

Lack of Effect of Theelin upon Somatogenic, Thyretropic, and Adrenotropic Activity of Hypophysis.

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It has been well established that rats treated with theelin undergo a diminution in the sex-stimulating power of the hypophysis.^{1, 2, 8} Nelson⁴ has recently demonstrated changes in the basophilic cells of the hypophyses of rats following injection of theelin which he interprets as indicating inhibition of secretory activity. Similar findings are recorded by Halpern and D'Amour.⁵ The same changes are described in the pituitaries of rats treated with pregnancy-urine extracts,^{4, 6, 7, 8} and these alterations are interpreted as secondarily due to increased secretion of the gonadal hormone.^{4, 6, 7, 9} There is some disagreement as to the changes in the acidophilic cells. Nelson⁴ records a decrease in the number of normal cells, with degranulated forms. Severinghaus⁷ finds little change in immature females, a reduction in number, size, and staining reaction in adult females and an increase in number, size, and staining reaction in adult males. Wolfe⁸ describes an increase in infantile females. Barnes, Reagan, and Nelson¹⁰ have demonstrated that in depancreatized dogs the injection of theelin has a similar effect to that of total hypophysectomy. Nelson and Overholser¹¹ have recently reported confirmatory experiments in depancreatized monkeys.

Since the initial work indicates very strongly that the administration of theelin has an inhibitory effect upon the histological pic-

¹ Meyer, R. K., Leonard, S. L., Hisaw, F. L., and Martin, S. J., *PROC. SOC. EXP. BIOL. AND MED.*, 1930, **27**, 702.

² Moore, C. R., and Price, D., *Am. J. Anat.*, 1932, **50**, 13.

³ Meyer, R. K., Leonard, S. L., Hisaw, F. L., and Martin, S. J., *Endocrinol.*, 1932, **16**, 655.

⁴ Nelson, W. O., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 452.

⁵ Halpern, S. R., and D'Amour, F. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 108.

⁶ Leonard, S. L., *Anat. Rec.*, 1933, **57**, 45.

⁷ Severinghaus, A. E., *Anat. Rec.*, 1934, **60**, 43.

⁸ Wolfe, J. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 214.

⁹ Wolfe, J. M., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 184.

¹⁰ Barnes, B. O., Reagan, J. F., and Nelson, W. O., *J. Am. Med. Assn.*, 1933, **101**, 926.

¹¹ Nelson, W. O., and Overholser, M. D., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **32**, 150.

ture of the anterior lobe of the hypophysis and suppresses its sex-stimulating power and diabetogenic activity, it seemed worth while to investigate any possible influence it might have upon the other anterior pituitary effects, somatogenic, thyreotropic, and adreno-tropic.

Litter-mate rats were divided into 3 groups. Group A, consisting of 3 males and 3 females, received daily injections of 9 rat units of theelin* in oil (0.03 cc.). Group B, comprising the same number of animals, was treated with injections of an equal quantity of Mazola oil. Group C, 2 males and 2 females, served as untreated controls. Injections were made daily from the 23d to the 90th day of life.

TABLE I.
Body Weight of Animals During Theelin Treatment, and of Controls.
Aver. Body Wt. in Gm.

Age in days	23	29	37	46	57	67	75	84	90
Group A	35	50	74	101	129	155	166	176	182
'' B	34	45	71	100	133	162	176	188	193
'' C	34	48	75	107	131	151	166	181	187

TABLE II.
Weights of Thyroids, Adrenals, and Gonads. No. of Animals Indicated in Parentheses. Both Gonads, Adrenals, and Thyroid Lobes Weighed Together.

	Thyroid, aver. wt. in gm.	Adrenals, aver. wt. in gm.	Ovaries, aver. wt. in gm.	Testes, aver. wt. in gm.
Group A	0.020 (6)	0.052 (6)	0.052 (3)	2.719 (3)
'' B	0.020 (6)	0.047 (6)	0.062 (3)	2.954 (3)
'' C	0.017 (4)	0.041 (4)	0.046 (2)	2.711 (2)

Results are shown in Tables I and II. No appreciable influence upon growth was noted, Groups A, B, and C averaging in weight respectively 35, 34, and 34 gm. at the outset, and 182, 193, and 187 gm. at the termination of the experiment. Nor was any essential difference found when the males and females of each group were considered separately. Likewise, no significant difference was observed in the weights of adrenals and thyroids of the treated animals as compared with those of the 2 control groups.

It is the common finding that the initial effect of theelin upon the gonads is an inhibition of growth and we have observed this regularly in other studies. That this effect is only temporary is indicated by this experiment, the testes and ovaries showing normal size after 67 days of treatment. The vaginae of group A were all open by the 27th day of life, those of groups B and C, from the 49th to the 59th day.

*The theelin was kindly supplied by Dr. O. Kamm, Parke, Davis and Company.

The histological picture of the adrenals, thyroids, testes, and ovaries of the theelin-treated animals differed in no respect from those of the 2 control groups.

Our experiments indicate that theelin has no effect upon the somatogenic, thyreotropic, or adrenotropic activity of the anterior pituitary of rats.

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Experimental Production of Glandular Cystic Hyperplasia of Endometrium with Estrogenic Substances of Parturient Urine.

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In a recent review of the important gynecological condition of glandular cystic hyperplasia of the endometrium, attention was called to the wide divergence of opinion concerning the amount of estrogenic substance necessary to produce it.¹ The enormous proliferation of the endometrium and the finding of increased amounts of an estrous inducing substance in the blood and urine of a certain percentage of these cases point to an excessive production of estrogenic hormones, as a result the disease is commonly referred to as an hyperestral one, or is said to exhibit hyperestrinism. Evans,² Novak,³ Siebke,⁴ Zondek,⁵ Frank,⁶ Kurzrok⁷ and Fluhmann⁸ all seem to favor this view. On the other hand the occurrence of the disease in sterile women, its close relation to amenorrhoea and its occurrence near the menopause and after partial castration indicate that there is a decreased function of the ovary and a lowered ovarian secretion. Seitz⁹ and Mazer and Goldstein¹⁰ have taken this latter view.

¹ Burch, John C., Phelps, Doris, and Wolfe, J. M., *Arch. Path.*, 1934, **17**, 799.

² Evans, H. M., *J. A. M. A.*, 1935, **104**, 464.

³ Novak, Emil, *Surgery, Gynecology and Obstetrics*, 1935, **60**, 330.

⁴ Siebke, Harold, *Zentralblatt f. Gyn.*, 1929, **53**, 2450.

⁵ Zondek, Bernhard, *Acta Obstet. et Gyn. Scandinavica*, 1934, **13**, 309.

⁶ Frank, Robert T., Goldberger, Morris A., Spielman, Frank, *J. A. M. A.*, 1934, **103**, 393.

⁷ Kurzrok, Raphael, *Endocrin.*, 1932, **16**, 361.

⁸ Fluhmann, C. F., *Surgery, Gynecology and Obstetrics*, 1931, **52**, 1051.

⁹ Seitz, L., *Munchen Med. Wochr.*, 1930, **77**, 133.

¹⁰ Mazer and Goldstein, W. B. Saunders, Philadelphia, 1932.