DIURNAL RHYTHM OF THE CORTICOSTEROID RESPONSE TO ACTH AND PHYSICAL EXERTION

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The 11-hydroxycorticosteroid (11-HCS) concentration in the peripheral blood of rats is maximal at 3 P.M. The greatest response to injection of exogenous ACTH was recorded at the same time. The maximum of changes in the 11-HCS concentration in the adrenals and peripheral blood in response to physical exertion does not coincide with the maximum of the basal level of corticosteroids or of the response to ACTH, but takes place during the evening or night, i.e., in the period of greatest physiological activity of the animals.

Attention has been drawn in recent years to the study of the circadian periodicity of physiological functions, reflecting adaptation of the body to external environmental conditions [5, 7]. Among many variables, the diurnal rhythms of corticosteroid regulation are of great importance, for according to some authorities [3, 8] they are synchronizers (endogenous timers) responsible for the temporal coordination of many peripheral intracellular processes. The sensitivity of the organism to stressors and to extreme stimuli has been shown to be linked with the corticosteroid rhythms [1, 6, 10]. Many aspects of the muscular activity of man and animals are known to depend on the functional state of the adrenal cortex [2, 4]. It can accordingly be postulated that the ability of animals and man to perform a particular volume of muscular work at different times of day or night will be connected with the diurnal rhythms of the corticosteroids.

This paper describes the results of experiments to study the diurnal rhythm of adrenocortical function, the reactivity of the adrenals to exogenous ACTH at different times of day or night, and the dependence of the corticosteroid response to physical exertion on the diurnal rhythm of activity of the animal.

EXPERIMENTAL METHOD

Experiments were carried out during the spring on 184 noninbred male albino rats weighing 130-180 g. Altogether 3 series of experiments were carried out.

Series I consisted of intact animals which were used to study the rhythm of adrenocortical function. To study the 11-HCS concentration the animals were decapitated in groups every 3 h during the 24-h period. The rats of series II were divided into groups which received ACTH by intramuscular injection in a dose of 3 units/100 g body weight at 2 and 8 A.M. and 2 and 8 P.M., and were decapitated 1 h after the injection. The rats of series III also were divided into groups and were compelled to swim at 30°C for 1 h, after which they were decapitated. The state of adrenocortical function was judged from the 11-HCS concentration in the peripheral blood plasma and in the adrenal tissue, determined fluorometrically [11].

EXPERIMENTAL RESULTS

The experiments revealed no significant changes in the total 11-HCS concentration in the adrenal tissues which could be assessed as diurnal rhythm, whereas on the basis of the plasma 11-HCS concentra-

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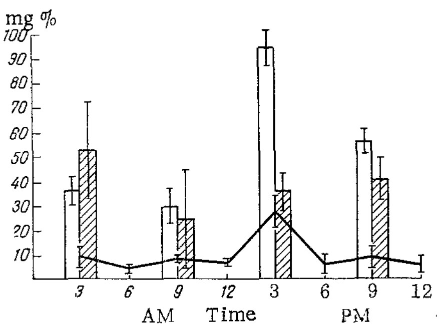

Fig. 1

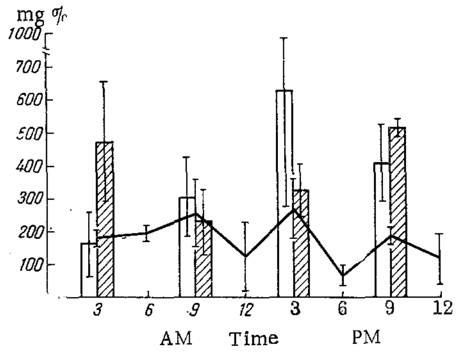

Fig. 2

Fig. 1. Effect of ACTH and physical exertion on 11-HCS concentration in peripheral blood plasma at different times of day and night. Curved line represents basal level of 11-hydroxycorticosteroids; unshaded columns show 11-HCS level after injection of ACTH; shaded columns show 11-HCS level after physical exertion.

