

Effect of Adrenotropic Extract upon the Accessory Reproductive Organs of Castrated Rats.

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A preliminary report¹ has been published concerning the effect of adrenotropic extracts of the pituitary upon the secondary sexual characteristics of castrate young male rats. Additional experiments confirming and enlarging upon this work are herein reported.

Enlargement of the prostate and seminal vesicles of young male castrates, associated with adrenal enlargement produced by treatment with adrenotropic extract, has been noted in this laboratory. The interpretation that the enlargement of the prostate and seminal vesicles depends upon the adrenal stimulation is supported by the additional experiments reported here.

1. *Effect of Adrenotropic Extracts upon Castrate Males.* Twenty-three-day-old male rats were castrated and allowed to rest for 5 days. On the sixth day injections of adrenotropic extract were begun and continued for 9 days, approximately 50 units being administered daily. The following day the animals were killed, the adrenals were weighed, and the prostates and seminal vesicles were weighed together. Tissues were fixed immediately and histological examination subsequently made.

Twelve animals, castrated and killed 15 days later, served as controls. The adrenal weights averaged 17 mg. (13-19 mg.) and the weights of the prostate and seminal vesicles averaged 39 mg. (28-47 mg.). Normal animals of the same age have adrenals of about 16 mg. and prostate and seminal vesicles averaging 100 mg. (82-128 mg.). In the experimental group the adrenal weights averaged 53 mg. (40-61 mg.) and the prostate and seminal vesicle weights averaged 56 mg. (50-63 mg.).

The enlargement of the prostate and seminal vesicles is definite. Histological examination showed marked repair of the prostate from the castrate level. The seminal vesicles showed little histological change, but were definitely larger than in the controls.

2. *Effect of Adrenotropic Extracts upon Hypophysectomized Castrate Males.* It has been known for some time that many non-specific substances (foreign proteins, drugs, etc.) produce an en-

¹ Davidson, C. S., and Moon, H. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 281.

largement of the adrenals. However, it is quite clear that only pituitary adrenal stimulating extracts are effective in the hypophysectomized animal.² It was felt necessary, therefore, to attempt to produce the secondary sexual changes in hypophysectomized castrated rats, to eliminate any non-specific effect of the extract.

Eighteen males were castrated at 30 days of age. Four days later they were hypophysectomized. Seven were then reserved as controls and the remaining 11 injected twice a day for 14 days with approximately 25 units of adrenotropic extract. On the 15th day (48 days old) the animals were killed, organs weighed and fixed. Hypophysectomy was complete in all cases.

The results summarized in Table I show a marked increase in weight of the prostate and seminal vesicles. Histological evidence again showed the typical changes in the prostate, much less so in the seminal vesicles.

TABLE I.

Adrenal Weights mg.		Prostate and Seminal Vesicle Weights mg.	
Experimental	Controls	Experimental	Controls
81	9	85	46
69	9.5	104	39
51	9	60	38
64	10	67	41
71	13	73	40
83	9	87	37
83	8	94	37
86		84	
57		84	
61		64	
56		65	
Aver. 67	9.5	72	40

The enlargement of the adrenals is to be noticed. Normal adrenal weights, in our colony, for animals 48 days old are between 25 and 30 mg. The enlargement here in the hypophysectomized animals is, therefore, to more than twice the normal weight. The enlargement is confined to the cortex, except that the vacuoles sometimes seen in the adrenal medulla of the hypophysectomized rat are absent. In fact, the medulla presents, on the whole, a much more normal appearance than the control. The cortical enlargement appears to be confined chiefly to cellular enlargement; no evidence of hyperplasia is to be seen.

² Collip, J. B., Anderson, E. M., and Thomson, D. L., *Lancet*, 1933, Aug. 12, p. 347.

Half the animals were injected subcutaneously and the others intraperitoneally. No differences in effectiveness of the extracts administered by these 2 routes were noted.

3. *Effect of Adrenotropic Extracts upon Castrated Adrenalectomized Males.* To show that the effect of the adrenotropic extracts is through the adrenals and not a direct effect of the extract on the prostate and seminal vesicles, a series of adrenalectomized animals were treated with the extract. Fifteen 23-day-old males were castrated and adrenalectomized 2 to 5 days later. Eight were then injected for from 5 to 9 days with adrenotropic extract. Organ weights are shown in Table II. These results show that the effect

TABLE II.

Prostate and Seminal Vesicle Weights mg.	No. of days treated
32	5
37	5
43	6
40	6
32	9
36	9
43	9
23	9
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Aver. 37	

Controls averaged 40 mg. (35-45 mg.).

of adrenotropic extracts on the secondary sex organs is through the adrenals, and does not occur in their absence.

Summary. 1. The effect of adrenotropic extracts of the pituitary upon the prostate and seminal vesicles of castrate young rats, previously reported, has been confirmed. 2. The response may be elicited in hypophysectomized animals. 3. The adrenotropic extract is without effect in adrenalectomized castrated rats. 4. The adrenotropic extract used causes marked enlargement of the adrenal cortex in normal animals, and not only prevents the adrenal atrophy following hypophysectomy but enlarges the cortex to more than twice the normal size. Some changes in the medulla of the adrenal are also reported.