

Mammary Growth in Hypophysectomized Male Mice Receiving Estrogen and Prolactin.*

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The first experiments revealing the lactogenic activity of hypophyseal extracts were inadequate for the demonstration of mammary growth.¹ Later experiments suggested a proliferation of the mammary glands of immature ovariectomized rabbits receiving hypophyseal extracts.² Other investigators detected little mammary growth in animals receiving prolactin.^{3, 4} In more recent experiments mammary growth occurred in ovariectomized, in male or in hypophysectomized mice, or in rats following implantation of hypophyseal tissue or injection of hypophyseal extracts.^{4, 6, 7, 8} Some investigators associated this mammogenic activity with the protein-components of such extracts,^{7, 8} others with the lipid soluble material of pituitary tissue.⁹

Although administration of estrogen results in mammary growth in intact rodents, the mammary response of hypophysectomized animals has been inconsistent.^{4, 5} The mammary glands of some hypophysectomized male mice developed slightly when estrogen, and progesterone or desoxycorticosterone were injected. Estrogen alone was least effective and the combinations most effective.⁹ The present experiments were concerned with the action of purified lactogenic hormone alone or in combination with estrogen on the mammary rudiments of hypophysectomized male mice.

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¹ Stricker, P., and Gruter, F., *Comp. rend. Soc. de biol.*, 1928, **99**, 1978.

² Corner, G. W., *Am. J. Physiol.*, 1930, **95**, 43.

³ Gardner, W. U., and Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bull.* 196, 1933.

⁴ Turner, C. W., "Mammary Glands," Chap. XI, *Sex and Internal Secretions*, E. Allen, C. H. Danforth and E. A. Doisy, Editors, Williams and Wilkins, Baltimore.

⁵ Nelson, W. O., *Physiol. Rev.*, 1936, **16**, 488.

⁶ Lewis, A. A., and Turner, C. W., *Mo. Agr. Exp. Sta. Res. Bull.* 310, 1938.

⁷ Reese, R. P., and Leonard, S. L., *Endocrinology*, 1941, **29**, 297.

⁸ Greep, R. O., and Staveland, H. E., *Endocrinology*, 1941, **29**, 18; Gardner, W. U., and White, A., unpublished.

⁹ Gardner, W. U., *Proc. Soc. Exp. Biol. and Med.*, 1940, **45**, 835.

Hybrid male mice from 4 to 8 weeks of age were hypophysectomized using the procedure described by Thomas.¹⁰ The mice were maintained on a diet of Fox Chow and water. Completeness of operation was checked by examination of serial sections of the sella. From 3 to 47 days after operation injections of lactogenic hormone or of the latter together with estrogen[†] were started, the former administered intraperitoneally and the latter subcutaneously on alternate days. On the tenth to thirteenth day the animals were killed and the mammary glands studied from stained and dissected preparations. As the glands of untreated intact, or of hypophysectomized male mice were always extremely rudimentary, only 2 untreated controls were included in this series. They failed to show mammary growth.

Five mice received a commercial preparation of prolactin (SC) which contained 12.5 I.U. per mg. A slight mammary growth occurred in 3 mice. Two of these were caged with animals receiving

TABLE I.
Mammary Responses in Hypophysectomized Mice Receiving Only Prolactin or Prolactin Together with Estrogens.

No. of mice	Treatment*	Period treated (days)	Days post-operative at start	No. complete operations	No. incomplete operations	No. mice showing mammary growth	
						Operations complete	Operations incomplete
3	DPB and SC	12	3	2	1	2	1
1	DPB and AW	10	6	1		1	
2	DPB and SC	11	26	2		2	
3	DPB and SP	9	30	3		3	
3	DPB and SP	9	46	3		3	
3	DPB and SP†	9	47	2	1	2	1
2	SC	12	3	2		2 slight	
2	AW	10	6	2			
2	AW†	10	6	1	1		
3	SC	11	26	2	1	1	
2	SP	9	30	2			
2	SP	9	46	1	1		
2	SP†	9	34	1	1		

Each prolactin preparation was given in a dose of 1 mg daily, except in groups marked † which received $\frac{1}{2}$ mg daily.

*SC—A prolactin preparation (Schering Corporation) containing 12.5 I.U. per mg.

AW—A purified prolactin preparation—35 I.U. per mg.†

SP—A purified prolactin preparation (Schering) containing 35 I.U. per mg.

DPB—Estradiol dipropionate 1 μ g every second day.

†This prolactin preparation was demonstrated to be homogeneous as shown by studies of its solubility, electrophoretic behavior, and sedimentation in the ultracentrifuge (unpublished results.)

¹⁰ Thomas, F., *Endocrinology*, 1938, **22**, 99.

† The estradiol dipropionate and 2 preparations of prolactin (SC and SP) were generously supplied by the Schering Corporation through the courtesy of Dr. E. Schwenk.

estrogen and may have acquired enough estrogen by contact to elicit some mammary response. A moderately extensive mammary growth occurred in all mice receiving both estrogen and the same preparation of prolactin (Table I).

The rudimentary glands were not stimulated in the 10 operated animals receiving either of the 2 preparations of highly purified prolactin (SP and AW) at either of the 2 different dose levels. The 10 operated mice receiving estrogen in addition to the purified lactogenic preparations showed mammary growth rated as ++ in 8 animals and + in the other two. At the time they were removed the glands were growing rapidly as indicated by the enlarged end buds containing numerous mitotic figures. The extent of mammary proliferation averaged somewhat less than that obtained in unoperated mice receiving estrogen, and was comparable to that induced in operated mice receiving estrogen and progesterone.⁹

The failure of mammary growth to occur in hypophysectomized rats receiving lactogenic hormone has been demonstrated.¹¹ Mammary growth likewise failed to occur in hypophysectomized male mice when given the purified preparation of lactogenic hormone used in this investigation. The mammary growth occurring when estrogen was administered together with the purified lactogenic hormone indicates that prolactin may either sensitize the mammary tissue of hypophysectomized mice to estrogen or improve the general condition of these animals so that mammary proliferation may occur.

Summary. The mammary rudiments grew in hypophysectomized male mice receiving either of 2 purified preparations of prolactin and estrogen. The injection of these preparations of prolactin alone was not followed by mammary growth.

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Some Effects of Thyrotropic Hormone on the Pregnant Rat.

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Grumbrecht and Loeser¹ reported death and maceration of the embryos in rats treated with thyrotropic hormone, whereas the ovaries

¹¹ Evans, H. M., Simpson, M. E., and Lyons, W. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **46**, 586.