PREVENTION OF DEATH OF RATS FROM RADIATION SICKNESS BY SCREENING PART OF THE BONE MARROW DURING IRRADIATION

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Experiments in which the hemopoietic organs of animals with radiation sickness were sreened [3], forming the basis of treatment of radiation sickness by bone marrow transplantation, have acquired new importance in connection with the possibility of using autotransplantation of bone marrow obtained from areas of that tissue screened during irradiation [1].

The object of the present investigation was to study the quantitative relationship between the effect of screening the bone marrow and the volume of the screened portion and the dose of radiation. The data available in the literature [2, 4-6, etc.] do not provide the solution to this problem.

EXPERIMENTAL METHOD

Experiments were carried out on 310 male Wistar rats weighing 160-180 g. During irradiation different volumes of bone marrow were screened from the action of the radiation by means of suitable lead aprons 4 mm thick.

Altogether 28 series of experiments were carried out. In each series 10-12 rats were used, consisting of control (totally irradiated) animals and animals in which certain parts of the bone marrow were protected.

Irradiation was given on the RUM-3 apparatus in the following conditions: 17 mA, 180 kV, skin-focus distance 50 cm, without tube, filters 0.5 Cu + 1 Al, dose rate 28 R/min. The rats were irradiated in the supine position, with their limbs tied to the bench. The doses of irradiation were 800, 720, and 650 R. The doses of x-rays used differed in their biological effect, causing death of the control animals at definite times after irradiation. For instance, after irradiation in a dose of 800 R, all the totally irradiated rats died in the period of the intestinal syndrome, on the 4th-7th day after irradiation. Irradiation in a dose of 720 R was followed by death of all the animals by the 11th day, 50% on the 4th-7th days and the rest on the 8th-11th days. A dose of irradiation of 650 R was not lethal for all the rats: by the 30th day after irradiation 20% of the animals remained alive. In these conditions of irradiation, few of the rats (about 20%) died from the intestinal syndrome, the rest died in the period of the bone-marrow syndrome. Throughout the period of the experiment the animals were kept in vivarium conditions on a normal diet.

Observations were made on the survival rate and the general condition of the animals, and their peripheral blood was investigated for a period of 3-4 months.

In different series of rats the following were screened: both femora and both humeri (4 limbs) 2 femora and 1 humerus (3 limbs), 2 femora, 1 femur, 1/2 and 1/10 of a femur.

To compare the effect of screening and autotransplantation of bone marrow, in a special series of investigations the number of nucleated bone marrow cells was determined in the femur and humerus of control, unirradiated rats (the bone marrow of the fragmented bones was separated in physiological saline with sodium citrate). This showed that the bone marrow of the femur contains about 20×10^7 cells and the bone marrow of the humerus 8×10^7 cells. On the basis of this count, the number of screened marrow cells could be calculated in each variant of the experiment.

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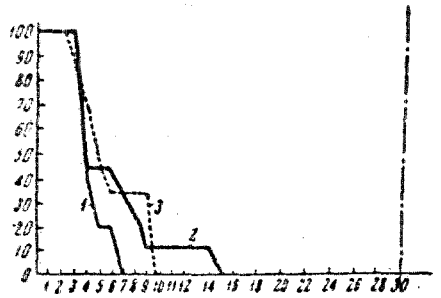

Fig. 1. Survival of rats following irradiation in a dose of 800 R. Here and in Figs. 2 and 3: along the axis of ordinates – survival rate (in %); along the axis of abscissas – days; 1) control animals (totally irradiated); 2) animals with screening of 4 limbs; 3) animals with screening of half of one femur.

EXPERIMENTAL RESULTS

The results of the experiments of Group 1 (irradiation in a dose of 800 R) are given in Fig. 1. This shows that all the control animals (18 rats, totally irradiated) died on the 4th-7th days after irradiation.

Screening of half a femur (18 rats) and of all 4 limbs (20 rats) had practically no protective action. All the experimental animals died by the 15th day after irradiation. Hence, the protection of even a considerable proportion of the bone marrow (in r limbs) during irradiation in large doses, causing death of all the control animals from an intestinal syndrome, was almost ineffective.

In the experiments of Group 2 the animals were irradiated in a dose of 720 R. During exposure protection against the action of radiation was given to the upper-third of 1 femur (23 rats), half of 1 femur (25 rats), the whole of 1 femur (28 rats), 2 femora (21 rats), and 3 (20 rats) and 4 limbs (28 rats). The results obtained are given in Fig. 2. This shows that after irradiation in this dose all the control animals (43 rats) died on the 4th-11th days, 50% of them on the 4th-7th days from the intestinal syndrome, and the rest on the 8th-11th days in the period of the bone marrow syndrome. Screening of one-tenth of the femur had practically no protective action. When half the marrow of 1 femur was protected, 12% of the irradiated rats survived. When the whole of 1 femur was protected, 30% of the rats survived. Protection of 2, 3, and 4 limbs gave almost an identical effect – by the 30th day 43-47% of the irradiated rats remained alive.

