The role of model investigations is particularly important in the study of such complex problems as sudden death. Since no single model can reproduce the natural course of coronary heart disease or give exhaustive information about its pathophysiology, we must rely on investigations conducted on a whole range of experimental models in order to elucidate problems connected with malignant arrhythmias, and to develop effective methods of their treatment and prevention.

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LIPID PEROXIDATION IN THE ADRENAL CORTEX IN EXHAUSTING STRESS

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Long-term exposures to extremal factors cause collapse of the adaptation process [4]. The reason for this phenomenon has not yet been explained. Nevertheless, it is logical to suggest that the collapse of adaptation may be connected with disturbance of the normal functioning of the endocrine system and, in particular, of the adrenal cortex. The adrenal cortex occupies a key position in the development of the adaptation syndrome, and the function of these glands is considerably depressed during prolonged, exhausting stress [4].

Lipid peroxidation (LPO), if activated excessively in many tissues, gives rise to destructive changes that are reflected in the rate of cellular metabolism and, consequently, in the specific function of tissue. In the adrenal cortex the existence of large amounts of biological antioxidants (ascorbic acid and α-tocopherol) evidently prevents the uncontrolled development of LPO [1, 6]. During exhausting stress, however, the situation may change.

The aim of this investigation was to determine the rate of LPO and the ascorbic acid and α-tocopherol levels in the adrenal cortex in the course of exhausting stress.

EXPERIMENTAL METHOD

Experiments were carried out on male rabbits (Soviet Chinchilla breed) weighing 2-2.5 kg and on noninbred male albino rats weighing 180-200 g. Stress was induced by immobilization by the limbs in the supine position for 6, 12, 24, 48, and 72 h. Each group consisted of six animals. After decapitation the adrenal cortex was separated from the medulla and used to determine concentrations of diene conjugates [7], α-tocopherol [12], and ascorbic acid derivatives [5]. 11-Hydroxycorticosteroids (11-HCS) in the blood plasma were determined by the method in [3].

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TABLE 1. Changes in Plasma 11-HCS Level and Concentrations of Diene Conjugates in Adrenal Cortex of Rabbits and Rats during Stress (in % compared with control, $M \pm m$)

Species of animals	Parameter	Duration of stress, h					
		0	6	12	24	48	72
Rabbits	11-HCS	100,0±14,1	216,2±18,4**	174,4±11,0*	147,8±11,2***	91,6±16,5	75,8±17,8
	Diene conjugates	100,0±5,5	95,9±7,3	87,8±19,5	117,2±13,4	127,6±11,0***	147,0±7,9**
Rats	11-HCS	100,0±5,9	307,2±2,6**	271,3±13,2*	268,9±13,8*	162,8±15,2*	67,6±13,8
	Diene conjugates	100,0±7,6	76,0±10,1	98,3±11,6	132,6±10,0	149,4±10,1	220,2±16,7**

Legend. $*p < 0.01$, $**p < 0.001$, $***p < 0.05$ compared with initial level.

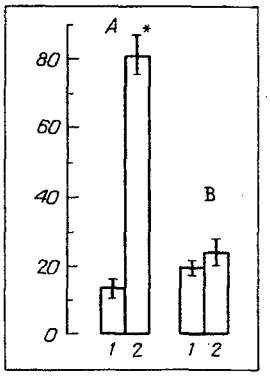

Fig. 1. Effect of ACTH on plasma 11-HCS levels in normal rats (A) and rats exposed for 72 h to immobilization stress (B). 1) Without ACTH, 2) 1 h after injection of 5 units ACTH. Ordinate, 11-HCS level (in μg%).

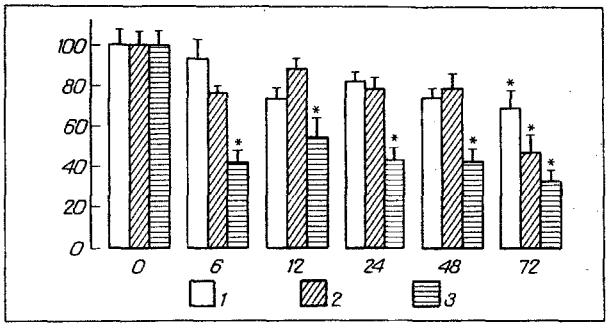

Fig. 2. Concentrations of α-tocopherol (1), ascorbic acid (2), and total concentration of dehydroascorbic and diketogulonic acids (3) in rabbit adrenal cortex during prolonged immobilization stress. Abscissa, duration of stress (in h); ordinate, levels of various parameters (in % of initial).

EXPERIMENTAL RESULTS

Prolonged exposure to immobilization stress led to a fall in the blood corticosteroid levels of the animals (Table 1). Compared with the stage of resistance, the fall was observed in both rabbits and rats toward the 48th hour of immobilization. Since the blood corticosteroid levels reflect the rate of steroid production in the adrenal glands [8] it can be postulated that prolonged stress leads to depression of adrenocortical function. However, the cause of this depression may be not only changes in metabolism in the adrenal glands themselves, but also reduced release of ACTH into the blood stream. Experiments were carried out to determine functional reserves of the adrenal cortex under normal conditions and after 72 h of stress by ACTH loading [9]. The results given in Fig. 1 show that administration of ACTH led to a sixfold increase in the blood steroid levels of normal animals. Meanwhile in stressed animals their levels did not rise significantly. Consequently, depression of adrenocortical function may be connected, not with ACTH deficiency, but with changes taking place in the adrenal glands themselves. Determination of diene conjugate levels in the adrenal cortex of the rats and rabbits showed (Table 1) that at times corresponding to a reduced rate of steroid production the concentrations of LPO products increased appreciably.

The adrenal cortex differs from other tissues in its high concentrations of unsaturated lipids [10] and of metals of transitional valency [2], and these constitute the basis for development of LPO. It has also been shown that cytochrome P-450-reductase, which is involved in steroid hydroxylation and is located in adrenocortical cells both on the endoplasmic reticulum and in mitochondria, may also be a component initiating free radical formation [11].

The adrenal glands are known to be rich in natural antioxidative compounds which prevent the development of LPO. In particular, they are rich in ascorbic acid [1] and α-tocopherol [6]. In high concentrations, naturally, they prevent activation of LPO.

It is interesting to study the time course of changes in the concentrations of these compounds in the adrenal cortex during prolonged stress (Fig. 2). A fall in the total concentration of ascorbic acid derivatives has been observed after exposure to the stress factor for as little as 6 h. This is the case mainly with dehydroascorbic and diketogulonic acids. The ascorbic acid concentration fell significantly only after 72 h. Changes in the α-tocopherol levels were exactly the same.

The results thus suggest that during prolonged stress associated with exhaustion of the functional resources of the adrenal cortex activation of LPO processes takes place in these glands. One possible cause of this activation of LPO is a fall in adrenocortical levels of ascorbic acid and α-tocopherol.

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