9451 P

Hyperglycemia and Increased Liver Glycogen Values in Hypophysectomized Rats on Chronic Administration of Adrenocorticotropic Hormone.*

LESLIE L. BENNETT. (Introduced by Herbert M. Evans.)

From the Institute of Experimental Biology, University of California.

Previous work from this laboratory has shown that the injection of small amounts of suitable anterior lobe extracts into 24-hour fasted hypophysectomized rats prevents the abnormal fall of muscle glycogen without affecting the blood glucose or liver glycogen.[1] To produce this effect the extract is given only during the fasting period, and the presence of the adrenals is not necessary. Further investigation has shown that this acute effect is not due to adrenocorticotropic hormone.[2] The present investigation is concerned with the effects of more chronic injection of adrenocorticotropic hormone. The extracts were prepared according to the method of Lyons,[3] and all chemical and operative procedures were carried out as reported previously.[1]

TABLE I.
Carbohydrate Levels of Hypophysectomized Rats Fasted for 24 Hours after 10-24 Days' Treatment with BA-2 or L 191-4

	Muscle Glycogen mg.%		Liver Glycogen mg.%		Blood Glucose mg.%	
	Mean	Range	Mean	Range	Mean	Range
Untreated Normal (13)*	500	480-545	22	11-33	79	60-89
Untreated Hypophysectomized (8)*	298	253-389	22	18-26	52	42-61
Attempted Maintenance, 10 mg. BA-2 daily for 10-11 days (6)*	464	369-529	429	149-774	106	90-127
Attempted Repair, 10 mg. BA-2 daily for 11-12 days (5)*	488	438-592	86	20-212	92	72-108
Hypophysectomized-adrenal Demedullated Attempted Maintenance, 10-18 mg. BA-2 daily for 10-11 days (6)*	425	372-529	11	6-17	58	54-64
Attempted Maintenance, 5 mg. L 191-4 daily for 10 days (2)*	385	363-405	8	6-9	57	56-59

*Number of animals in the group.

* Aided by the Presnell Fund for the study of the metabolic relations of the anterior hypophysis, contributed by Robert R. Presnell, Frank Tuttle, Arthur Stebbins, and Mrs. Gordon Kahn, of Los Angeles.

1 Russell, J. A., and Bennett, L. L., PROC. SOC. EXP. BIOL. AND MED., 1936, **34**, 406.

2 Bennett, L. L., *Am. J. Physiol.* In press.

3 Lyons, W. R., PROC. SOC. EXP. BIOL. AND MED., 1937, **35**, 645.

In Table I are summarized various experiments dealing with 10-24 days' injection of BA-2 (adrenocorticotropic hormone) and a purified lactogenic preparation. For the sake of convenience these experiments are called maintenance (injections started immediately after hypophysectomy) or repair (injections started 10-12 days after hypophysectomy). All extracts were injected 3 times during the fasting period in addition to the previous treatment. These data show that after longer treatment with adrenocorticotropic hormone there is a significant increase in liver glycogen and blood glucose. Not only are these values higher than those of the untreated hypophysectomized rat, but they are also far higher than those found in untreated normal rats. The adrenals of the maintenance group were much larger than those of the repair group, an average of 32.5 mg. as compared with 22 mg. These values should be compared with 25 mg. for untreated normal rats, and 10 mg. for untreated hypophysectomized rats. The only known contamination of BA-2 was one unit of lactogenic hormone per mg. The effects produced by BA-2 cannot be due to this contamination, as 50 units of lactogenic (5 times the amount administered in BA-2) were administered daily in L 191-4 (a potent lactogenic preparation supplied by Dr. W. R. Lyons) with clear-cut negative results.

The animals of one group were adrenal-demedullated about a week previous to hypophysectomy and after the latter operation maintained with BA-2. These animals grew normally during the interval between operations, and at autopsy serial sections of the adrenal remnants showed the presence of cortical tissue only. The blood glucose and liver glycogen values of these rats were not raised by treatment. This suggests that the effects are being mediated through the adrenal medulla. However, it is more likely that there was insufficient cortical tissue present to produce the elevation in blood glucose and liver glycogen. (In no case was the weight of the cortical remnant equal to the weight of the intact adrenals.) This interpretation is borne out by the observation of much higher carbohydrate levels in the maintenance than in the repair experiments. It is further supported by the fact that a large group of preliminary experiments, in which adrenocorticotropic extracts of varying potency were used, showed that a high degree of positive correlation existed between blood glucose level and the amount of adrenal repair.

These observations are in sharp contrast to the resistance which hypophysectomized rats develop to the metabolic effects of crude anterior lobe extracts after 10 to 20 days' treatment.[4]

[4] Bennett, L. L., PROC. SOC. EXP. BIOL. AND MED. In press.