

THE INFLUENCE OF THYROIDECTOMY ON ALIMEN- TARY GLYCOSURIA.¹

By JOHN McCURDY.

(From the Hunterian Laboratory of Pathological Physiology, Johns Hopkins University, Baltimore.)

For some years there have been reports in the literature of a lowered carbohydrate assimilation limit on the feeding of thyroid extract. A lowered assimilation limit was noted in Basedow's disease by Kraus and Ludwig (1), Chvostek (2), Goldschmidt (3) and Straus (4). Hirschl (5) and Knöpfelmacher (6) have reported a rise in the assimilation limit with thyroid insufficiency. Recently Falta (7) reports experiments indicating that removal of the thyroids to some extent inhibits artificially produced glycosuria. But since it is necessary to preserve the parathyroid glands in order to observe the influence of the thyroid gland alone, I have decided to test the effect of removing thyroid tissue only, enough parathyroid tissue being left to fulfil the functions of the parathyroids completely.

Alimentary glycosuria was chosen as the condition most easily produced for study. At first lactose was fed by the stomach tube, this sugar being chosen on account of its low assimilation limit. Efforts to determine what quantity can be assimilated were highly unsatisfactory for reasons which may be understood, if one considers the fate of a carbohydrate administered *per os*. Carbohydrate may pass out with the feces; it may be absorbed by the lymphatics of the intestine, and so reach the general blood stream, or it may be changed in the intestine to dextrose and reaching the liver be stored there as glycogen.

Schlesinger has shown that glycosuria results only when sugar passes by the lymphatics into the general blood stream. Such conditions therefore as retard or accelerate digestion and the progress of food through the intestinal canal will determine the amount of sugar which passes to the liver and the amount which is lost with the

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feces, and these two variables are inconstant enough to prejudice the accuracy of a series of experiments. As only that sugar which gains direct access to the general blood stream produces glycosuria, it is obvious that the internal secretions of the thyroid glands can affect only the fate of this sugar. It was therefore decided to continue this work by injecting a given amount of dextrose into one of the systemic veins.

The urine was collected by a catheter (female dogs with perineal section being employed) at the end of each hour subsequent to injection; the urine was tested quantitatively by Benedict's method and qualitatively by the polarimeter.

Blumenthal (8), working with rabbits, found that 0.8 gram of dextrose per kilo of body weight was the smallest quantity which produced glycosuria after injection. The first injections were made with half that amount, the intention being to increase the amount until the limit of assimilation was reached. It was found, however, that all the dogs experimented with excreted a satisfactory quantity of dextrose after injection of 0.4 gram at most per kilo.

EXPERIMENT I.—White female fox terrier; weight 6 kilos. The experiment was started by feeding lactose, but the animal was found to have an extraordinary susceptibility and continued excreting sugar long after a time when lactose had doubtless been assimilated. Only urine of twenty-four hours was examined. Thus on December 11, 1908, the last administration of 14 grams of lactose was made. Excretion of reducing substances continued till February 11, 1909. On December 18 a sample of the urine was collected and allowed to ferment; since it lost all its reducing power, only dextrose was being eliminated.

The first intravenous injection of dextrose was made on February 19. On account of the high susceptibility of the animal, only 0.2 gram per kilo was used, or 6.2 c.c. of a 19.2 per cent. solution of dextrose. Elimination was completed in twenty-four hours and amounted to 0.4 gram.

A second injection of the same quantity was made on February 23. The twenty-four hour urine on February 24 contained 1.0 gram of dextrose. This is practically the same as the amount injected. The urine each day till March 8 showed the following content of dextrose in grams: 0.17, 0.15, 0.48, 0.12, 0.18, 0.34, 0.15, 0.15, making a total excretion in nine days of 2.74 grams of dextrose, whereas 1.2 grams were injected. From this discrepancy it was considered that the animal had been poisoned, so that it was unable to burn all the carbohydrate of its normal food.

