

### Induced Postpartum Lactation in Hypophysectomized Rats.\*

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Although lactation has been induced in the hypophysectomized, postpartum guinea pig by injecting crude pituitary extracts, or purified lactogenic hormone supplemented by salt, cortin or adrenocorticotrophic hormone,<sup>1-3</sup> Nelson and Gaunt using similar methods failed to maintain lactation in hypophysectomized, lactating rats.

To obtain further evidence on this point 14 rats were hypophysectomized 5-24 hours before delivery. Four of these rats were retained as controls, and the remaining 10 were injected twice daily with relatively large subcutaneous doses of a lactogenic preparation containing adrenocorticotropin, but no thyrotropin, gonadotropin or somatotropin. All rats were given 1.0 cc. of a 20% glucose solution twice daily.

Four rats received a total dose of 0.5 gm. of a sheep pituitary extract equivalent to approximately 2,500 pigeon macro-units of mammotropin<sup>6</sup> and 10 rat units of adrenocorticotropin,<sup>7</sup> over a period of 10 days. The young, although nursed, did not obtain

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<sup>1</sup> Gomez, E. T., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 404.

<sup>2</sup> Nelson, W. O., and Gaunt, R., *ibid.*, 1936, **34**, 671.

<sup>3</sup> Gomez, E. T., and Turner, C. W., *ibid.*, 1936, **35**, 365.

<sup>4</sup> Gomez, E. T., and Turner, C. W., *ibid.*, 1937, **36**, 78.

<sup>5</sup> Nelson, W. O., and Gaunt, R., *ibid.*, 1937, **36**, 136.

<sup>6</sup> Lyons, W. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **35**, 645.

<sup>7</sup> Moon, H. D., *ibid.*, 1937, **35**, 649.

#### FIG. 1.

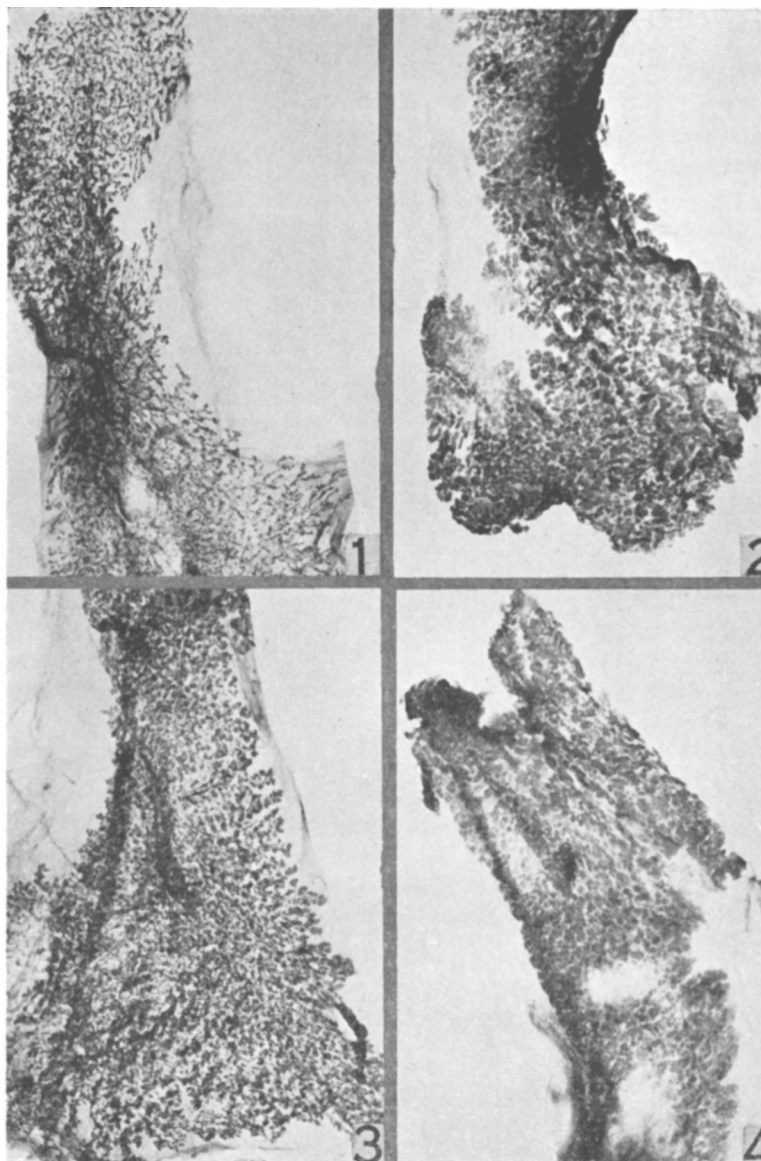
Mammary gland from a rat hypophysectomized 1 day antepartum and sacrificed on the 11th day postpartum. Alveoli have regressed to the small bud stage. No milk.

