EFFECT OF BONE MARROW AUTOGRAFTS ON POSTRADIATION RECOVERY OF THE INTESTINE

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After uneven irradiation of rats (of the intestine in a dose of 1,050 R and the rest of the body in a dose of 735 R), leading to 100% mortality among the animals in the course of 3.5-5 days, bone marrow autografts speeded up recovery of the DNA content in the mucous membrane and weakened the inhibition of the enzyme-secreting function of the intestine. Many (40%) of the irradiated rats with bone marrow autografts survived up to the 30th day of observation.

It is generally considered that death of animals irradiated in doses of more than 1,000 R (acute intestinal radiation death) in the course of 3.5 days is due to injury to the gastrointestinal tract [2, 8, 9]. At the same time, if part of the bone marrow is screened or grafted into animals irradiated in superlethal doses some of them will survive for this period of time [1, 5-7]. However, it is not yet clear to what extent the favorable effect of screening or transfusions of bone marrow is reflected in the state of the gastrointestinal tract. Only limited experimental data on this question are available. It is merely stated that if dogs irradiated in doses of 1,000-2,400 R are treated with transfusions of bone marrow or blood and injections of antibiotics and electrolytes, and if they survive for 3-4 days (all the control animals died by this time), regeneration of the intestinal epithelium was complete by the ninth day after treatment [7]. However, the use of this combined treatment makes it difficult to assess the role of marrow transfusions in the mechanism of intestinal recovery.

The object of this investigation was to study the role of bone marrow in postradiation recovery of the intestine in rats after uneven irradiation leading to death in the course of 3.5-5 days.

EXPERIMENTAL METHOD

Male albino rats weighing 180-200 g were used. In the case of irradiation of the intestine in a dose of 1,050 and of the rest of the body in a dose of 735 R 100% of the rats died after 3.5-5 days. The effect of

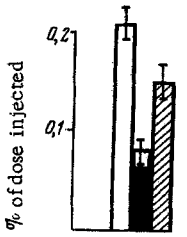

Fig. 1. Incorporation of thymidine-C^{14} into DNA of duodenal mucous membrane of irradiated rats on third day after irradiation. Unshaded column – irradiated animal, undergoing mock operation (control); black column – intact rats, unevenly irradiated (group 1); obliquely shaded column – unevenly irradiated rats with bone marrow autografts (group 2).

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TABLE 1. Effect of Bone Marrow Autografts on DNA Content in Duodenal Mucous Membrane and on Intestinal Alkaline Phosphatase Activity (M ± m)

Group of rats	Time after irradiation (days)									
	2		3		5		7		10	
	DNA (μg per organ)	alkaline phosphatase activity (units)	DNA (μg per organ)	alkaline phosphatase activity (units)	DNA (μg per organ)	alkaline phosphatase activity (units)	(DNA (μg per organ)	alkaline phosphatase activity (units)	DNA (μg per organ)	alkaline phosphatase activity (units)
Intact irradiated (1)	1114±54,2 (5)	11 400±2 300 (5)	960±73,7 (15)	3351±364 (7)	1857±304 (7)	—	—	—	—	—
Irradiated, receiving bone marrow autografts (2)	1137±145 (5)	10 400±1 711 (5)	1332±96,3 (17)	5128±692 (8)	2494±192 (8)	—	3285±292 (5)	4940±441 (5)	3481±306 (5)	6680±1344 (5)
P	0,84	0,77	0,0027	0,05	0,095	—	—	—	—	—

Note: The DNA content in the duodenal mucous membrane of the control (mock operation) was 2380 ± 85.6 μg and intestinal alkaline phosphatase activity in the small intestine was 11,400 ±480 to 13,400 ±80 units. The number of animals used is given in parentheses.

bone marrow autografts on postradiation recovery of the intestine was studied in animals irradiated in this way. The animals were irradiated on the RUM-17 apparatus under the following conditions: 250 kV, 15 mA (filters 1 mm Cu + 1 mm Al). Irradiation was carried out with the intestine exteriorized from the abdomen under hexobarbital anesthesia, with observance of the rules of asepsis and antisepsis. Bone marrow was obtained before irradiation from the femur by puncture, placed in physiological saline with citrate, and kept during irradiation under sterile conditions in the cold. After irradiation, about 40×10^6 bone marrow cells were injected intravenously.

