HYPERGLYCEMIA IN PYRIDOXINE DEFICIENT RATS

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Xanthurenic acid, an abnormal metabolite of tryptophan (1, 2), which is produced in pyridoxine-deficient rats, is said to cause diabetes mellitus (3).

In our laboratory Lin et al. (4) suggested that the deficiency of pyridoxine alone for a long time might cause, independently of the diabetogenic action of xanthurenic acid, abnormal carbohydrate metabolism leading to continuous hyperglycemia. The authors have studied the blood sugar levels of the rats fed on a pyridoxine-deficient casein diet without adding tryptophan particularly.

Thirty white Wistar strain male rats weighing 120–170 g were divided into three groups of ten rats each and were kept on the following diet for more than ninety days: (A) natural diet or wheat with fish meal, (B) pyridoxine-deficient casein diet (5), (C) 5 μg of pyridoxine hydrochloride, a dose considered to be a sufficient amount to keep normal growth, was added to each g of the above-mentioned pyridoxine-deficient diet. Each rat was housed in an individual screen-bottomed cage with drinking water freely available. Animals were given 15 g of the diet every day. The results are shown in Fig. 1.

In the growth curve (Fig. 1), Groups A and C showed a natural gain in the body weight. On the contrary, Group B showed no further increase after thirty days from the beginning of the experiment. It is worthy of mention that the pyridoxine-deficient rats at this period of time showed neither sudden decrease nor any further increase in body weight, but the growth of some animals ceased.

The urinary xanthurenic acid was estimated by the method of Rosen, Huff and Perlweig (6). Since tryptophan was not added particularly to the diet, these urinary xanthurenic acid is considered to be originated from the diet. Taking the mean values of the urinary xanthurenic acid of ten rats of each group into consideration, Group B showed a value higher than those of Groups A and C, indicating the deficiency of pyridoxine in the rats of Group B.

In each individual of Group B, the volume of 24-hour urine increased

1 Preliminarily reported at the Kanto-Sectional Meeting of the Japanese Biochemical Society held November 8, 1958.
distinctly, the lie of hair was poor and a remarkable anemia was observed. Some of them showed acrodynia and exophthalmus. The blood sugar was estimated in a fasting state according to King and Garner (7). The mean blood sugar levels of pyridoxine-deficient rats were considerably higher than those of Groups A and C. Furthermore, the levels of Group C were always higher than those of Group A. Some factors other than pyridoxine deficiency might have been joined in causing hyperglycemia in the rats of Group B. To ascertain the nature of the hyperglycemia observed in the rats of Group B, glucose tolerance test was carried out: 2g of glucose per kg body weight was given per os to the rats of Group B and control animals. The tolerance curve of control animals showed a normal decline, but that of the pyridoxine-deficient rats was not the case as given in Fig. 2. It is thus evident that an abnormal sugar metabolism took place in the pyridoxine-deficient rats. The result of insulin-glucose tolerance test is also presented in Fig. 2.

It is a significant fact that unambiguous hyperglycemia occurs in the rats

![Blood Sugar Curves and Growth Curves and Amount of Urinary Excreted Xanthurenic Acid. Each Curve and Rectangle Represent the Averages of Ten Rats of Each Group](image)

- ○: pyridoxine-deficient rats (Group B)
- ×: control rats fed synthetic diet (Group C)
- ●: control rats fed natural diet (Group A)

![Glucose Tolerance Curve and Insulin Glucose Tolerance Curve](image)

- ○: pyridoxine-deficient rats (Group B)
- ×: control rats fed synthetic diet (Group C)
- ●: control rats fed natural diet (Group A)
of Group B without particular addition of tryptophan to the diet, that is, under an experimental condition differing from Kotake's. Kotake et al. could cause diabetes mellitus to rats by injecting 120 mg of xanthurenic acid per kg body weight.

Matsuura found that xanthurenic acid did not produce hyperglycemia until it was given in such a large dose as 400—500 mg per kg of rats. The average amount of urinary xanthurenic acid in pyridoxine-deficient rats in this experiment was not more than 0.17 mg a day. A hundred days later from the beginning of the experiment, the animals were minced and xanthurenic acid expected to be accumulated in the body was estimated. Its average value in the rats of Group B was not more than 0.5 mg per rat, an amount considered to be too small to cause hyperglycemia. As the blood sugar was determined in this experiment by the method of King and Garner utilizing the reducing action of sugar, there may be some doubt whether the high blood sugar level is really due to glucose or to some non-sugar reducing substance which might have appeared in the blood as a result of the privation of pyridoxine. Therefore, the blood sugar was again estimated by the manometric method of Keilin and Hartree (8), using glucose oxidase or notatin, which is known to have a definite specificity for glucose. The values of glucose in blood estimated by the manometric technique coincided with those estimated by the method of King and Garner. Thus the hypothesis that some non-sugar reducing substance might have increased in pyridoxine deficiency is excluded.

Consequently it is evident that a continuous hyperglycemia occurs in the rats fed on pyridoxine-deficient diets for a long time. But the cause of this hyperglycemia seems scarcely to be attributable to the accumulation of xanthurenic acid in the body.

REFERENCES