Hence, with a dose of 720 R, maximal protection was obtained by screening two femora, and a further increase in the volume of screened marrow gave hardly any increase in the effect. In these conditions approximately 47% of the animals survived, i.e., the proportion which, in the control series, died in the period of the bone marrow syndrome after total irradiation.

It is interesting to compare these results with those obtained in the author's laboratory after autotransplantation of bone marrow. It was shown that the injection of 20×10^6 bone marrow cells, equivalent to about 1-10th of the total number of cells in the femur, into the blood stream led to the survival of 45% of the irradiated animals, compared with death of all the control animals at the same time as in the experiment now described. It may be concluded from a comparison of the results obtained that with this dose of irradiation, the therapeutic effect of screening 40×10^7 marrow cells was equivalent to that of autotransplantation of approximately 1-20th their number – 20×10^6 cells. The results of the present investigation thus confirm the conclusion drawn by the authors cited above, that transplantation and the associated repopulation with unirradiated cells has a much greater therapeutic effect than the unirradiated portion of the bone marrow of corresponding size left behind in the irradiated organism. Evidently, after a certain dose of x-ray irradiation, when screening of a large volume of bone marrow enabled most of the animals dying in the period of a lethal bone-marrow syndrome to survive, autotransplantation of the bone marrow must be ineffective.

The results of the third group of experiments are given in Fig. 3. After total irradiation in a dose of 650 R (20 rats) 20% of the totally irradiated animals survived until the 30th day. In this case screening of the bone marrow gave a still greater protective effect than after irradiation in a dose of 720 R (see Figs. 2 and 3). In these conditions of irradiation, when hardly any cases of death from the intestinal syndrome were observed, protection of the bone marrow in all four limbs (20 rats) enabled all the irradiated animals to survive, and even protection of half of 1 femur (16 rats, 10×10^7 cells) saved 50% of the irradiated rats. Screening of one-tenth of 1 femur (10 rats) evidently was ineffective.

The results obtained after irradiation in a dose of 650 R, when some of the animals survived even without screening, showed that in these conditions a therapeutic effect may be achieved by screening a smaller proportion of the bone marrow than when a lethal dose of irradiation was given. This demonstrates that autotransplantation of bone marrow from screened areas during irradiation in these conditions can still be effective only if the volume of unirradiated bone marrow in the organism is relatively small. Hence,

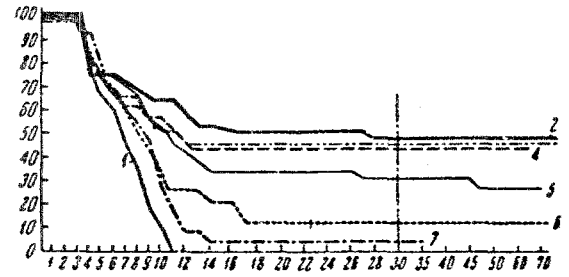

Fig. 2. Survival of rats after irradiation in a dose of 720 R. 1) Control animals (totally irradiated); 2) animals with screening of 4 limbs; 3) animals with screening of 3 limbs; 4) animals with screening of 2 limbs; 5) animals with screening of 1 femur; 6) animals with screening of half of 1 femur; 7) animals with screening of one-tenth of 1 femur.

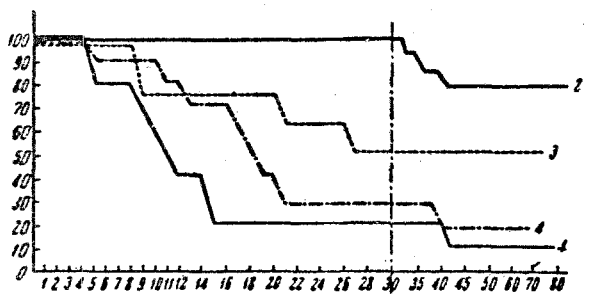

Fig. 3. Survival of rats after irradiation in a dose of 650 R. 1) Control animals (totally irradiated); 2) animals with screening of 4 limbs; 3) animals with screening of half of 1 femur; 4) animals with screening of one-tenth of 1 femur.

the protective effect of screening the bone marrow depends both on the volume of bone marrow protected and on the dose of radiation. The smaller the dose of irradiation and the larger the area of bone marrow screened, the higher the survival rate among the animals after irradiation by comparison with the controls. After sublethal doses of irradiation, when some of the rats survived and when few die in the period of the intestinal syndrome, if a certain proportion of the bone marrow is screened during irradiation, 100% of the animals survive. A further increase in the volume of bone marrow screened is ineffective in these circumstances. Following total irradiation in lethal doses the survival rate is limited mainly by death of the rats from the intestinal syndrome, against which protection of the bone marrow usually has little effect. An increase in the volume of bone marrow screened in this case also is effective only up to a certain limit, which increases with an increase in the dose of radiation.

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