

Effects of Prolactin and Cortical Hormones on Body Weight and Food Intake of Adrenalectomized Pigeons.

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Earlier publications^{1,2} have shown that in pigeons both prolactin and adrenal cortical hormones can prevent or reduce the loss in weight of body and viscera which otherwise occurs during the 10 days immediately following hypophysectomy. The clear demonstration of this action of cortical hormones made it necessary to learn whether the similar action of prolactin on body weight and food intake is mediated by the adrenals. Although it was known that most of the preparations of prolactin used in these particular studies^{1,2} were almost free of any ability to enlarge the adrenals of 2-day chicks and 21-day rats only tests of effects of prolactin in completely adrenalectomized pigeons could resolve this question. Since cortical hormone preparations had shown additive effects with prolactin on body weight and food intake of hypophysectomized pigeons² two cortical preparations were included in the present study. War conditions have made it necessary to discontinue this work before all contemplated tests could be made, but the results already obtained seem to warrant publication.

Methods. Carneau pigeons aged 1.5 months from hatching were adrenalectomized in 2 stages under nembutal anesthesia with an interval of one week between the operations. The technic is essentially similar to that independently developed by Bülbring.³ Each adrenal is removed in one piece by blunt dissection. At death or at killing the completeness of removal was determined by histological examination of any doubtful tissue. Incomplete removal of the adrenals was relatively

rare and data from such animals are not included here. Immediately before the second operation 1 mg of desoxycorticosterone acetate was injected. During experimental periods salt (NaCl, .75 g, NaHCO₃, .125 g) in gelatin capsules was given twice daily unless the birds were injected with a cortical hormone.

All injections were begun on the day of the second operation. Adrenal cortex extract* (ACE) was given twice daily and desoxycorticosterone acetate† (DCA) or prolactin once daily. The preparation of prolactin used contained, according to our methods of assay,⁴ the following units per mg of hormones: prolactin, 17; gonadotrophin, <.004; thyrotrophin, 0.06; corticotrophin, .024. The total amount of food and water consumed in each period was measured and the average daily intake per bird calculated.

Results. When given salt as noted above adrenalectomized young Carneau pigeons have an average survival period of 9 days after removal of the second adrenal; none has lived longer than 17 days without cortical hormone therapy. Drakes are reported⁵ to survive 8 to 10 hours, whereas fowl are said⁵ to live for as long as 82 days after adrenalectomy. Adrenalectomized pigeons lose weight slowly at first and then rapidly during a day or two before death (Fig. 1). Daily food intake in the 10-day period after operation is reduced

* Adrenal cortex extract was supplied through the courtesy of Dr. David Klein, The Wilson Laboratories.

† Desoxycorticosterone acetate was supplied through the courtesy of Dr. Erwin Schwenk, Schering Corporation.

⁴ Bates, R. W., Riddle, O., and Miller, R. A., *Endocrinology*, 1940, **27**, 603.

⁵ Herrick, E. H., and Torstveit, O., *Endocrinology*, 1938, **22**, 469.

¹ Schooley, J. P., Riddle, O., and Bates, R. W., *Am. J. Anat.*, 1941, **69**, 123.

² Miller, R. A., and Riddle, O., *Abst. in Anat. Rec. Suppl.*, 1942, **84**, 40; complete paper, *Endocrinology*, 1943, in press.

³ Bülbring, E., *J. Physiol.*, 1937, **80**, 64.

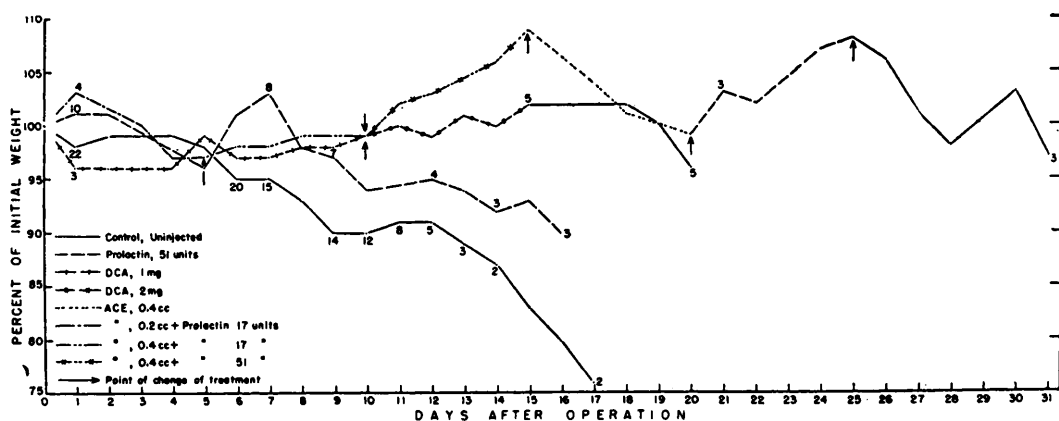


Fig. 1.

Changes in body weight of adrenalectomized pigeons injected with cortical hormones and prolactin. The figures on each curve indicate the number of surviving animals.

to about one-fifth the amount eaten by normal unoperated pigeons (Table I). Water intake was apparently unaffected by adrenalectomy but it was increased markedly when salts were given.

