AUTOREACTIVITY OF SPLEEN CELLS OF OLD MICE AND HYDROCORTISONE-TREATED ANIMALS

A. N. Meilikhova, D. N. Mayanskii, and V. A. Kozlov

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KEY WORDS: graft versus host reaction; hydrocortisone; autoreactivity.

During aging autoantibodies against various organs and tissues have been reported to appear, probably in connection with a reduction in suppressor activity of the lymphoid cells which normally inhibit immunologic reactivity against autoantigens [7, 12]. There is evidence in the literature of the important role of adrenocortical hormones in the regulation of reactions of cellular immunity [2, 5]. It has been shown that suppressor cells of splenic origin, participating in antibody formation and reactions of cellular immunity in an allogeneic system, are sensitive to glucocorticoids [2, 6, 8]. It was decided to study the effect of glucocorticoids on suppressor activity of lymphoid cells in reactions to autoantigens.

In the investigation described below the ability of spleen cells of old donors and of animals treated with hydrocortisone to induce a local graft versus host reaction (GVHR) in the popliteal lymph node of syngeneic recipients was studied.

EXPERIMENTAL METHOD

Female CBA or (CBA × C57BL)F_1 mice weighing 18-22 g were used as donors. Spleen cells of these animals were obtained by the method described previously [1] and injected into syngeneic recipients in a dose of 5×10^6 or 10×10^6 subcutaneously into the left hind paw. The reaction was read on the 7th day and assessed by means of a lymph node index (LNI), equal to the ratio of the weight of the left popliteal lymph node (experiment) to that of the contralateral node (control). Some donors were given hydrocortisone acetate (from Gedeon Richter, Hungary) in a dose of 125 mg/kg, others received 50 mg/kg of hydrocortisone acetate intraperitoneally 3 days before transplantation. In the experiments of series III, (CBA × C57BL)F_1 donors aged 18 months were used. Donors for the control were intact mice aged 4 months. The statistical analysis was carried out by Student's t-test.

EXPERIMENTAL RESULTS

As Table 1 shows, transplantation of spleen cells in a dose of 10×10^6 from (CBA × C57BL)F_1 donors aged 18 months into a syngeneic recipient caused a twofold increase in weight of the popliteal drainage lymph node compared with the contralateral node ($P < 0.01$), whereas the same dose of spleen cells from a young donor caused virtually no increase in weight of the popliteal lymph node.

After injection of hydrocortisone into the CBA donors their spleen cells, in a dose of 5×10^6, caused a twofold increase in weight of the popliteal lymph node when given in doses of both 50 mg/kg and 125 mg/kg ($P < 0.05$); injection of spleen cells from intact CBA donors, however, caused virtually no change in weight of the lymph node (Table 2).

The results in Table 3 show that spleen cells from intact donors and from (CBA × C57BL)F_1 donors treated with 50 and 125 mg/kg hydrocortisone, transplanted in a dose of 5×10^6 into syngeneic recipients, caused no significant increase in weight of the drainage lymph node. However, 10×10^6 spleen cells from donors receiving 50 mg/kg hydrocortisone caused a marked increase in weight of the popliteal lymph node in the syngeneic recipients compared with intact cells ($P < 0.05$).

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TABLE 1. Changes in Absolute Weight (in mg) of Popliteal Lymph Node and LNI after Transplantation of 10×10^6 Spleen Cells from (CBA × C57BL)F_1 Donors Aged 4 and 18 Months into Syngeneic Recipients (M ± m)

Material transplanted	No. of recipients	Weight of left lymph node (expt.)	Weight of right lymph node (control)	LNI
Spleen cells from donors aged 4 mos.	12	1,80±0,13	1,53±0,09	1,14±0,08
Spleen cells from donors aged 18 mos.	12	3,76±0,43	1,98±0,18	2,02±0,28

TABLE 2. Changes in Absolute Weight (in mg) of Popliteal Lymph Nodes and LNI after Transplantation of 5×10^6 Spleen Cells from CBA Donors Treated with 50 and 125 mg/kg Hydrocortisone into Syngeneic Recipients (M ± m)

