

EFFECT OF CATECHOLAMINES AND CORTICOSTEROIDS ON BLOOD ANTITHROMBIN ACTIVITY OF INTACT AND ADRENALECTOMIZED ANIMALS

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Adrenalin and noradrenalin increase the total antithrombin activity of the blood serum and activate antithrombins II, III, and IV in intact and adrenalectomized rats. These indices remain substantially unchanged after administration of hydrocortisone and deoxycorticosterone acetate.

Evidence of the highly important role of antithrombins in blood coagulation is given by the close relationship which exists between their level and the coagulating activity of the blood [1, 6, 7] and by changes in the antithrombin activity during disturbances of hemocoagulation [2-4]. The hormonal regulation of antithrombin activity has received little study although changes in the hormonal background are known to be accompanied by changes in the antithrombin level [5, 8]. Links between individual antithrombins and adrenal hormones have not been investigated.

The character of the relationship between antithrombins II, III, and IV and the total antithrombin activity of the blood, on the one hand, and the adrenal hormones on the other hand was accordingly investigated.

EXPERIMENTAL METHOD

Noninbred albino rats (521 animals) weighing 150-250 g were kept on a mixed diet. Adrenalin (A) and noradrenalin (NA) were injected intramuscularly in doses of 30 and 150 μ g/100 g body weight respectively 5, 15, 30, and 120 min before blood samples were taken. Control animals received injections of 0.85% sodium chloride solution. Hydrocortisone (HC) and deoxycorticosterone acetate (DOCA) were injected intramuscularly 4, 8, and 24 h before blood samples were taken (in doses of 5 and 0.025 mg/100 g body weight respectively). Control rats received distilled water or peach oil.

Bilateral adrenalectomy was performed in one stage through a dorsal approach. Experiments were carried out on the 8th day after the operation. At this time, as preliminary observations showed, the antithrombin level in animals undergoing a mock operation was the same as in intact animals. After the operation the animals were given 0.85% sodium chloride solution to drink. Some adrenalectomized animals received HC and DOCA (separately and combined) for 30 days. The total antithrombin activity was estimated by the degree of inactivation of thrombin solution by native serum and the activity of antithrombins II, III, and IV was determined from the degree of inactivation of thrombin by serum which had first been heated (to remove antithrombin II) or extracted with ether (to remove antithrombins II and III), using Perlick's method [9].

EXPERIMENTAL RESULTS

The total antithrombin activity, expressed as deviation from the control level of 100%, for intact and adrenalectomized animals receiving catecholamines and corticosteroids respectively is shown in Figs. 1 and 2.

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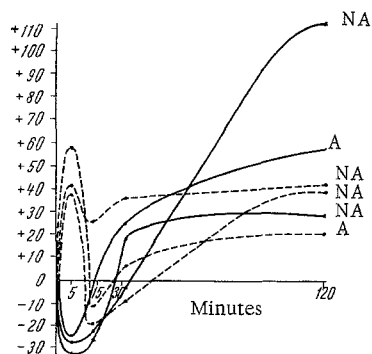


Fig. 1

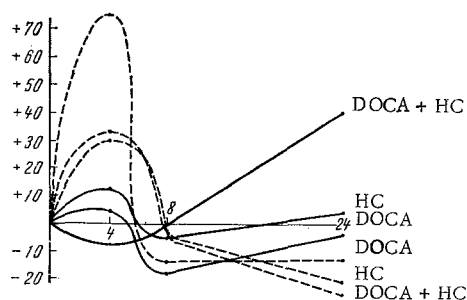


Fig. 2

Fig. 1. Total antithrombin activity after administration of catecholamines. Abscissa, time of taking blood samples (in min); ordinate, deviation of index from control level (100%); continuous lines represent intact, broken lines adrenalectomized animals. Compound administered is indicated opposite appropriate curve.

Fig. 2. Total antithrombin activity after administration of corticosteroids to animals. Abscissa, time of taking blood samples (in h). Remainder of legend as in Fig. 1.

Administration of A and NA both together and separately led to a decrease in the antithrombin activity of the intact animals (Fig. 1) 5 min after injection on account of a decrease in the antithrombin II level (after administration of A by 5 ± 1.3 of NA by 4 ± 1.5 , and by A + NA 5 ± 1.6 ; in the control by 10 ± 1.7 sec; in all cases $P < 0.05$). The low level of total antithrombin activity still persisted 15 min after injection of the catecholamines (together or separately), but by this time the normal level of antithrombin II was restored and the level of antithrombin IV had fallen (after administration of A by 26 ± 0.3 , of NA by 27 ± 3.1 , and of A + NA 22 ± 1.8 ; in the control by 34 ± 1.7 sec; in all cases $P < 0.05$). The total antithrombin activity 30 min after injection of the catecholamines was higher than initially on account of an increase in the antithrombin IV level. This change was even more marked 120 min after separate and combined injections of the hormones, when it was due to an increase in the level of both antithrombins II and III and also, to a lesser degree, of antithrombin IV.

In the adrenalectomized animals the total antithrombin activity 5 min after injection of A and NA (separately or together) was increased on account of an increase in the level of antithrombin III (after administration of A by 16 ± 4.3 , of NA by 10 ± 3.2 , and of A + NA by 10 ± 2.3 ; in the control by 3.0 ± 1.7 sec; in every case $P < 0.05$). No significant differences from the control were found 15 min after administration. An increase in the total antithrombin activity was found after 30 min, and it was more marked still after 120 min. It was due to approximately equal activation of antithrombins II and IV.

Changes in the total antithrombin activity after administration of corticosteroids are shown in Fig. 2. In intact animals no significant changes in antithrombin activity were found 4 and 8 h after injection of HC and DOCA (separately and together). Not until 24 h after simultaneous administration of HC and DOCA was an increase in total antithrombin activity found, when it was due to significant activation of antithrombin II (8 ± 2.1 compared with 3 ± 0.6 sec in the control; $P < 0.05$). In the adrenalectomized animals the total antithrombin activity was increased on account of an increase in the antithrombin IV level (after administration of HC by 30 ± 5.3 , of DOCA by 27 ± 4.4 , and of HC + DOCA by 24 ± 1.5 ; in the control by 17.0 ± 1.8 sec; $P < 0.05$). By the end of the observations (24 h) a tendency was observed for the total antithrombin activity to decrease in animals receiving HC or DOCA separately, and there was a significant decrease in its level after administration of both hormones together. The decrease in total antithrombin activity was accompanied by only a slight decrease in the level of antithrombin IV (after administration of HC and DOCA by 19 ± 1.2 ; in the control by 27 ± 4.0 sec; $P < 0.1$). During administration of corticosteroids for 30 days there was no change in the activity of the antithrombins.

Analysis of these results show that catecholamines and corticosteroids lead to different changes in the antithrombin activity of the blood serum in intact and adrenalectomized animals. After administration of catecholamines the changes in the levels of the individual antithrombins are not synchronized.

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