portion of the process. It may be that the intermediate phase is not observed, because the amino group of p-aminobenzoic acid reacts with the red substance (halochrome) to give soluble anilino-like compounds which undergo auto-oxidation to a brownish melanin more soluble than that derived from tyrosine alone. Pugh and Raper[11] did not observe aniline to form an anilino compound with tyrosine oxidized by tyrosinase, but isolated anilino compounds when catechol or p-cresol was oxidized by tyrosinase and oxygen. Moreover, they found that aniline alters melanin formation, an observation confirmed by the data of Table I, since no black pigmentation occurred when tyrosine was acted upon by tyrosinase in the presence of the aromatic amine.

In view of the above, it is conceivable that p-aminobenzoic acid modifies in the animal organism the type of melanin produced from the oxidation of dopa by dopa oxidase, an enzyme which has been found in skin by Bloch and Schaaf.[12] The nature of this enzyme is not clearly defined. Whether it will eventually be found to be a specific dopa oxidase[1] or an inh'bited tyrosinase,[13, 14] is immaterial as far as the data presented are concerned, because p-aminobenzoic acid appears to enter the non-enzymatic portion of the reactions leading to the formation of melanin.

Summary. Para-aminobenzoic acid modifies the formation of melanin; sulfanilamide has an apparently similar effect; under identical conditions, calcium pantothenate has no influence.

13027

Inability of Desoxycorticosterone to Maintain Lactation.*

ROBERT GAUNT.

From the Department of Biology, Washington Square College of Arts and Science, New York University, New York City.

The following facts have established the adrenal cortex as an important factor in lactation: (1) adrenalectomized rats do not

[11] Pugh, C. E. M., and Raper, H. S., *Biochem. J.*, 1927, **21**, 1370.

[12] Bloch, B., and Schaaf, F., *Biochem. Z.*, 1925, **162**, 181.

[13] Raper, H. S., *Physiol. Rev.*, 1928, **8**, 245.

[14] Figge, F. H. J., PROC. SOC. EXP. BIOL. AND MED., 1941, **46**, 269.

* This work was aided by a grant from the American Philosophical Society. We are indebted to Dr. Erwin Schwenk, the Schering Corporation, for the desoxycorticosterone acetate (cortate) used here.

lactate normally.[1-5] This deficiency can be corrected by cortin but only if relatively large doses are given;[6] (2) changes are apparent histologically in the mammary glands of lactating, adrenalectomized rats;[7] (3) the induction of an experimental lactation is facilitated in rats by cortin injections;[8] (4) the hypophysectomized guinea pig can be made to lactate with purified lactogenic hormone only if cortin, adrenotropin or salt is concomitantly given.[9] The latter point may not be true of the hypophysectomized rabbit.[10] Brownell, Lockwood and Hartman believed that the lactation-supporting factor of the adrenal cortex, which they designated *cortilactin,* was chemically separable from the life-maintaining factor.[3] The study of crystalline cortical substances is of obvious importance in elucidating the physiology of the above-mentioned phenomena.

This report concerns the effect of desoxycorticosterone acetate (DCA) on the lactation of rats adrenalectomized within 24 hours after delivery. The growth rate of the suckling young was used as an index of lactation. All litters were reduced to 6 each. Although the growth curves included here are shown for the first 30 days, they serve as a measure of lactation only up to 15 to 20 days, at which time the young began to eat. Well-nourished litters of normally lactating mothers began to eat earlier that the various dwarfed litters. Treatments were usually discontinued at 20 days if the litters lived that long. I. The normal growth rate for this rat colony is shown in curve 1 for 15 unselected litters, reduced to 6 young each. The mortality from all causes was 5% and probably in no case was due to lactation failure. II. In 7 untreated adrenalectomized mothers lactation was sub-normal but no deaths of young occurred before 15 days and 34% were raised to weaning (curve 3). This result is somewhat better than we previously found, probably because the adrenalectomies were delayed until after parturition. The mothers lost an average of only 5% of their body weight while

