GLUCOCORTICOID HORMONES AND THE IMMUNE RESPONSE IN CBA AND C57BL MICE OF DIFFERENT AGES

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Genetic control of the intensity of the immune response to a number of antigens is now a firmly established fact [6]. Realization of genetic information determining the intensity of a complex process such as immunogenesis can be mediated not only at the molecular and cellular levels but also, evidently, through nonspecific factors involved in regulation of the intensity of the immune response in the intact organism.

The object of this investigation was to study possible correlation between the functional state of the hypothalamo-hypophyseo-adrenocortical system (HHACS) and differences in the intensity of immunologic responses in mice of two different lines.

EXPERIMENTAL METHOD

Experiments were carried out on male CBA and C57BL mice aged 8-20 and 28-40 weeks, obtained from the "Rappolovo" Nursery, Academy of Medical Sciences of the USSR, during the summer. The animals were kept in standard plastic boxes, 20 in each box, and they received a balanced diet and adequete water.

The mice were immunized with previously washed sheep's red blood cells (SRBC) in a dose of 5×10^8 cells per animal, intraperitoneally in a volume of 0.5 ml. The magnitude of the immune response was estimated on the 6th day after immunization by counting the number of rosette-forming cells (RFC) in the spleen by the immune rosette-formation test [12].

To determine the concentration of 11-hydroxycorticosteroids (11-OHCS) in the blood plasma mice were decapitated between 10 a.m. and noon. Heparinized blood plasma from five or six mice was pooled. The 11-OHCS concentration in the samples was determined fluorometrically [4]. The number of immune RFC was expressed in log units [4].

The results were subjected to statistical analysis by the Wilcoxon–Mann–Whitney nonparametric test [2].

EXPERIMENTAL RESULTS

The immune response to SRBC in CBA and C57BL mice was characterized by a marked increase in the number of immune RFC in the spleen. In the group of animals aged 8-20 weeks the number of spontaneous RFC in the spleen before immunization was greater in C57BL than in CBA mice, but at the height of the immune response this relationship was reversed (Table 1). In mice aged 28-40 weeks interlinear differences in the intensity of the immune response were preserved and there was a tendency for the numbers of spontaneous RFC to differ. The results agree with data in the literature [5]. On the basis of the increase in the number of RFC in the spleen of the two lines of mice immediately after immunization, it can be postulated that the immune response in CBA mice is characterized by greater proliferative activity of the RFC population than in C57BL mice, and that this rule extends to both age groups.

Various investigators have observed weakening of immunologic responses to different antigens with advancing age in man and naimals. The results of the present experiments are

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TABLE 1. Number of RFC in Spleen of Young and Old CBA and C57BL Mice

Group of animals	No. of RFC per 10^6 spleen cells, log	P
Before immunization		
1. Young CBA	2,40±0,10	$P_{1-2}<0,05$
2. Young C57BL	2,69±0,09	$P_{2-4}>0,05$
3. Old CBA	2,50±0,06	$P_{1-3}>0,05$
4. Old C57BL	2,80±0,22	$P_{3-4}>0,05$
On 6th day after immunization		
1. Young CBA	3,93±0,06	$P_{1-2}<0,05$
2. Young C57BL	3,76±0,03	$P_{2-4}<0,05$
3. Old CBA	3,88±0,06	$P_{1-3}>0,05$
4. Old C57BL	3,56±0,06	$P_{3-4}<0,01$

TABLE 2. Plasma 11-OHCS Level in Young and Old CBA and C57BL Mice (M ± m)

Group of animals	11-OHCS concn., μg/100 ml	P
Before injection of antigen		
Intact		
1. Young CBA	15,0±1,4	$P_{1-2}>0,05$
2. Young C57BL	18,3±1,7	$P_{2-4}<0,05$
3. Old CBA	17,8±0,8	$P_{1-3}>0,05$
4. Old C57BL	12,7±1,5	$P_{3-4}<0,05$
2 h after injection of antigen		
1. Young CBA	27,1—1,5	$P_{1-2}>0,05$
2. Young C57BL	30,2±1,6	$P_{2-4}<0,01$
3. Old CBA	25,5±1,0	$P_{1-3}>0,05$
4. Old C57BL	24,3±1,0	$P_{3-4}>0,05$

evidence of depression of the immune response to SRBC in mice of the weakly responding C57BL line in the older age group, whereas in the strongly responding CBA line no weakening of the immune response took place with age.

