Effect of Corticosterone and Aldosterone Upon Milk Yield In the Rat.* (30964)

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It has been reported that cortisone and hydrocortisone acetate injection(1) increased milk yield in the rat, as measured by growth rate of their litters. However, the observation that the predominant secretions of the rat adrenal cortex are aldosterone and corticosterone(2) suggested that these compounds be tested. Anderson and Turner(3) found that 25 μg aldosterone and 1 mg corticosterone acetate per day maintained lactation at approximately 80% of the normal level in adrenalectomized rats and suggested that daily requirements of aldosterone and corticosterone in maintenance of normal lactation in the rat exceed 25 μg per day for aldosterone and 1 mg per day for corticosterone.

It became of interest, therefore, to determine the influence of these hormones on lactation of normal rats. The objective of the present study was to determine the effect of corticosterone and aldosterone separately and together in augmenting the milk yield of normal lactating rats.

Materials and methods. Pregnant Sprague-Dawley-Rolfsmeyer rats were maintained in individual litter cages, fed Purina Lab Chow and water *ad libitum*. The animal room was maintained at a temperature of 78 ± 1°F. On day 4 of lactation, litters were standardized to 6 pups.

Aldosterone-21-acetate was dissolved in sesame oil in a concentration of 25 μg per 0.1 ml carrier. Graded levels of corticosterone were suspended in physiological saline. From day 7 to 19 of lactation, the dams were injected subcutaneously, once daily, approximately at the same time as follows: 1) 44 controls were injected with physiological saline, 2) 9 rats were injected with 0.75 mg corticosterone, 3) 21 rats were injected with 1 mg corticosterone, 4) 24 rats were injected with 1.25 mg corticosterone, 5) 10 rats were injected with 1.5 mg corticosterone, 6) 18 rats were injected with 25 μg aldosterone-21-acetate, and 7) 16 rats were injected with 25 μg aldosterone-21-acetate + 1 mg corticosterone.

On days 14, 16, 18 and 20, milk yields were estimated from the increases of litter weights during a 30-minute nursing period following 10 hours of isolation from the mother. One USP unit of oxytocin was injected subcutaneously into the dams immediately before nursing and a second unit after 15 minutes of nursing to aid in complete milk removal. Student's "t" test was used in statistical treatment of the data.

Results. The estimated milk yield from day 14 to 20 for a group of 90 control animals (Group 1) has been determined in this laboratory (Table I). Of this group, 44 control animals were involved in the present experiment (Group 2). The effect of various hormone treatments will be compared with Group 2. Lactating rats injected with 0.75 mg corticosterone/day showed no beneficial effect on lactation (Table I). Administration of 1 mg/day increased milk yield 12.0% ($P<0.20$) on day 14, 13.2% ($P<0.05$) on day 16, 13.3% ($P<0.05$) on day 18, and 27% ($P<0.001$) on day 20. Injection of 1.25 mg/day increased milk yield on days 14 to 20; however, only on days 14 and 20 was milk production significantly increased ($P<0.05$). The animals injected with 1.5 mg/day showed a 12% decrease in milk yield on day 14 and 6% on day 16; however, it increased 21% ($P<0.01$) on day 20. Administration of 25 μg aldosterone alone failed to show a response to the hormone. The combination of 25 μg aldosterone and 1 mg corticosterone increased milk yield 34.8% ($P<0.001$) on day 14, 24% ($P<0.01$) on day 16, 12.6% ($P<0.05$) on day 18, and 12.7% ($P<0.05$) on day 20.

Discussion. Lactogenic hormone is believed

* Contribution from Mo. Agr. Exp. Sta. Journal Series No. 3012. Approved by Director. This investigation was supported in part by a grant from USPHS.

TABLE I. Effect of Corticosterone and Aldosterone on Lactation in the Rat.

Group	Treatment	No. of animals	Milk yield after 10 hr separation (g)* Day 14	% change	P	Day 16	% change	P	Day 18	% change	P	Day 20	% change	P
I	Control†	90	9.8	—		12.4	—		13.8	—		10.7	—	
II	Control	44	9.2 ±.54	—		12.0 ±.71	—		14.3 ±.76	—		12.6 ±.64	—	
III	.75 mg corticosterone	9	8.6 ±.78	-6.5	<.30	11.0 ±.74	-9.1	<.20	13.0 ±1.00	-9.1	<.20	12.0 ±.70	-4.8	<.30
IV	1.0 mg "	21	10.3 ±.74	12.0	<.10	13.7 ±.60	13.2	<.05	16.2 ±.61	13.3	<.05	16.0 ±.72	27.0	<.001
V	1.25 mg "	24	11.1 ±.65	20.7	<.025	12.5 ±.88	3.3	<.40	15.0 ±.84	4.9	<.30	14.4 ±.76	14.3	<.05
VI	1.50 mg "	10	8.1 ±.89	-12.0	<.10	11.4 ±1.12	-5.8	<.40	14.6 ±.76	2.1	<.40	15.3 ±.68	21.4	<.005
VII	25 μg aldosterone	18	9.7 ±.73	5.4	<.30	13.6 ±.91	12.4	<.20	14.2 ±1.12	-.7	>.50	11.5 ±.77	-8.7	<.20
VIII	*Idem* + 1.0 mg corticosterone	16	12.4 ±.62	34.8	<.001	15.0 ± .73	24.0	<.005	16.1 ± .76	12.6	<.05	14.2 ±.69	12.7	<.05