The effects of prolactin, DCA and ACE on body weight and on food and water consumption are presented in Table I and Fig. 1. One mg daily of DCA partially supported food consumption for two 5-day periods but did not cause an increase in body weight; 2 mg restored growth rate and food intake to levels characteristic of normal unoperated pigeons. Water intake was not appreciably changed by DCA. It is notable, however, that similar amounts of DCA markedly stimulated the water consumption of hypophysectomized pigeons.² When no treatment was given during a final 5-day period (15-20 days) following 2 mg DCA daily body weight remained constant for a few days and then declined. In this case prolonged absorption of DCA from the sesame oil solution injected during the preceding 15 days probably accounts for the temporary maintenance of body weight and a level of food intake somewhat higher (Fig. 1) than that found in other untreated adrenalectomized pigeons.

Prolactin caused an increase in the weight of adrenalectomized pigeons when adrenal insufficiency was not acute. All of the pigeons of Group III regained at least some of the weight lost after adrenalectomy and most of them became considerably heavier than at operation; all of them, however, lost weight

sooner or later as adrenal insufficiency developed even though prolactin was being administered. In the averages presented for birds of Group III (Table I, Fig. 1) the marked gains in weight by some pigeons are largely concealed by the heavy losses in other moribund animals. The ability of prolactin to stimulate an increase in the body weight of adrenalectomized pigeons was again clearly demonstrated by the animals of Group V (Fig. 1) during the fifth period (20-25 days) after operation. These pigeons had been maintained previously with adrenal cortical extract. It seems probable that the loss of weight during the immediately preceding period (15-20 days) was not the result of insufficient dosage with ACE but the result of discontinuing an earlier series of injections of prolactin (Table I, Fig. 1).

Either prolactin or ACE partially maintained food consumption, and this partial support of appetite by each hormone appears to be additive when both substances were injected into the same adrenalectomized pigeons (Table I). When amounts of ACE similar to those given here were injected into hypophysectomized pigeons water intake was greatly stimulated.²

Discussion. The above results, and the literature cited, demonstrate that prolactin stimulates more than normal increases in the weight of pigeons in the absence of either the adrenals or the anterior pituitary, while cortical hormones restore a normal rate of growth in adrenalectomized pigeons but only partially

TABLE I.
Effects of Adrenal Cortical Hormones and Prolactin on Food and Water Intake and on Body Weight of Adrenalectomized Young Carneau Pigeons.

Group	Substance injected	Daily dose	Days after operation	Data obtained end of each period		Intake	
				Wt change, %	No. of birds	Food per day, g	Water per day, cc
I	Normal, uninj.	—	1-10	+ 5	15	31	56
II	Uninj.*	—	Adrenalectomized. 1-10	—10	12	7	120
III	Prolactin*	51 u	1- 5	— 4	10	19	139
	"	51 u	5-10	— 3	7	16	140
	"	51 u	10-16	— 4	3	23	93
IV	DCA	1 mg	1- 5	— 1	3	18	77
	"	1 mg	5-10	— 0	3	19	52
	"	2 mg	10-15	+ 3	3	39	60
	Uninj.	—	15-20	— 6	3	22	58
V	Prolactin + ACE	17 u 0.2 cc	1- 5	— 3	4	22	56
	Prolactin + ACE	17 u 0.4 cc	5-10	+ 2	4	26	58
	Prolactin + ACE	51 u 0.4 cc	10-15	+10	4	44	70
	ACE	0.4 cc	15-20	—10	4	26	57
	Prolactin*	51 u	20-25	+ 9	3	28	111
	Uninj.*	—	25-31	—11	3	8	97

*Salt mixture given by mouth twice daily (total, 1.5 g NaCl; 0.25 g NaHCO₃).

support the weight of hypophysectomized pigeons. It is evident therefore that prolactin is of primary importance in this aspect of growth in pigeons and that this action of prolactin is not mediated through the adrenal. One of us⁶ earlier reported some data which indicate that the ability of prolactin to increase the basal heat production of pigeons is also not mediated by the adrenals. In adrenalectomized rats Long⁷ observed that although anterior pituitary extract caused a gain in weight (rats maintained on salt), still better responses were always observed if the animals received cortical extract in addition. It should be remembered, however, that for pigeons the main growth promoting pituitary factor is prolactin and for the rat it is some other

pituitary factor or a combination of factors.

Summary. Adrenalectomized young Carneau pigeons fed 1.75 g of a salt mixture daily showed an average period of survival of 9 days. Such pigeons eat little food and lose weight. Prolactin induced more than normal gains in body weight when adrenal insufficiency was not acute and restored food intake to a level almost equal to that of unoperated birds. Either adrenal cortical extract or desoxycorticosterone acetate maintained life in adrenalectomized pigeons. Daily doses of 2 mg of desoxycorticosterone acetate fully restored the rate of increase of body weight and the daily food consumption to levels characteristic of normal unoperated pigeons. A group of birds given high dosage of both prolactin and adrenal cortical extract showed more rapid gains in body weight and larger food intake than has ever been observed in normal unoperated pigeons of the age used here.

⁶ Riddle, O., and Smith, G. C., *Proc. Soc. Exp. Biol. and Med.*, 1940, **44**, 499.

⁷ Long, C. N. H., *Cold Spring Harbor Symposia*, 1942, **10**, 91.