PRIMATOLOGY

Hormonal Function of the Adrenal Glands in Men and Monkeys in Hemoblastoses and during Aging

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Similar changes in the functioning of the adrenal glands (activation of cortisol synthesis due to a more complete utilization of its biochemical precursors and reduced formation of dehydroepiandrosterone and its sulfate fraction) are demonstrated in men and monkeys in hemoblastoses and during aging. It is assumed that being adaptive and nonspecific in nature, these changes lead to hormonal imbalance promoting the development of senile involution processes in patients and animals with severe chronic disease.

Key Words: *adrenal cortex; chronic stress; aging*

Systemic studies of the function of the adrenal cortex in leukemic patients have demonstrated a dissociation between the plasma level of cortisol and most of its biosynthetic precursors as well as adrenal androgens in the majority of patients [3-5]. The content of pregnenolone (Δ5P), 17-hydroxypregnenolone (17-Δ5P), 17-hydroxyprogesterone (17-Δ4P), and dehydroepiandrosterone (DHA) was decreased against the background of increased or unchanged concentration of cortisol. Possible adaptive and nonspecific nature of these phenomena was discussed [4,5]. Similar changes in the level of cortisol, its biochemical precursors, and DHA were noted in healthy men during aging [6,12]. This finding points to the presence of a universal, most probably adaptive, reaction of the adrenal cortex in men during chronic stress induced by pathological process and during aging.

In light of this and taking into account the fact that human and simian adrenals produce similar amounts of DHA and its sulfate fraction (DHAS), it seems interesting to study the endocrine function of the adrenal glands in hemoblastoses and during aging not only in men but also in laboratory monkeys. This study allowed us to evaluate, on the one hand, the universal biological nature of this relationship and, on the other hand, the prospects of using primates as an experimental model in the study of problems related to chronic stress induced by pathological process and endocrinological problems of aging.

The present study presents a comparative investigation of the functioning of the adrenal glands in men and monkeys (*Papio hamadryas*) in hemoblastoses and during aging.

MATERIALS AND METHODS

The study was performed on 93 healthy men aged 22-90 years (residents of the Krasnodar region, Adygy, and Abkhazia) and 37 male hamadryas baboons (*Papio hamadryas*) aged 6-26 years from Sukhumi and Adler breeding centers. The men were divided into 4 age groups: 25-35 years (group 1, n=11), 36-60 years (group 2, n=43), 61-74 years (group 3, n=27), and 75-90 years (group 4, n=12). The monkeys were also divided into 3 groups: 6-9 years (group 1, n=20), 10-15 years (group 2, n=14), and 20-26 years (group 3, n=3).

Twenty-six patients with chronic lymphoid leukemia were examined; of them 14 patients had chronic myeloleukemia and 13 patients had acute leukemia.

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Twelve male hamadryas baboons had pronounced clinical symptoms of hemoblastosis [1]. Blood from patients with leukemia was obtained from the clinics, blood samples from monkeys with hemoblastoses were provided by the Institute of Medical Primatology, Russian Academy of Medical Sciences, Sochi. The patients were examined before treatment. Their somatic state corresponded to the state of marked clinical manifestations; the history of the disease varied from several weeks to 2 years.

The function of the adrenal glands was assessed by the content of steroid hormones and their precursors in peripheral blood. Blood was drawn at 10:00-11:00. from the ulnar vein using heparin as anticoagulant. The content of DHA, Δ5P, 17-Δ5P, and 17-Δ4P was measured by radioimmunoassay (RIA) after purification of the steroids on celite columns, DHAS and 11-deoxycortisol were measured by RIA without chromatography, and cortisol was determined by competitive binding. The data were processed using the Student's *t* test.

RESULTS

The content of cortisol was considerably increased in all groups of leukemic patients and monkeys. The level of 11-deoxycortisol, a direct biochemical precursor of cortisol, was practically unchanged. The concentration of other precursors (Δ5P, 17-Δ5P, and 17-Δ4P) and adrenal androgens (DHA) was significantly or insignificantly decreased (Table 1), these changes being more pronounced in younger patients.

Similar changes in adrenal steroidogenesis were previously noted not only in leukemia but also in other cancer and noncancer diseases [5]. Analogous shifts in the content of cortisol and DHA were observed by other researchers [11] in some severe chronic diseases. In hamadryas baboons, a long-term stress (experimental hypokinesia or repeated immobilization) also induce dissociation between the content of cortisol and its major biochemical precursors [2].

No considerable changes in the content of cortisol and 11-deoxycortisol were found in healthy men and monkeys of different ages (Figs. 1 and 2). However, the content of Δ5P, 17-Δ5P, and 17-Δ4P as well as blood concentration of DHA and DHAS progressively decreased during aging, being minimal in old individuals (Figs. 1 and 2).

Thus, we observed similar shifts in the blood level of adrenal steroids in men and monkeys with hemoblastoses and during aging, which is indicative of a universal reaction of the adrenal glands to pathology and aging.

