75 Gy. At the same time, the number of SS-groups of protein origin in the small intestine of females in three months after γ -irradiation at a total dose of 1.0 Gy was lower than in females irradiated at a dose of 0.75 Gy. With regard to the non-protein part of the thiol disulfide system the content of SH- and SS-groups in females in three months after γ -irradiation at a total dose of 0.75 Gy, was significantly higher than in those irradiated at a dose of 1.0 Gy.

Thus, under the conditions of prolonged γ -irradiation at a total dose of 1.0 Gy for the 3rd month after the lesion there is a decrease in the functional activity of the thiol disulfide system and especially its low molecular weight link both in males and females, compared with those irradiated at a dose of 0.75 Gy while more significant deviations took place in males. The depletion of thiol-disulfide metabolism was quite noticeable, which was a sign of a decrease in nonspecific resistance of these animals.

In three months after the end of the action of γ -irradiation in a total dose of 1.0 Gy, the content of SH-groups of protein origin in the small intestine of 12-month-old males in relation to the same age control was 63.6%, and SS-groups - 135.8%.

Due to this increase in the content of protein SS groups, the redox potential of the protein molecule decreased and amounted to 46.7% relative to intact males of this age. At this stage of research in the small intestine of radiation-affected males, the content of SH-groups of non-protein origin also decreased, both in relation to similar values of the previous term, and in relation to the same age control, equal to 88.4%. In parallel with this, there was an increase in the content of non-protein SS-groups by 30.3% compared with the same age non-irradiated males. After increasing the ratio of low molecular weight thiol compounds, there was a corresponding decrease in the redox potential by 33.7% relative to the control. Quite significant deviations were detected when comparing the thiol-disulfide system in the small

intestine of males in 6 months after prolonged γ -irradiation at a total dose of 1.0 and 0.75 Gy. For example, the content of protein SH-groups in the small intestine of males irradiated at a total dose of 1.0 Gy was 13.2% lower than in irradiated at a dose of 0.75 Gy, and SS-groups content was 46.9% lower, but the redox potential was practically the same. In the small intestine of 6 months males after the end of prolonged exposure to ionizing radiation at a total dose of 1.0 Gy, the content of SH-group of non-protein origin was 35.2% lower than in those irradiated at a dose of 0.75 Gy and SS groups content was lower at 16.7%. The redox potential in males in 6 months after irradiation at a total dose of 0.75 Gy, prevailed over irradiated peers at a dose of 1.0 Gy by 33.9%.

Thus, prolonged γ -irradiation at a total dose of 1.0 Gy causes deeper changes in the thiol disulfide system in the small intestine of males than 0.75 Gy irradiation. This difference is particularly clear in the more distant periods after radiation damage, which is obviously due to the labeling of radiation and involutionary processes on the one hand and on the other hand depletion of the buffer capacity of antiradiation mechanisms due to more powerful γ -irradiation.

Studies of the state of protein and non-protein parts of the thiol disulfide system in the small intestine of 6 months females after the end of prolonged exposure to ionizing radiation at a total dose of 1.0 Gy also revealed a number of features and differences compared to males of the same age.

For example, in 6 months after the end of long-term exposure to γ -irradiation at a total dose of 1.0 Gy, the content of protein SH-groups in the small intestine of 12-month-old females was lower than in the same age control group animals by 24.6%, and SS-groups almost did not differ from the latter. It is noteworthy that in absolute values, the content of protein SH-groups in females was higher by 34.1%, and SS-groups by 10.2% of the values irradiated in this dose of the same age males. The redox potential in 6 months after γ -irradiation at a total dose of 1.0 Gy in females was lower than the indicators of the same age control group animals by 23.5%, but prevailed the indexes of males of this age group by 21.9%.

