THE EFFECT OF PRELIMINARY RADIOISOTOPE ADMINISTRATION ON THE PERIPHERAL BLOOD COMPOSITION AND THE SURVIVAL OF ANIMALS SUBSEQUENTLY X-IRRADIATED WITH A LETHAL DOSE

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Certain radioactive isotopes have been used lately for a preliminary irradiation of animals in order to increase their survival rate following a subsequent exposure to ionizing radiations in lethal doses.

N. V. Luchnik and V. G. Kulikova [4] noted an increase of radioresistance in mice which had a preliminary injection of a Ce^{144}, a source of mild β and γ-radiations.

P. N. Kiselev et al. [3] used P^{32} for preliminary irradiation, but did not obtain a positive effect.

TABLE 1. Results of Experiments with Rats

Number of animals in experiment		Amount of isotope administered per animal (in μC)	Period between administration of isotope and general irradiation (in days)	Number of animals surviving		Percentage survival on the 30th day		Increase of survival in experiment as compared to control (in %)
control	experimental			control	experimental	control	experimental	
Preliminary administration of I^{131}								
20	19	40	55	10	11	50	58	8
16	17	20	45	7	10	43	58	15
Preliminary administration of P^{32}								
16	15	20	45	7	9	43	60	17
40	30	20	15	12	13	30	43	13
Preliminary administration of S^{35}								
20	19	20	55	10	14	50	73	23
9	10	20	45	6	9	67	90	23
40	40	20	15	12	14	30	35	5

L. Dimitrov [7] reported that the use of radioactive isotopes of cobalt and of sulfur-labelled thiamine increased the resistance of dogs to a subsequent action of an ionizing radiation in lethal doses.

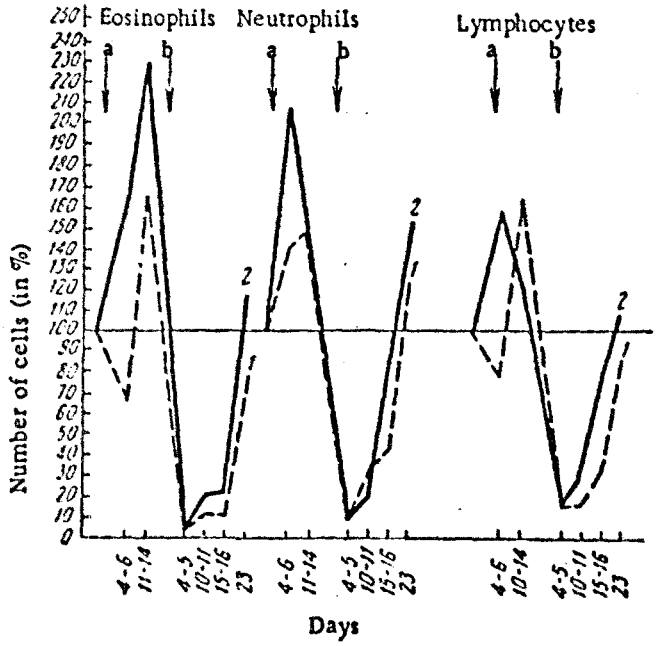
The purpose of this work was to study the effects of a preliminary administration of radioactive isotopes, having different radiation patterns, on the damage and repair of different systems of the organism, following a subsequent exposure to ionizing radiations in a lethal dose. In the preliminary irradiation of animals we have used radioactive I^{131}, P^{32} and S^{35}.

According to I. S. Belokonskii [1] the protective action of β-mercaptoethylamine and of aminoethyllysothiuronium is due to their ability to lower the oxygen consumption of animals during irradiation. Through an administration of radioactive iodine, and consequently, through a lowering of the thyroid function, he has attempted to lower the rate of basal metabolism of the organism, and thus to increase its resistance.

TABLE 2. Results of Experiments with Mice

Number of animals in experiment			Amount of isotope administered per animal (in μC)	Period between administration of isotope and general irradiation (in days)	Number of animals surviving			Percentage survival on the 30th day		
control	experimental	biocontrol			control	experimental	biocontrol	control	experimental	biocontrol
Preliminary administration of P^{32}										
29	50	20	2	15	12	10	16	41	20	80
Preliminary administration of S^{35}										
29	100	20	2	15	12	79	16	41	79	80

P. N. Kiselev and V. A. Semina [2] explained the increased survival of mice following a preliminary irradiation, by a development of immunity to the products of breakdown of their own proteins. They have used radioactive phosphorus to produce necrotic foci in the bone marrow, which eventually stimulated the production of immunity. Considering the importance of the epithelial tissue in the "acceptance" of the radiation damage and in the subsequent development of the radiation syndrome, they have used radioactive methionine, which becomes distributed mainly within the epithelium of the skin and of the gastro-intestinal tract.