1 Carr, J. L., PROC. SOC. EXP. BIOL. AND MED., 1931, **29**, 131.

2 Gaunt, R., *Am. J. Physiol.*, 1933, **103**, 494.

3 Brownell, K. A., Lockwood, J. E., and Hartman, F. A., PROC. SOC. EXP. BIOL. AND MED., 1933, **30**, 783.

4 Britton, S. W., and Kline, R. F., *Am. J. Physiol.*, 1936, **115**, 627.

5 Tobin, C. E., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 599.

6 Gaunt, R., and Tobin, C. E., *Am. J. Physiol.*, 1936, **115**, 588.

7 Levenstein, I., *Anat. Rec.*, 1937, **67**, 477.

8 Reece, R. P., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 25.

9 Reviewed by Nelson, W. O., and Gaunt, R., *Cold Spring Harbor Symp. Quant. Biol.*, 1937, **5**, 398.

10 Fredrikson, H., *Acta Obst. et Gynec. Scand.*, 1939, **19**, Suppl. 1, 1.

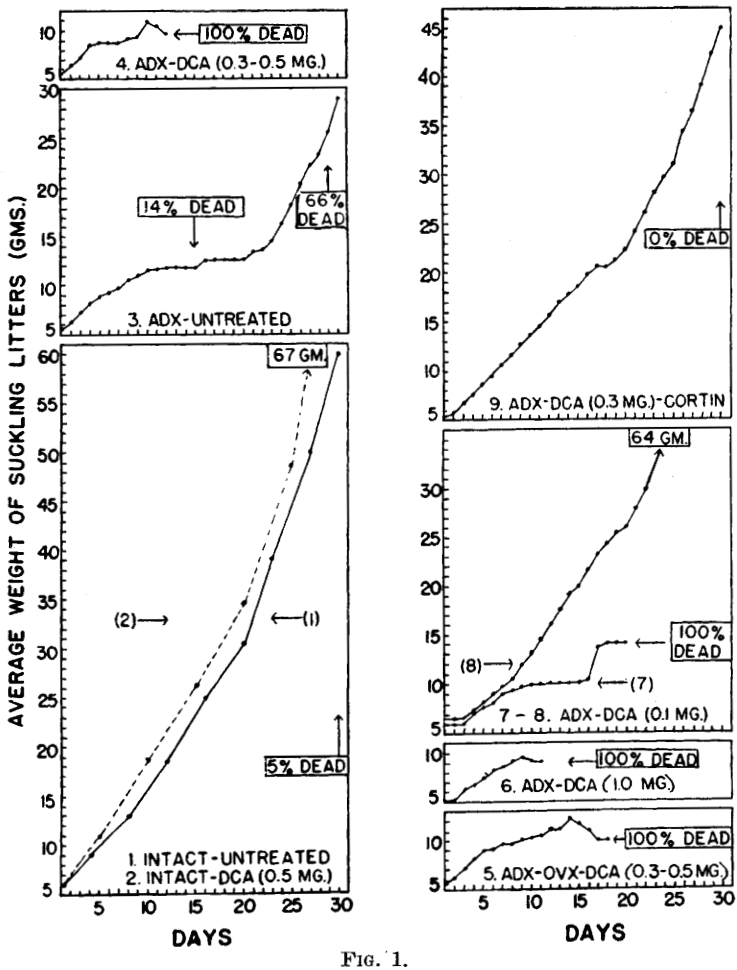

FIG. 1.

Average growth curves of rat litters from mothers receiving various treatments. Curve 1 is the average of 15 litters; curve 2, 4 litters; curve 3, 7 litters; curves 4, 5 and 9, 4 litters each; curve 6, 2 litters; curve 7, 1 litter; curve 8, 3 litters. Abbreviations are as follows: Adx.—adrenalectomized; Ovx—ovariectomized; DCA—desoxycorticosterone acetate.

lactating. Shortly after lactation stopped adrenal insufficiency became more severe and all but one mother died.

Previous work showed that cortin, given in adequate dosage to such adrenalectomized animals, supports a completely normal lactation.[6] III. DCA was given to a total of 14 adrenalectomized mothers in doses ranging from 0.1 to 1.0 mg per day (curves 4-8). Of this group 13 litters died, and one, anomalously, grew normally (curve 8), although the mother later died of adrenal insufficiency. The failure of lactation in these cases occurred despite freedom from

all obvious symptoms of adrenal insufficiency. All but one of the 14 animals gained weight while lactating, with average increments as follows: those shown in curve 4 gained 8%; curve 5, 17.8%; curve 6, 12%; curve 7, 4%; and curve 8, 15%. Normal untreated mothers (curve 1) gained 4.2% during the first 20 days of lactation. Thirteen of the mothers died after treatment was discontinued.

It is clear that DCA will not support lactation. There is also a suggestion in these results, first, that lactation is worse instead of better with the larger doses of DCA, and, secondly, that litters of untreated mothers fared better than those of treated mothers, *i. e.*, that DCA inhibited lactation. We do not consider that the differences were great enough to establish this as fact, but if it eventually proves to be true a reason may be found in the observation that DCA is a mammary-growth stimulant,[11] and therefore might be expected to inhibit lactation when given in proper dosage.[12]

IV. There was no significant influence of 0.5 mg DCA per day on the lactation of intact rats (curve 2), indicating that if this substance is a lactation inhibitor its effects are counteracted (at this dose level) by other cortical secretions. The same conclusion is indicated by the near normal response of adrenalectomized mothers given DCA plus 2 cc per day of an old and relatively weak batch of cortin (curve 9).

V. The dose of estrogen needed to inhibit lactation is about 10× greater in castrate than intact rats.[13] We thought, therefore, that ovarian removal might modify the response of adrenalectomized mothers given DCA. A comparison of curves 4 and 5 suggests that possibly the castrates lactated a little better than animals with ovaries intact, but the difference was of questionable significance.

Summary. The necessity of adrenal cortical secretions for the support of lactation in rats was confirmed. Desoxycorticosterone acetate, unlike adrenal cortical extract, was of no benefit at all in correcting this deficiency, and may have further depressed lactation.†

11 Van Heuverswyn, J., Folley, S. J., and Gardner, W. U., PROC. SOC. EXP. BIOL. AND MED., 1939, **41**, 389.

12 Folley, S. J., *Lancet*, 1941, **1**, 40.

13 Edelmann, A., and Gaunt, R., *Physiol. Zool.*, in press.

† Since the above experiments were completed tests have been made, in collaboration with Dr. E. C. Kendall, on the lactation-maintaining potency of other adrenal compounds. This work is still in progress but the following facts have been established: Kendall's compound A (dehydrocorticosterone) and compound E (17-hydroxy-11-dehydrocorticosterone) were about equally effective, and in daily doses approximating 0.5 mg maintained a growth rate in suckling young which approached but did not reach normal (9 of 10 litters survived). Kendall's cortin was distinctly more effective than his amorphous fraction when given in doses that were of equal potency in maintaining adrenalectomized dogs.