To determine any possible participation of adrenocortical hormones in the mechanism of these interlinear differences in the intensity of the immune response, basic 11-OHCS levels were studied in mice of both lines and age groups, with parallel determination of the intensity of the response of HHACS to antigenic stimulation. The experiments revealed no significant differences in the basic 11-OHCS level in mice aged 8-20 weeks (Table 2). Meanwhile, in the group of animals aged 28-40 weeks a statistically significant decrease in the 11-OHCS concentration was found in mice of the weakly responding C57BL line. These results agree with those obtained by other workers [7] who found a higher 11-OHCS level in CBA than in C57BL mice. However, it should be pointed out that different techniques were used by the present writers and those cited above. Sememkov et al. obtained blood for determination of the 11-OHCS concentration from the retro-orbital sinus. That procedure evidently gives rise to greater stress than instant decapitation, which we used, as is shown also by the values given by the authors in [7]. For instance, the blood 11-OHCS concentration was 78.4 μg% in CBA mice and 38.5 μg% in C57BL mice, i.e., considerably higher than the values we obtained. For comparison it may be noted that, according to Gorbalenya et al. [1] the plasma 11-OHCS concentration in C57BL mice was 22.8 μg%.

Injection of an antigen is known to raise the glucocorticoid hormone level [3, 8]. We investigated changes in the plasma 11-OHCS concentration in mice of both lines and age groups in response to injection of SRBC. The maximal increase in 11-OHCS concentration in mice of both lines was observed 2 h after injection of the antigen. The intensity of the response of HHACS was equal, irrespective of genetic differences. There was only a tendency for the intensity of the hormonal response to diminish with age, but a significant decrease was found only in C57BL mice, with a weak response to SRBC.

Differences in the immune response and hormonal status thus revealed were thus due mainly to a considerable decrease in the values of the parameters with age in C57BL mice.

We are not inclined to regard weakening of reactivity of the HHACS as a factor responsible for the lower level of immunologic reactivity. For example, the possiblity cannot be ruled out that a higher immune response may be observed in C57BL mice to other antigens differing from SRBC. However, the results revealed correlation between the intensity of the immune response to T-dependent antigen and the level of HHACS function, and this correlation was particularly strong in animals with a particular genotype during agine.

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STATE OF ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY AND *IN VITRO* EFFECT OF INTERFERON ON K CELL FUNCTION IN CHILDREN WITH CHRONIC VIRUS HEPATITIS B

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Recent investigations have demonstrated the role of cell-mediated cytotoxic reactions in the pathogenesis of virus hepatitus B (VHB). It has been shown that expression of antigens on the surface of liver cells, arising during intracellular replication of hepatitis B virus, cytolytic immune processes aimed at eliminating infected hepatocytes are activated. The possibility of involvement of T killer cells, natural killer cells, and K cells in the mechanism of destruction in acute and chronic VHB also have been demonstrated [1, 5, 9]. K cells mediate antibody-dependent cellular cytotoxicity (ADCC). With the aid of a receptor for the Fc fragment of IgG, found on their surface, K cells bind with antibodies, reacting with antigens of target cells, and exert a cytolytic reaction [12]. In chronic hepatitis B (CHB) all the conditions are found for induction of ADCC. The presence of antibodies of the IgG class, directed against the expressed virus antigen (HB_cAg) [14] in the serum and on the surface of the hepatocytes, and the discovery of antibodies against hepatocyte membrane antigen (LSP) [10] are evidence that the conditions are met for cytolysis by circulating K cells.

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