Changes in the number of cells in peripheral blood of rats. 1) Control rats; 2) experimental rats; a) time of administration of radioactive substances; b) time of general x-irradiation.

METHODS

Our experiments were performed on white rats weighing 180-200 g and on mice weighing 20-25 g. Prior to experiments, the animals were kept for 10-15 days under new living conditions, in order that they might become adapted to them. Living conditions and all experimental manipulations were made as similar as possible for the experimental and the control animals. In mouse experiments, in addition to the experimental and the control groups, there was also a biocontrol group. Radioactive isotopes were administered as solutions in normal saline. Control animals were administered with saline in the same volume as experimental ones were administered with the isotope solution. The animals were weighed every 5-7 days; the composition of peripheral blood and the total number of erythrocytes, leucocytes, as well as the leucocytic formulas were determined in rats. Mortality among the animals was recorded daily.

The isotope activity varied, but it was sufficient in order to observe blood changes. Periods between the administration of radioactive substances and the subsequent x-irradiation also varied. The time of the maximal functional changes in one or another physiological system was noted. Irradiation was made with filtered rays under standard conditions, in doses of 800 r for rats, and 600 r for mice; these doses corresponded on the average to $LD_{0/30}$.

RESULTS

The results of experiments are presented iif Tables 1 and 2.

As seen in Table 1, when rats were given radioactive isotopes 15, 45 and 55 days before a general irradiation with x-rays in a lethal dose, there was a 5-23% increase of survival, as compared with controls. With the administration of methionine, survival was higher in those groups, in which the intervals of time between the administration of the isotope and the subsequent general x-irradiation were longer. In mice, when the period between the administration of the isotope and the subsequent general irradiation was equal to 15 days, methionine considerably increased their survival after exposure to lethal doses of ionizing radiation, (Table 2).

Survival among mice, which had a preliminary dose of methionine, was 38% higher than that among the controls, while survival in the biocontrol group was 80%. The general appearance and behavior of mice indicated a more favorable course of radiation sickness, if they had received a preliminary dose of methionine. The weight of experimental mice was greater than that of the controls. Thus, an administration of radioactive methionine 15 days perior to a general irradiation protected against damage inflicted by an ionizing radiation equal to 600 r.

A careful study of the morphology of peripheral blood revealed differences between the experimental and the control groups of animals. Rats, which had received a preliminary dose of methionine, had more erythrocytes on the 10th and the 20th days of radiation sickness than those which had a preliminary dose of saline alone. The total number of leucocytes was greater throughout the entire duration of sickness in animals which had received a preliminary dose of methionine. There was an increase in the number of all leucocytes, especially neutrophils and eosinophils, following the administration of radioactive isotopes (see figure).

A few publications have been concerned with the problem of the mechanism of aquired radioresistance. Pape and Pendl [8] and Betz et al. [5] thought that it was related to an increased regeneration of blood following preliminary irradiations. P. N. Kiselev et al. [3] and L. A. Dimitrov [6] considered the increased radioresistance following preliminary irradiations as a result of a developed immunity. Dokvisto (1959) left the problem of the mechanism of acquired radioresistance open.

The experimental data obtained have shown that in animals with an increased radioresistance, following a preliminary administration of methionine, there is an increased number of neutrophils and eosinophils, i.e. of elements of the marrow, and not the lymphatic hemopoiesis.

SUMMARY

To increase the radioresistance radioisotopes – I^{131}, P^{32} and methionine-S^{35} – were administered to rats 15, 45 and 55 days prior to the total x-irradiation. The survival of rats, to which 20 C of the isotope was previously administrated, increased by 5-23% in comparison with controls, depending on the type of isotope and the interval between the isotope administration and the subsequent x-irradiation in a dose of 800 r. The survival of the mice, to which methionine was administered 15 days prior to the x-irradiation in a dose of 600 r, increased by 38%. The number of the peripheral blood leukocytes increased after the administration of radioisotopes to rats. A relatively high leukocyte count in experimental rats was retained after the total x-irradiation. As demonstrated, this rise was mainly due to the increased number of neutrophils and eosinophils.

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