

The Adrenals and Pituitary in Initiation of Lactation.

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The authors¹ have shown, and Gomez and Turner² confirmed, that a purified pituitary lactogenic extract, unlike crude pituitary extract, will not produce lactation in hypophysectomized guinea pigs, but will do so if adrenal cortical hormone is simultaneously administered. A further analysis of factors permitting lactation in the guinea pig is reported here.

Mammary glands of guinea pigs, male or female, were developed by oestrin* injections of 30 or more R.U. per day for not less than one month. Purified lactogenic hormone* was used in doses of 10 mg. or more of powder daily. Glucose solutions were injected after hypophysectomy.

I. It was again found that lactogenic hormone would not, after 8 days' treatment, start lactation in hypophysectomized pigs (3 cases). It would, however, cause lactation if cortical hormone* were given simultaneously (3 cases).

II. That either crude pituitary extract alone or purified lactogenic hormone plus cortical hormone will induce lactation, suggested that the adrenotropic fraction is the missing factor in purified extracts. This assumption was verified by experiments in which 4 hypophysectomized pigs were treated with lactogenic hormone plus 2 cc. daily of adrenotropic hormone.* All animals lactated within 1-3 days. One of these pigs was treated for a week with lactogenic hormone, without lactating, before treatment with adrenotropic hormone was begun. Another was treated 6 days with adrenotropic hormone, without lactating, before treatment with lactogenic hormone was begun. A fifth animal, treated for a week with adreno-

¹ Nelson, W. O., and Gaunt, Robert, *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **34**, 671.

² Gomez, E. T., and Turner, C. W., *PROC. SOC. EXP. BIOL. AND MED.*, 1936, **35**, 365.

* This work was made possible by gifts of the following materials, for which the authors are indebted: Adrenal cortical extract—Dr. W. W. Swingle, Princeton University; crude pituitary extract (sheep), lactogenic hormone and theelin—Dr. Oliver Kamm, Parke-Davis and Co.; amniotin—Dr. J. A. Morrell, E. R. Squibb and Sons; adrenotropic hormone—Dr. J. B. Collip, McGill University.

tropic hormone only, failed to lactate. These facts suggest that adrenotropic and lactogenic fractions are not identical.

III. Since salt therapy is known to alleviate symptoms of adrenal insufficiency, attempts were made to induce lactation in hypophysectomized pigs treated with lactogenic hormone and high doses of NaCl. Salt was given by subcutaneous or intraperitoneal injection, in drinking solution, or by stomach tube, in amounts regulated to prevent diarrhea. Any type of salt therapy tried plus purified lactogenic hormone induced lactation within 4-5 days (7 cases).

IV. Attempts to induce lactation in adrenalectomized pigs were difficult because the guinea pig is quickly susceptible to adrenal insufficiency, and crude pituitary extracts hasten death. Pigs were treated for 36 hours after adrenalectomy with cortical extract and salt to assist in recovery from the severe operation. Twenty-four hours after the last cortical hormone injections, lactogenic extracts were begun, and salt therapy continued. Eleven cases of complete adrenalectomy were thus obtained which lived from 3 to 12 days after the beginning of lactogenic injections. None lactated. Five of these had received purified lactogenic hormone, living an average of 8 days after lactogenic hormone injections began. Six received crude pituitary extract, living an average of 4.6 days. With longer survival it is possible, but improbable, that salt-treated, adrenalectomized pigs on crude extract might eventually have lactated.

In completely adrenalectomized pigs, if cortical extract and pituitary extract were given throughout the period after adrenalectomy (one case) or after pituitary extracts alone had failed to induce lactation (3 cases) milk secretion started.

Incompletely adrenalectomized pigs lactated within 60 hours after either crude or purified lactogenic extracts were given (6 cases).

An amount of cortical hormone, or tissue, insufficient to prevent adrenal insufficiency (asthenia, weight loss, anorexia) or even to maintain life, will generally permit lactation. This was unexpected because the hypophysectomized pig, without any marked symptoms of adrenal insufficiency, must nevertheless have more cortical hormone than its own adrenals will release in order to lactate. The theory that lactation failure in adrenalectomized animals is due primarily to disturbances in fluid and electrolyte balance, which explains satisfactorily the phenomenon observed in adrenalectomized lactating rats,^{3,4} and in salt-treated hypophysectomized guinea pigs is

³ Gaunt, Robert, and Tobin, C. E., *Am. J. Physiol.*, 1936, **115**, 588.

⁴ Levenstein, Irving, *Anat. Rec.*, 1937, (in press).

less well illustrated, but not precluded, in adrenalectomized pigs. In the latter animals clear serum was nearly always expressible from the nipples during the observation period. If cortical hormone or tissue was present this fluid quickly became milk. Sufficient fluid for milk flow was probably present.

In guinea pigs lactating normally after parturition, production of "artificial adrenal insufficiency"⁵ by intraperitoneal injection and subsequent withdrawal of isotonic glucose solution for 2 successive days, either entirely or almost, stopped lactation (4 cases). Lactation was quickly reinstated by salt solutions given orally.

Conclusion. Experiments of several types indicate that adrenal cortical hormone is necessary for milk production, and that the disturbance of cortical function produced by hypophysectomy, or adrenalectomy prevents the initiation of lactation in the guinea pig.

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Horizontal Respiratory Graphs by Automatic Feed of Oxygen into a Basal Metabolism Apparatus.

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When respiratory tracings are taken of a subject breathing air, oxygen must be added to maintain the oxygen concentration at the desired level. A previous method employed a calibrated air pump by which the experimenter forced into the gas circuit sufficient oxygen to maintain the graph approximately horizontal. The oxygen concentration in the circuit was subject to considerable variation depending on the frequency with which the oxygen consumed by the patient was replenished. Furthermore, the graphs were difficult to calculate accurately, since the oxygen admitted was reflected intermittently on the tidal air curve. The "concertina apparatus" was used by Haldane¹ for gases of fixed concentrations but the expiratory phase on the graph was traced as a result of the refilling of the concertina from a gas source other than the lungs. Poulton² em-

⁵ Gilman, Alfred, *Am. J. Physiol.*, 1934, **108**, 662.

¹ Haldane, J. S., "Respiration," new edition, University Press, London, 1935, p. 208.

² Poulton, E. P., *Guys Hospital Gazette*, 1935, **49**, 346.