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Growth of the Mammary Glands in Hypophysectomized Mice.*

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Many investigations have indicated that the hypophysis is essential for mammary growth in animals receiving estrogen (see ¹ and ² for review). The above observations, however, have not been uniform in animals of different species or, in some instances, among animals of the same species observed in different laboratories. In hypophysectomized male mice the injection of large amounts of estrogens for prolonged periods³ did not induce mammary growth. On the other hand mammary growth followed the injections of a lipid extract of the pituitary gland and led to the assumption that the pituitary produced a mammogenic hormone.⁴

Recent experiments have demonstrated that estrogens will induce a local growth of the breast tissue of rabbits⁵ and monkeys⁶ if properly applied while adjacent mammary glands in the same animal are not affected. Similar experiments conducted with mice have given comparable results.⁷ Mammary growth has also occurred in young male mice receiving injections of progesterone,⁸ several androgens and desoxycorticosterone as well as estrogens.⁹ The apparently contradictory observations listed above indicated the desirability of further studies on the estrogen-hypophyseal-mammary relationship.

One-hundred-one hybrid mice from 30 to 80 days old were hypo-

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¹ Turner, C. W., *Mammary Glands*, Chapter XI, Sex and Internal Secretions, E. Allen, C. H. Danforth and E. A. Doisy, Editors, Williams & Wilkins, Baltimore; Nelson, W. O., *Physiol. Rev.*, 1936, **16**, 488.

² Fredrikson, H., *Acta Obst. et Gynec. Scand.*, **19**, Suppl. 1.

³ Gomez, E. T., Turner, C. W., Gardner, W. U., and Hill, R. T., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **36**, 287.

⁴ Lewis, A. A., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1938, **39**, 435; *Mo. Agr. Exp. Sta. Res. Bul.* 282, 1938.

⁵ Lyons, W. R., and Sako, Y., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **44**, 398.

⁶ Speert, H., *Science*, 1940, **92**, 461.

⁷ Gardner, W. U., *Yale J. Biol. and Med.*, in press.

⁸ Gardner, W. U., and Hill, R. T., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 718.

⁹ Van Heuverswyn, J., Folley, S. J., and Gardner, W. U., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 389.

physectomized using the parapharyngeal method described by Thomas.¹⁰ Testosterone propionate, desoxycorticosterone acetate or progesterone† alone or in combination with estrogens or estrogen alone were administered for periods of 12 to 15 days starting from 1 to 89 days postoperatively. All hormones were dissolved in sesame oil and injected subcutaneously. The mice were fed Purina Fox Chow and water. The mammary glands were removed on the skins and prepared as "whole mounts". The completeness of hypophysectomy was checked by examination of serial sections of the sella turcica and surrounding tissues.

The 7 groups of mice in the present experiment are listed in Table I. Each of these groups was composed of smaller units of 3 to 6 animals. Each of the animals of these smaller groups received the same amount of hormone while the amounts varied among the groups. The range of the daily doses administered is indicated in the table.

All of the substances used induced mammary growth in hypophysectomized mice except the testosterone propionate. The relative number of mice showing mammary growth and the extent of mammary growth was greatest in those receiving desoxycorticosterone acetate + estradiol dipropionate, or progesterone + estradiol dipropionate. The glands were markedly enlarged, and from

TABLE I.
Summary of the Treatment and Mammary Response of Completely and Partially Hypophysectomized Mice Receiving Several Hormones.

Treatment hormones used	No. of mice	No. with complete hypophysectomy	No. with incomplete hypophysectomy	Treatment amt daily	No. of mammary responses	
					Complete hypophysectomy	Incomplete hypophysectomy
TP*	16	11	5	.25 to 1.25 mg	0	1
DC	10	7	3	.25 mg	2	2
P	12	4	8	.125 to 0.25 mg	1	3
E	19	10	9	.05 μ g to 1 μ g	5	8
DC and E	18	14†	4	DC and E‡	12	3
P and E	16	12	4	P and E‡	11	4
TP and E	10	7	3	TP and E‡	0	0

*TP—Testosterone propionate; DC—Desoxycorticosterone acetate; P—Progesterone; E—Estradiol dipropionate.

†One mouse in this group had no mammary glands.

‡The amounts of the various hormones used in these groups varied as indicated above.

¹⁰ Thomas, F., *Endocrinology*, 1938, **23**, 99.

† The testosterone propionate and progesterone were generously supplied by Dr. E. Schwenk of the Schering Corporation and the desoxycorticosterone acetate and estradiol dipropionate by Drs. Mautner and Oppenheimer of Ciba Pharmaceutical Products.

20 to 50 mitotic figures were counted in individual terminal buds of the proliferating ducts. The total size of the glands averaged less than those of intact animals similarly treated. The response of the glands of the incompletely operated animals was usually quite similar to that of the completely hypophysectomized except in a few instances. The very small amount of pituitary tissue remaining in some incompletely operated animals, no anterior lobe-tissue in some instances, did not greatly alter the quantitative response of the glands.

The amount of mammary growth occurring and the relative number of mice responding was smaller in the completely operated animals of the groups receiving desoxycorticosterone acetate, progesterone or estradiol dipropionate. The glands of these animals were only slightly enlarged and comparatively few dividing cells were present in the end buds of the ducts. The glands of the incompletely operated mice receiving desoxycorticosterone acetate, progesterone or estradiol dipropionate were all more extensively developed if anterior lobe tissue remained.

The complete lack of mammary growth in the mice receiving testosterone propionate + estradiol dipropionate cannot be explained at this time as both of these hormones alone induced a definite but slight mammary growth. The more extensive mammary proliferation of the mice receiving desoxycorticosterone acetate + estradiol dipropionate or progesterone + estradiol dipropionate is not considered to be only an additive effect.

Summary. Slight growth of mammary glands of some hypophysectomized male mice was induced within 15 days by the injection of desoxycorticosterone acetate, progesterone and estradiol dipropionate. A more extensive and more rapid proliferation of the mammary ducts of hypophysectomized mice occurred when desoxycorticosterone acetate or progesterone was injected with the estradiol dipropionate.