THERAPEUTIC VALUE OF BONE MARROW IN MICE IRRADIATED WITH HIGH-ENERGY PROTONS

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The action of protons on biological substrates is a subject of increasing interest to investigators [1], for protons are one of the principal factors of cosmic radiation. The question of biological protection and experimental treatment is of great theoretical interest and practical importance in relation to irradiation with protons.

Following the successful use of bone marrow transfusions after exposure to certain types of ionizing radiation [2-4], the efficacy of this method has been studied in the case of injury due to protons. An isologous radiation chimera was used as model for the investigation.

EXPERIMENTAL METHOD

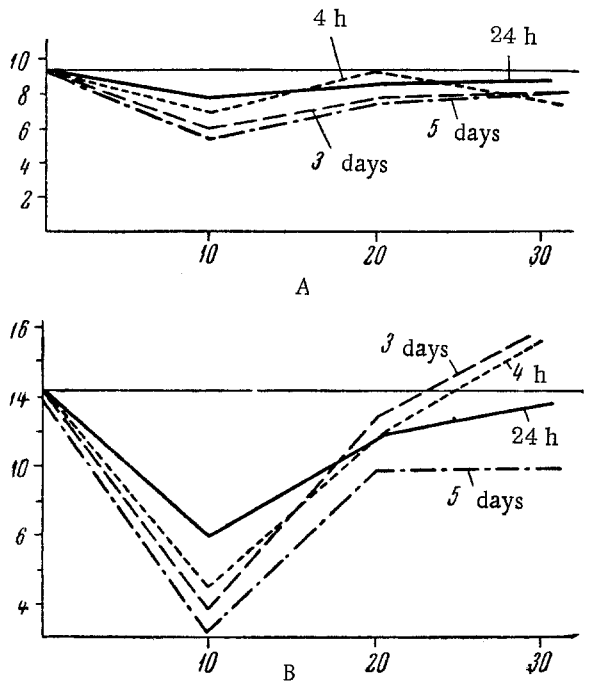
Experiments were carried out on male mice of the CBA line weighing 20-24 g, which were irradiated on the synchrocyclotron of the Joint Institute for Nuclear Research in Dubno, with a proton beam with an energy of 240 MeV; the dose of irradiation was 950 + 50 rad at a rate of 1.13 rad/sec. After various intervals of time the recipient mice were given an intravenous injection of isologous bone marrow cells suspended in medium No. 199. Each animal received $2.7-3.0 \cdot 10^6$ viable nucleated cells in 0.3-0.4 ml of fluid. The mice of the control group received an injection of the corresponding volume of medium No. 199. In the course of the experiment the mice (in groups of five) were kept in special cages. Every 10 days the erythrocyte and leukocyte counts were determined in 4-5 mice in each experimental group.

EXPERIMENTAL RESULTS

The therapeutic efficacy of the bone marrow injections was assessed by the survival rate of the animals and the state of their peripheral blood. Figures showing the survival rate of the mice irradiated with high-energy protons

Therapeutic Efficacy of Bone Marrow after Irradiation with High-Energy Protons

Procedure	Interval between exposure and transfusion	Dose of cells ($\cdot 10^6$)	No. of animals	Survival rate (in weeks)				Proportion surviving until 30th day (in %)
				1st	2nd	3rd	4th	
Irradiation	–	–	40	23	2	2	2	5
Irradiation + bone marrow	4 h	2.85	10	8	8	8	8	80
	24 h	3.0	40	37	37	36	36	90
	3 days	2.7	40	25	11	11	11	27.5
	5 days	3.0	38	27	8	7	7	18.5



Dynamics of changes in blood cells in mice of line CBA irradiated with high-energy protons and treated with isologous bone marrow. Along the axis of the abscissas – time after irradiation (in days); along the axis of ordinates – A – erythrocytes (millions), B – leukocytes (thousands). The times of injection of the hemopoietic tissue are indicated.

and treated with isologous bone marrow are given in the table. A dose of 950 + 50 rad corresponds to $LD_{95/30}$ in all the experimental groups; the animals died mainly in the 1st or 2nd week after irradiation.

Administration of isologous bone marrow gave an undoubted therapeutic effect, although this became weaker as the interval between irradiation and transfusion became longer. Transfusions were most effective during the first 24 h after exposure (survival rate 80-90%); injection of bone marrow after 5 days was much less successful (survival rate 18.5%).

The dynamics of the changes in the blood cells in mice protected by isologous bone marrow after irradiation with protons are illustrated in the figure. The radiation erythropenia was less severe in the animals receiving bone marrow 24 h after exposure. The radiation leukopenia in these mice was relative slight (the leukocyte count on the 10th day after irradiation was 40% of the original), but it was more marked in the other groups.

The results of these experiments showed that transplantation of isologous bone marrow into animals irradiated with high-energy protons is therapeutically effective. The degree of its efficacy may be very high (80-90%) if the bone marrow transfusion is given during the first 24 h after irradiation; however, it falls as the length of time increases between exposure and injection of the hemopoietic tissue. The optimal time for manifestation of the effect of bone marrow therapy for proton injury, as for injury by other types of ionizing radiation [5, 6], is 24 h after exposure.

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