SENSITIVITY OF MICE IRRADIATED WITH X-RAYS TO ACUTE HYPOXIA

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Despite its undoubted practical importance and considerable theoretical interest, the problem of the effect of various doses of ionizing radiation on the sensitivity of animals to acute hypoxia has recived little attention in the recent literature. Conflicting results have been obtained by different workers [2, 3, 11-14], possibly because they used different experimental conditions: different doses of irradiation, different intervals between irradiation and carrying out the experiments, animals of different species and sex, and different techniques to produce hypoxia and differences in its degree.

The object of the present investigation was to examine the sensitivity of irradiated mice to hypoxia in the initial period of acute radiation sickness depending on the dose of irradiation.

EXPERIMENTAL METHOD

Experiments were carried out on 100 male mice weighing 18-22 g and 18 male rats weighing 120-200 g.

The experiments were divided into 6 series: in series I-IV the resistance of the animals to high altitudes was determined after a single exposure to whole-body irradiation (10 mice in a dose of 200 R, 11 in a dose of 400 R, 10 in a dose of 600 R, and 19 mice in a dose of 800 R; in series V the lactic acid concentration was determined in the blood of the irradiated animals (3 rats irradiated in a dose of 400 R and 3 rats in a dose of 800 R); in series VI the oxygen consumption of the irradiated animals was investigated (3 rats irradiated in a dose of 800 R). The animals were irradiated with x-rays by means of a type RUM-3 apparatus (voltage 185 kV, current 15 mA, filter 0.5 mm Cu, skin-focus distance 40 cm, dose rate 40 R/min). The animals were irradiated in boxes divided by partitions. One box contained 5 mice and the other 2 rats. The time between irradiation and exposure to hypoxia was 96 h for the mice irradiated in dose of 200 R, 75-70 h for the mice irradiated in doses of 400 and 600 R, 56 h for mice irradiated in a dose of 800 R, and 73 h for rats irradiated in doses of 400 and 800 R.

The mice were placed in a vacuum exsiccator with a capacity of 6 liters and "raised" at the rate of 30 m/sec to an "altitude" of 10 000 m and then lowered from this altitude at the rate of 5 m/sec until the time of death. Two mice—control and irradiated—were "raised" at the same time. The criterion used to indicate the resistance of the animals to high altitudes was their resistance to progressive hypoxia during the "ascent" in the exsiccator until the onset of terminal convulsions and respiratory arrest.

The lactic acid in the blood of the control and irradiated rats was determined quantitatively by the method of Barker and Summerson [1]. Blood was taken from the tail vein of the animals in a volume of 1 ml. A type SF-4 spectrophotometer was used for the colorimetric determination.

The oxygen consumption of the experimental and intact rats was determined by E. V. Gubler's method [5]. The determination was carried out over a period of 10 min.

EXPERIMENTAL RESULTS

In these experiments (Fig. 1) the resistance of the mice irradiated in a dose of 200 R to high altitudes was higher than that of the control animals ($P = 0.01$). The mice irradiated in doses of 400, 600, and 800 R were less resistent to high altitudes than control mice (the values of P corresponding to these doses of

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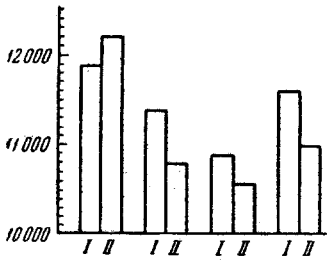

Fig. 1. Comparative resistance of control and irradiated mice to high altitudes in the latent period of radiation sickness. Along the axis of abscissas – doses of irradiation (in R); along the axis of ordinates – altitude reached (in m). Here and in Fig. 2 and 3: I – control, II – experiment.

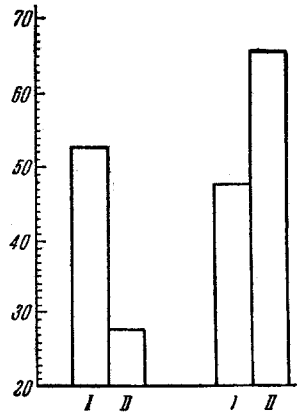

Fig. 2. Changes in lactic acid concentration in the blood of rats depending on dose of irradiation. Along the axis of abscissas – doses of irradiation (in R); along the axis of ordinates – lactic acid (in mg%).

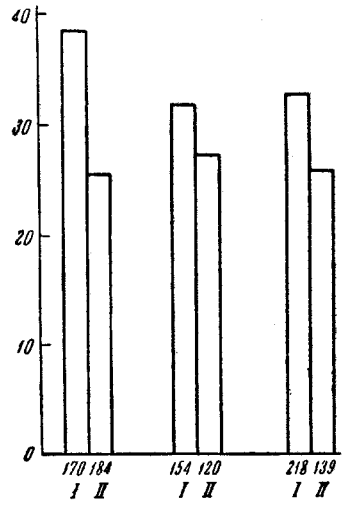

Fig. 3. Oxygen consumption of rats irradiated in a dose of 800 R and control rats. Along the axis of abscissas – weight of rats (in g); along the axis of ordinates – oxygen consumption (ml/kg body weight/min).

irradiation were 0.05, >0.2, and 0.005). A significant difference in the behavior of the animals during the "ascent" was observed only in the case of the mice irradiated with 800 R. In the animals of this series of the experiments the number of convulsions was 35% greater than in the controls, and in most of them the intensity and duration of the convulsions was greater. However, in 3 mice of this series of experiments no well marked terminal convulsions were seen. In one experiment the animals showed no convulsions whatever, and in 2 other experiments only a few weak spasms were observed.

These expermental results suggest that the resistance of the irradiated mice to hypoxia is determined mainly by the typological properties of the central nervous system and its functional state during irradiation [8]. Whole-body irradiation of animals causes disturbances of higher nervous activity, occurring in 3 successive phases [4, 7]. The first phase arises during the latent period of acute radiation sickness and corresponds to the times of the present series of experiments. It is characterized by weakness of internal inhibition and by more intensive excitation. In turn, the increased excitation lowers the resistance of the animals to acute hypoxia [10]. In the present experiments in which mice were irradiated with large doses of x-rays the increased excitability of the central nervous system had a decisive effect in relation to lowering the resistance of the animals to high altitudes.

In the case of the mice irradiated in a dose of 200 R the combined affect of a moderate dose of ionizing radiation and of hypoxia evidently led to stimulation of the adaptive reactions of the irradiated animals (central nervous system, endocrine glands, etc), thereby increasing the resistance of the animals to high altitudes [9].

To determine the extent of the change of tissue respiration toward anaerobic glycolysis after irradiation of rats with doses of 400 and 800 R and to examine the effect of this factor on the decrease in resistance to hypoxia, the blood was investigated biochemically by quantitative estimation of the lactic acid in the intact and experimental animals. It is clear from Fig. 2 that the lactic acid concentration in the rats irradiated in a dose of 800 R was higher than in the healthy rats, whereas in the animals irradiated in a dose of 400 R it was smaller. However, the difference between these values and the controls were not statistically significant ($0.2>P<0.5$).

The fall of 23% in the gas exchange of rats irradiated in a dose of 800 R by comparison with that in control animals, observed in these experiments (Fig. 3), suggests that large doses of ionizing radiation may have a depressant effect on oxidative metabolism.

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