whereas it requires one unit to cause a 50% increase in the adrenal weights of 21-day-old rats. We believe that 4-day-old rats afford a more satisfactory method of assay for A-C-T because of greater sensitivity.

Summary. The response of 4-day-old rats to various anterior pituitary extracts has been described. It was noted that 4-day-old rats responded with adrenal hypertrophy and thymic atrophy to much smaller amounts of A-C-T than 21-23-day-old rats. Mammotropic and growth preparations did not cause adrenal hypertrophy and thymic atrophy. It is concluded that the 4-day-old rats will be a more sensitive test animal for A-C-T preparations.

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Effect of Adrenocorticotropic Hormone on the Thymus of Rats.*

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It was reported in earlier papers that the administration of adrenocorticotropic hormone (A-C-T) to immature rats resulted in adrenal hypertrophy[1, 2] and thymic atrophy.[2, 3] It has also been noted that large amounts of A-C-T will also cause a depression of somatic growth, whereas the viscera continue to grow. These findings have been studied considerably more in detail in this laboratory.†

A-C-T, prepared and assayed by the method previously published,[1] was given at various levels to 21-23-day-old normal male rats in 3 daily injections. The rats were autopsied 24 hours after the last injection. It was noted that the thymic atrophy was proportional to the amount of A-C-T administered as seen in Table I.

Atrophy of the thymus following the administration of the gonadotropic hormone of pregnant mare serum was reported by Evans and

* Aided by grants from the Board of Research of the University of California and Rockefeller Foundation of New York City. Assistance was rendered by the Federal Works Progress Administration, Project O.P. 65-1-08-62 Unit A-5.

1 Moon, H. D., PROC. SOC. EXP. BIOL. AND MED., 1937, **35**, 649.

2 Moon, H. D., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 34.

3 Evans, H. M., Moon, H. D., Simpson, M. E., and Lyons, W. R., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 419

† Results on the inhibition of growth to be published later.

TABLE I.
Effect of A-C-T on Normal Immature Male Rats.

No. of rats	Age at autopsy, days	A-C-T units	Length of treatment, days	Adrenals, mg	Thymus, mg
80	26-28	Controls	3	16.9	174
5	26	⅛	3	18.2	146
5	26	¼	3	18.6	133
5	26	½	3	19.6	116
10	26-27	1	3	24.1	78
6	27	2	3	33.1	33
6	27	4	3	49.9	19

Simpson.[4] This atrophy was mediated through the gonads as shown by the effectiveness of the sex hormones in causing thymic atrophy.[5]

In order to rule out the possibility of adrenocorticotropic hormone causing thymic atrophy through the gonads, extracts were given to castrate rats. Table II shows that A-C-T caused just as marked atrophy of the thymus in castrate rats as in normal rats.

TABLE II.
Effect of A-C-T in Castrate Rats.

No. of rats	Age at autopsy, days	A-C-T units	Length of treatment, days	Avg wt of adrenals, mg	Avg wt of thymus, mg
6 males	26	1.0	3	26.0	96.0*
6 "	25	1.25	3	28.5	78.5*
12 "	26	Controls		19.0	220.0*
6 females	46	40	25	125.0	33.0
8 "	46	Controls		44.0	462.9

*Compare with Table I.

To determine whether or not the action of the A-C-T on the thymus was mediated through the adrenals, adrenalectomized animals were injected with A-C-T. Male rats were adrenalectomized when 21 to 22 days old. Injections were begun on the day following operation and given in 3 daily doses. The animals were autopsied 24 hours after the last injection. Table III shows that A-C-T had no effect on the thymus of adrenalectomized rats.

TABLE III.
Effect of A-C-T in Adrenalectomized Rats.

No. of rats	Age at operation, days	Age at autopsy, days	A-C-T units	Length of treatment, days	Thymus, mg
6 males	22	26	4	3	197
8 "	22	26	Controls	—	178

[4] Evans, H. M., and Simpson, M. E., *Anat. Rec.*, 1934, **60**, 423.

[5] Schacher, J., Browne, J. S. L., and Selye, H., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 488.

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 Adrenocorticotropic Hormone.*

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It has been reported by McQueen-Williams[1] and Emery and Winter[2] 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 Marine[3] 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

* Aided by grants from the Board of Research of the University of California and Rockefeller Foundation of New York City. Assistance was rendered by the Federal Works Progress Administration, Project O.P. 65-1-08-62 Unit A-5.

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.