

0.8 cc. of a normal woman's urine. The 2 samples showing the highest unitage happened to have been taken in the mid-interval and therefore when a ripened or recently ruptured Graafian follicle may have been influential.

8462 C

Reactions of Mammary Glands of Normal and Hypophysectomized Male Guinea Pigs to Female Sex Hormone.

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It has become increasingly important during these last few years of intensive experimentation on the hormonal control of the mammary apparatus to discriminate between the respective rôles played by the primary female sex hormone (estrin) and the anterior pituitary mammary-stimulating hormone (mammatropin), in inducing growth and secretory activity of the breast.

Several years ago in the course of experiments on the effects of purified gonadotropic hormone in hypophysectomized rats¹ it was noticed that although the female genital tract responded to the hormones of the stimulated ovaries, the mammary apparatus showed only a poorly-developed duct system. These findings pointed to a greater importance of the anterior pituitary as a source of a mammary growth-promoting factor than is admitted by some investigators. To further determine the degree of mammary stimulation possible through estrin, it was decided to use hypophysectomized male guinea pigs, since Laqueur and others² have shown that the intact male guinea pig responds to estrin treatment by mammary growth and lactation. Asdell and Seidenstein³ found the development of the mammary glands of ovariectomized, hypophysectomized rabbits injected daily for 15 days with 25 rat units of estrin plus 4 rabbit units of progestin almost the same as ovariectomized, non-hypophysectomized rabbits similarly treated. Apparently they did not study the effect of estrin alone.

¹ Evans, H. M., Pencharz, R. I., and Simpson, M. E. Unpublished observation.

² Laqueur, E., Borchardt, E., Dingemanse, E., and De Jongh, S. E., *Deut. med. Wchnschr.*, 1928, **54**, 465.

³ Asdell, S. A., and Seidenstein, H. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1935, **32**, 931.

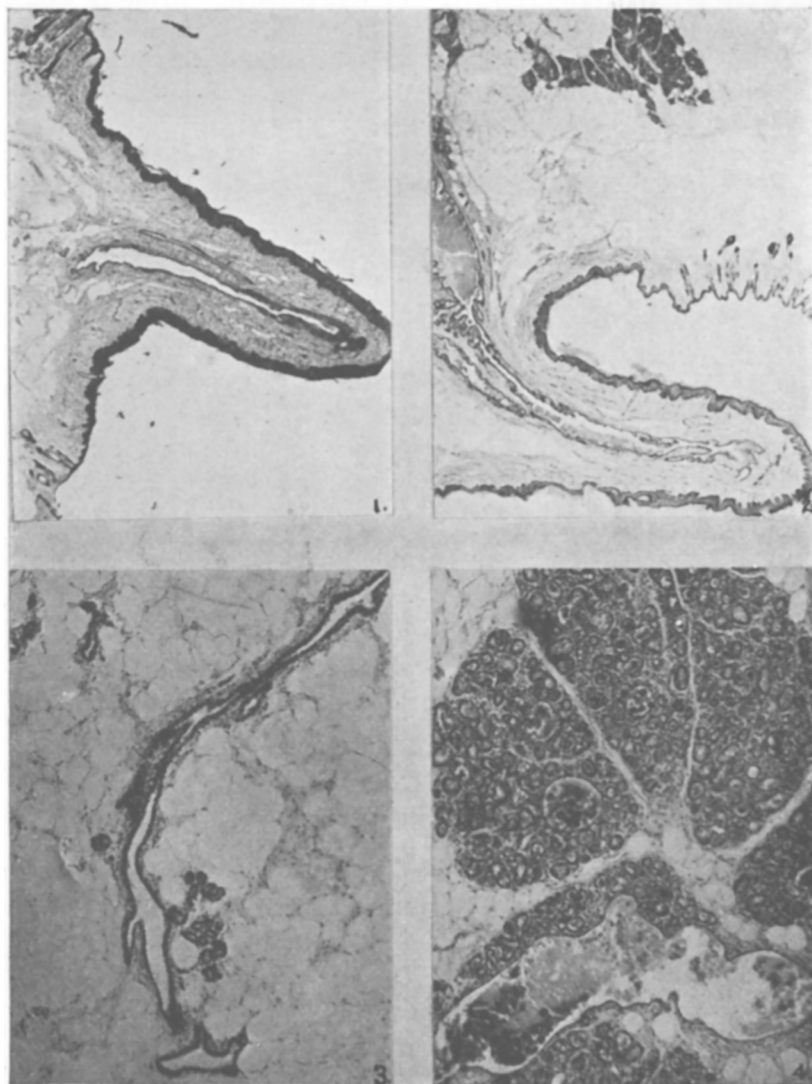


FIG. 1.

Section of nipple of hypophysectomized male guinea pig injected with estrin. x 10.

