

EFFECT OF ADRENAL CORTICAL HORMONES ON I^{131} ABSORPTION
BY THE THYROID AND ON THE RESPIRATION OF ITS PARENCHYMA

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Reports in the literature regarding the effect of the adrenal cortical hormones on the glands of internal secretion, and especially on the thyroid, are extremely conflicting. Many writers report a depression of the thyroid function by cortisone and DOCA, as shown by a decreased intensity of absorption [3, 4, 9, 10, 12, 18] and elimination [6, 7] of I^{131} by the gland, by a decrease in the amount of protein-bound iodine in the blood serum [5, 10, 12, 21], and by a decrease in the basal metabolism [4, 12, 21], the weight of the thyroid [16], and the height [16] and number [13] of the cells of the thyroid epithelium. Other writers report completely opposite findings [8, 11, 12]. Sometimes it is denied that these hormones have any action on the thyroid [17, 19].

Another unsolved problem is that of the point of action of the adrenal cortical hormones. It is considered, for instance, that these substances act on the hypophysis and depress the production of thyrotropic hormone [15] or depress the action of hypophyseal thyrotropin on the thyroid [20]. Some authors maintain that the increased elimination of iodine by the kidneys under the influence of cortisone creates an iodine deficiency in the body, which indirectly affects the thyroid function [3, 4]. At the same time, findings have been obtained suggesting that the adrenal cortical hormones may have a direct action on the thyroid [14].

The object of this investigation was to discover whether these conflicting results are due to differences in the dose of adrenal cortical hormones and in the duration of their action.

EXPERIMENTAL METHOD

The effect of the adrenal cortical hormones on the absorption of I^{131} by the thyroid was studied in male albino rats weighing 140-170 g. Cortisone acetate and DOCA were injected intramuscularly in various doses, and I^{131} was injected intraperitoneally in doses of 1.0 and 0.3 μ Ci, in 1 ml isotonic NaCl solution.

The degree of radioactivity of the thyroid was measured in the extracted glands by means of a gas-discharge Geiger-Müller beta counter and B apparatus, or in vivo by means of radiometers of types B and PS-5M, with gas-discharge and scintillation gamma counters, housed in lead collimators with an aperture of 1 cm².

On the basis of I^{131} fixation curves obtained for each animal, the mean curve for each group of animals was plotted. The results of similar determinations made on intact animals acted as controls.

To discover if adrenal cortical hormones could act directly on the thyroid, the effect of these substances was studied on oxygen absorption by the isolated thyroid parenchyma, incubated in a Warburg's apparatus. The thyroids of male rats weighing 130-250 g were carefully dissected and minced in the cold to give a homogeneous mass, 50 mg of which was placed in each vessel. The incubation mixture consisted of rats' blood serum (3 ml) to which was added cortisone acetate (0.4, 1.0, and 4.7 mg) or DOCA (0.6, 1.5 and 7.2 mg). In control determinations nothing was added to the serum. The action of the test hormones was judged by the amount of oxygen absorbed in micro-liters per milligram dry weight of gland tissue, for the intensity of the respiration of the thyroid is a measure of its functional activity [1,2]. The numerical results obtained were analyzed statistically.

EXPERIMENTAL RESULTS

Injection of DOCA (for the first 24 h the preparation was injected every 2 h and thereafter once daily; the first injection was given 2 h before injection of the isotope) was reflected in the I^{131} absorption by the thyroid, and

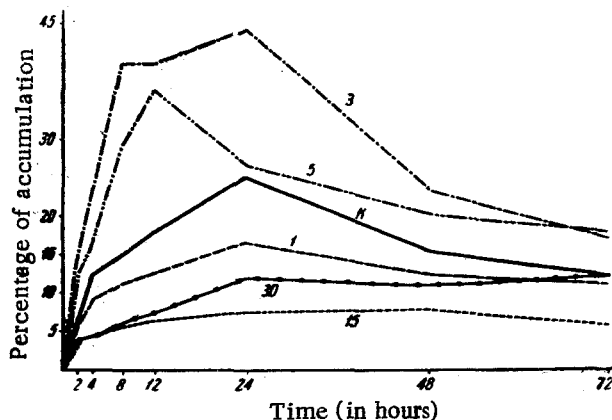


Fig. 1. Effect of DOCA on I^{131} absorption by the thyroid following repeated injection of the hormone for 1, 3, 5, 15, and 30 days in a daily dose of 1.5 mg/100 g body weight (K - control).

