CXII. THE EFFECT OF THE ADMINISTRATION OF GLYCINE TO PIGEONS ON A DIET DEFICIENT IN VITAMIN B.

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It is believed by various authorities [see Funk, 1914; Funk and Collazo, 1925; Randoin and Simonnet, 1924, 1, 2] that protein metabolism requires less vitamin B than that of carbohydrate. In fact these authors consider vitamin B as specially associated with the utilisation of carbohydrates, the last-named authors even believing that experimental animals (*e.g.* pigeons and rats) can be kept alive in a good state of nutrition on dietaries deprived both of vitamin B and of carbohydrates. Such theories have been fully dealt with in a previous communication [Kon and Drummond, 1927], in which observations were reported in disagreement with them. It seemed worth while, however, to ascertain whether the alleged sparing action attributed to proteins could be explained by reference to their specific dynamic action, leading to increased cell metabolism and possibly to liberation of the body reserves of vitamin B. In order to investigate this question, it was decided to administer to pigeons fed on a diet deficient in vitamin B sufficient amounts of glycine to raise markedly their metabolism. Three lots of pigeons, each consisting of four birds, were used. The initial average weights were 428, 421 and 411 g. respectively. At first they were fed on polished rice for 12 days until the typical decrease in appetite was manifested, by which time the average weights were 393, 388 and 362 g. respectively. The actual experiment was then started, the first lot receiving daily a solution of 2 g. of pure synthetic glycine in 25 cc. of water, the second a solution of 1.6 g. of glucose in 12 cc. of water (glycine gives rise to 80 % of its weight of glucose [Ringer and Lusk, 1910]), the third 25 cc. of water. Ample supplies of polished rice and water were also provided for each group. All the liquids were introduced into the crop by means of a small funnel and a piece of rubber tubing. The weight of the birds, their food intake and cloacal temperature were determined daily. The glycine and glucose solutions were diluted as far as convenient for administration in order to avoid the introduction of strongly hypertonic fluids. Nevertheless, the glucose solution had roughly 2.4 times the osmotic pressure of blood, and the glycine 3.3. Vomiting was observed in all the pigeons of the glycine group. It was not present in the two remaining sets. Vomiting was frequently observed by Csonka [1915] after administering glycine to dogs.

Effects of dosage. The birds receiving glycine died in the course of 30, 24, 21 and 25 days respectively (on the 18th, 12th, 9th and 13th days after the administration of glycine was commenced) without showing any characteristic symptoms other than loss of appetite, weakness and in two cases paralysis. Nothing of interest was revealed on *post mortem* examination with the exception of a marked enteritis in one case (pigeon 3). One of the pigeons receiving sugar developed opisthotonos on the 28th day of the experiment, one died without marked symptoms on the 27th day. The experiment was terminated on the 31st day, after all the pigeons receiving glycine had died. Two of the sugar group and all the birds of the water group were still surviving at that time.

Body weight. After 8 days of actual experiment (up to the death of the first pigeon of the glycine group) the average weights were 339, 339 and 321 g. respectively, the pigeons on glycine having lost 54 g., or an average of 6.8 g. daily, those on sugar 49 g., or an average of 6.1 g. per day, and the birds receiving water 41 g., or 5.1 g. daily.

Food intake. The average daily food intake, that is, the voluntary consumption of polished rice, for the same period of time was 0.5 g. in the glycine group, 1.6 g. in the sugar group and 4.2 g. in the water group. It appeared that administration of glycine and glucose interfered with the voluntary food intake, in the former case more strongly than the latter.

Body temperature. The average temperatures at the beginning of the actual experimental period were 41.7°, 41.9° and 41.8°; at the end of the experiment these had dropped to 39.6°, 40.7° and 40.4°, the heaviest drop being manifested by the glycine group.

It is evident that the administration of a substance having a marked specific dynamic action had no beneficial effect on pigeons deprived of vitamin B and that on the contrary these birds declined rapidly. There is little doubt that glycine had no toxic action *per se*, and that probably the bad effects were caused by the high molecular concentration of the liquid administered. The molecular concentration of the glucose was lower and hence the untoward results were much less marked. It will be remembered that in pigeons forcibly fed deficient diets, the crop does not function normally [Kon and Drummond, 1927], and that the hypertonic fluid consequently could not be disposed of so easily as in normal animals.

Funk and Paton [1922] observed occlusion of the crop and death in pigeons fed forcibly a mixture of glucose and egg-albumin, and attributed these symptoms to a difference in osmotic pressure of the sugar solution and the body fluid. Collazo [1923] introduced large amounts (10 g.) of various carbohydrates into the crops of vitamin B-deficient and normal pigeons and found that beriberi symptoms and death, or death without previous symptoms, ensued invariably in the former. Glucose, galactose and fructose showed the highest, and starch the lowest toxicity, whereas the disaccharides sucrose, lactose and maltose, occupied an intermediate position. No symptoms were

produced in normal animals even by larger doses. Collazo [1923] concludes from his experiments that in vitamin B avitaminosis, the carbohydrate metabolism becomes aberrant and toxic intermediate substances are produced. It seems that a much simpler explanation is that, the emptying of the crop being impaired in vitamin B-deficient pigeons, they were killed by the enormous osmotic pressure of the solutions. Collazo does not give the concentration but it was surely not less than 20 % as even the administration at once of 50 cc. of liquid would present difficulties¹. In normal pigeons the rapid emptying of the crop not only exposes the hypertonic liquid to the large surface of the gut and thus ensures prompt dilution and excretion, but also enables the birds to drink water. The supposition is further strengthened by the fact that the toxicity of the substances administered was inversely proportional to their molecular weight (starch, disaccharides, monosaccharides). It is to be noted that in the dog administration of glucose (100 g.) never caused death, but vomiting, a symptom observed by Cowgill [1921] even when vitamin B-containing extracts were given by the stomach tube to vitamin B-deficient dogs. Collazo also found that administration of 1 g. glucose daily to a pigeon, previously kept for 1 week on a vitamin B-deficient ration, caused convulsions and death in the course of 3 days. As already reported, out of four pigeons receiving nearly twice this dose, two died 12 and 16 days respectively after the administration was commenced. Two were still surviving after 31 days of vitamin B-free feeding and 19 days of sugar administration.

SUMMARY.

Administration of glycine has no beneficial effects on pigeons fed on diets deficient in vitamin B. The opinion of Collazo that the carbohydrates administered to vitamin B-deficient pigeons are toxic *per se* is not corroborated. The effects are attributed to the high osmotic pressure of the solutions administered and to the inability of the deficient birds to empty their crops normally.

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¹ It would appear from a subsequent publication of Rubino and Collazo [1923] that the carbohydrates were administered as 50 % solutions.