

Functional Activity of the Adrenal Cortex in Mice of Opposite Strains with Candidiasis

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Experiments were performed on two opposite strains of mice differing in the basal blood glucocorticoid concentration in the blood. Infection of animals with *C. albicans* fungi led to the development of hypocorticism. C57Bl/6 and CBA mice with progressive candidiasis showed a persistent and phasic course of hypocorticism, respectively.

Key Words: mice of opposite strains; candidiasis; cortisol; progesterone

Studies of the interaction between *Candida* fungi and macroorganism mainly focus on activity of the immune system [2]. Little is known about the response of endocrine glands, including the adrenal glands (AG), to candida infection. Individual differences in functional activity of the adrenal cortex can be genetically determined. They determine the development and severity of inflammation (*e.g.*, mycotic inflammation), since corticosteroids interact with the immune system and modulate various immune functions [1,5]. It was hypothesized that glucocorticoids and other steroid hormones can modify pathogenicity of *C. albicans*. It is associated not only with modulation of antiinfectious protection in the organism, but also with the direct effect of these hormones on microorganisms that have steroid-binding proteins [11,12].

Here we studied functional activity of the adrenal cortex in mice of two opposite strains (CBA and C57Bl/6) under normal conditions and during the response to mycotic inflammation produced by candida infection.

MATERIALS AND METHODS

Experiments were performed on male inbred CBA ($n=52$) and C57Bl/6 mice ($n=58$) weighing 20-30 g and obtained from the nursery of the Institute of Cytology and Genetics (Siberian Division of the Russian

Academy of Sciences). Candidiasis was produced by intraperitoneal injection of *C. albicans* in a single dose of 2.5×10^6 microbial bodies. The development of systemic mycosis (candidiasis) was verified histologically. Typical infiltrates and granulomas consisting of macrophages and epithelioid cells were revealed in the liver, lungs, and lymph nodes [7].

The blood and AG were sampled before (control mice) and 10, 28, and 56 days after infection. AG were weighted and homogenized in phosphate buffer. Homogenates were centrifuged. Supernatants were extracted with diethyl ether (1:10); extracts were evaporated. The solid residue was dissolved in 0.1% bovine serum albumin. Serum concentration of cortisol and contents of cortisol and progesterone in extracts of AG were measured by radioimmunoassay and enzyme immunoassay using commercial kits Cortisol-RIA (Immunotech) and Steroid IFA-progesterone (Alkor Bio).

The results were analyzed by Kruskal—Wallis analysis of variance and nonparametric Mann—Whitney test (Bonferroni-adjusted multiple comparison procedure).

RESULTS

Blood cortisol concentration in control CBA mice was 3.9-fold lower than in C57Bl/6 mice (15.8 ± 2.7 and 61 ± 5 nmol/liter, respectively, $p < 0.01$).

On day 10 after infection blood cortisol concentration decreased in mice of both strains (Fig. 1). Blood

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cortisol concentration in CBA mice increased to the basal level after 28 days, but decreased by the 56th day. Cortisol concentration in C57Bl/6 mice remained low in various periods after treatment.

We revealed no significant interstrain differences in the concentrations of cortisol and progesterone in AG of control animals (Table 1, Fig. 2). It can be hypothesized that the differences in blood cortisol concentration in animals of these strains are associated with intensive binding of the hormone to plasma transcortin in C57Bl/6 mice, which decelerates its elimination from the circulation [4].

Adrenal cortisol concentration in CBA mice tended to decrease on days 10 and 28, but increased by 1.7 times on day 56 (compared to the previous stage of study). It should be emphasized that cortisol concentration in AG progressively decreased in C57Bl/6 mice. Interstrain differences in adrenal cortisol concentration were revealed 56 days after infection and associated with opposite changes in the level of this hormone.

Adrenal progesterone concentration in mice of both strains decreased 10 days after infection. Progesterone concentration in AG increased by 2-3 times on day 28. By the 56th day adrenal progesterone concentration was below the basal level in CBA mice, but remained high in C57Bl/6 mice.