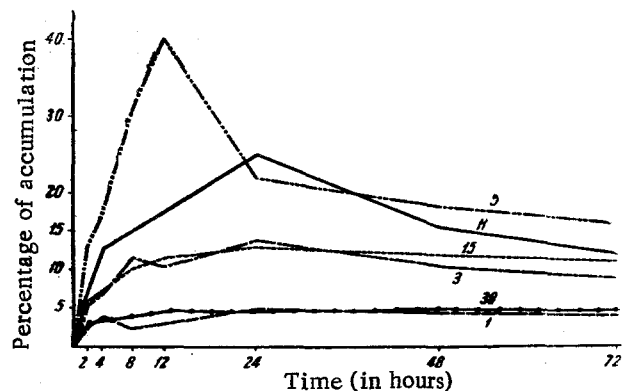


Fig. 2. Effect of cortisone on I^{131} absorption by the thyroid following repeated injection of the hormone for 1, 2, 5, 15, and 30 days in a daily dose of 1 mg/100 g body weight (K - control).

the character and degree of the changes in the curves were dependent on the dose of the mineralocorticoid given. For instance, whereas DOCA in a dose of 0.1 mg/100 g body weight caused a slight decrease in I^{131} absorption (by 9.4% after 4 h, 18.4% after 12 h, and by 5% after 24 h) by comparison with the controls, in a dose of 0.4 mg it gave the opposite effect (absorption was increased by 75.2% after 4 h, and by 12.3% after 12 h), and the effect of a dose of 10 mg was still more marked (absorption was increased by 126.5% after 4 h, by 47.4% after 12 h, and by 6.5% after 24 h). Meanwhile injection of DOCA in all these doses caused considerable slowing of the elimination of I^{131} from the thyroid.

In the experiments with cortisone acetate injected as described above, measurement of the radioactivity of the thyroid in vivo gave the following results. Cortisone in a dose of 0.1 mg/100 g body weight did not produce a significant decrease in the accumulation of I^{131} by comparison with that in the intact animals. The other doses of cortisone acetate (0.2 and 10 mg/100 g body weight) caused a sharp fall in the level of the I^{131} absorption curves.

Comparison of the results indicated certain differences in the action of cortisone acetate and DOCA on the absorption and elimination of I^{131} by the thyroid, especially when large doses were given. For instance, whereas 10 mg DOCA caused a considerable and rapid absorption of the isotope (maximum $35.3 \pm 9.5\%$ over a period of 8 h) and retarded its elimination ($20.4 \pm 4.7\%$ of I^{131} remained in the thyroid after 72 h), 10 mg cortisone acetate lowered the maximum of absorption to $8.0 \pm 2.8\%$.

In the next series of experiments the action of cortisone and DOCA on the thyroid function was compared in vivo in animals receiving cortisone acetate and DOCA (in doses of 1.0 and 1.5 mg/100 g body weight, respectively) daily for different periods.

A single injection of DOCA lowered the I^{131} absorption by the thyroid (Fig. 1). Further injections of this hormone for 3 days greatly increased the intensity of absorption, so that the greater part of the isotope accumulated over a period of 8 h. The intensity of absorption continued at a high level after 5 daily injections of DOCA, but the maximum of absorption of I^{131} was slightly lowered and lasted for a shorter time. This period of high radioactivity was followed by a decrease, which was observed when the daily injections were prolonged for 15 and 30 days. At these times the accumulation of I^{131} in the thyroid was considerably retarded (the maximum of accumulation was reached only after 48 h). Elimination of the isotope also was slowed.

