By immunocytochemical analysis it was thus possible to estimate production of IL-1β at the cellular level and to study the temporal parameters of its synthesis by human blood monocytes.

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EFFECT OF IMMUNOMODULATORS ON MACROPHAGAL 5′-NUCLEOTIDASE ACTIVITY AND BLOOD CORTISOL LEVEL IN INBRED MICE

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In recent years, a close connection has been found between the neuroendocrine and macrophagal systems. Macrophages play an active part in the regulation of hormones, including glucocorticoids. In turn, glucocorticoids occupy a special place among the hormones controlling the mononuclear phagocyte system [4, 5, 7]. However, the concrete mechanisms and particular features of interaction between macrophages and glucocorticoids, especially under the influence of immunomodulators, have not been adequately studied.

Accordingly, an investigation was carried out with the aim of studying the effect of immunomodulators of bacterial origin on the level of activity of the ecto-5′-nucleotidase (EC 3.1.3.5) of the peritoneal exudate macrophages (BEM) and the blood cortisol level in mice of different lines.

EXPERIMENTAL METHOD

Experiments were carried out in the winter on male mice aged 3 months, weighing 16-18 g, and belonging to the CBA, C57BL/6, and BALB/c lines and (CBA·C57BL/6)F_1 hybrids. Preparations of bacterial origin were used as immunomodulators: the polysaccharide salmosan, obtained from the N. F. Gamaleya Research Institute of Epidemiology and Microbiology, Academy of Medical Sciences of the USSR (Director, Professor M. A. Tumanyan) from *Salmonella typhiabd.*, and the protein product staphylococcal enterotoxin A, produced by Ufa Research Institute of Vaccines and Sera. Salmosan

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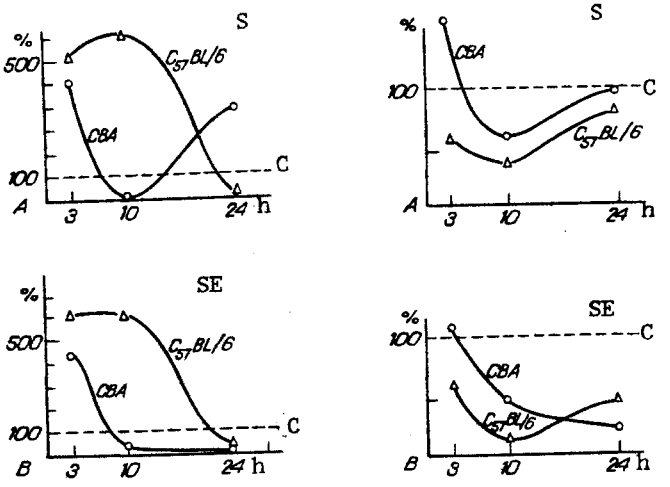

Fig. 1 Fig. 2

Fig. 1. Changes in cortisol level (in % of control level — C) with time in CBA and C57BL/6 mice after subcutaneous injection of S (Fig. 1A) and SE (Fig. 1B).

Fig. 2. Changes with time in ecto-5'-nucleotidase activity of PEM (in % of activity of control animals (C)) in CBA and C57BL/6 mice after subcutaneous injection of S (Fig. 2A) and SE (Fig. 2B).

(S) and staphylococcal enterotoxin A (SE) were injected subcutaneously in a dose of 100 and 1 μg per mouse, respectively. During the first 24 h after injection of the immunomodulators the blood cortisol level was determined by a fluoroimmunometric method (DELFIA) [14]. In parallel tests on these same animals, activity of ecto-5'-nucleotidase was determined in the membrane of residual intact PEM by the method described in [11]. For each experimental group, consisting of at least six animals, there was a corresponding control group, the mice of which received an injection of isotonic sodium chloride solution. The experimental and control animals were kept under identical standard conditions. The experimental data were subjected to linear regression analysis. A technique of statistical conclusions was used, incorporating exponential smoothing methods [8].

EXPERIMENTAL RESULTS

The experiments showed that injection of immunomodulators into different lines of mice was accompanied by marked changes in the blood cortisol level. These differences were most marked in CBA and C57BL/6 mice.

Changes in the serum cortisol level of CBA and C57BL/6 mice with time after injection of S and SE into the animals are shown in Fig. 1. Changes in the blood cortisol level were similar in type in C57BL/6 mice receiving S and SE: a sharp increase in the hormone concentration in the first 10 h after injection followed by a decrease until 24 h below the control level. In CBA mice, changes in the cortisol level in response to S and SE were similar in character only during the first 10 h of the investigation, and they differed sharply at later stages. For instance, in the first 3 h after injection of both S and SE there was a sharp rise in the hormone level. By 10 h, however, not only had the hormonal level not returned to normal, but it had fallen below the control level, and after injection of S it fell to zero values, and of SE to 24% compared with the control. Later, with the course of time, the blood cortisol level rose again in mice receiving S, and after 24 h it was 4 times higher than in the control. In animals receiving injections of SE, however, the cortisol concentration continued to fall virtually to zero values throughout this period.

Changes in 5′-nucleotidase activity of PEM with time are shown in Fig. 2. Comparison of Figs. 1 and 2 shows that the curve of 5′-nucleotidase activity in CBA mice repeated in general features the curve showing the change in the blood cortisol level. After the same period of time, maximal and minimal values of the parameters were observed on these curves. In C57BL/6 mice, by contrast with CBA, the curve of 5-nucleotidase activity was apparently a mirror image of the curve demonstrating changes in blood cortisol.

The investigations thus showed the existence of correlation between the blood cortisol level and the 5-nucleotidase level of PEM. In CBA mice this correlation was positive, but in C57BL/6 mice it was negative in character.

These results showing correlation between 5′-nucleotidase activity of PEM and the cortisol level under the influence of immunomodulators are in agreement with previous data showing that different hormones can influence 5-nucleotidase activity [3, 6, 9]. Data in the literature, relating to the structure and function of 5′-nucleotidase, its functional connection with cAMP phosphodiesterase [12], and its role in the regulation of cAMP — a mediator of the action of hormones on many biological systems [13], likewise do not contradict the results of the present investigation.

It was shown previously that S and SE cause considerable changes in various functional, morphological, and biochemical characteristics of macrophages, including in enzymes of adenosine metabolism [1]. It can be tentatively suggested that interlinear differences in the character of the effect of immunomodulators on the macrophagal system and, in particular, on 5′-nucleotidase activity [10], are determined by differences in their action on the hormonal balance in mice of different lines, and depend on individual differences in neuroendocrine regulation.

Considering that neuroendocrinological relations play a key role in the regulation of homeostasis, the continuation of research in this direction will help to create a more complete picture of the mechanisms of the immunomodulating action of different preparations and to establish new mutually regulating links between the immune and neuroendocrine systems.

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