On March 9, therefore, the thyroid glands were removed. (All the thyroidectomies were performed by Dr. W. G. MacCallum.) Unfortunately the anatomical relations of the glands were such that it was possible to leave only two small parathyroids on the left side, and these were left with their circulation im-

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paired. Urine collected during the sixteen hours subsequent to the operation contained 0.12 gram of dextrose. No more elimination of sugar took place. Two days after operation the dog developed tetany, and death two weeks later showed that there had been too great a destruction of parathyroid tissue.

Removal of the thyroids in this case stopped glycosuria that had existed for ten days and was apparently analogous to a condition that had lasted for two months.

The results obtained with the next animal were more conclusive.

EXPERIMENT II.—Large female spaniel; weight 19.3 kilos. It was found that the glycosuria resulting from injection of 0.4 gram of dextrose per kilo lasted for five hours and reached about 1 gram in total. After the thyroid extirpation (when a large parathyroid was left on each side with circulation intact) the amount excreted and time taken by excretion gradually sank to zero. The following table gives the exact figures:

Date.	Cubic centimeters of injection.	Percentage of dextrose in injection.	Sugar eliminated.					Total.
			1st hr.	2d hr.	3d hr.	4th hr.	5th hr.	
April 20	26.0	30.4	0.360	0.235	0.150	0.055	0.100	0.900
" 24	26.0	30.4	0.060	0.300	0.660	0.270	0.065	1.355
" 27	26.0	30.4	0.420	0.160	0.170	0.160	0.110	1.020
May 3	Thyroids removed.							
" 6	29.0	27.0	0.125	0.312	0.80	0.042	0.035	0.694
" 11	29.0	27.0	0.125	0.140	0.075	0.040	0.000	0.380
" 13	29.0	27.0	0.070	0.035	0.082	0.009	0.000	0.196
" 20	29.0	27.0	0.055	0.045	0.085	0.000	0.000	0.196
June 3	32.5	24.0	0.000	0.000	0.000	0.000	0.000	0.000

A third confirmatory experiment was made.

EXPERIMENT III.—White female setter; weight 17.1 kilos. The following table gives the results.

Date.	Cubic centimeters of injection.	Percentage of dextrose in injection.	Sugar eliminated.					Total.
			1st hr.	2d hr.	3d hr.	4th hr.	5th hr.	
May 15	26.0	27.0	0.080	0.016	0.185	0.040	0.000	0.321
" 18	26.0	27.0	0.100	0.172	0.053	0.000	0.000	0.325
" 25	Thyroids removed: one good parathyroid left on each side.							
June 2	29.0	24.0	0.040	0.060	0.000	0.000	0.000	0.100
" 4	29.0	29.0	0.075	0.052	0.003	0.000	0.000	0.130

Lack of time prevented continued estimation of sugar eliminated by this third dog during a month.

A word may be said as to the probable action of the internal secretion of the thyroids. It is evident that it inhibits the combustion of carbohydrate. It may do this in two ways: by inhibiting

that action of the pancreatic and muscle ferments which causes the actual oxidation of dextrose or by inhibiting the transport of dextrose to the muscles. That the former possibility is true has been shown *in vitro* by King (9). Were the latter condition also a factor in the normal metabolism, we should expect that, when the inhibitory action of the thyroids was removed, any dextrose injected would cause a rush of sugar from the liver to the blood stream, and as a result, a greater amount of glucose would be excreted in the first hour after injection. But the results of Experiments II and III show that such excretion does not occur. To settle this question finally it would be necessary to perform similar experiments on animals in which an Eck's fistula had been produced.

Falta suggests that a compensating factor may be developed when thyroid irregularities have occurred. There is no such change within a month at least (Experiment II).

SUMMARY.

1. Removal of the thyroid glands causes a rise in the assimilation limit for dextrose.
2. If the parathyroids are left, this result is permanent.
3. The thyroids probably inhibit normally the direct combustion of the sugar in the muscles.

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