

13. L. G. Lajtha, The Use of Isotopes in Hematology [Russian translation], Moscow (1963).
14. H. Maurer, Disc Electrophoresis and Related Techniques of Polyacrylamide Gel Electrophoresis, De Gruyter, New York (1971).
15. A. G. E. Pearse, Histochemistry: Theoretical and Applied, Little, Brown and Co., Waltham, Mass. (1960).
16. R. H. Reiff, J. Y. Nutter, D. M. Donohue, et al., Am. J. Clin. Path., 30, 199 (1958).
17. S. A. Rosenberg and G. Guidotti, J. Biol. Chem., 243, 1985 (1968).

# FUNCTIONAL STATE OF THE HYPOTHALAMO-HYPOPHYSEO-ADRENAL SYSTEM IN GUINEA PIGS EXPOSED TO RADIAL ACCELERATION

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The effect of an increased gravitational field on activity of the hypothalamo-hypophyseo-adrenal system was studied in experiments on guinea pigs. A single exposure led to activation of this system; however, during repeated exposure to radial acceleration the animals ceased to respond by an increase in the blood corticosteroid level, evidently on account of adaptation of the central components of the system and not of exhaustion of the adrenal cortex.

KEY WORDS: *Hypothalamo-hypophyseo-adrenal system; radial acceleration; corticosteroids.*

The study of the action of acceleration and the associated overloading on the neuroendocrine regulatory mechanism is an urgent problem in aviation and space medicine [2].

In this investigation the effect of single and repeated exposure to radial acceleration on the state of the hypothalamo-hypophyseo-adrenal system, the hormones of which have an important influence on the resistance of the body to unfavorable environmental factors [6, 7], was studied.

## EXPERIMENTAL METHOD

Experiments were carried out on 96 male guinea pigs weighing 320-400 g. In these animals, as in man, the main adrenocortical hormone is cortisol (17-HCS) [4, 8]. Its concentration was determined in the blood plasma [5] of the animals after they had been spun in a special centrifuge with a lever 60 cm long. Twenty minutes before exposure to radial acceleration (11g for 10 min) the guinea pigs received an intraperitoneal injection of methyl-diazine (10 mg/kg), chlorpromazine (10 mg/kg), or physiological saline. Control animals received physiological saline over a period of 11 days. Blood samples were taken from the heart in the morning. The results were subjected to statistical analysis [1].

## EXPERIMENTAL RESULTS AND DISCUSSION

The 17-HCS concentration in the blood plasma of the guinea pigs 90 min after a single spinning was much higher than in the control animals. During repeated acceleration, starting from the sixth day, the 17-HCS concentration was almost unchanged after spinning (Table 1).

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TABLE 1. Effect of Increased Gravitational Field on 17-HCS Concentration in Blood Plasma of Guinea Pigs ( $M \pm m$ )

Day of experiment	17-HCS concn., $\mu\text{g}\%$		P
	control	expt.	
1	38,6 $\pm$ 3,3*	80,4 $\pm$ 4,6	<0,05
3	48,6 $\pm$ 2,3	64,4 $\pm$ 4,8	<0,05
6	40,3 $\pm$ 3,2	45,7 $\pm$ 5,7	>0,05
9	38,4 $\pm$ 4,2	54,3 $\pm$ 9,1	>0,05
11	46,6 $\pm$ 3,1	47,5 $\pm$ 8,7	>0,05

\*Each figure is mean of 6-8 determinations.

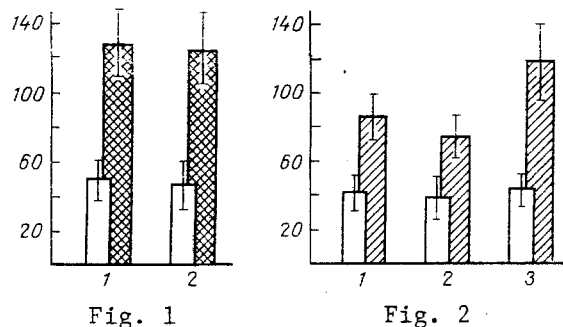


Fig. 1. Effect of ethimizole on blood plasma 17-HCS concentration in guinea pigs. Ordinate, 17-HCS concentration (in  $\mu\text{g}\%$ ). 1) Intact animals; 2) animals exposed to repeated spinning on centrifuge. Unshaded columns) before injection; shaded columns) 2 h after injection of ethimizole. Values of  $M \pm m$  shown.