Characteristic of this stage of research was that in the small intestine of irradiated females the content of SH- and SS-groups of non-protein origin did not differ from the same-age control, but the level of redox potential remained lower than the latter by 10.1%. All these indicators differed positively in females compared to those in males. Thus, the above facts indicate that prolonged γ -irradiation at a total dose of 1.0 Gy even in 6 months after its

completion leads to profound changes in the thiol-disulfide system of the small intestine of females.

The analysis done showed that in 12-month-olds irradiated at a dose of 1.0 Gy, the content in the small intestine of SH-groups of protein origin did not differ from that of irradiated at a dose of 0.75 Gy, and the number of SS-groups of protein origin at this time, females irradiated at a dose of 1.0 Gy was lower than those irradiated at a dose of 1.0 Gy, was lower than those irradiated at a dose of 0.75 Gy by 34.5%. It was also characteristic that in females irradiated at a dose of 0.75 Gy, on the 6th month after its completion, the content of non-protein SH- and SS-groups significantly exceeded the indicators of the same age females irradiated at a dose of 1.0 Gy.

Thus, the results obtained show that prolonged fractionated γ -irradiation at low doses causes long-term and stable shifts in the thiol-disulfide system, the components of which, among other things, are responsible for the body's resistance to adverse environmental factors. Moreover, it is obvious that the detected changes affect not only the tissues of the small intestine, but also the body as a whole. It is also characteristic that prolonged total γ -irradiation at a total dose of 1.0 Gy causes more significant changes than at a dose of 0.75 Gy and this is especially evident in the longer term after its action. Obviously, the latter is a consequence of the depletion of the buffer capacity of anti-radical processes. It should also be noted that the resistance of small intestinal tissues to the effects of ionizing radiation in females is much higher than in males.

The results of studies of the state of the glutathione redox system in the small intestine of males and females in different periods after prolonged γ -irradiation at a total dose of 1.0 Gy were as following. It was found (Table 2) that on the 12th day after prolonged total exposure to γ -irradiation at a total dose of 1.0, the content of reduced glutathione in the small intestine of males exceeded the control indicators by 26.7%. In parallel, there was an increase in the activity in the small intestine of these males glutathione peroxidase by 10.3% and glutathione S-transferase by 11.6%, compared with the same age non-irradiated rats. It is noteworthy that the content of reduced glutathione in the small intestine of 3-month-old males irradiated at a dose of 1.0 Gy was higher than that of the same age animals exposed to ionizing radiation at a total dose of 0.75 Gy. The activity of glutathione peroxidase and glutathione-S-transferase in the small intestine of 3-month-old males irradiated at a dose of 1.0 Gy, also significantly exceeded similar values at the animals irradiated at a dose of 0.75 Gy.

Table 2.

The state of the glutathione redox system in the small intestine of rats irradiated at a total dose of 1.0 Gy; $M \pm m$; $n = 10$; $\mu\text{mol} / \text{g}$

Conditions of the experiment			GSH	GP	GT
Animal's age	Term after irradiation	Sex			
3 mns	Control	M	174.4±0.87	81.4±4.06	55.9±2.80
		F	23.30±1.16	109.10±5.45	71.26±3.56
	The 12 th day	M	22.4±1.11* 128.7	89.80±4.48* 110.3	62.40±3.11* 111.6
		F	32.36±1.62* 138.9	128.52±6.42* 117.8	85.60±4.30* 120.1
6 mns	Control	M	19.9±0.99	85.2±4.26	54.1±2.85
		F	22.2±1.11	102.6±7.18	68.6±4.8
	3 mns	M	20.6±1.02 103.4	55.6±2.78* 65.3	32.5±1.63* 60.1
		F	25.66±1.28* 115.6	72.02±3.60* 70.2	50.50±2.52* 73.6
12 mns	Control	M	14.96±0.75	77.10±3.85	49.40±2.46
		F	17.2±0.86	91.89±6.43	60.1±3.0
	6 mns	M	13.10±0.65* 87.4	54.60±2.73* 70.8	35.22±1.76* 71.3
		F	17.8±0.90 103.3	70.39±3.52* 76.6	41.40±2.07* 68.9

