

A-C-T has also been given to hypophysectomized rats at various levels to determine the amount of repair of the adrenal cortex as well as to demonstrate thymic atrophy. It was noted that when a total of 1 unit or less of A-C-T was given, that no consistent decrease in the thymus could be demonstrated although this amount of A-C-T stimulated the adrenals. However, when more than 2.5 units were given over a period of 10 days there was always marked atrophy of the thymus.

Conclusions. 1. A-C-T caused acute thymic atrophy in normal 21-23-day-old rats. 2. Castration did not prevent thymic atrophy produced with A-C-T. 3. This atrophy was observed in hypophysectomized rats although to a lesser degree. 4. A-C-T did not cause thymic atrophy in adrenalectomized rats. 5. It would seem likely that thymic atrophy produced with A-C-T is through the adrenal cortical steroids.

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Response of Thyroidectomized Rats to Adrenocorticotrophic Hormone.*

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It has been reported by McQueen-Williams¹ and Emery and Winter² that adrenal hypertrophy could not be obtained in thyroidectomized rats with the administration of pituitary substance. This has been interpreted as evidence for a pituitary factor which acts on the adrenals through the thyroid. Recently Rosen and Marine³ have presented data showing a decreased response of the adrenal cortex of guinea pigs to prolonged injections of an acetic acid extract of pituitary following thyroidectomy.

The evidence presented by McQueen-Williams and Winter and

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¹ McQueen-Williams, M., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 296.

² Emery, F. E., and Winter, C. A., *Anat. Rec.*, 1934, **60**, 381.

³ Rosen, S. H., and Marine, D., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 647.

Emery⁴ for a directly acting adrenocorticotrophic hormone is the compensatory adrenal hypertrophy after unilateral adrenalectomy in thyroidectomized rats. Recently there has been increased evidence for a directly acting adrenocorticotrophic hormone. In a previous paper from this laboratory,⁵ there was a footnote stating that removal of the thyroid gland did not effect the adrenal hypertrophy obtained in immature male rats treated with adrenocorticotrophic hormone. Atwell⁶ has reported repair of the interrenal bodies in hypophysectomized thyroidectomized tadpoles with pituitary extracts. Jores and Boecker⁷ were able to obtain adrenal hypertrophy with adrenocorticotrophic extracts in thyroidectomized guinea pigs.

Adrenocorticotrophic hormone (A-C-T) prepared and assayed by the method described in a previous paper⁴ was injected intraperitoneally (1% solution) into normal and thyroidectomized† male rats (22 to 23 days old) daily for 3 days. The animals were sacri-

TABLE I.
Normal Rats.

No. of rats	A-C-T injected, units	Wt of 2 adrenals	
		Range, mg	Avg, mg
75	0	9.9-22.0	16.7
6	0.2	15.0-23.2	18.6
6	0.4	19.0-24.3	21.5
6	0.8	19.4-25.0	22.6
6	1.2	22.0-32.0	26.0
6	2.0	30.2-36.0	33.8
6	5.0	50.0-66.2	59.4

TABLE II.
Thyroidectomized Rats.

No. of rats	A-C-T injected, units	Wt of 2 adrenals	
		Range, mg	Avg, mg
26	0	11.5-22.0	16.6
8	0.75	16.5-24.0	20.0
8	1.50	20.0-36.5	27.9
6	3.40	23.2-40.4	35.4

⁴ Winter, C. A., and Emery, F. E., *Am. J. Physiol.*, 1936, **116**, 164.

⁵ Moon, H. D., *Proc. Soc. Exp. Biol. and Med.*, 1937, **35**, 649.

⁶ Atwell, W. J., *Am. J. Physiol.*, 1937, **118**, 452.

⁷ Jores, A., and Boecker, W., *Z. f. ges. Exp. Med.*, 1937, **100**, 332.

† All thyroid tissue visible under a dissecting microscope was removed. The region was dissected and examined at autopsy. Although there was the possibility of the presence of microscopic remnants of thyroid tissue, it was considered that if thyroid activity was concerned in the adrenal hypertrophy with adrenocorticotrophic hormone, there would be a significant decrease in such activity after relatively complete thyroidectomy. Injections were begun on the rats on the day following thyroidectomy.

TABLE III.
Desiccated Thyroid and A-C-T in Normal Immature Male Rats.

No. of rats	Desiccated thyroid, mg	A-C-T units	Wt of 2 adrenals	
			Range, mg	Avg, mg
6	25	0	14.5-19.0	16.2
6	25	1	20.9-26.9	24.6
6	0	1	22.1-27.0	25.2

ficed on the day following the last injection. The adrenals were removed, weighed and fixed in Bouin or 10% formol.

Normal male rats were given desiccated thyroid alone and in combination with A-C-T. The desiccated thyroid was given in an aqueous suspension by stomach tube. A single administration was given and the animals autopsied on the fourth day. A-C-T injections were begun on the day that the desiccated thyroid was given, and the injections were given daily for 3 days.

The results in Table III show that the administration of desiccated thyroid produced no augmentation of the effect of A-C-T on the adrenals. The efficacy of the desiccated thyroid was indicated by the fact that all the rats given the desiccated thyroid lost from 2 to 4 g from their initial body weight (A-C-T preparations cause an inhibition of growth but not a *loss* in body weight).

Celloidin sections stained with iron haematoxylin and aniline blue, and frozen section stained with Sudan III and haematoxylin showed no significant differences between the adrenals of normal and thyroidectomized animals treated with adrenocorticotrophic hormone.

Conclusions. The adrenal hypertrophy of normal and thyroidectomized rats has been shown to be directly proportional to the amount of adrenocorticotrophic hormone administered. There was no evidence that the presence of the thyroid gland was necessary for the adrenal cortical hypertrophy produced by adrenocorticotrophic preparations when given immediately after thyroidectomy. The administration of desiccated thyroid to normal rats did not augment the adrenal hypertrophy caused by adrenocorticotrophic hormone. Further work will be necessary to determine whether or not a certain minimal amount of a thyroid principle is necessary in the production of adrenal hypertrophy.