Fig. 2. Response of hypophyseo-adrenal system of guinea pigs to single exposure to an increased gravitational field: 1) animals receiving physiological saline; 2) animals receiving methyldiazine; 3) animals receiving chlorpromazine. Unshaded columns) control; shaded columns) 90 min after spinning. Remainder of legend as in Fig. 1.

The gradual weakening of the response of the adrenal cortex to repeated radical acceleration could be attributed either to habituation (training) of the central mechanisms or to exhaustion of the reserves of the glands. To study this question the substance ethimazole (ethylamide of imidazolecarboxylic acid), which increases adrenocortical activity in guinea pigs through its influence on the hypothalamic regulation of ACTH secretion [3], was used. Ethimazole was injected intraperitoneally into the guinea pigs 20-24 h after the last spinning in a dose of 20 mg/kg, and blood samples were taken from the heart 2 h later. The stimulating effect of ethimazole on the adrenal cortex was completely preserved in animals exposed to radial acceleration for 11 days (Fig. 1). Weakening of the response of the hypophyseo-adrenal system to repeated radial acceleration was thus the result not of exhaustion of this system but of adaptation of the central mechanisms to the corresponding procedure. This conclusion is also confirmed by the fact that some autonomic responses arising in guinea pigs during exposure to an increased gravitational field (an increase in the heart and respiration rates, disturbances of movement coordination) gradually diminished and disappeared completely on the 6th-11th day of spinning.

To study the possible role of central cholinergic and adrenergic mechanisms in the action of the increased gravitational field on the hypophyseo-adrenal system the effectiveness of preliminary injection of the central muscarinic cholinolytic drug methyldiazine (10 mg/kg) or the adrenergic blocking drug chlorpromazine (10 mg/kg) was studied. Neither substance had any significant effect on the manifestation of the adrenocortical response to a single spinning (Fig. 2). Consequently, stimulation of the function of the hypothalamo-hypophyseo-adrenal system during a single exposure to radial acceleration evidently is not dependent on integrity of the central cholinergic or adrenergic mechanisms.

#### LITERATURE CITED

1. M. L. Belen'kii, Elements of Quantitative Evaluation of a Pharmacological Effect [in Russian], Leningrad (1963).
2. V. V. Parin, Selected Works, Vol. 2, Space Biology and Medicine. Cybernetics [in Russian], Moscow (1974).
3. V. E. Ryzhenkov, "The action of central neurotropic drugs on the pituitary-adrenocortical system in its various states," Author's Abstract of Doctoral Dissertation, Leningrad (1968).
4. N. A. Yudaev and S. A. Afinogenova, Probl. Éndokrinol., No. 2, 12 (1962).
5. N. A. Yudaev and Yu. A. Pankov, Probl. Éndokrinol., No. 2, 35 (1958).
6. K. Lissak and E. Endröczi, Neuroendocrine Regulation of Adaptive Activity [in Russian], Budapest (1967).
7. H. Selye, Essays on the Adaptation Syndrome [Russian translation], Moscow (1960).
8. G. Telegdy, E. Endröczi, and K. Lissak, Acta Physiol. Acad. Sci. Hung., 18, 211 (1960).

#### EFFECT OF CYTOSTATIC AGENTS ON DEVELOPMENT OF THE FEBRILE REACTION TO INJECTION OF BACTERIAL PYROGEN

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The development of the febrile reaction to injection of bacterial lipopolysaccharide (pyrogenal) in rabbits after preliminary treatment with actinomycin D and cortisone was studied. This treatment did not change the reactivity of the temperature regulating centers of the rabbits to endogenous pyrogen. After intravenous injection of the bacterial pyrogen the febrile reaction was considerably shortened, and after intracisternal injection of the pyrogen the reaction was sharply inhibited. These results indicate an important role of polymorphonuclear leukocytes and of endogenous pyrogen formation by these cells in the mechanism of fever in response to the action of bacterial pyrogen.

KEY WORDS: *Fever; pyrogens; inflammation; cytostatic agents.*

In the modern view the development of fever in various pathological conditions is due to endogenous pyrogens formed by the blood cells, mainly by polymorphonuclear leukocytes and monocytes. Endogenous pyrogens are considered to be natural and adequate stimuli for the temperature regulating centers, and the role of bacterial pyrogens is simply to stimulate the synthesis of endogenous pyrogens by the leukocytes [2, 4, 6, 10]. At the same time, it is known that a high fever can be observed in patients with agranulocytosis or severe granu-

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