* Mean ± standard error.
† Mean of Group II + 46 control animals of another experiment.
P = Student's *t* probability: significance of difference from controls.

to play a primary role in stimulating milk secretion. However, other hormones are believed to synergize with lactogen in stimulating increased milk yield. In the lactating rat, it has been shown that exogenous oxytocin administered at the time of nursing aids in complete milk removal(4). During recent years, in a series of studies from this laboratory, the possible effect of a number of hormones upon the yield of milk has been studied. The following hormones have been shown to stimulate increased milk yield: growth hormone(4), thyroxine(5), lactogenic hormone(6) and parathyroid hormone(7), administered separately and together(8). Recently, it was shown that insulin also stimulated increased milk secretion(9). The present report is a continuation of this study. It was suggested that lactating rats show a dose response to the action of corticosterone and at an optimal level of corticosterone can increase established milk yield in the rat. Although aldosterone alone was ineffective, the combination of the 2 adrenal steroids increased milk yield on days 14 to 20 compared with control animals; however, there is no statistically significant difference when the 2 hormones were compared with 1 mg/day corticosterone alone, except a 20.4% increase ($P<0.025$) on day 14 and a 11.2% decrease ($P<0.05$) on day 20, indicating that the effectiveness of the combination is due mainly to the action of corticosterone.

Summary. Daily subcutaneous administration of 1 mg of corticosterone to Sprague-Dawley-Rolfsmeyer rats from day 7 to 19 of lactation stimulated increased milk secretion on days 14 to 20. On day 14 milk yield was increased 12.0%, on day 16, 13.2%, on day 18, 13.3%, on day 20, 27.0%. Higher levels of the hormone depressed milk yield, whereas a lower level of corticosterone was ineffective. Twenty-five μg aldosterone alone was either of no benefit or only slightly effective. Although the combination of 1 mg corticosterone plus 25 μg aldosterone increased milk yield on days 14 to 20 compared with control animals, it appears that the increased milk yield is due primarily to the effect of corticosterone alone.

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Received October 18, 1965. P.S.E.B.M., 1966, v121.

Evidence from Cross Circulation Studies for a Humoral Mechanism In the Natriuresis of Saline Loading. (30965)

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Sodium excretion by the kidney is dependent upon both the amount of sodium filtered at the glomerulus and renal tubular reabsorption. Although a rise in the filtered load of sodium (F_{Na}) plays an important role in the natriuresis resulting from saline loading, experiments by de Wardener *et al*(1) demonstrated that an increase in sodium excretion occurs even when the glomerular filtration rate (GFR) is reduced. This dissociation between urinary sodium excretion and filtered sodium load was subsequently confirmed by Levinsky and Lalone(2). Rector and coworkers(3) provided indirect evidence that decreased proximal tubular reabsorption of sodium occurs during saline loading. Direct confirmation of decreased proximal reabsorption of fluid in saline diuresis was recently reported by Dirks, Cirksena and Berliner(4) using micropuncture methods in the dog.

It has been suggested from cross circulation experiments by de Wardener and associates(1,5) and from studies in an isolated kidney preparation by Lichardus and Pearce(6) that a humoral sodium excreting factor contributes to the natriuresis of saline loading but the evidence presented failed to exclude the possibility that an increase in GFR produced the increase in sodium excretion.

In the present study, blood was cross circulated from saline loaded donor dogs through normal recipients in which a reduction in GFR was produced by aortic constriction immediately above both renal arteries. In 9 of 12 experiments an increase in sodium excretion occurred in the recipient in the presence of a decreased filtered sodium, a finding which suggests a decrease in fractional renal tubular reabsorption by a humoral mechanism.

Material and methods. The experiments were performed in 15-25 kg female mongrel dogs. Blood from each pair of dogs was cross matched to insure compatibility. All dogs were fed a synthetic diet containing 60 mEq of sodium and 18 mEq of potassium per day. The last feeding was 20-24 hours before the experiment but water was allowed *ad libitum*. The donor dogs received 15 mg of desoxycorticosterone acetate in oil intramuscularly per day for 2 days prior and 30-60 minutes before the experiment was begun. The animals were anesthetized with sodium pentobarbital 30 mg/kg intravenously and endotracheal intubation performed.

Two series of animals were studied. In Series I blood was cross circulated from normal non-saline loaded donors through normal recipients. In Series II the blood was cross circulated from saline loaded donors. Saline loading of the donor was accomplished by infusing 1 liter of normal saline intravenously as rapidly as possible and continu-

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