Material transplanted	No. of recipients	Weight of left lymph node (expt.)	Weight of right lymph node (control)	LNI
Spleen cells from intact donors	20	1,80±0,12	1,62±0,13	1,30±0,12
Spleen cells from hydrocortisone-treated donors:				
50 mg/kg	12	3,10±0,38	1,42±0,10	2,07±0,25
125 mg/kg	18	2,43±0,13	1,31±0,06	1,86±0,11

TABLE 3. Changes in Absolute Weight (in mg) of Popliteal Lymph Nodes and LNI after Transplantation of Various Doses of Spleen Cells from (CBA × C57BL)F_1 Donors Treated with 50 and 125 mg/kg Hydrocortisone, into Syngeneic Recipients (M ± m)

Material transplanted	No. of recipients	Weight of left lymph node (expt.)	Weight of right lymph node (control)	LNI
$5 \cdot 10^6$ Spleen cells from intact donors	9	2,2±0,18	1,5±0,13	1,39±0,05
$5 \cdot 10^6$ Spleen cells from hydrocortisone-treated donors:				
50 mg/kg	10	2,26±0,20	1,46±0,12	1,63±0,16
125 mg/kg	11	2,30±0,18	1,46±0,23	2,07±0,44
$10 \cdot 10^6$ Spleen cells from intact donors	17	1,80±0,10	1,50±0,26	1,20±0,08
$10 \cdot 10^6$ Spleen cells from donors treated with 50 mg/kg hydrocortisone	17	2,00±0,13	1,30±0,07	1,60±0,17

The results thus show that under the influence of hydrocortisone spleen cells become capable of inducing a local GVHR in syngeneic combinations CBA → CBA and (CBA × C57BL)F_1 → (CBA × C57BL)F_1, although genotype does have some effect on the character of the reaction produced. Cells of animals aged 18 months acquire the ability to induce a local GVHR in a syngeneic recipient.

The results can be explained by an age-related decrease in the suppressor population of T lymphocytes. The cause of this may be involution of the thymus with age, and the accompanying decrease in the secretion

of thymic humoral factors, which according to Small and Irainin [11] is responsible for regulation of suppressor activity of T lymphocytes. Thymectomy on adult donors is in fact followed by their becoming capable of inducing a GVHR in a syngeneic recipient [4]. The appearance of activity in GVHR induction by spleen cells of donors treated with large doses of hydrocortisone can be attributed to elimination of cells with suppressor activity by the hormone and to a relative increase in activity of lymphocytes which participate in processes of immunologic recognition. Just as in reactions in an allogeneic system [2, 6], suppressor T lymphocytes modulating processes of recognition of autoantigens, are evidently sensitive to hydrocortisone. Population changes connected with a decrease in suppressor activity may perhaps take place in connection with age changes in the pituitary-adrenal system, either acting directly on lymphocytes or leading to age involution of the thymus [9], the role of which in the development of autoimmune pathology is no longer in dispute [10]. It can be tentatively suggested that clones of lymphoid cells responding to autoantigens exist in the body, but under normal conditions their function is inhibited by the activity of hydrocortisone-sensitive suppressor cells.

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IMMUNOBIOLOGICAL STUDY OF HETEROGENEOUS ANTIGENS TO UROPATHOGENIC STRAINS OF *Escherichia coli*

I. I. Podoplelov, A. S. Samoilenko, N. I. Shchipkova, V. I. Burtsev, and D. Ya. Bakanova

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Much attention is currently being paid to the study of heterogeneous (cross-reactivity) antigens common to macro- and microorganisms. This is explained by their important role in the development of immunopathological processes and weakening or distortion of the immune response. These properties of bacteria which contain heterogeneous antigens may lead to the formation of a bacterial carrier state, enabling an infectious disease to be converted into a chronic form. Meanwhile the presence of antigens in bacteria identical with those of human erythrocytes may be the reason why an infectious disease affects particular population groups selectively [1-3, 5].

The object of this investigation was to study the role of heterogeneous antigens of the ABO type in strains of Escherica coli in the formation and course of chronic pyelonephritis in man.

Research Laboratory of Experimental Immunobiology, Academy of Medical Sciences of the USSR, Moscow.

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