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Carbohydrate Oxidation in Hypophysectomized Rats.

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It was noted that rats hypophysectomized* for 6 to 8 weeks, with metabolic rates 70% of those of normal controls (as determined gravimetrically by the Haldane method), frequently showed high respiratory quotients (R.Q.) after a fasting period of 24 hours. Values as high as 0.78 to 0.81 were sometimes observed, the average of a series of 19 observations being 0.75, while the average of 19 controls was 0.72. If the hypophysectomized rats were fasted longer than 30 hours, the R.Q. usually dropped to 0.73, though in a few instances it remained high for nearly 40 hours. Changes in the acid-base equilibrium were apparently not responsible for the high R.Q., as shown by determinations of the CO_2 content of the blood. Glycogen determinations after a 24-hour fast showed that the hypophysectomized animals contained considerably less muscle and liver glycogen than did normal controls. Hypoglycemia was always present, the blood sugar being around 50 mg. %.

These findings suggested that the regulatory mechanism which leads to the preservation of glycogen during fasting is disturbed after hypophysectomy. The low glycogen reserves and the tendency to hypoglycemia in hypophysectomized animals might be due, among other factors, to the removal of an inhibitory influence on carbohydrate oxidation. In order to test this assumption, a standard amount of glucose (500 mg. per 100 gm. of body weight) was fed to normal and hypophysectomized rats after a fasting period of 24 hours, the aim being to determine (a) how much glucose was oxidized in the first few hours during the period of active absorption and (b) what length of time was required for the complete disposal of the ingested sugar by oxidation.

In the first 4 hours the normal animals oxidized an average of 192 and the hypophysectomized animals an average of 160 mg. of glucose per 100 gm. of body weight.† The glucose fed was dis-

* The completeness of the operation was checked in each case at autopsy.

† Attention is called to the fact that hypophysectomized rats show a diminished rate of intestinal absorption of glucose, as Phillips and Robb (*Am. J. Physiol.*, 1934, **109**, 82) have shown and as we are able to confirm.

posed of by oxidation in about the same length of time (21.7 hours in the normal and 20 hours in the hypophysectomized animals), but since the latter had a 29% lower O_2 consumption than the controls, they derived a correspondingly larger proportion of their energy from carbohydrate oxidation. The hypophysectomized rats excreted less urinary nitrogen than the controls but slightly more than rats thyroidectomized for 4 weeks. The animals were on a high carbohydrate diet prior to the experiments.

In another series of observations normal and hypophysectomized rats were kept for 2 days on a high fat (butter) diet prior to the glucose test meal. Fat feeding depressed carbohydrate oxidation in the normal but had little effect in the hypophysectomized animals; the former oxidized an average of 144 and the latter of 190 mg. per 100 gm. of body weight per 4 hours.

Hypophysectomized rats are about 8 times more sensitive to the convulsive action of insulin than are normal rats. It might be argued, therefore, that removal of the pituitary results in a relative excess of insulin in the body and that the greater proportion of carbohydrate used for oxidation is due to this factor. Houssay has shown, however, that an extra-pancreatic factor is also involved, since extirpation of the pituitary in depancreatized dogs enabled them to oxidize carbohydrate.

Summary. Hypophysectomized rats continue to oxidize carbohydrate for a longer period of time during fasting and they derive a larger proportion of their energy from carbohydrate after glucose feeding than do normal rats. A high fat diet prior to glucose feeding reduces carbohydrate oxidation in normal rats but has little effect in hypophysectomized rats; the latter oxidize more sugar in the first 4 hours after the glucose feeding than the former in spite of a lower O_2 consumption and a reduced rate of intestinal absorption.