Twenty-four hours after injection of cortisone the thyroid accumulated only very small amounts of I^{131} (Fig. 2). After the injections had continued for 3 days the percentage of accumulation rose sharply, yet remained lower than in the controls. Not until daily cortisone injections had been given for 5 days did the accumulation of I^{131} attain its maximal level. The absorption curve of the isotope at this period was characterized by a rapid rise (the maximum of accumulation was reached after 12 h), and the curve was at a higher level than that of the controls. Further saturation of the body with cortisone for 15, and still more for 30 days, again lowered the I^{131} absorption. The character of the I^{131} absorption curves obtained in the 30-day and 15-day experiments differed only very slightly from that of the 1-day and 3-day experiments.

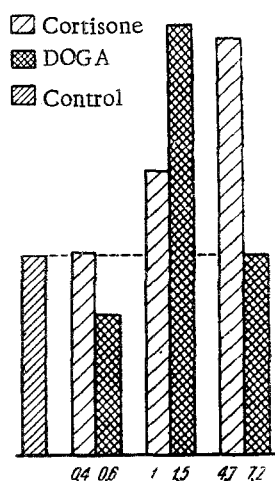


Fig. 3. Effect of various doses of cortisone and DOCA (in mg) on oxygen absorption by thyroid tissue.

($2.48 \pm 0.23 \mu\text{l/mg}$), but cortisone in a dose of 1 mg increased this absorption by 42.3% ($3.53 \pm 0.26 \mu\text{l/mg}$). The addition of a large dose of cortisone (4.7 mg) to the incubation medium increased the oxygen absorption still further ($5.19 \pm 0.55 \mu\text{l/mg}$).

In the experiments with DOCA a dose of 0.6 mg of this hormone depressed the respiration of the isolated thyroid (the oxygen absorption fell to $1.75 \pm 0.10 \mu\text{l/mg}$). At the same time the addition of a larger dose (1.5 mg) gave the opposite effect: the oxygen absorption rose by 116.9% over the control figure to $5.38 \pm 0.61 \mu\text{l/mg}$. If the dose of DOCA was increased to 7.2 mg, the respiration of the thyroid tissue remained within the limits of variation of the control indices ($2.49 \pm 0.11 \mu\text{g/ml}$).

It should be noted that in the experiments with cortisone a parallel was observed between the increase in the dose of hormone and the volume of oxygen utilized: whereas a small dose of cortisone (0.4 mg) left the respiration practically unchanged, an increase in the dose to 1.0 and 4.7 mg was accompanied by an intensive respiration. In the experiments with DOCA, on the other hand, the large dose of this hormone (7.2 mg) was inactive whereas the small dose (0.6 mg) depressed respiration. Only in a dose of 1.5 mg did DOCA stimulate the respiration of the thyroid parenchyma to a marked degree.

SUMMARY

The influence of cortisone-acetate and desoxycorticosterone acetate (DOCA) on absorption and excretion of I^{131} by the thyroid gland depends on the dose and the length of action of the hormonal preparations. The action of DOCA (1.5 mg per 100 gm of body weight) and of cortisone (1.5 mg per 100 gm of body weight) varies; this is manifested in different periods of appearance of the maximal iron radioactivity (in experiments with DOCA - 3 days, with cortisone - 5), its value (in DOCA more, than in cortisone), and in the nature of action (on the 3rd day DOCA increases, and cortisone reduces the isotope absorption as compared to control).

In experiments in vitro carried out in a Warburg apparatus cortisone-acetate and DOCA changed the respiration of the thyroid gland tissue. A rise in the cortisone dose (0.4-1.0-4.7 mg) caused a parallel rise in the oxygen intake by the thyroid gland, whereas DOCA intensified the respiration of the thyroid parenchyma only in a medium dose (1.5 mg).

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