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Effect of Hypophysectomy and Replacement Therapy on Lactation in Guinea Pigs.*

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Under favorable conditions, lactation has been induced experimentally in the normal rabbit, dog, sow, guinea pig, cat, cow and goat by means of the lactogenic hormone. Hypophysectomy in late pregnancy or during lactation either prevents the initiation[1] or causes the rapid cessation of lactation.[2] In hypophysectomized dogs,[3, 4] cats and ferrets,[5] the induction of lactation has been reported to be stimulated by extracts of the anterior pituitary gland containing the lactogenic hormone.

The present study was aimed to determine the immediate effect of hypophysectomy on lactation and of replacement therapy in the initiation or maintenance of lactation in the guinea pig. Hypophysectomized lactating females and experimentally cryptorchid males carrying functional ovarian grafts from 6 to 8 weeks were used. The operation, carried on by the parapharyngeal route, was well tolerated and the high post-operative mortality experienced in earlier work was successfully controlled by the daily administration of glucose.

Seven lactating guinea pigs were hypophysectomized during the first week after delivery. Lactation at this time was well established and would normally continue for 2 to 3 weeks. All the animals showed a rapid decline in milk secretion the first day after hypophysectomy, being completely dry in 2 to 3 days. These observations confirm and extend the report of Nelson[1] in which the cessation of lactation followed hypophysectomy in 2 animals. Five

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1 Nelson, W. O., PROC. SOC. EXP. BIOL. AND MED., 1935, **33**, 222.

2 Selye, H., Collip, J. B., and Thompson, D. L., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 589; **31**, 82.

3 Evans, E. D., *U. S. D. A. Yearbook*, 1934, 360.

4 Houssay, B. A., *Comp. rend. Soc. Biol.*, 1935, **120**, 496.

5 McPhail, M. K., *Proc. Roy. Soc. B.*, 1935, **117**, 34, 45.

of these animals were given the purified lactogenic hormone‡ (galactin) in amounts varying from 20 to 50 mg. daily for periods from 9 to 12 days immediately after the cessation of milk secretion. The 5 injected and the 2 uninjected animals showed no evidence of secretion during a period of 10 days. The glands at autopsy and later verified by microscopic examination showed marked involution of the glandular parenchyma.

In addition, 6 animals which upon autopsy were found to be incompletely hypophysectomized, showed a decline in milk secretion during the first few days following hypophysectomy, but soon returned to a level which was sufficient to raise their young without other feed. The glands of these animals at autopsy showed abundant milk secretion.

A total of 10 lactating females was hypophysectomized. Four were given galactin by subcutaneous injection in varying amounts from 10 to 40 mg. immediately after hypophysectomy and continued daily thereafter for 10 days. Three of the animals were completely dry in 2 to 4 days after hypophysectomy, while the fourth was in milk throughout the observation period. At autopsy, the latter animal was found to be incompletely hypophysectomized. Two were given 10 mg. of acetone dried anterior pituitary powder daily immediately after hypophysectomy. Both animals died on the third and fourth days, respectively, after the first injection. The glands at the time of death were well hypertrophied but secretion was present only in the lumina of the large ducts. Two were given a ground aqueous suspension of ¼ of a fresh whole sheep pituitary gland daily. One of the animals died 10 days after the first injection and the second was sacrificed after 20 days. The glands of both animals at autopsy were engorged with milk comparable to normal lactating females. One animal was given 0.5 cc. of an alkaline extract (1 cc. = 1.8 gm. fresh tissue) daily. Lactation declined the day after operation. On the fourth day milk was no longer present in the glands.

Five unilaterally castrated and experimentally cryptorchid male guinea pigs carrying functional ovarian grafts for 6 to 8 weeks were hypophysectomized. (In these animals the existence of functional ovarian grafts in the cryptorchid testis causes a complete development of the mammary gland. In intact animals, the injection of galactin or the removal of the testis-grafts is followed by the secretion of milk.[6]) Three of the animals were given 10 mg.

‡ Three daily injections of 5 mg. of this preparation produced copious lactation in experimentally cryptorchid males carrying functional ovarian grafts.

[6] Turner, C. W., and Gomez, E. T., *Mo. Agr. Exp. Sta. Res. Bul.*, 206, 1934.

of galactin daily beginning immediately after hypophysectomy, while in the other 2 the testis was removed. In addition, 3 cryptorchid intact males were given 5 mg. daily as controls. One of the injected hypophysectomized animals died on the second day after the first injection and the other two 6 days later. The untreated animals were sacrificed after 10 days. Lactation did not occur in any of the hypophysectomized animals. Lactation was well established after 3 daily injections in the intact cryptorchid males.

Summary. Hypophysectomy in lactating guinea pigs is immediately followed by a rapid decline in lactation and a complete cessation within 2 to 3 days after operation. Galactin was not able to initiate lactation in hypophysectomized experimentally cryptorchid males or to re-initiate and maintain lactation following hypophysectomy at any stage during the first week of lactation. The injection of a suspension of ground fresh whole sheep pituitary gland tissue was able to maintain lactation in 2 cases.

The failure of galactin to initiate or maintain lactation in the hypophysectomized guinea pig is believed to emphasize the importance of the products of the other endocrine glands controlled by the hypophysis in lactation. The importance of the thyroid[7] and of the adrenal cortex[8] has been indicated. Carbohydrate metabolism is also intimately concerned in milk secretion.

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Maintenance of Carbohydrate Levels in Fasted Hypophysectomized Rats Treated with Anterior Pituitary Extracts.*

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It has previously been reported by one of us[1] that hypophysectomized rats, while they have normal carbohydrate levels in

[7] Graham, W. R., Jr., *Biochem. J.*, 1934, **28**, 1368.

[8] Gaunt, R., and Tobin, C. E., *Anat. Rec.* (Supp.), 1936, **64**, 18.

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[1] Russell, J. A., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 279.