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REACTION OF LYMPHOID TISSUE DURING COMPENSATORY REGENERATION OF THE SALIVARY GLANDS IN MICE

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After unilateral removal or burns of a single submaxillary salivary gland and also after amputation of the lower incisors in CBA mice the ability of the spleen cells to form antibodies and to take part in the graft versus host reaction was studied and the number of hematopoietic stem cells was counted by the splenic colonies method. Each of the experimental procedures on the salivary glands was shown to be accompanied by increased migration of stem cells, and the ability of the lymphocytes to induce a graft versus host reaction was increased. The ability of splenic lymphocytes to react to an additional antigenic stimulus is enhanced by amputation of the lower incisors, which was followed by enlargement of the salivary glands, and is sharply reduced by removal or burns of the submaxillary salivary gland, neither of which induces hypertrophy of the salivary glands.

KEY WORDS: immune reactions; hypertrophy of salivary glands; amputation of lower incisors.

Regeneration of the liver and compensatory hypertrophy of the kidney are accompanied by a combination of changes in the functional properties of the lymphoid organs [1-4]. To decide to what extent these changes are characteristic of regenerative processes and how they correlate with the regenerative power of the organs, the reactive properties of splenic lymphocytes were studied during various forms of regenerative growth of the salivary glands in mice. This organ was chosen as the test object because of wide variation in its ability to undergo hypertrophy, ranging from absence after unilateral sialadenectomy to intensive hypertrophy of the glands following repeated amputation of the lower incisors.

EXPERIMENTAL METHOD

Experiments were carried out on 300 CBA mice. The antibody-forming capacity of spleen cells to sheep's red blood cells (SRBC) was studied by Jerne's method [5] 4, 17, and 48 h after unilateral sialadenectomy, burns of one submaxillary salivary gland, and amputation of the lower incisors. At the specified time after the operations the mice were killed, a suspension of their spleen cells was prepared, and was injected in a dose of 1×10^7 cells into lethally irradiated syngeneic recipients together with 2×10^8 SRBC. Control recipients received the same number of SRBC and spleen cells from intact mice. The number of antibody-forming cells (AFC) was determined on the 8th day after transfer of the lymphocytes and immunization. Changes in the ability of the lymphocytes to give a graft versus host reaction (GVHR) were determined at the same times after the operation by Möller's method [6]. The number of hematopoietic stem cells (CFU) in the spleen of the experimental animals also was determined by counting macroscopic colonies 8 days after transplantation of splenocytes of irradiated recipients in the usual way [7].

EXPERIMENTAL RESULTS

The experiments showed that each of the experimental procedures on the salivary glands (extirpation, unilateral burns, or repeated amputation of the lower incisors) was accompanied by an increase in the migrating capacity of the stem cells, as reflected in an increase in the number of exogenous colonies in the spleen of recipients of splenocytes of the experimental mice. This was clearly revealed 17 h after the beginning of

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TABLE 1. Changes in Functional Activity of Mouse Splenocytes in Different Forms of Compensatory-Adaptive Growth of the Submaxillary Salivary Gland ($M \pm m$)

Type of operation	Time after operation, h	CFU		GVHR		AFC	
		experiment	control	experiment	control	experiment	control
Extirpation of one submaxillary salivary gland	4	8	5	380±76.5	1450±97.4	543±103.3	1188.3±58.2
	17	15	10	865.5±201	2150±158	147±89	313±99
	48	Confluent	12	1780±204.8	3251±305	—	—
Burns of one submaxillary salivary gland	4	4	7	673±72.8	2950±275	635±58	1188±208
	17	10	7	1500±190	3000±280	820±33	2100.3±145.3
	48	17	10	2733±35.5	3251±193	—	—
Amputation of lower incisors	4	—	—	2828±144	4240±778.6	2620±320	2352±180
	17	15	10	1900±110	3800±290	2733±58.5	1936.6±108.3
	48	Confluent	12	—	—	—	—

the experiment, but after 48 h far higher values were obtained. The migrating capacity of the stem cells was particularly considerably increased at this period after unilateral sialadenectomy and amputation of the lower incisors. Identical changes in stem cell activity following operations leading to different manifestations of compensatory growth of the salivary glands are evidence that the ability of these glands to regenerate is not directly dependent on stimulation of stem cells (Table 1). As Table 1 shows, the ability of the splenic lymphocytes to react to an additional antigenic stimulus after experimental procedures on the salivary glands depends mostly on the degree of manifestation of compensatory growth of the gland. For instance, in the absence of salivary gland hypertrophy after unilateral sialadenectomy, or when the manifestations of hypertrophy were weak (after unilateral burns of the gland), not only was the ability of the spleen cells to form antibodies not increased, as in the case of regeneration of the liver [2] but, on the contrary, it was sharply reduced compared with the control ($P=0.02$). Meanwhile amputation of the lower incisors, leading to marked hypertrophy of the salivary glands, like regeneration of the liver, was accompanied by increased ability of the lymphocytes to respond by enhanced antibody formation to injection of SRBC. The clearest differences in the antibody-forming capacity of the splenocytes were seen 17 h after the operation. It will be clear from Table 1 that each of the experimental procedures used on the salivary glands increased the ability of the lymphocytes to induce the GVHR.

In all cases the number of antibody-forming cells (AFC) in recipients of lymphocytes from the experimental animals was smaller and, consequently, the number of their immunocompetent cells fell by a greater degree after the GVHR than in recipients of lymphocytes from control mice. This change in the reactivity of the lymphocytes can be explained by an increase in the number or functional activity of the T-lymphocytes, which are mainly responsible for this reaction. These changes were apparent 4 h after the operation. During regeneration of the liver, by contrast with the operation used in the present experiments, the ability of the splenocytes to induce the GVHR was reduced. This is evidence that the GVHR is not the result of stress. Of the various indices used to characterize activity of lymphoid tissue during compensatory growth, the one which correlates most closely with the regenerative power of the organ is the ability of the lymphocytes to respond to an additional antigenic stimulus. On the whole, the results are evidence that the operation and repair processes in the organs are accompanied by a sharp change in the activity of the immunity system.

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