CIRCADIAN RHYTHMS OF PLASMA ANDROGEN LEVELS IN *Papio hamadryas* MALES

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KEY WORDS: androgens; circadian rhythm; adaptation; steroid hormones.

A cyclic pattern of function has now been established for the gonads and adrenals of man and animals [1-3, 5]. Changes in biological rhythms due to exposure to various factors have recently begun to engage the attention of research workers. Investigations of this kind have so far been few in number and contradictory in their results. For various reasons such investigations cannot be carried out on man.

The aim of this study was to examine the character of circadian rhythms of the content of androgens, namely testosterone, 5α-dihydrotestosterone, androstenedione, and dehydroepiandrosterone, in the blood plasma of male baboons (*Papio hamadryas*) depending on the ecologic conditions under which they live.

EXPERIMENTAL METHOD

Experiments were carried out on 18 clinically healthy mature male baboons aged 12-18 years and weighing 25-35 kg. The animals were divided into two groups. Group 1 consisted of intact control baboons kept with a group of females and young in large open-air cages. The animals of group 2 were adapted to the experimental conditions: For 15-30 days they were kept in individual metabolic cages, with simulation of blood taking daily, involving temporary fixation of the animals. Blood for determination of steroid hormones was taken in a volume of 8-10 ml from the cubital vein into centrifuge tubes with heparin before adaptation, during the period of adaptation on the 2nd, 4th, 7th, 10th, 15th, 23rd, and 30th days, in the morning, and again at 3-hourly intervals for 24 h. Plasma was obtained by centrifuging the blood at 3000 rpm for 5 min and was kept in the frozen state at −20°C. The blood androgen levels were determined by radioimmunoassay, and the compounds were isolated in a pure form on columns with Celite, using highly specific antisera [4]. Calculation of the standard curve, determination of the steroid concentrations in the samples, and statistical analysis of the results by Student's t test were carried out on the D-3-28 computer by the use of special programs.

EXPERIMENTAL RESULTS

During the period of adaptation considerable changes occurred in the sex steroid hormone levels (Fig. 1). The blood testosterone level of intact males kept in the "harem" averaged from 18 to 24 nmoles/liter. However, the hormone level rose readily during the 30 days of adaptation to reach 50 nmoles/liter, i.e., it increased by 2.5 times.

The concentration of 5α-dihydrotestosterone, the main metabolite of testosterone, also increased statistically significantly ($P < 0.01$), to reach a maximum by the end of the period of adaptation.

The androstenedione level rose by 1.5-2 times during adaptation, but unlike the preceding hormones, it did not rise steadily throughout the period of adaptation.

There was no significant difference in the concentrations of dehydroepiandrosterone in the intact and adapted males. Throughout the 30-day adaptation period its concentration lay between 15 and 20 nmoles/liter.

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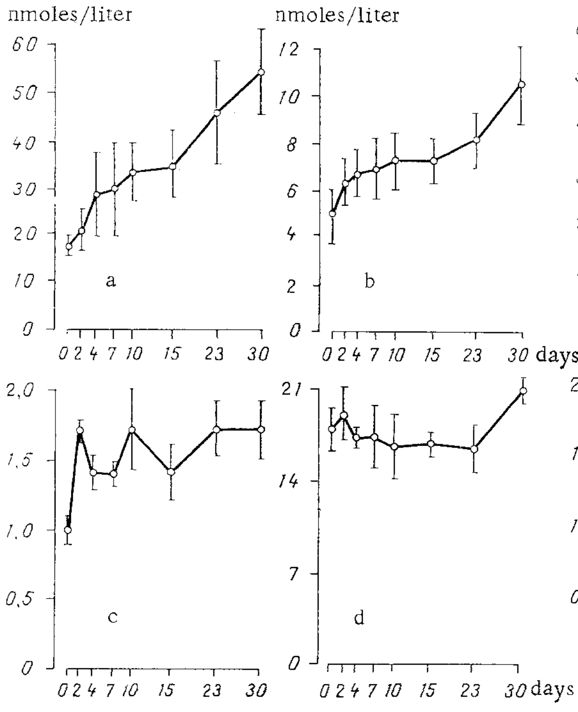

