Labilization of particles following injection of suramin, it must be noted, is connected with the formation of autophagosomes, which have greater "fragility" [10]. Autophagy is observed after injection of Triton WR 1339, suramin, and some other LTAs and may be a manifestation of a nonspecific cellular reaction to injection of these substances.

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ACTION OF PREDNISOLONE ON ^{3}H-CATECHOLAMINE SYNTHESIS IN RAT ADRENALS DURING PHYSICAL FATIGUE

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It was shown previously that during severe physical fatigue noradrenalin and adrenalin synthesis in the adrenals from tyrosine and dopa is inhibited in rats [3]. Glucocorticoids both in vivo and in vitro normalize catecholamine synthesis in such animals but do not affect the synthesis of these amines in intact rats. It has been found that the stimulating effect of glucorticoids on depressed catecholamine synthesis is manifested only if tyrosine is used as the precursor [5]. Under the influence of hydrocortisone, synthesis of ^{3}H-noradrenalin and ^{3}H-dopamine from ^{3}H-tyrosine also is activated in the rat CNS [6]. These facts suggest that glucocorticoids are evidently universal regulators of the intensity of catecholamine synthesis both in the central and in the peripheral regions of the sympathico-adrenal system.

In the present investigation, which was aimed at studying the effect of the glucorticoid prednisolone on the ability of the adrenals to synthesize catecholamines during physical fatigue in animals, a radioisotopic method was used. By so doing, by contrast with previous studies [1, 2], it was possible to use the principal precursor of these amines, namely tyrosine, in low physical concentrations and also to investigate dopamine synthesis under these conditions. Animals in a state of severe physical fatigue after swimming for 8 h served as the experimental model.

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TABLE 1. Synthesis of ^{3}H-Catecholamines (in cpm/g tissue) in Adrenals of Rats during Physical Fatigue and after Administration of Prednisolone (M ± m, n = 12)

Group of adrenals	^{3}H-adrenalin + ^{3}H-noradrenalin	P	^{3}H-dopamine	P
1 (control)	84 103±7 738	—	133 607±7 850	—
2 (swimming)	63 451±2 286	<0,02	124 883±7 986	>0,05
3 (prednisolone)	84 036±3 442	>0,05	159 757±10 222	>0,05
4 (swimming + prednisolone)	109 252±7 835	<0,05* <0,01 †	195 147±15 405	<0,01* <0,01 †

*Compared with group 1.
†Compared with group 2.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred male rats weighing 200-250 g in two groups: controls, and after swimming for 8 h at 30-32°C. Synthesis of ^{3}H-catecholamines was investigated in four groups of adrenals: 1) adrenals of control rats, 2) adrenals of control rats incubated in the presence of prednisolone, 3) adrenals of swimming rats, 4) adrenals of swimming rats incubated in the presence of prednisolone.

The animals were electrocuted and decapitated. The adrenals were incubated in Tyrode's solution in 5-ml chambers at 37°C, saturated with oxygen. The adrenals of all groups were preincubated in Tyrode's solution for 30 min. After the change of solution, prednisolone was added to the adrenals of groups 1 and 3 in a final concentration of 20 μg/ml, after which incubation was resumed for 30 min. Next, ^{3}H-tyrosine (specific activity 124.1 mCi/mmole, concentration in incubation medium 20 μCi/ml) was added to all the samples. The adrenals were incubated with the labeled precursor for 30 min. At the end of incubation, the preparations in all the tests were washed five times with Tyrode's solution. After washing, the adrenals were homogenized in 5 ml of 0.2 M $HClO_4$ with 0.5% EDTA and centrifuged after 30 min at 2000g. The supernatant was neutralized to pH 6.5. Chromatographic separation of the catecholamines was carried out on columns with the ion-exchange resin Dowex-50 (from Serva, West Germany) in the sodium form. The mixture of ^{3}H-noradrenalin and ^{3}H-adrenalin was eluted from the columns with 5 ml 1 M HCl, after which the ^{3}H-dopamine was eluted with 5 ml of 2 M HCl [1]. Radioactivity was measured on an Intertechnique SL-30 (France) liquid scintillation counter with external standard.