Changes in adrenal steroidogenesis in hemoblastoses are most probably adaptive in nature and reflect the reaction of the adrenal cortex to chronic stress induced by pathological process. Unlike acute stress accompanied by a concordant rise of the content of cortisol, all its precursors, and adrenal androgens in the peripheral blood, decreased concentrations of Δ5P, 17-Δ5P, 17-Δ4P, and DHA during chronic stress probably reflect an adaptive rearrangement of the adrenal steroidogenesis directed towards a long-term maintenance of an optimal level of cortisol, a vital hormone, and prevention of adrenal cortex depletion through a more complete utilization of cortisol precursors and suppressed biosynthesis of other corticosteroids (in particular, DHA and DHAS).

TABLE 1. Peripheral Blood Content of Cortisol, 11-Deoxycortisol, Δ5P, 17-Δ5P, 17-Δ4P, and DHA in Patients and Male Hamadryas Baboons with Hemoblastoses (*M*±*m*, nmol/liter)

Groups (age, years; number of individuals)	Cortisol	11-Deoxy-cortisol	Δ5P	17-Δ5P	17-Δ4P	DHA
Men						
Healthy (67±0.7; *n*=27)	367.0±33	11.6±1.5	3.9±0.5	2.4±0.3	2.2±0.2	6.3±0.6
(49±1.2; *n*=43)	375.0±38	11.2±0.9	7.7±0.5	4.2±0.3	4.1±1.0	12.3±0.9
With chronic lymphoid leukemia (66±1; *n*=26)	486.0±22**	12.4±0.6	3.1±0.5	2.1±0.2	2.2±0.2	4.3±03**
With chronic myeloleukemia (50±2; *n*=14)	530.0±61*	13.0±1.6	3.1±0.3**	3.8±0.6	3.6±0.5	9.7±1.4
With acute leukemia (49±3; *n*=13)	610.0±70**	14.2±1.0	3.3±0.3***	2.5±0.6*	2.8±0.4	6.6±0.7***
Monkeys						
Healthy (9.5±0.4; *n*=32)	888.0±18.0	27.0±2.5	2.3±0.3	15.3±1.8		26.3±1.8
With hemoblastoses (9.0±0.8; *n*=12)	2090.0±380.0***	34.2±10.0	2.0±0.7	10.1±2.0*		16.5±1.9***

Note. *p<0.05, **p<0.01, ***p<0.001 compared with healthy men or monkeys of the same age.

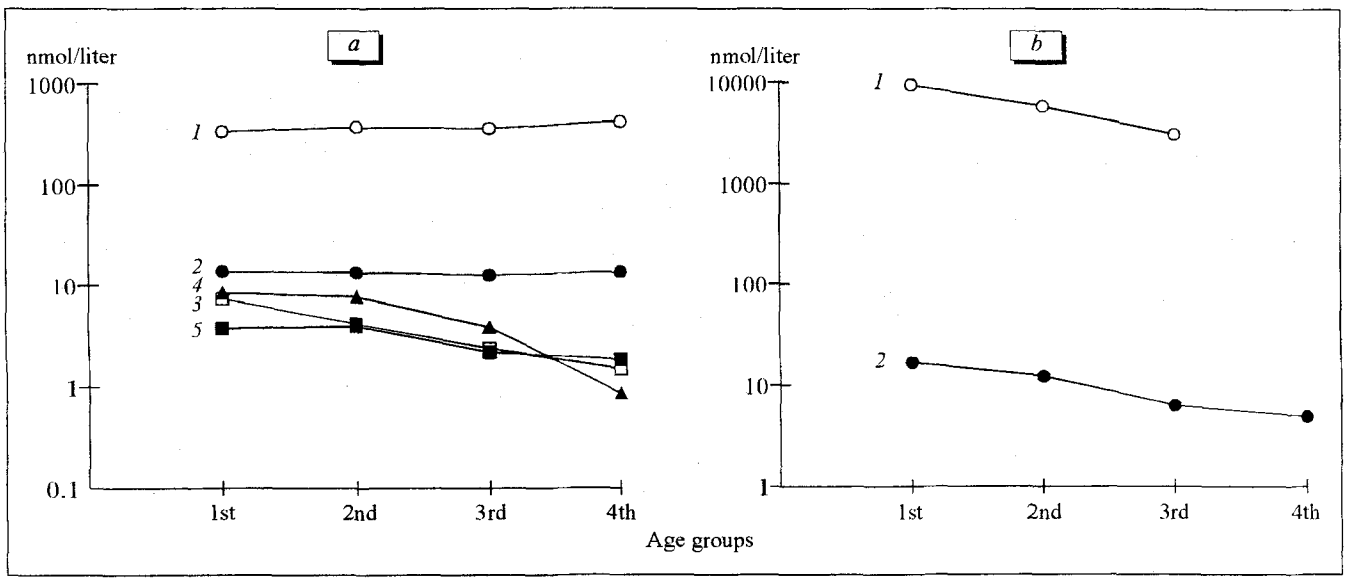

Fig. 1. Peripheral blood content (logarithmic scale) of cortisol (*1*), 11-deoxycortisol (2), 17-Δ5P (3), Δ5P (*4*), and 17-Δ4P (5) (graph *a*); the content of DHA (*1*) and DHAS (2) (graph *b*) in men of different age.

