6. R. I. Mishell and E. W. Dutton, J. Exp. Med., 126, 423 (1967).
7. B. S. Nilsson, B. M. Sultzer, and W. Bullock, J. Exp. Med., 137, 127 (1973).
8. F. Parenti, P. Frangeschini, and G. Farti, Biochim. Biophys. Acta, 123, 181 (1966).
9. B. Phillips and E. Weisrose, Clin. Exp. Immunol., 16, 383 (1974).
10. J. Quintaus and I Lefkovitz, J. Immunol., 113, 1373 (1974).
11. C. S. Ripps and K. Hirschhorn, Clin. Exp. Immunol., 2, 377 (1967).
12. T. W. Tao, Science, 146, 247 (1964).
13. E. R. Unanue and B. A. Askonas, J. Exp. Med., 127, 915 (1968).

EFFECT OF VARIOUS ANTISERA ON INTENSITY OF THE IMMUNE RESPONSE DURING INDUCTION OF ANTIBODY FORMATION BY ALLOGENEIC MACROPHAGES

T. V. Anfalova and V. G. Galaktionov

UDC 612.017.1.014.46:615.365.018.51/.53

Data on the effect of various antisera on the induction of antibody formation by immune allogeneic macrophages are described. A considerable decrease in the intensity of the immune response was observed after injection both of allogeneic antiserum and of antimacrophagal serum during the first 2 days after transplantation of the allogeneic macrophages. Injection of these sera on the following days had no significant effect on the intensity of the immune response. Antierythrocytic serum prevented the accumulation of antibody-forming cells if injected at various times after transplantation of the allogeneic macrophages.

KEY WORDS: macrophages; induction of immune response; antimacrophagal serum; allogeneic antiserum.

In previous investigations [1, 2] the writers showed that incompatibility between the donor of antigen-treated macrophages (MPH) and recipient with respect to the H-2 locus leads to marked depression of the immune response compared with its induction under conditions of complete syngeneity of the donor of immune MPH and the recipient.

To study whether immune rejection by an incompatible recipient is the decisive factor in the observed decrease in the accumulation of antibody-forming cells (AFC), the effect of various antisera was studied on the induction of antibody formation by immune allogeneic MPH in the early and later stages of induction. Antimacrophagal and allogeneic antisera were used as the model factor destroying the donor's MPH.

EXPERIMENTAL METHOD

Mice of strains CBA and DBA/2 were used, for this particular allogeneic pair gives the most marked depression of the immune response in the nonsyngeneic transfer system. Immune MPH were obtained as described earlier [2].

Mouse antierythrocytic serum was prepared from the blood of CBA mice immunized twice with sheep's red cells. The hemagglutinin titer was 1:64,000.

Rabbit antimacrophagal serum was prepared as described by Shortman and Palmer [5]. Anti-DBA/2

Institute of Medical Genetics, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR P. D. Gorizontov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 9, pp. 1094-1096, September, 1976. Original article submitted October 31, 1975.

serum was obtained from CBA mice after repeated intraperitoneal immunization with spleen cells of DBA/2 mice. The titers of antisera in the cytotoxic test were 1:64–1:128. The intensity of the immune response was determined from the number of AFC in the spleen, detected by Jerne's method [4] on the 5th day after injection of immune macrophages.

EXPERIMENTAL RESULTS

In the experiments of series I the action of specific anti-DBA/2 serum prepared against spleen cells was studied. It will be clear from Fig. 1 that the anti-DBA/2 serum had a depressive action only if injected during the first 2 days after injection of the immune MPH. The number of AFC was reduced by more than half. Subsequently the anti-DBA/2 serum had no appreciable effect on the intensity of the immune response. The depressive effect of the antiserum was presumably connected with the induction period. According to data in the literature [6, 7], the duration of induction is 1-2 days. To clear up this point in the concrete situation (induction of the immune response by allogeneic MPH) experiments were carried out to study the effect of antimacrophagal serum on the induction process. The scheme of the experiments in this case was the same as in the previous series.

As Fig. 1 shows, the heterologous rabbit antimacrophagal serum had a depressive action when injected during the first 2 days after injection of MPH. On the following days the antimacrophagal serum did not affect AFC accumulation. The marked decrease in the intensity of the immune response after injection of the antimacrophagal serum during the first 2 days after transfer of antigen-processing peritoneal exudate cells confirmed that induction of the immune response took place during the first 2 days. In this situation it is impossible to speak of the effect of antiserum only on the transplanted MPH. The serum used also acted on the receipient's MPH because of its polyspecificity. However, the main conclusion that induction of the immune response took place during the first 2 days after injection of the antigen-processing MPH appears to be perfectly valid.

