

EXPERIMENTAL BIOLOGY

EFFECT OF LYMPHOCYTES OF UNILATERALLY NEPHRECTOMIZED MICE ON PROLIFERATIVE ACTIVITY OF THE KIDNEYS AND LIVER OF INTACT RECIPIENTS

A. G. Babaeva, N. A. Kraskina,
and L. D. Liozner

UDC 612.46+612.35/.014.3:612.6-0.6:/616.155.32-
02:616.61-089.87-031.4-092.9

Transplantation of splenic lymphocytes of unilaterally nephrectomized CC57Br and C57Bl mice to intact syngeneic recipients led to an increase in proliferative activity of the tubular epithelium of the kidneys and reticulo-endothelial cells of the liver after 49-50 h. Lymphocytes of intact mice and of mice undergoing resection of the kidney did not possess stimulating properties.

The writers showed previously [1, 2] that transplantation of splenic lymphocytes of partially hepatectomized mice into intact syngeneic recipients led to an increase in mitotic activity in the hepatocytes and reticulo-endothelial cells.

To analyze the changes in the properties of the lymphocytes taken from animals undergoing the operation it was essential, first, to discover whether the lymphocytes become capable of inducing increased mitotic activity only after the operation on the liver or whether similar changes are observed after extensive resection of other organs; second, to discover whether the action of lymphocytes on the proliferative activity of the recipient's organs is organ-specific.

To answer these questions an investigation was carried out to determine how the transplantation of lymphocytes obtained from animals after removal or resection of the kidney is reflected in the proliferative activity in the liver and kidney by comparison with the effect observed in animals undergoing partial hepatectomy.

EXPERIMENTAL METHOD

The experimental animals consisted of 120 male mice of line CC57Br with a mean weight of 19 g (series I) and 95 male mice of line C57Bl with a mean weight of 21 g (series II and III). Either the whole of one kidney or a small part of its convex surface (along the long axis) was removed from the group of mice which subsequently acted as donors of lymphocytes. The donors of series I were killed 17-19 h after the operation and those of series II and III 19-21 h after the operation with chloroform vapor and suspensions of their spleen cells were prepared in medium No. 199 for intravenous injection into intact syngeneic recipients [3] in doses of 80 million cells per recipient of series I and 62 million cells per recipient of series II and III. The recipients of series I and II were autopsied 49-50 h, and those of series III 73 h after the injection, at 8-10 A.M., after receiving a preliminary (2 h beforehand in series I and 4 h beforehand in series II and III) injection of colcemid in a dose of 5 mg/kg. Intact mice and recipients of splenic lymphocytes from intact mice were used as the controls. The mitotic activity was determined by the method used previously [1, 2]. The numerical results were subjected to statistical analysis by the Fisher-Student method.

Laboratory of Growth and Development, Institute of Human Morphology, Academy of Medical Sciences of the USSR. Laboratory of Immunology, Moscow Institute of Epidemiology and Microbiology, Ministry of Health of the USSR. (Presented by Academician of the Academy of Medical Sciences of the USSR A. P. Avtsyn.) Translated from *Byulleten' Éksperimental'noi Biologii i Meditsiny*, Vol. 75, No. 2, pp. 78-80, February, 1973. Original article submitted July 7, 1972.

© 1973 Consultants Bureau, a division of Plenum Publishing Corporation, 227 West 17th Street, New York, N. Y. 10011. All rights reserved. This article cannot be reproduced for any purpose whatsoever without permission of the publisher. A copy of this article is available from the publisher for \$15.00.

TABLE 1. Mitotic Activity of Kidney and Liver of Mice Receiving Lymphocytes

Series	Group of mice	Character of operation on donor	No. of recipients	Mitotic index of recipient's cells, % ₀₀ (M ± m)		
				tubular epithelium of kidney	hepatocytes	reticulo-endothelium of liver
I	Control		17	0,15±0,05	0,32±0,11	3,50±0,67
	Exptl.	Unilateral nephrectomy	17	0,52±0,14	0,35±0,21	5,53±0,75
II	Exptl.	Resection of the kidney	17	0,26±0,11	0,22±0,09	2,16±0,40
	Intact		10	0,15±0,03	0,30±0,13	3,29±0,90
	Control	Unilateral nephrectomy	11	0,22±0,08	0,28±0,17	3,70±1,09
	Exptl.		10	0,47±0,12	0,37±0,19	6,45±1,82
III	Intact	Unilateral nephrectomy	8	0,22±0,06	0,29±0,10	0,69±0,23
	Control		9	0,14±0,05	0,14±0,05	1,02±0,56
	Exptl.	Unilateral nephrectomy	9	0,31±0,11	0,09±0,03	2,00±0,80

TABLE 2. Relative Increase in Proliferative Activity of Liver and Kidney Cells in Recipients of Lymphocytes

Group of animals	Increase in mitotic activity (in percent of control)			
	liver		kidney	
	epithelium	reticulo-endothelium	epithelium	reticulo-endothelium
Recipients of lymphocytes of partially hepatectomized mice	328*	385*	155	184*
Recipients of lymphocytes of unilaterally nephrectomized mice	109	158*	346*	—
The same	159	192	320*	190

* Differences significant.