* $P < 0.05$ relative to the same age animals in control group

In the small intestine of 3-month-old females on the 12th day after γ -irradiation in a total dose of 1.0 Gy, the content of reduced glutathione exceeded the indicators of age control by 38.9%, which was also 44.5% higher than in the same age-old males, irradiated at this dose. The activity of glutathione peroxidase and glutathione transferase in the small intestine of 3-month-old females on the 12th day after irradiation at a total dose of 1.0 Gy, exceeded the level of age control by 17.8 and 20.1%, respectively, which was also higher than in the same age-old males irradiated at this dose. In 3-month-old females on the 12th day, after prolonged exposure to γ -irradiation at a total dose of 1.0 Gy, all indicators of glutathione redox system in the small intestine significantly prevailed similar to those irradiated at a dose of 0,75 gr.

Three months after the end of prolonged exposure to ionizing radiation at a total dose of 1.0 Gy, the content of reduced glutathione in the small intestine of 6-month-old males decreased relative to the previous term, and relative to control and constituted 103.4%. In parallel with that indicated in the small intestine of these males we observed a decrease in

glutathione peroxidase and glutathione-S-transferase activity both relative to the previous values and relative to control by 34.7 and 39.9%, respectively.

In 3 mns after irradiation at a dose of 1Gy it was found that the content of reduced glutathione and the activity of glutathione peroxidase and glutathione-S-transferase in the small intestine of males significantly outweighed the changes in the animals irradiated at a dose of 0.75 Gy.

In 6-month-old females, three months after radiation injury at a dose of 1.0 Gy, the content of reduced glutathione in the small intestine relative to the same age control group animals was 115.6%. The indicators of the content of reduced glutathione in these females were lower than similar values of females of the previous term by 20.7%. The activity of glutathione peroxidase and glutathione-S-transferase in this case was lower than the control values, respectively, by 29.8 and 26.4%. Comparison of the results obtained after γ -irradiation at a total dose of 1.0 Gy showed that the content of reduced glutathione, glutathione peroxidase and glutathione-S-transferase activity in the small intestine of females three months after γ -irradiation at a total dose of 0.75 Gy were significant. The latter was evidence that in females irradiated at a dose of 1.0 Gy there is a depletion of the functional capacity of the glutathione redox system and a sharp decrease in nonspecific resistance. Six months after the end of ionizing radiation at a total dose of 1.0 Gy, the content of reduced glutathione in the small intestine of 12-month-old males decreased significantly relative to similar values in all previous stages of the study and was 87.4% relative to control. At the same time, a decrease in the activity of glutathione peroxidase and glutathione-S-transferase was observed both in relation to the indicators of the previous stages of the study and control and, in relation to the latter, was equal to 70.8 and 71.3%, respectively. In addition, the detected changes in the content of reduced glutathione and the activity of glutathione peroxidase and glutathione-S-transferase in the small intestine of males in 6 months after irradiation at a total dose of 1.0 Gy were significantly greater than at irradiation at a dose of 0.75 Gy.

The content of reduced glutathione in the small intestine of females in 6 months after radiation damage in a total dose of 1.0 Gy did not differ from the indicators of the same age intact animals, but was significantly lower than the value in all previous experiments.

The content of reduced glutathione in the 12 –months-old females irradiated at a dose of 1.0 Gy was higher than that of the same age radiation-affected males. The activity of glutathione peroxidase and glutathione-S-transferase in the small intestine of females in 6 months after γ -irradiation at a total dose of 1.0 Gy also decreased and, relative to control, was 76.6 and 68.9%, respectively, but in both cases it was higher than in males. All detected

changes in the functional state of the glutathione redox system in the small intestine of females in 6 months after radiation damage at a dose of 1.0 Gy were more pronounced than when irradiated at a dose of 0.75 Gy.

