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Blood Sugar Studies Following Hypophysectomy and Experimental Lesions of Hypothalamus.*

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It is not clear whether the relation of hypophysis and hypothalamus to carbohydrate metabolism is due primarily to one or the other, or to an interaction between both. We wish to record the following progress report pertaining to the subject.

All operations were made under nembutal† by the subtemporal approach with excellent visibility and little or no hemorrhage.

Fasting Blood Sugars. In 45 normal dogs, the fasting blood sugars determined by a modified Folin-Wu method ranged from 75 to 139 mg. %, with only 2 cases below 80. We consider values of 70 and below abnormal. After complete hypophysectomy, abnormally low blood sugars were observed in 7 out of 11 cases, values

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† Courtesy Abbott Laboratories, Chicago.

of 34, 43, 59, 63, 69, and 70 being recorded. Removal of the anterior lobe alone in one specimen resulted in hypoglycemia (40). In each case, the low blood sugar was accompanied by symptoms typical of cachexia hypophysoprivea. These crises were spontaneous and varied in their onset from 1 day to 3 months postoperative. In 4 cases in which glucose was given, immediate recovery was effected; one animal still survives. In 2, symptoms were reprecipitated by a short period of starvation. These results are in exact agreement with those reported by Houssay and Biasotti.[1] Two of the remaining dogs died the first day postoperative without low blood sugars, one, after several weeks and one is still living after 3 months.

Hypoglycemic crises similar to those following hypophysectomy were observed in 5 out of 13 dogs with bilateral transverse lesions at the chiasmal level of the hypothalamus (68, 68, 50, 65, 68). These occurred on the first and second days and were followed by death in 4 cases; the fifth recovered on administration of glucose and maintained a normal blood sugar until death on the fifth day. Four of the remaining 8 retained normal blood sugars until terminated 1 to 2 months after operation. The other 4 died within the first 4 days without showing low blood sugars. It is possible that a hyperglycemia due to the excitement which is a characteristic result of these lesions overshadowed the hypoglycemic effect. Values from 150 to 166 occurred during periods of excitement.

No abnormally low fasting blood sugars appeared in 6 animals with bilateral transverse lesions at the middle of the hypothalamus; 4 with bilateral transverse prechiasmal lesions; 4 with ventral third of hypothalamus removed; 2 with maceration of the whole hypothalamus.

Hyperglycemia (except during excitement) did not occur, even transiently, except with complete removal of the hypothalamus and after transection of the brain stem caudal to the hypothalamus.

Glucose Tolerance was determined by analyzing blood samples at the ½, 1 and 2 hour intervals following administration of 2 gm. per kilo of glucose by stomach tube. In 26 determinations on 23 unoperated dogs, the distribution was: 6 low, never over 150; 15 normal, under 200, ending below 150; 4 high, above 200, but below 150 at end; 1 high prolonged, over 200 and ending above 150. Standards were chosen arbitrarily.

[1] Houssay, B. A., and Biasotti, A., *Endocrinol.*, 1931, **15**, 511.

Tests made after operation (1-14 days) on 6 dogs with chiasmal lesions, 1 with ventral third of hypothalamus removed, 1 with anterior lobe removed, 1 with posterior lobe removed, and 6 with complete hypophysectomy, as well as 2 with hemorrhage at the base of the brain, but no experimental lesion, all showed high or high prolonged curves. In those dogs which could be followed, including one or more of each group, the curves returned to normal within from 9 to 20 days.

Starvation on Tolerance Curve. One chiasmal, 1 posterior lobe, 2 hypophysectomized dogs, and 1 with stalk detached, in all of which the tolerance curve had returned to normal, were starved, tests run at 4, 8, and 14 days, and the results compared with 3 starving, unoperated dogs. All gave high or high prolonged curves, but with these striking differences: At the end of the 4 and 8 day periods, blood sugars in the control and posterior lobe dogs were normal or only slightly high at the end of the second hour, while the other operated dogs were highest at this time (above 200). After 14 days of starvation, blood sugars of the control and posterior lobe animals were normal or falling at the end of the fourth hour, while those of the other operated dogs were higher than at any time earlier in the test (255-357). Curves were thus higher and more prolonged in the 4 operated than in the control and posterior lobe dogs at the same period of starvation. (Excessively high blood sugars lasting for from 4 to 6 hours were observed when glucose was given to dogs with hypoglycemia.)

Several of the dogs, in which the crises occurred several days or more after operation, exhibited marked degeneration of the liver. In 3 instances—2 hypophysectomy, 1 chiasmal—large duodenal ulcers were present which simulate experimental ulcers produced by ligation of the bile ducts.

Since it is impossible to duplicate lesions exactly, histological studies, now in progress, may modify groupings and explain discrepancies.