These changes can be partially determined by activation of the latter enzymes of cortisol biosynthesis (for instance, 17α-, 11β-hydroxylases) observed after injection of adrenocorticotropic hormone [8,9].

The observed changes in adrenal steroidogenesis during aging are most probably related to attenuated transformation of cholesterol to D5P, presumably due to inhibition of cholesterol desmolase caused by impaired oxygenation. There are data [7] on reduced activity of mitochondrial enzymes in the adrenal glands of aging men.

However, in both cases changes in adrenal steroidogenesis lead to analogous hormone imbalance in peripheral blood: an absolute or relative rise of cortisol and its immediate precursor 11-deoxycortisol against the background of a reduced content of other cortisol precursors (Δ5P, 17-Δ5P, and 17-Δ4P) as well as DHA and DHAS. Taking into account the important role of adrenal cortex in the integration of nonspecific adaptation processes in the organism, similar changes in the functioning of adrenal cortex in response to chronic stress caused by the disease and during aging can hardly be attributed to an accident. By contrast, numerous clinical and experimental data indicate a close relationship between aging and pathological process, in particular, hemo-

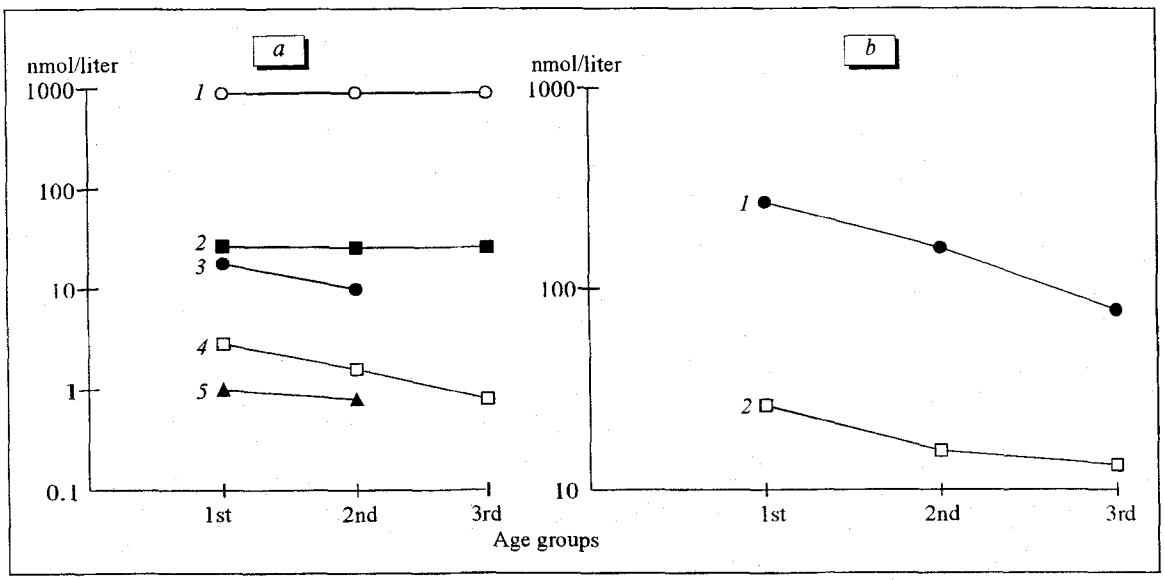

Fig. 2. Peripheral blood content (logarithmic scale) of cortisol (*1*), 11-deoxycortisol (2), 17-Δ5P (3), Δ5P (*4*), and 17-Δ4P (5) (graph *a*); the content of DHA (*1*) and DHAS (2) (graph *b*) in monkeys of different age.

blastosis. In patients with leukemia, the signs of aging develop more rapidly that in healthy subjects of the same age.

Reduced level of adrenal androgens, which may play an important role in the inhibition of aging, accelerate aging against the background of chronic diseases. Clinical and experimental studies showed that DHA (DHAS) possesses antiatherogenic and antitumor activity, prevents the development of such age-related disorders as insulin-independent diabetes mellitus, neurodegenerative processes, and immune disturbances. The decreased level of Δ5P involved in the regulation of brain neuronal activity, and 17-Δ4P, a putative arterial pressure regulator [10], can also be involved.

Of crucial importance is the fact that the adrenal cortex in men and monkeys similarly reacts to pathological process and aging. Taking into account the absence of appreciable secretion of DHA (DHAS) in other animal species, these findings attest to evolutional unity of primates and substantiate the prospects of using hamadryas baboons as an experimental model for studying endocrinological problems of aging and chronic stress induced by a pathological process.

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