EXPERIMENTAL RESULTS

The results of determination of the mitotic activity of the lymphocytes in the kidney and liver of the recipient mice are given in Table 1. From 49 to 50 h after transplantation the tubular epithelium of the recipients' kidney responded to the injection of lymphocytes of the unilaterally nephrectomized mice by a significant increase in proliferative activity ($P=0.01$). Its mitotic index (MI) was more than three times higher than MI of the tubular epithelium of the control recipients receiving a suspension of lymphocytes from intact mice (series I) and in intact animals (series II). Virtually no mitoses were present in the connective-tissue cells of the kidney of the experimental and control animals of series I, while in the mice of series II the increase in mitotic activity was not significant.

The number of dividing cells in the tubular epithelium 73 h after transplantation was down to the control level.

The mitotic index of the hepatocytes of the recipients 49-50 h after transplantation was unchanged under the influence of the lymphocytes of the unilaterally nephrectomized animals, but after 73 h it was significantly reduced ($P=0.001$) by comparison with the intact animals (Table 1). The reticulo-endothelial cells of the recipient's liver responded to this procedure by a small increase ($P=0.03$) in the number of mitoses both 49-50 h and 73 h after transplantation (series I and II) by comparison with the intact mice (series III) and control recipients, injected with lymphocytes of intact mice (series I). Consequently, unilateral nephrectomy modifies the properties of the lymphocytes; they cause an increase in the intensity of proliferation of the tubular epithelium and reticulo-endothelial cells of the liver in the recipient. The absence of any increase in the intensity of proliferation in the liver cells shows that lymphocytes do not acquire the ability to stimulate the mitotic activity of these cells under the influence of unilateral nephrectomy.

The results obtained by counting the number of mitoses in the liver and kidneys of recipients of the lymphocytes from unilaterally nephrectomized mice are compared in Table 2 with the changes discovered previously [1, 2] in the mitotic activity in the liver and kidneys of recipients of lymphocytes from partially hepatectomized mice. It will be clear from Fig. 2 that the action of the lymphocytes at the times studied exhibited definite, but not absolute, organ specificity.

In experiments in which lymphocytes were transplanted from animals undergoing operation on the liver, the increase in intensity of proliferative activity affected mainly the recipients' liver cells. Some increase in mitotic activity was observed in connective-tissue cells of the kidneys, but the specific renal tissue did not respond by any significant changes in its mitotic index to the injection of lymphocytes from partially hepatectomized donors. Conversely, when lymphocytes from unilaterally nephrectomized mice were injected, the increase in proliferative activity affected chiefly the kidney tissue, as was found in two experiments.

The study of mitotic activity of the liver and kidneys of the recipients injected with a suspension of lymphocytes from mice undergoing resection of a small area of the kidney (series I) showed that under these experimental conditions the phenomenon of increased proliferative activity was not observed. The injected lymphocytes caused no significant changes in the mitotic index either of the tubular epithelium of the recipient's kidneys or the reticulo-endothelial and other cells of the liver (Table 1).

The results of these experiments can be summarized by saying that unilateral nephrectomy, like partial hepatectomy, modifies the properties of the lymphocytes, as a result of which they become capable of stimulating the proliferative activity of the tubular epithelium of the recipient's kidney and the reticulo-endothelial cells of the recipient's liver. The ability of lymphocytes from an animal undergoing an operation to induce increased proliferation is to a considerable extent organ-specific.

LITERATURE CITED

1. A. G. Babaeva, N. A. Kraskina, and L. D. Liozner, *Tsitologiya*, No. 12, 1511 (1969).
2. A. G. Babaeva, N. A. Kraskina, and L. D. Liozner, *Byull. Éksperim. Biol. i Med.*, No. 7, 91 (1969).
3. N. A. Kraskina, *Function of the Lymphoid Tissue in the Formation of Postvaccinal Immunity* [in Russian], Moscow (1968).