The state of the intestine was estimated from the DNA content in the duodenal mucous membrane [4] based on the incorporation of thymidine-C^{14} into DNA. Alkaline phosphatase activity was investigated in the mucous membrane of the small intestine [3]. The animals were decapitated on the 1st, 2nd, 3rd, 5th, 7th, and 10th days after irradiation. The rats of group 1 were intact, irradiated animals and those of group 2 were irradiated rats receiving bone marrow autografts. Unirradiated rats undergoing the same operation were used as the control.

EXPERIMENTAL RESULTS

All the rats died within 3.5-5 days after irradiation of the intestine in a dose of 1,050 R and simultaneous irradiation of the rest of the body in a dose of 735 R. Autografting of bone marrow considerably modified the dynamics of the mortality. In the 5-day period about 30% of the animals died. About 40% of the animals survived until the 30th day after irradiation.

Data showing the state of the intestine of the intact irradiated rats and the rats receiving bone marrow autografts are given in Table 1. They show that by the second day after irradiation there was a considerable, and practically equal, decrease in the DNA content in the duodenal mucous membrane of the two groups of animals. By the third day after irradiation the DNA content in the rats of group 1 continued to decline – to 960 ± 73.7 μg, whereas in the rats of group 2 the DNA level was actually slightly increased – to 1332 ± 96.3 μg ($P = 0.0027$). In the rats of group 1, which survived until the 5th day, the DNA content in the mucous membrane did not reach its initial level although it was higher than on the 3rd day, whereas in the rats of group 2 the DNA content reached the control level and actually exceeded it by the 7th and 10th days.

On the third day after irradiation, when the decrease in the DNA content in the mucous membrane was greatest in the intact irradiated animals, a tendency toward recovery was observed in the animals with bone marrow autografts. This conclusion is supported by the data for incorporation of thymidine-C^{14} into the DNA of the mucous membrane at this period

of observation (Fig. 1). Incorporation of the label in the rats of group 2 was significantly higher than in group 1 (Fig. 1). Their specific radioactivity also was higher, evidence of more intensive DNA synthesis in the cells.

Intestinal alkaline phosphatase activity in the rats of group 2 was lowered to a lesser degree than in group 1. Bone marrow autografts apparently delayed the decrease in enzyme activity. Meanwhile restoration of alkaline phosphatase activity in the rats of group 2 took place more slowly than recovery of the DNA content. Whereas the DNA level in the duodenal mucous membrane reached the control value by the 5th day, alkaline phosphatase activity was not fully restored until the 10th day after irradiation.

These results thus show that bone marrow damage plays an essential role in the mechanism of death of the irradiated animals. Bone marrow autografts after uneven irradiation reduced the mortality of the rats in the "intestinal phase" (3.5-5 days).

These experiments showed that injection of bone marrow stimulates repair processes in the intestine, direct proof of the role of the bone marrow in the mechanism of postradiation recovery of the intestine in rats irradiated in super-lethal doses.

LITERATURE CITED

1. S. N. Aleksandrov, K. F. Galkovskaya, and T. I. Baidachenko-Rostovtseva, Vopr. Onkol., No. 10, 77 (1965).
2. B. Raevskii, Problems in Radiobiology [in Russian], Moscow (1956), p. 133.
3. L. S. Fomina, in: Modern Methods in Biochemistry [in Russian], Moscow (1964), p. 292.
4. W. C. Schneider, J. Biol. Chem., 161, 293 (1945).
5. L. Cole, Brookhaven Symposium in Biology, No. 20, 263 (1968).
6. L. I. Cole, I. G. Harbermeyer, and P. C. Wowel, Radiat. Res., 7, 139 (1957).
7. E. B. Hager, F. W. Ferrebee, and E. D. Thomas, Radiobiol.-Radioter. (Berlin), No. 4, 1 (1963).
8. H. Quastler, E. F. Lanz, M. E. Keller, et al., Am. J. Physiol., 164, 546 (1951).
9. H. Quastler, Radiat. Res., 4, 303 (1956).