#### FIG. 2.

Same from a normal rat 11th day postpartum. This rat was suckling a normal litter, and therefore some of the lobules have been partially drained, while others are filled with milk.

#### FIG. 3.

Same from a rat hypophysectomized 1 day antepartum and injected for 10 days with 2,500 units mammotropin and 10 units adrenocorticotropin. Sacrificed on the 11th day postpartum. Some of the lobules have been maintained in a func-



tional state and contain milk, but due to insufficient dosage considerable regression has occurred.

FIG. 4.

Same from a rat hypophysectomized 1 day antepartum and injected for 10 days with 10,000 units mammotropin and 40 units adrenocorticotropin. Microscopically, as well as grossly, this gland could not be distinguished from a normal lactating gland. Its lobules appear more engorged with milk than those in Fig. 2.

All figures  $\times 1\frac{1}{2}$ . Glands stained *in toto* with alum carmine, and cleared with methyl salicylate.

sufficient milk and died after 5 days. The mothers were sacrificed on day 11. Fig. 3 shows a mammary gland representative of this group. The alveolar units show considerably better development than is found in the rapidly regressing glands of the hypophysectomized control animals (Fig. 1). They were, however, less well developed than those of normal 10-days postpartum animals (Fig. 2).

Two rats received 1.0 gm. (5,000 macro-units mammotropin and 20 units adrenocorticotropin) over a period of 5 days. The mammary glands were well developed and lactating, but the young, though nursed, were not sustained. All died of inanition by day 5.

The remaining 4 rats received 2.0 gm. (10,000 macro-units of mammotropin and 40 units of adrenocorticotropin) over a 10-day period. Milk could be expressed from the nipples throughout the injection period, and was observed through the abdominal wall in the stomachs of the young. The mothers exhibited normal nesting and nursing behavior, and the young were almost continuously attached to the greatly elongated nipples. But even in this group lactation was deficient, and the original litters died by day 5. Three 5-day-old foster young from normal mothers were then given to each of these mothers. Although they were successful in obtaining milk from their foster mothers for the remaining 5 days of the experiment, they also gradually lost weight. The mammary glands of these mothers appeared grossly (Fig. 4) and microscopically like those of the normal lactating controls.

The thyroids and ovaries of the injected and control hypophysectomized rats showed regression. The thymus glands of the injected, but not of the control hypophysectomized, rats had atrophied to about one-tenth the normal weight, as a result, apparently, of adrenal stimulation. The adrenals of the injected hypophysectomized rats were not only maintained by the adrenocorticotropin, but were hypertrophic (in one case the 2 adrenals weighed 357 mg.). It is not likely, therefore, that an adrenal deficiency was the limiting factor in this experiment.

*Summary.* It was possible to induce postpartum lactation in hypophysectomized rats, and to maintain a functional development of their mammary glands by injections of combined mammotropic and adrenocorticotropic hormones. That this treatment did not constitute complete substitution therapy was shown, however, by the fact that sufficient milk was not available for sustenance of the young.