Fig. 2. Effect of ACTH and physical exertion on 11-HCS concentration in adrenals at different times of day and night. Legend as in Fig. 1.

TABLE 1. Dynamics of 11-HCS Concentration in Blood Plasma (in $\mu g\%$) after Physical Exertion and Administration of ACTH at Different Times of Day and Night

Group of animals	Time of determination			
	3 AM	9 AM	3 PM	9 PM
Intact	9,8±1,9	8,7±0,5	27,6±2,89	9,2±2,07
Injection of ACTH (5 units intramuscularly)	36,4±2,8*	30,0±3,2*	94,0±7,2*	55,7±6,0*
Swimming (1 h)	52,0±9,0*	23,7±9,2	36,1±3,8	40,9±4,1*

*Here and in Table 2 difference statistically significant ($P < 0.05$) compared with figures for diurnal rhythm of intact rats.

tion these changes were clearly marked. Determination of the total fluorescent substances in homogenates of adrenal tissue evidently does not give a correct idea of the diurnal dynamics of the corticosteroid concentration in the adrenals. The lowest 11-HCS level in the blood plasma is observed in rats in the morning (6-9 A.M.), when the experimental animals are in a state of minimal motor activity. The basal corticosteroid level reaches a maximum at 3 P.M., but by 6 P.M. the blood hormone level was significantly reduced, thereafter remaining substantially unchanged (Fig. 1). There are reports in the literature of circadian fluctuations of a similar character in the plasma corticosterone level in albino rats [1, 9]. In the experiments in which ACTH was given, judging from changes in the 11-HCS concentration in the blood plasma and adrenals, the maximum of the response coincided with the maximum of the basal rhythm of adrenal function, confirming results described previously [10]. The adrenals continued to give a marked response to injection of exogenous ACTH during the evening (Tables 1 and 2). During the next 12 h there was a significantly smaller increase in the 11-HCS concentration in the plasma in response to injection of ACTH. Between 3 and 9 A.M. the increase in plasma corticoid concentration was 26-21 $\mu g\%$, compared with the 66–47 $\mu g\%$ recorded between 3 and 9 P.M. Administration of ACTH at 3 and 9 P.M. led to an increase of more than twice in the 11-HCS concentration in the adrenals. During the morning no such effect was observed (Fig. 2).

The reactivity to ACTH was thus maximum during the afternoon and evening.

In the experiments with physical exertion the increase in the 11-HCS concentration at 3 P.M. (the period of maximal basal level and maximal reactivity to injection of ACTH) was very small. Physical exertion induced a considerable increase in the 11-HCS concentration in the blood plasma and adrenals in the opposite phase, at 3 A.M. It will be noted that the second point of marked response to physical exertion

TABLE 2. Dynamics of 11-HCS Concentration in Adrenals (in $\mu g\%$) after Administration of ACTH and Physical Exertion at Different Times of Day and Night

Group of animals	Time of determination			
	3 AM	9 AM	3 PM	9 PM
Intact	180,3±11,9	254,3±47,8	271±40	182±20,3
Injection of ACTH (5 units intramuscularly)	159,8±42,8	303±66,1	620±153	408±59,5*
Swimming (1 h)	471,5±86,8*	225±45,7	319,6±36,2	513,4±24,4*

occurred at 9 P.M. Considering the activity of the animals and their behavior at this time of day, the coincidence of the phase of maximal adrenal response to physical exertion with the period of maximal physiological activity of the animals will be noted. The discrepancy between the times of the most marked corticosteroid response to injection of ACTH and to physical exertion cannot be attributed to the exogenous nature of the ACTH injected. The maximal adrenal response to injection of ACTH coincided with the maximum of the basal level of 11-HCS in the peripheral blood and adrenal tissues. The evident discrepancy between the diurnal rhythm of the response to injection of ACTH and of the basal 11-HCS level, on the one hand, and the response to physical exertion on the other hand, requires further experimental analysis. Presumably the absence of changes in the state of adrenal function during physical exertion in the morning and afternoon is connected with the level of tuning of the central mechanisms leading to the response of the hypophyseo-adrenal system to motor activity.

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