

**Effect of Testosterone on Pituitary and Mammary Gland.\***

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The injection of estrogens into ovariectomized<sup>1</sup> or normal female rats<sup>2</sup> increases the lactogen content of their pituitary glands and causes an extension and arborization of the duct system of the mammary gland.<sup>3, 4, 5</sup> The administration of testosterone to spayed rats induces mammary proliferation<sup>6, 6, 7</sup> and marked milk secretion.<sup>6</sup> We were interested, therefore, in determining the influence of testosterone injections on the lactogen content of the pituitary gland.

Thirty-six sexually mature female rats were paired on the basis of body weight. All of the animals were ovariectomized and a mammary gland removed from 4 of the animals. One of each pair was injected subcutaneously daily for 15 days with 200 gamma of testosterone propionate (Oreton†). The other animal of each pair served as a control. Control and experimental animals were sacrificed the day following the last day of injection of the experimental animals. The mammary glands were removed from both groups of animals and studied in whole mounts and in histological sections. The pituitary glands were removed, weighed, and assayed for their lactogen content by injecting the suspended tissue intradermally over the crop glands of common pigeons. Pituitaries from the control and experimental animals were injected into the same group of birds.

Wolfe and Hamilton<sup>8</sup> showed that the injection of 500 gamma of

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<sup>1</sup> Reece, R. P., and Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bul.*, 1937, 266.

<sup>2</sup> Reece, R. P., *Proc. Soc. Exp. Biol. and Med.*, 1938, **39**, 77.

<sup>3</sup> Turner, C. W., *Sex and internal secretions*, 1932, chapter 12 (E. Allen, ed.), Williams and Wilkins Co., Baltimore.

<sup>4</sup> Nelson, W. O., *Physiol. Rev.*, 1936, **16**, 488.

<sup>5</sup> Astwood, E. B., Geschickter, C. F., and Rausch, E. O., *Am. J. Anat.*, 1937, **61**, 373.

<sup>6</sup> Selye, H., McEuen, C. S., and Collip, J. B., *Proc. Soc. Exp. Biol. and Med.*, 1936, **34**, 201.

<sup>7</sup> Nelson, W. O., and Merekel, C. G., *Proc. Soc. Exp. Biol. and Med.*, 1937, **36**, 823.

† The Oreton used in this study was kindly supplied by Dr. E. Schwenk of the Schering Corporation.

<sup>8</sup> Wolfe, J. M., and Hamilton, J. B., *Endocrinology*, 1937, **21**, 603.

testosterone acetate into spayed rats did not alter the weight of the pituitary gland. In our work the dosages employed also failed to alter pituitary weight, the average weight of the pituitary glands from injected animals (10.4 mg) being nearly identical with that of the control animals (10.1 mg). Hamilton and Wolfe<sup>9</sup> also demonstrated that the daily administration of 500 gamma of testosterone propionate reduced the gonadotropic properties of the pituitary gland. In this work the injection of testosterone propionate elicited a 41% increase in the lactogen content of the pituitary glands. Considering the pairs separately, 15 of the pituitaries from the injected rats contained more lactogen than did the glands from the control rats, one was equal to, and 2 contained less lactogen. The fact that the mammary glands of the experimental animals showed evidence of secretory activity suggests that testosterone propionate injections stimulate the pituitary gland to secrete and to discharge into the blood the lactogenic hormone. It would seem, therefore, that the inhibition of lactation in the rat<sup>10</sup> and perhaps in woman<sup>11</sup> by testosterone injections cannot be attributed either to the suppression of lactogen secretion or to the suppression of its discharge into the blood. In contrast to the action of estrogens in bringing about an increase in the lactogen content of the pituitary gland,<sup>1</sup> testosterone propionate augments the lactogen content by increasing the concentration of the hormone in the pituitary tissue and not by inducing an increase in pituitary weight.

The mammary glands of the animals at the time of ovariectomy showed an extensive duct system with numerous end-buds. Signs of involution were present in the mammary glands of the control animals at the time of sacrifice. The mammary glands of the injected animals showed an extensive development of the lobule-alveolar system. This extensive development of the lobule-alveolar system, however, has been brought about not only by hyperplasia but also by hypertrophy inasmuch as secretory activity had been induced in the acini.

*Conclusions.* The daily injection of 200 gamma of testosterone propionate for 15 days into sexually mature spayed rats augmented the lactogen content of their pituitary glands about 40%, caused no change in pituitary weight, induced an extensive development of the lobule-alveolar system of the mammary glands, and initiated secretory activity. It is suggested that the action of testosterone on the pituitary gland is sufficient to account for the hyperplasia and hypertrophy of the mammary glands of males.

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<sup>9</sup> Hamilton, J. B., and Wolfe, J. M., *Endocrinology*, 1938, **22**, 360.

<sup>10</sup> Folley, S. J., and Kon, S. K., *Proc. Roy. Soc., B*, 1938, **124**, 476.

<sup>11</sup> Kurzrok, R., and O'Connell, C. P., *Endocrinology*, 1938, **28**, 476.