Progression of candidiasis in mice of both strains was accompanied by the development of hypocorticism. C57Bl/6 and CBA mice showed a persistent and phasic course of hypocorticism, respectively. These data are consistent with the results of clinical observations. Published data show that candidiasis is often accompanied by adrenal insufficiency [13]. Progesterone serves as a precursor of glucocorticoids. We found that adrenal progesterone concentration increases in C57Bl/6 mice. These animals exhibited low concentration of cortisol in the blood and AG during the late postinfection period. Our findings suggest that the early and late stages of steroidogenesis in AG are uncoupled during candida infection.

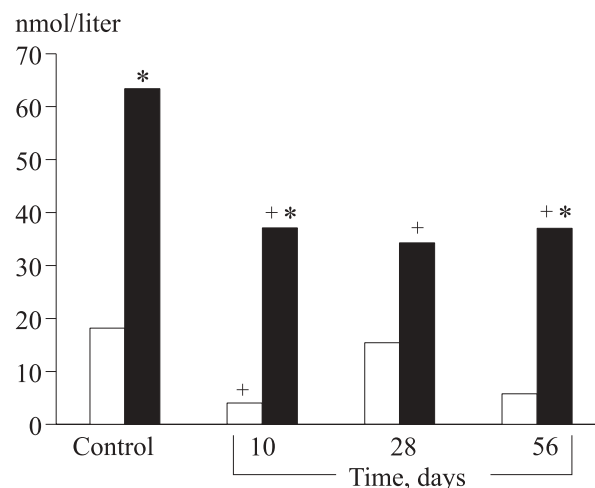


Fig. 1. Blood cortisol concentration in mice of opposite strains with progressive experimental candidiasis. Here and in Fig. 2: light bars, CBA; dark bars, C57Bl/6. * $p < 0.01$ compared to CBA; + $p < 0.02$ compared to the control.

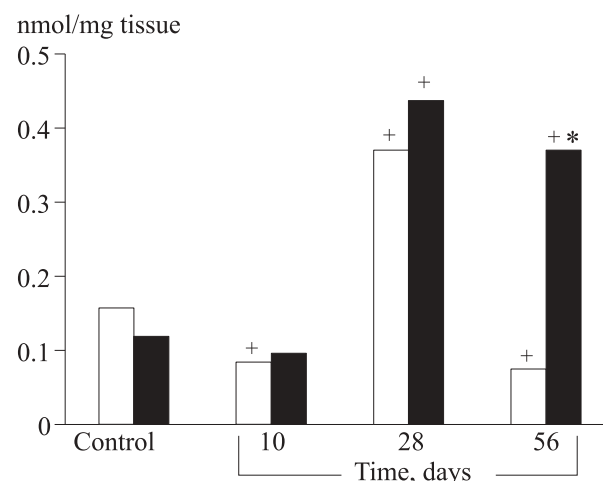


Fig. 2. Adrenal progesterone concentration in mice of opposite strains with progressive experimental candidiasis.

Infection of experimental animals with *C. albicans* can modulate functional activity of the adrenal cortex. One of the mechanisms for this effect suggests

TABLE 1. Adrenal Cortisol Concentration in Mice of Opposite Strains with Progressive Experimental Candidiasis ($M \pm m$, nmol/mg tissue)

Postinfection period, days	Strain					
	CBA			C57Bl/6		
	median	25%	75%	median	25%	75%
0	5.68	4.3	7.57	3.51	1.77	6.44
10	4.57	3.73	5.62	3.11	1.67	5.57
28	4.12	3.92	4.22	4.13	2.24	4.37
56	7.22	5.92	8.42	2.36*	1.09*	2.52*

Note. 25% and 75%, interquartile ranges. * $p < 0.01$ compared to CBA (Mann—Whitney test).

that microorganisms synthesize signal substances typical of higher animals (*e.g.*, steroid hormones) [10].

CBA and C57Bl/6 mice differ in the subcellular organization of AG [9], metabolism of steroid hormones in the liver [8], and genetically determined nonspecific resistance and immune response [3,6].

Our results indicate that functional activity of the adrenal cortex in mice of opposite strains undergoes various changes during candidiasis. These findings complement published data on symbiotic relationships between *C. albicans* and macroorganism. We conclude that host genotype can determine the variability of these relationships.

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