

# KINETICS OF HEMATOPOIETIC STEM CELLS IN THE BONE MARROW OF HEPATECTOMIZED MICE

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Two thirds of the liver was removed from (CBA × C57BL/6j)F<sub>1</sub> female mice. On the 5th day after the operation a significant increase was observed in the number of endogenous colonies in the spleen of the partially hepatectomized animals. This increase was not connected with a change in the number of stem cells in the bone marrow, for partial hepatectomy at different times after the operation did not affect the number of colony-forming units in the bone marrow.

KEY WORDS: partial hepatectomy; colony-forming units; spleen; bone marrow.

Factors influencing the kinetics of the pluripotent hematopoietic stem cells at the different stages of individual development and during pathological processes have been insufficiently studied. The writers previously found an increase in the number of endogenous colonies in the spleen of mice sublethally irradiated during the first 5 days after resection of two thirds of the liver compared with nonhepatectomized irradiated animals. The maximal effect was observed on the 5th day [1, 3]. It was suggested that this observation reflects connections between the liver and the hematopoietic tissue and that it may be useful for their experimental study. In the writers' opinion this phenomenon could be based either on intensified proliferation of stem cells in the bone marrow and their subsequent migration into the spleen or intensification of proliferation of stem cells in the spleen of sublethally irradiated hepatectomized mice.

This paper gives the results of experiments carried out to test the first hypothesis.

## EXPERIMENTAL METHOD

Female (CBA × C57BL/6j)F<sub>1</sub> mice weighing 21-22 g from the Stolbovaya nursery, Academy of Medical Sciences of the USSR, were used. The mice were divided into three groups: partially hepatectomized, undergoing the mock operation, and intact. Two thirds of the liver was removed from the mice of the first group [2]. The mock operation consisted of laparotomy followed by suture of the wound. The operations were performed under hexobarbital anesthesia. At various times after the operation the absolute number of nucleated cells and of colony-forming units (CFU) in the bone marrow was determined in all the animals. The CFU were studied by the method of determining the number of exogenous colonies in the spleen of lethally irradiated mice [4]. Recipient mice were irradiated in a dose of 1200 R. An intravenous injection of  $5 \times 10^4$  nucleated bone marrow cells was given to the animals 24 h after irradiation. The bone marrow suspension consisted of the combined pool of cells taken from the femora of four mice of one group. The viability of the cells was tested by means of trypan blue. The colonies were counted 8 days after injection of the suspension. The number of endogenous colonies in the spleen of the lethally irradiated mice did not exceed 0.8 per spleen.

To determine the number of endogenous colonies in the spleens of the partially hepatectomized mice, mice undergoing the mock operation, and the intact mice, the animals were irradiated in a dose of 650 R on the 5th day after the operation. The results were subjected to statistical analysis using Student's *t* test. Differences between means were regarded as significant for which  $P \leq 0.05$ .

## EXPERIMENTAL RESULTS

In three experiments the considerable increase in the number of endogenous colonies in the spleens of mice subjected to partial hepatectomy and irradiated in a dose of 650 R 5 days after the operation compared with the number of endogenous colonies in nonhepatectomized irradiated animals was confirmed completely.

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**TABLE 1. Number of Endogenous Colonies in Spleens of Mice Irradiated on 5th Day after Partial Hepatectomy ( $M \pm m$ )**

No. of experiment	Number of endogenous colonies		
	control	mock operation	partial hepatectomy
1	$4,2 \pm 0,8$ (n=9)	$7,1 \pm 1,8$ (n=8)	$23,1 \pm 3,2^*$ (n=9)
2	$5,8 \pm 1,0$ (n=25)	$6,9 \pm 1,0$ (n=10)	$20,7 \pm 2,9^*$ (n=10)
3	$5,6 \pm 0,8$ (n=17)	$10,3 \pm 2,6$ (n=17)	$24,3 \pm 3,8^*$ (n=17)

\*P < 0.01 compared with value for control animals and animals undergoing mock operation.

**TABLE 2. Number of Stem Cells in Bone Marrow after Partial Hepatectomy ( $M \pm m$ )**

Time after operation, days	Number of exogenous CFU in bone marrow (per $5 \times 10^4$ nucleated cells)		
	control	mock operation	partial hepatectomy
1-2	$11,7 \pm 0,9$ (n=6)	$9,1 \pm 1,0$ (n=9)	$13,4 \pm 1,9$ (n=9)
1	$12,6 \pm 1,1$ (n=23)	$14,2 \pm 0,8$ (n=15)	$13,5 \pm 0,9$ (n=29)
2	$10,5 \pm 0,6$ (n=9)	$14,6 \pm 4,1$ (n=5)	$15,6 \pm 0,8$ (n=36)
5	$10,8 \pm 0,5$ (n=22)	$18,9 \pm 2,0$ (n=16)	$9,8 \pm 0,6$ (n=53)
10	$11,9 \pm 0,7$ (n=21)	$12,2 \pm 1,1$ (n=24)	$13,1 \pm 0,9$ (n=23)

**Legend.** Number of cells in bone marrow was unchanged after operation.

The small increase in the number of endogenous colonies in the animals undergoing the mock operation was not statistically significant compared with the control and was probably due to operative trauma (Table 1).

In the next series of experiments the hypothesis of possible intensification of proliferation of stem cells in the bone marrow under the influence of the regenerating liver was tested. For this purpose the absolute number of nucleated cells and of CFU in the bone marrow of the hepatectomized mice was studied at different times after the operation. The results of these experiments are summarized in Table 2. They show that partial hepatectomy had no significant effect on the number of CFU in the bone marrow of the animals undergoing the operation. The mock operation itself led to an increase in the number of stem cells in the bone marrow. This increase was significant 5 days after the operation.

The increase in the number of endogenous colonies in hepatectomized mice irradiated 5 days after the operation is thus not connected with a change in the number of stem cells in the bone marrow.

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