Fig. 1

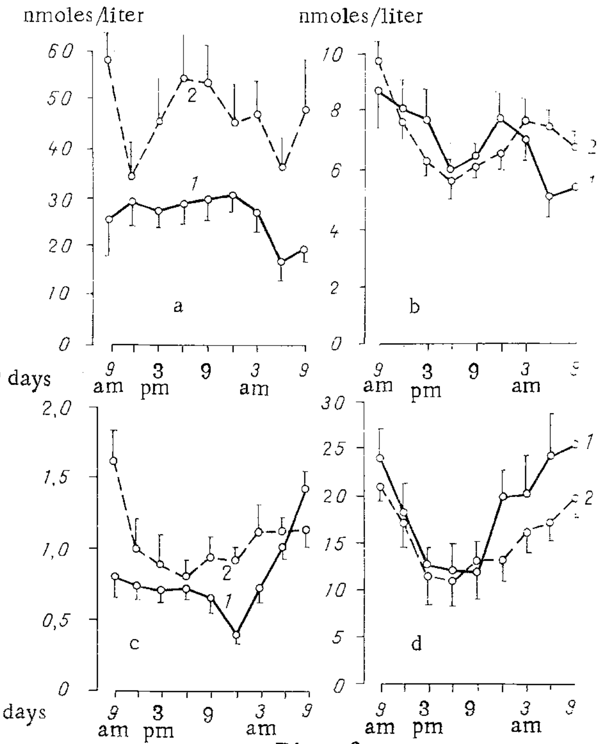

Fig. 2

Fig. 1. Blood androgen levels in male baboons during adaptation (M ± m). Abscissa, duration of adaptation (in days); ordinate, androgen concentration (in nmoles/liter): a) testosterone, b) 5α-dihydrotestosterone, c) androstenedione, d) dehydroepiandrosterone.

Fig. 2. Blood androgen level in male baboons during the 24-h period (M ± m). Abscissa, clock time. 1) Intact animals, 2) adapted animals. Remainder of legend as to Fig. 1.

TABLE 1. Mean Daily Concentration (in nmoles/liter) of Androgens in Blood Plasma of Male Baboons during Adaptation to Experimental Conditions (M ± m)

Androgen	Animals		P
	intact	adapted	
Testosterone	26,8±2,0	47,8±4,3	<0,01
5α-Dihydrotestosterone	7,0±0,8	7,3±0,5	<0,05
Androstenedione	0,7±0,04	1,0±0,10	<0,02
Dehydroepiandrosterone	18,5±3,2	15,6±2,4	<0,05

Preliminary adaptation of the animals to the experimental conditions and the blood-taking procedure had a marked effect on the mean daily basal level of the androgens and the character of their circadian rhythms. In the first place, the mean daily blood testosterone level in the adapted males was higher than that of the intact animals (Table 1).

A distinct circadian rhythm of testosterone was found in the adapted males without a fall in its concentration at 9 a.m. on the following day, characteristic of intact males (Fig. 2). The fact will be noted that monkeys with the lowest initial testosterone level in the morning were found to have the lowest mean daily concentration of this hormone, whereas animals with a maximal morning testosterone concentration had the highest values of mean daily concentration. This indicates that even if the blood hormone level of the adapted monkeys is determined only once a day, this can adequately reflect individual differences in testicular hormonal activity.

Adaptation of the animals was shown to have no significant effect on the character of the dynamics of the plasma 5α-dihydrotestosterone level during the 24-h period. Both in intact and in adapted animals negative correlation was observed between it and the testosterone concentration.

Adaptation of the animals to the experimental conditions led to a very small increase in the mean daily androstenedione level (Table 1). As Fig. 2 shows, there was a moderate decrease in the steroid concentration in the blood of animals adapted for 1 month in the second half of the day, but in the morning its concentration also was a little below the initial level.

The dehydroepiandrosterone level fell steadily during the afternoon in both intact and adapted animals to reach a minimum during the evening. A distinct circadian rhythm of the steroid was found with its acrophase in the early morning.

Thus 5α-dihydrotestosterone, androstenedione, and dehydroepiandrosterone were characterized by a fall in their blood concentration in the evening and a rise in the early morning, whereas in the case of testosterone, one of the principal sex hormones, synthesized in the testes, a circadian rhythm was found with its acrophase in the evening. The clearest circadian rhythms were noted for testosterone and dehydroepiandrosterone.

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IMMUNOCOMPETENT CELLS IN THE BED OF A FULL-THICKNESS SKIN ALLOGRAFT TRANSPLANTED AT DIFFERENT TIMES OF DAY

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The possibility of using natural biological time factors (rhythms) to change the state of a graft has been demonstrated by studies of the chronobiology of skin grafts [10]. The effect of the time of day when the transplantation was done on the degree of destruction of the epithelium of the skin graft and its infiltration by polymorphonuclear leukocytes and lymphocytes, and on the number of viable epitheliocytes was also demonstrated previously [2].

The object of this investigation was to compare the dynamics of the number of immunocompetent cells in the bed of a skin allograft in mice in the course of its rejection, depending on the time of the day of the skin grafting operation.

EXPERIMENTAL METHOD

The organization and conditions of the experiments, the technique of transplantation, the method of obtaining material, and the histological treatment of the grafted skin were all described previously [2]. The number (in units/mm^3) of lymphocytes, immunoblasts, plasmablasts, and juvenile and mature plasma cells was counted in a standard volume of tissue ($648 \cdot 10^{-6}$ mm^3) in the bed of the graft. The significance of differences was determined by the Wilcoxon–Mann–Whitney criterion and also by Student's t test for series with tied pairs.

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