

EFFECT OF PARTIAL HEPATECTOMY ON INDUCTION OF CELLS INHIBITING DEVELOPMENT OF THE HUMORAL IMMUNE RESPONSE

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It has been shown that partial hepatectomy inhibits the induction of cells exerting a suppressant effect on the development of humoral immune response.

KEY WORDS: specific suppression; nonspecific suppression; humoral immune response; partial hepatectomy.

Regeneration in several organs is accompanied by changes in the properties of the lymphocytes and in the immunologic status of the organism [1-3]. In particular, at certain times (4-21 h) after resection of two-thirds of the liver in mice the antibody-forming potential of the spleen cells is increased. Hence it has been suggested that these changes are due to depression of suppressor function.

To test this hypothesis the experiments described below were carried out to study the effect of partial hepatectomy on induction of cells causing specific suppression of the immune response when transplanted into intact animals, in the mouse spleen by immunization, and also to study the ability of spleen cells to induce nonspecific suppression of the immune response during development of the graft versus host reaction (GVHR).

EXPERIMENTAL METHOD

Experiments were carried out on CBA mice and (CBA \times C57BL/6) F_1 hybrids.

Nonspecific suppressor activity was studied on Möller's model [7]. Spleen cells from CBA mice in a dose of 50×10^6 were injected into intact (CBA \times C57BL/6) F_1 mice. Two-thirds of the liver was removed from some of the donors 19 h before sacrifice, or a mock operation was performed. The recipients were immunized 7 days after transplantation of the spleen cells with sheep's red blood cells (SRBC) in a dose of 5×10^8 .

Induction of specific suppressor activity was studied on Whisler's model [10]. CBA mice were immunized with SRBC in a dose of 3×10^9 . Two-thirds of the liver was resected from some mice 19 h before immunization. Spleen cells of immunized animals were injected into intact mice (50×10^6) 2 weeks later. The recipients of the spleen cells were immunized the same day with SRBC (2×10^8).

On the 5th day after immunization the number of antibody-forming cells (AFC) in the recipients' spleen was determined by Jerne's method [6].

The numerical results were subjected to statistical analysis and the geometric mean and its confidence limits at $P = 0.01$ were determined.

EXPERIMENTAL RESULTS

When the mice receiving injections of spleen cells from syngeneic immune donors were immunized with SRBC, the number of AFC formed was only one-tenth of that found in control mice (injection of SRBC only; Table 1).

As other investigations have shown [5, 10], the inhibition in this model is specific in character: The immune response only to the antigen with which the donors of the splenocytes were immunized is depressed. In this case the suppression is mediated by T-cells.

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TABLE 1. Effect of Partial Hepatectomy on Induction of Cells Producing Specific Suppression of Immune Response

Donors of immune cells	No. of recipients	Number of AFC
Control	6	101 900 (60 390—166 300)
Intact	9	10 250 (6 227—16 890)
Mock operation	5	12 360 (5 376—28 400)
Hepatectomized	14	47 880 (38 650—59 300)

TABLE 2. Effect of Partial Hepatectomy on Cells with Nonspecific Suppressive Action

Donors of CBA cells	No. of recipients	Number of AFC
Control	6	126 800 (76 960—209 800)
Intact	8	22 170 (16 800—20 070)
Mock operation	5	19 260 (10 600—34 940)
Hepatectomized	11	52 840 (43 410—64 330)

Immunization of the donors thus induced accumulation of specific suppressors in them.

When mice partially hepatectomized 19 h before immunization with SRBC were used as donors of spleen cells, inhibition of the immune response was not so marked (to only half the control level).

After injection of spleen cells from mice undergoing a mock operation the immune response of the recipients was inhibited just as strongly as after transplantation of cells from immune, intact donors.

The results indicate that induction of cells producing specific suppression of the immune response, by means of immunization in partially hepatectomized mice, takes place much less effectively than in intact animals.

As Table 2 shows, injection of spleen cells of intact CBA mice or CBA mice undergoing a mock operation into (CBA \times C 57BL/6) F_1 hybrids leads to considerable inhibition of the immune response to SRBC injected 7 days after transplantation of the cells.

Inhibition of the immune response (Table 2) was much weaker when spleen cells from hepatectomized mice were transplanted into the hybrids. Special experiments showed that AFC in this model were mainly of recipient origin.

Inhibition of the immune response was unconnected with the toxic effect of the GVHR. Direct proof was obtained that nonspecific inhibition of the immune response was connected with the appearance of actively suppressing cells during the GVHR [8, 9].

Consequently, under the influence of partial hepatectomy the formation of nonspecific suppressor spleen cells during development of the GVHR is considerably reduced.

Partial hepatectomy thus inhibits induction of cells with a suppressive influence on the development of the humoral immune response. This is evidently connected with the fact that after partial hepatectomy a factor blocking suppressors (or, more exactly, their precursors) appears in animals.

It was shown previously [4] that a factor [the $F(ab)_2$ fragment of the IgG molecule] capable of potentiating the immune response in homologous recipients appears in the spleen of partially hepatectomized animals. The possibility cannot be ruled out that the potentiating action of this factor on the immune response also is mediated through blocking of suppressors.

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