

Effects of Hypophysectomy, ACTH, Cortisone and Estradiol on the β -Glucuronidase Activity of Adrenal Gland in the Rat.* (20486)

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That a relationship exists between the activity of the enzyme β -glucuronidase in certain tissues and the circulating level of estrogens, androgens and probably adrenal cortical steroids is well established. Thus, estrogens notably increase the β -glucuronidase concentrations in the accessory organs of reproduction(1,2), androgens that in the kidney(3) and cortisone has been reported to effect a rise in the plasma levels of this enzyme in man(4). Although the nature of this hormone-enzyme relationship is still obscure, its elucidation may lead to a better understanding of the mechanisms involved in steroid hormone synthesis, utilization and metabolism. The occurrence of relatively high concentrations of β -glucuronidase in the adrenal glands of the rat(5) and the cow(6) seemed of interest in this regard and an investigation of adrenal β -glucuronidase activity under a variety of experimental conditions was therefore initiated.

Materials and methods. Male rats of the Sprague-Dawley strain were hypophysectomized by the parapharyngeal route, the control animals being subjected to sham procedures. At the time of operation 30,000 units of penicillin in oil were administered and 10% glucose was made available as the drinking fluid.

The 3 hormones were administered subcutaneously in one daily dose: estradiol benzoate in oil, cortisone acetate in aqueous suspension and ACTH in gelatin solution (ACTHAR gel Armour, Lot L-47704). The animals were sacrificed the day following the last injection of estradiol and cortisone and 3 hours after the last injection of ACTH.

The adrenals were trimmed, weighed on a torsion balance and analyzed for β -glucuronidase activity by the method of Talalay, Fishman and Huggins(5). In the hypophysectomized groups aliquots of the whole adrenal

homogenates were utilized for the estimation of enzyme activity, total nitrogen determinations being performed on aliquots of the same homogenates by micro-Kjeldahl analysis.

Results. 1. *Effect of ACTH.* 2 mg of ACTH per day for 4 and 10 days effected a statistically significant increase in adrenal weight and treatment for 10 days resulted in a significant reduction of body weight (Table I). These expected changes were not associated with an increase in adrenal β -glucuronidase activity when expressed in terms of enzyme activity per mg of adrenal tissue, wet weight (Table I).

2. *Effect of cortisone acetate.* 3 mg of cortisone acetate per day for 10 days failed to effect a significant change in adrenal β -glucuronidase activity despite the marked regression in adrenal weight induced by this treatment (Table II).

3. *Effect of estradiol benzoate.* As in the case of ACTH and cortisone, estradiol (100 μ g per day for 10 days) did not alter the β -glucuronidase concentrating adrenal tissue although the effects of this hormone on adrenal weight and somatic growth could be demonstrated. (Table II).

4. *Effect of hypophysectomy.* β -glucuronidase activity in the adrenal glands 6 days following hypophysectomy was increased significantly above the control concentrations ($P < .01$ in Exp. 1 and 2; Table III). When expressed in terms of enzyme activity per mg of nitrogen this increase was less marked but still significant at the 5% level (hypox.: 90.4 ± 7.9 units per mg of nitrogen; control: 70.3 ± 2.9 units per mg of nitrogen; 15 degrees of freedom).

Discussion. The increase in adrenal β -glucuronidase concentration following hypophysectomy is difficult to interpret. It should be noted that cortisone administration, while effecting an involution of the adrenals comparable to that obtained by hypophysectomy, did not result in a rise of enzyme activity.

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TABLE I. Effect of ACTH on Adrenal β -glucuronidase Activity.

Exp.	No. animals	Final body wt	Adrenal wt	Units enzyme per mg adrenal*
		g	mg	
Control	6	195 $\pm$ 8†	25.4 $\pm$ 1.5	6.96 $\pm$.51
2 mg ACTH/day for 4 days	7	186 $\pm$ 6	32.4 $\pm$ 2.1	6.70 $\pm$.26
Control	5	228 $\pm$ 9	29.8 $\pm$ 2.5	7.92 $\pm$.70
2 mg ACTH/day for 10 days	6	201 $\pm$ 1	41.2 $\pm$ 3.6	8.16 $\pm$.28

* Wet wt.

† Mean $\pm$ stand. error of the mean.TABLE II. Effect of Estradiol Benzoate and Cortisone Acetate on Adrenal β -glucuronidase Activity.

Exp.	No. animals	Final body wt	Adrenal wt	Units enzyme per mg adrenal*
		g	mg	
Control	9	206 $\pm$ 7†	26.3 $\pm$ 1.4	8.50 $\pm$.54
100 μ g estradiol benzoate/day for 10 days	10	152 $\pm$ 5	31.8 $\pm$ 2.0	7.97 $\pm$.46
3 mg cortisone/day for 10 days	8	162 $\pm$ 8	12.8 $\pm$.5	9.70 $\pm$.61

* Wet wt.

† Mean $\pm$ stand. error of the mean.TABLE III. Effect of Hypophysectomy (6 Days) on Adrenal β -glucuronidase Activity.

Exp.	No. animals	Final body wt	Adrenal wt	Units enzyme per mg adrenal*
		g	mg	
I				
Control	9	153 $\pm$ 3†	28.6 $\pm$.7	10.28 $\pm$.27
Hypox.	15	100 $\pm$ 3	15.9 $\pm$.1	11.73 $\pm$.35
II				
Control	10	164 $\pm$ 4	29.4 $\pm$.8	10.59 $\pm$.48
Hypox.	15	105 $\pm$ 3	16.1 $\pm$.5	13.80 $\pm$.37

* Wet wt.

† Mean $\pm$ stand. error of the mean.

Whatever the physiological significance of β -glucuronidase may be, its stability in the adrenal gland with reference to the experimental procedures employed suggests that the functions of the enzyme in this organ may be different from that in the uterus or the kidney where the response to hormonal stimulation or deprivation is a striking one.

Summary. The effects of hypophysectomy and ACTH, cortisone acetate and estradiol benzoate administration on the β -glucuronidase activity of the adrenal gland in the rat have been investigated. ACTH, cortisone and estradiol, while producing their characteristic effects on adrenal and body weights, failed to modify the β -glucuronidase concentrations in the gland. Hypophysectomy, on the other hand, effected a statistically significant in-

crease in adrenal β -glucuronidase activity.

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