POSSIBILITY OF INCREASING THE PROTECTIVE ACTION OF SCREENING PART OF THE BONE MARROW DURING IRRADIATION OF RATS AND MICE

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During subtotal irradiation of mice and rats, blood loss increases the protective effect of screening part of the bone marrow. Blood loss in totally irradiated animals does not increase their rate of survival.

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Screening of part of the hematopoietic tissue during irradiation increases the survival rate of animals [6]. The protective action of screening is nowadays associated with the liberation of polypotent stem cells from the protected zone into the damaged organism, and to their migration, proliferation, and differentiation [5]. G. S. Strelin and co-workers experimentally increased the protective effect of screening an area of the bone marrow in the femur of a rat by autotransplantation of marrow tissue from a zone of hematopoiesis which was undamaged during irradiation into the venous system. In a previous investigation [4], similar results were obtained in experiments on rats using blood loss as the stimulator of hematopoiesis. The erythropoietin secreted under these circumstances promotes, in our opinion, the increased liberation of polypotent stem cells from the screened area of hematopoietic tissue. In turn, liberation of stem cells may help to increase the area of active hematopoiesis, the basis for successful treatment of the bone-marrow syndrome in acute radiation sickness.

In the present investigation we studied the possibility of obtaining the observed effect in mice, the spontaneous migration of stem cells in which is more intensive than in rats [2], and the relationship between the effect obtained and the size of the screened area of bone marrow was examined.

EXPERIMENTAL METHOD

Experiments were carried out on 264 rats (160-190 g) and 290 mice (20-24 g). In each experiment the animals were divided into four groups: group 1, whole-body irradiation; group 2, whole-body irradiation with preliminary blood loss (control group); group 3, irradiation with screening of part of the bone marrow; group 4, subtotal irradiation with preliminary blood loss (experimental groups).

The source of ionizing radiation was a type RUM-11 apparatus. The dose of irradiation was 760-800 R for rats and 800 R for mice. The rats were irradiated while fixed on their back to a wooden bench, and the mice in pairs (control and experimental) in a special box made of organic glass. The area of the limb to be protected from irradiation in the rats and mice was covered by a lead sleeve.

Bleeding was carried out 10 days before irradiation. In the rats blood (2% of the body weight) was taken by puncture from the heart, and in mice (2.5% of body weight) from the optic plexus.

EXPERIMENTAL RESULTS

The criterion for assessment of the experimental results was the survival rate of the animals on the 20th day after irradiation when endogenous hematopoiesis was actively restored in animals saved from radiation death by homotransplantation of bone marrow.

In the experiments described the dose of radiation used was one which, if given to the whole body, caused death of all (in rats) or nearly all (in mice) the animals by the 12th day. Under these conditions blood loss was ineffective: the survival rate was not increased (Figs. 1 and 2, a).

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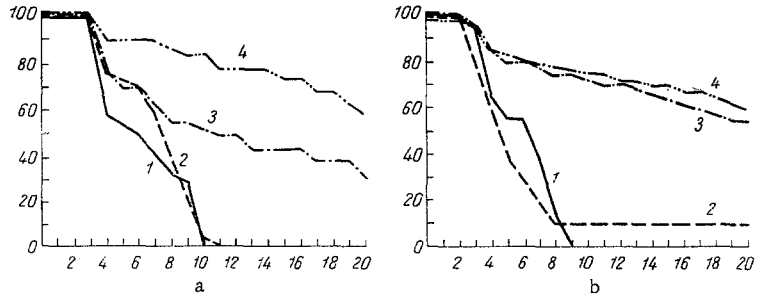

Fig. 1. Effect of blood loss on results of screening in rats. a) Screening of one leg; b) screening of four limbs; 1) whole-body irradiation; 2) whole-body irradiation combined with preliminary blood loss; 3) subtotal irradiation; 4) subtotal irradiation combined with preliminary blood loss. Abscissa, survival rate (in percent); ordinate, days after irradiation.

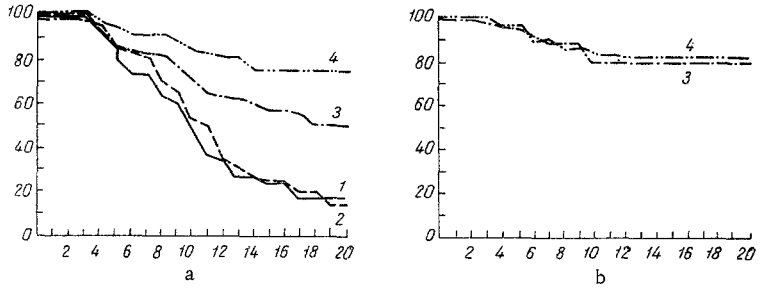

Fig. 2. Effect of blood loss on results of screening in mice. a) Screening of foot; b) screening of leg. Legend as in Fig. 1.

As was previously shown [4], blood loss in rats whose leg was screened increased the action of screening and produced a higher survival rate of the animals (33 and 66% respectively; Fig. 1).

In the present experiments the leg was screened in some of the mice, and this led to survival of 80% of subtotally irradiated animals without blood loss and of 84% of such animals in combination with blood loss (Fig. 2, a).

Screening the leg alone in mice thus gave a significant protective effect; for this reason, to elucidate the role of blood loss during subtotal irradiation, the size of the area screened was reduced in the experiment (one foot was screened). As a result 55% of the mice survived after subtotal irradiation, but when blood loss was combined with screening of the foot the survival rate was 76% (Fig. 2). The difference between the groups is statistically significant.

A similar relationship must evidently exist for rats also.

Since screening of all four limbs in rats at the time of irradiation gives maximal protective effect in the period of development of the bone marrow syndrome [1], in the experimental group all four of the rat's limbs were screened with lead sleeves at the moment of irradiation in one group of the experiment, while in the other group the same procedure was adopted in conjunction with blood loss (Fig. 1, a). The survival rate of 57-60% respectively, i.e., an increase in the area of screening makes the positive effect of blood loss.

The protective effect of screening of part of the bone marrow can thus be intensified in both mice and rats by stimulating hematopoiesis by means of blood loss. Erythropoietin probably brings about an increase in the number of polypotent stem cells leaving the screened zone for the injured part of the body, thus increasing the area of active hematopoiesis compared with that in the animals which were simply screened. This results in a higher survival rate among the animals. With an increase in the area screened

the observed effect disappears: in this case the hematopoietic function of the screened part of the bone marrow and, above all, the liberation of an adequate number of stem cells from it, play a direct role in this case.

Stimulation of hematopoiesis after irradiation with a lethal dose is evidently worthwhile only in the case of subtotal or unequal irradiation.

The beneficial action of stimulation of hematopoiesis in rats after screening of a relatively larger area of the bone marrow than in mice can be explained by the lower mobility of the stem cells in rats.

The essential feature of this experimental model is a combination of stimulation of hematopoiesis with the presence of intact hematopoietic tissue in the irradiated animals.

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