EXPERIMENTAL RESULTS

The development of physical fatigue in the rats as a result of swimming for 8 h was accompanied by a significant increase in weight of the adrenals. For instance, whereas in rats of the control groups they weighed 100 ± 6 mg, in the rats after swimming this was increased to 130 ± 4 mg, evidence of the development of considerable changes due to stress in the animal.

The results of investigation of ^{3}H-catecholamine synthesis in the rats' adrenals showed (Table 1) that after swimming for 8 h the intensity of synthesis of ^{3}H-adrenalin and ^{3}H-noradrenalin in the adrenals was significantly reduced by 25%. Synthesis of ^{3}H-dopamine also was reduced, but not statistically significantly. These results agree with data in the literature [3, 4], indicating depression of the synthetic capacity of the adrenal medulla during prolonged physical exertion, probably due to inhibition of functional activity of the enzymes of catecholamine synthesis [2].

After the addition of prednisolone to the medium with adrenals of the control rats, no significant changes were found in the rate of ^{3}H-catecholamine synthesis. Meanwhile, some stimulation of ^{3}H-dopamine synthesis was observed under these conditions. The absence of any marked effect of prednisolone on catecholamine synthesis in the adrenals of intact rats, incidentally, corresponds with data in the literature showing that the action of glucocorticoids on this process in the adrenals is manifested only after exposure of the animals to procedures such as hypophysectomy, denervation, or stress [5, 7-10]. However, it may be that the absence of a clear effect of glucocorticoids in the intact adrenals is connected with the fact that glucocorticoids accelerate catabolism of catecholamines at the same time as they activate their synthesis. This is shown by the results of experiments in which the activating action of hydrocortisone on synthesis of ^{3}H-noradrenalin and ^{3}H-dopamine from ^{3}H-tyrosine was manifested only when iproniazid, a monoamine oxidase inhibitor, is added at the same time to the medium [6]. The combination of these two processes, proceeding in opposite directions, may probably ultimately lead to an increase in the rate of turnover of catecholamines although their level in the organ remains constant.

Under the influence of prednisolone on the adrenals of the experimental rats marked activation of synthesis of labeled catecholamines was observed. The formation of ^{3}H-noradrenalin and ^{3}H-adrenalin was increased under these circumstances by 75% relative to their level observed in the swimming rats, whereas ^{3}H-dopamine synthesis was increased by 56%. Stimulation of catecholamine synthesis by prednisolone against the background of physical fatigue was so considerable that the rate of ^{3}H-catecholamine synthesis in this case not only reached the control level, but actually exceeded it. For instance, under the influence of prednisolone the rate of synthesis of ^{3}H-noradrenalin and ^{3}H-adrenalin in the adrenals of the experimental rats was 30% higher than in the control, and the rate of synthesis of ^{3}H-dopamine was 46% higher.

Consequently, the decrease in catecholamine synthesis in the adrenals of rats during fatigue due to prolonged physical exertion is completely compensated by the action of the glucocorticoid prednisolone. The results confirm the previous hypothesis that glucocorticoids restore catecholamine synthesis, depressed as a result of physical exertion, through their action on tyrosine hydroxylase. This conclusion is also supported by data showing that the stimulating effect of glucocorticoids on depressed catecholamine synthesis is manifested only when tyrosine, and not dopa, is used as the substrate for synthesis [5].

These results demonstrate once again the close connection between hormones of the adrenal cortex and-medulla, which is manifested particularly clearly during the action of extremal factors on the organism. Glucocorticoids may evidently change the intensity of catecholamine synthesis in the adrenals by influencing the activity of the enzyme tyrosine hydroxylase, which is the factor limiting the velocity of synthesis of these amines.

The results of these experiments, in conjunction with data in the literature, show that one of the main causes of the decrease in intensity of catecholamine synthesis following severe physical exertion is exhaustion of the synthetic capacity of the adrenal cortex, leading to depression of the glucocorticoid level in the body which, in turn, reduces the activity of tyrosine hydroxylase, the key enzyme of catecholamine synthesis. Under these conditions, administration of exogenous glucocorticoids completely restores the level of catecholamine synthesis in the adrenals when depressed as a result of physical fatigue.

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