To continue the analysis of the character of induction of the immune response in the allogeneic organism the effect of antierythrocytic serum was studied. Antiserum against sheep's erythrocytes was injected intraperitoneally into the mice in a dose of 0.2 ml. The results of this series of experiments are given in Fig. 1. Injection of antierythrocytic serum on the day of transplantation of MPH and on the day after transplantation led to almost total abolition of the immune response, evidently in connection with the total blocking of the erythrocytic determinants bound with MPH. The accumulation of AFC was largely suppressed also when the antiserum was injected on the 4th day after transplantation of the immune MPH. However, the decrease in the intensity of the immune response at these times was evidently not connected with macrophagal induction, but reflected disturbances of the subsequent stages of antibody formation.

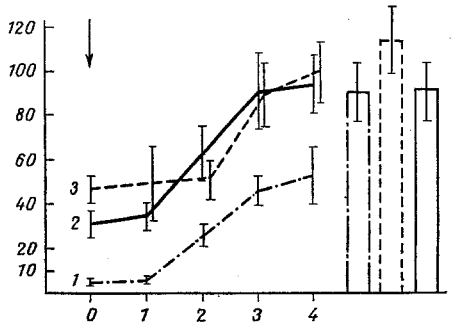

Fig. 1. Effect of different antisera on immune response of CBA mice during induction of antibody formation by macrophages of DBA/2 mice: 1) antierythrocytic serum; 2) antimacrophagal serum; 3) anti-DBA/2 srum. Arrow indicates injection of macrophages. Columns show intensity of immune response in appropriate control. Ordinate, number of AFC per 10^6 spleen cells; abscissa, days of injection of antisera.

Depression of the intensity of the immune response after injection of the anti-DBA/2 and antimacrophagal sera on the first 2 days after transplantation of the antigen-processing cells of the peritoneal exudate evidently indicated that MPH induced antibody formation during the first 2 days after their transplantation into the recipient, and that it was at that time that the antisera prevented interaction between the donor's MPH and the recipient's immunocytes. However, the number of AFC never fell to the background level as was observed after injection of antierythrocytic serum. If anti-DBA/2 serum was injected on the first 2 days after transplantation of the cells the intensity of the immune response corresponded to values obtained when free antigen was used [2]. It can be postulated that specific destruction of the immune MPH by anti-DBA/2 antibodies injected on the 3rd-4th day after transplantation of the antigen-processing peritoneal exudate cells did not effect the final intensity of the immune response, because the induction process was already complete. Consequently, it is extremely likely that the immune rejection was unable to exert its eliminating action for the induction period ended before maturation of the rejection factors could be completed.

Other workers using adherent and nonadherent spleen cells of two inbred strains and allogeneic antiserum against adherent cells also reached similar conclusions [3]. Analysis of the accumulation of AFC in a nonsyngeneic combination between the donor of immune MPH and the recipient suggests that the effectiveness of induction depends not only on the immunogen of the MPH cell surface and the antigen-recognizing receptors of the immunocytes, but also on the genetic correspondence (structural similarity) of the interacting cellular units. The most effective induction by immune MPH takes place under conditions of complete genotypical similarity of the interacting immunocompetent cells.

LITERATURE CITED

1. V. G. Galaktionov and T. V. Anfalova, Dokl. Akad. Nauk SSSR, 212, 751 (1973).
2. V. G. Galaktionov and T. V. Anfalova, Zh. Obshch. Biol., 35, No. 3, 365 (1974).
3. H. Cosenza and L. D. Leserman, J. Immunol., 108, 418 (1972).
4. N. Jerne and A. Nordin, Science, 140, 405 (1963).
5. R. Shortman and I. Palmer, Cell. Immunol., 5, 299 (1972).
6. E. R. Unanue, Advances Immunol., 15, 95 (1971).
7. B. Vernon-Roberts, The Macrophage, Cambridge Univ. Press, London, (1972).

PARTICIPATION OF PHYTOHEMAGGLUTININ-TRANSFORMED MOUSE LYMPHOCYTES IN THE GRAFT VERSUS HOST REACTION

V. G. Nesterenko and L. V. Koval'chuk

UDC 616-056.3-02:612.6.02.017.1+612.6.02.017.1-06:612.112.94

Transformed lymphocytes obtained by stimulating lymph node cells of CBA mice with phytohemagglutinin (PHA) do not give the graft versus host reaction (GVHR) if injected into sublethally irradiated (CBA x C57BL/6)F_1 hybrids. In a population of PHA-stimulated cells the GVHR was induced by small lymphocytes having the same concentration of antigens, detectable by antilymphocytic serum, as intact lymphocytes.

KEY WORDS: phytohemagglutinin; blast transformation; graft versus reaction.

It was shown previously that cultivation of lymph node cells with phytohemagglutinin (PHA) for 44 h led to a considerable reduction in their activity in the graft versus host reaction (GVHR). It was suggested that

Department of Immunology, Medico-Biological Faculty, N. I. Pirogov Second Moscow Medical Institute.

(Presented by Academician of the Academy of Medical Sciences of the USSR Yu. M. Lopukhin.) Translated from Byulletin' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 9, pp. 1096-1098, September, 1976. Original article submitted February 9, 1976.