FIG. 2.

Section of nipple of normal male guinea pig injected with estrin. Part of the alveolar system and ducts distended with milk are shown. x 10.

FIG. 3.

Section of mammary gland of hypophysectomized male guinea pig injected with estrin. x 50.

FIG. 4.

Section of mammary gland of normal male guinea pig injected with estrin. x 50.

Our experimental material included 6 normal and 6 hypophysectomized male guinea pigs. The operation had been carried out by the parapharyngeal route, an approach which permits removal of all the pituitary tissue below the diaphragma sellae, but leaves the infundibular stalk with its accompanying pars tuberalis cells intact.

All of the animals were injected with Progynon* for one month. During this period each had received approximately 1800 rat units of female sex hormone.

The nipples of the hypophysectomized animals had grown from an original length of 2 mm. to 6 mm., those of the intact guinea pigs from 2 mm. to 8 mm. None had lactated as yet, but during the second month by injecting 200 rat units of estrin daily for 2 days, and then 2 rat units daily for the next 5 days as suggested by De Jongh and Dingemanse,⁴ it was possible to cause lactation in all of the intact animals within a month (2 lactating within a week). Four of the 6 hypophysectomized animals survived 2 months of injections and showed nipple development almost equal to that in the intact series, but one could express from their mammary glands only a few drops of a clear serous fluid such as may be obtained from the normal guinea pig at estrus. From the 6 intact animals milk could be readily expressed in small streams.

The accompanying photomicrographs illustrate histologically the main findings. Fig. 1 and 2, nipple sections of the hypophysectomized and intact estrin-injected males, respectively, show that this part of the male breast responds equally well in normal and hypophysectomized guinea pigs, attaining the dimensions of a normally-lactating female. Fig. 3 shows the limited growth of ducts and alveolar buds obtained in the hypophysectomized animals. Estrin promoted mitotic proliferation of solid outgrowths from the ducts with subsequent canalization. Fig. 4 shows a gland section of one of the injected intact males with functional alveolar development comparing favorably with that of normal lactation.

Since hypophysectomized male guinea pigs appear no less susceptible than normals to the effect of estrin as shown by nipple growth, and since this hormone does not cause in them lactation or growth approximating that of the intact animal similarly injected, it would seem that the presence of the pituitary is necessary for functional growth of the mammary gland. This is consistent with our former finding that the mammary glands of guinea pigs hypo-

* The progynon in oil kindly supplied to Dr. H. M. Evans by Schering Corporation contained 10,000 R.U. per cc.

⁴ De Jongh, S. E., Dingemanse, E., *Arch. Neerl. de Physiol.*, 1931, **16**, 288.

physectomized in pregnancy rapidly regress, especially following parturition.⁵

8463 C

The Dopa Reaction in Amphibia.

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Considerable evidence has accumulated indicating that the dopa reaction is specific for distinguishing melanoblastic cells in mammals (Bloch¹). According to Bloch the dopa is oxidized to dopa-melanin by a specific oxidase which is present only in cells capable of forming melanin normally. The theory further assumes that dopa (3,4-dioxyphenylalanin) which is an intermediate oxidation product of tyrosine² is the normal precursor of melanin in animals. In mammals the reaction occurs only in pigmented regions of the epidermis, never in white areas. However, in adult amphibia dopa reacts in all regions of the epidermis whether pigment is present or not.³ The reaction is most intense in the outer layers of the epidermis in contrast to the conditions in mammals where the reaction is most intense in the basal cells (*stratum germinativum*).

In the present work the skin of 4 different urodeles was used with results which confirm those of Schmidt (Table I). Laidlaw's technic⁴ was used with the exception that frozen sections were not made. Small pieces of skin were fixed for 2 hours in 5% formalin, washed 10 minutes in distilled water and placed in 0.1% buffered dopa solution at a temperature of 36°C. for 6-11 hours. The controls were put in the phosphate buffer solution without dopa. The pieces of skin were then imbedded and sectioned in the usual way. Apparently, the dopa solution penetrates the epidermis rapidly, since the reaction is the same at the cut edges as elsewhere.

⁵ Pencharz, R. I., and Lyons, W. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **31**, 1131.

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¹ Bloch, B., *Z. ges. exp. Med.*, 1917, **5**, 179; *Centralbl. Haut- und Geschlechts-Krankheit*, 1923, **8**, 1; also, summary by Biedermann, W., *Ergebn. d. Biol.*, 1928, **4**, 360.

² Raper, H. S., *Physiol. Rev.*, 1928, **8**, 245.

³ Schmidt, W. J., *Dermatol. Z.*, 1919, **27**, 284.

⁴ Laidlaw, G. F., *Anat. Rec.*, 1932, **53**, 477.