

XI. GLYOXALASE IN AVIAN BERIBERI.

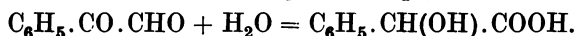
BY GEORGE MARSHALL FINDLAY.

From the Royal College of Physicians' Laboratory, Edinburgh.

(Received December 20th, 1920.)

ALTHOUGH the relationship of beriberi to vitamin B has by now been firmly established there are still those [Walshe, 1918] who maintain that the disease is in reality a toxæmia. This view is by no means new though the original theory has undergone many modifications as our knowledge of beriberi has progressed. At present it is believed that in the absence of vitamin B there is a breakdown in metabolism, more particularly in regard to the metabolism of carbohydrates. Toxins are formed and as a result of their action on the central and peripheral nervous systems, there occur changes very similar to those seen in other forms of toxic polyneuritis. In support of this hypothesis may be cited the curious fact that birds that have been fed on a diet lacking in vitamin B develop symptoms of beriberi more rapidly when their diet contains an excess of carbohydrate. It may, however, be noted that according to Mellanby [1920] carbohydrates have a similar effect in hastening the onset of rickets in puppies deprived of vitamin A. So far, however, no toxin has been isolated from the blood or tissues of animals suffering from beriberi nor has there been demonstrated any interference with the normal metabolism of carbohydrates. In order to investigate the carbohydrate metabolism in avian beriberi the following experiments were carried out on the glyoxalase content of the liver in avian beriberi. Glyoxalase, as was first pointed out by Dakin and Dudley [1913, 1], is an enzyme with an important rôle in the metabolism of sugar. It is widely distributed in nearly all tissues, more especially in the liver and muscles and has the power of transforming "glyoxals" of various compositions into compounds of lactic acid. In the body the chief "glyoxal" so acted upon is pyruvic aldehyde, or as it is sometimes called methylglyoxal. Pyruvic aldehyde is an intermediate stage between glucose and lactic acid. Glyoxalase also plays a part in the conversion of *d*-alanine to lactic acid, while the relationship of pyruvic aldehyde to pyruvic acid is of considerable interest in view of the fact that, as pointed out by Smedley [1912], the higher fatty acids can be synthesised by starting with pyruvic acid. The presence of glyoxalase in the tissues is thus of importance in relation to the metabolism of proteins, fats and carbohydrates.

In the present investigation estimations were made of the glyoxalase content of the livers in control pigeons, in pigeons suffering from beriberi and in pigeons "cured" of beriberi by the administration of vitamin B. Preliminary estimations of the water content of the livers showed that the variation between healthy and beriberic pigeons was practically negligible. The glyoxalase was estimated by the method already employed by Dakin and Dudley [1913, 2, 3], which consists essentially in allowing a 20 % watery extract of the tissues to act on phenylglyoxal, when the phenylglyoxal is converted into mandelic acid according to the equation—



The mandelic acid is then extracted and estimated by titration in terms of *N*/10 NaOH.

In the present instance 15 cc. of a 20 % tissue extract were allowed to act on 0.1 g. of phenylglyoxal for 24 hours at 37°. The acidity obtained is shown in the following table:

	Control pigeons	Beriberic pigeons	"Cured" pigeons
Experiment 1	4.2	1.9	2.8
" 2	4.3	0.9	3.4
" 3	4.7	2.1	3.0
Average ...	4.4	1.6	3.1

It will thus be seen that in pigeons suffering from beriberi there is as compared with control birds a reduction in the glyoxalase content of the liver by more than one-half. The administration of vitamin B produces a definite rise in the amount of glyoxalase present.

Very similar results were obtained in the case of liver catalase by Dutcher [1918], who believed that vitamin B acted as a co-enzyme for catalase. An attempt was therefore made to determine whether vitamin B acted as a co-enzyme for glyoxalase. For this purpose experiments were performed by adding vitamin B to a watery extract of the liver of beriberic pigeons. The vitamin B was obtained from yeast extract, which had been previously heated to 100° for an hour to destroy its glyoxalase. Three grams of this yeast extract were then added to the mixture of phenylglyoxal and tissue extract and allowed to stand for 24 hours at 37° as before. The average acidity obtained from three observations was 1.72, a result scarcely differing from that found in beriberic birds. Vitamin B can thus only lead to an increased production of glyoxalase when it acts through the intact cell; it cannot therefore be regarded as a true co-enzyme of glyoxalase.

There is thus some evidence to show that in avian beriberi a definite breakdown in carbohydrate metabolism occurs though whether such a breakdown is followed by the production of toxic substances in the tissues is still undetermined.

The writer desires to take this opportunity of thanking Prof. Barger and Mr E. Stedman for their kindness in preparing the phenylglyoxal used in these experiments.

CONCLUSIONS.

- (1) The glyoxalase content of the liver in pigeons with beriberi is less than that in control pigeons.
- (2) The administration of vitamin B to a beriberic pigeon is followed by an increase in the glyoxalase content of the liver.
- (3) Vitamin B does not act as a co-enzyme of glyoxalase.

REFERENCES.

- Dakin and Dudley (1913, 1). *J. Biol. Chem.* **14**, 155.
——— (1913, 2). *J. Biol. Chem.* **14**, 423.
——— (1913, 3). *J. Biol. Chem.* **15**, 127
Dutcher (1918). *J. Biol. Chem.* **36**, 63.
Mellanby (1920). *Brit. Med. J.* **ii**, 328.
Smedley (1912). *J. Physiol.* **45**, 24.
Walshe (1918). *Brit. J. Child. Dis.* **15**, 25