Thus, prolonged total γ -irradiation at a total dose of 1.0 Gy, leads to profound and lasting changes in the functional state. Its essence is to activate this system in the initial stages, and followed by inhibition. At the same time, sexual dimorphism in the manifestations of radio-induced changes in the functional state of this system is also clearly traced.

Studies of acetylcholinesterase activity in the small intestine of males in 12 days after radiation injury, showed (Table 3) that it exceeded the indicators of the same age animals in the control group by 80.5% and was higher than in males of this age, irradiated at the total dose 0.75 Gy.

In the small intestine of 3-month-old females in 12 days after radiation damage in a total dose of 1.0 Gy, acetylcholinesterase activity exceeded the level of the same age control group animals by 52.2% and was lower than in radiation-affected males of this age group.

The detected changes in acetylcholinesterase activity in 12 days after radiation injury at a total dose of 1.0 Gy in the small intestine of males and females decreased sharply relative to previous values, but exceeded the level of age control by 20.4 and 10,6% respectively.

Table 3

Acetylcholinesterase activity in the small intestine of male and female rats irradiated at a total dose of 1.0 Gy; $M \pm m$; $n = 10$; $\mu\text{mol} / \text{g}$

Conditions of an experiment			Acetylcholinesterase Activity
Animal's age	Term after irradiation	Sex	
3 mns	Control	M	492.0±24.6
		F	554.03±27.7
	The 12 th day	M	888.06±44.40* 180.5
		F	843.2±42.16* 152.2
6 mns	Control	M	479.3±23.96
		F	565.3±28.3
	3 mns	M	577.1±28.85* 120.4
		F	625.22±31.26*
12 mns	Control	M	352.2±17.6
		F	447.8±22.4
	6 mns	M	283.90±14.19*
		F	395.4±19.80±

P < 0.05 relative to the same age control

In the small intestine of 3-month-old females in 12 days after radiation damage in a total dose of 1.0 Gy, acetylcholinesterase activity exceeded the level of the same age animals

of the control group animals by 52.2% and it was lower than in radiation-affected males of the same age. The changes detected in acetylcholinesterase activity in 12 days after radiation injury at a total dose of 1.0 Gy in the small intestine of males and females decreased sharply relative to previous values, but exceeded the level of the same age control group animals by 20.4 and 10.6%, respectively. The activity of acetylcholinesterase in the small intestine of males in three months after γ -irradiation at a total dose of 1.0 Gy was 20.1% lower than when irradiated at a total dose of 0.75 Gy. In females these figures were almost the same. In six months after prolonged exposure to γ -irradiation at a total dose of 1.0 Gy, the activity of acetylcholinesterase in the small intestine of males and females decreased in relation to all previous terms and control and was equal to the latter, respectively, 80.6 and 88.3%. The detected changes were lower than in irradiated males and females of this age, respectively, by 69.6 and 25.13%.

Thus, the analysis of acetylcholinesterase activity in the small intestine of males and females irradiated at a total dose of 1.0 Gy, allows us to identify three periods of its functional capacity. The first period is characterized by a sharp activation of the enzyme, and it aimed at eliminating the effects of radiation. The second period is characterized by relative stabilization of its activity and even normalization. The third period is characterized by a sharp inhibition of enzyme activity, which is obviously a sign of depletion of nonspecific resistance. Dose, urgency and sex dependence of the detected changes are also characteristic.

Conclusions

1. Under physiological conditions there are clear gender and age differences in the functional state of thiol-disulfide, glutathione redox system and acetylcholinesterase activity.
2. Prolonged total γ -irradiation in the total dose of 0.75 and 1.0 Gy causes quite stable and profound changes in the functional state of the systems under study.
3. The dependence of the detected changes on the time elapsed after radiation damage, the dose of γ -irradiation and the sex of the animals is clearly monitored.
4. Females have been shown to be more radioresistant than males.

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