ANTAGONISTIC ACTION OF PYRIDOXINE TO TOXOPYRIMIDINE ON THE GROWTH OF MICE

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It was reported by the authors (1-4) that B₆ group-vitamins had a strong atoxopyrimidine action. Watanabe and Shintani (5) proved the antagonistic action between B₆ group-vitamins and toxopyrimidine¹ (TXP) in rats.

In the present paper evidence will be given indicating an antagonistic action between pyridoxine and TXP on the growth of young weanling male DD mice.

EXPERIMENTAL

Materials and Method

Young weanling male DD mice were given a synthetic diet for a certain period. Mice fed with a diet containing TXP deficient in pyridoxine lost weight rapidly and died (Fig. 1, E). When pyridoxine was added to this diet, the mice recovered weight promptly (Fig. 2, curve 3).

The basal diet consisted of, in per cent, purified starch, 60; purified casein, 20; lard, 15 and McCollum salt mixture (No. 185), 5. One drop of cod liver oil per day per animal was also administered. A vitamin-mixture consisting of 1 mg of thiamine hydrochloride, 0.4 mg of riboflavin, 0.1 mg of pyridoxine hydrochloride, 3 mg of calcium pantothenate, 10 mg of inositol, and 25 mg of *p*-aminobenzoic acid was added to each 100 g of the basal ration. The

FIG. 1 Average Body-weight Curves of Young Male DD Mice fed with Diet A, B, C, and E

A, 8 mice fed with diet A; B, 7 mice fed with diet B; C, 8 mice fed with diet C; E, 8 mice fed with diet E; †, all the animals of group E died in 13-15 days.

¹ 2-Methyl-6-amino-5-hydroxymethylpyrimidine

FIG. 2 Average Body-weight Curves of Young Male DD Mice Fed with Diets A, C, and D

1, 7 mice fed with diet A; 2, 7 mice fed with diet D followed by C; 3, 7 mice fed with diet C followed by D; 4, 2 mice fed with diet C; †, all the animals of this group died in 37 days.

The animals were fed with diets A, B, C, and E, respectively, for 21 days. Mice fed with diet A continued to grow normally. Mice fed with diet E lost body weight rapidly, manifesting the symptoms resembling those of vitamin B₆ deficiency within 7–10 days and died within 13–15 days (Fig. 1, E). The clinical symptoms of the deficiency were lifelessness, loss of hair especially around the nostril, on the ventral side of both the neck, and abdomen, bristling up or lying of hair, reddishness and swelling of the hind legs, loss of glossiness and drying of the tail skin, *etc.* as given in Table I.

In mice fed with diet C, increase in body weight was considerably suppressed, and symptoms of vitamin B₆ deficiency appeared, but not a mouse

animals received each of the following 5 kinds of diet;

Diet A, the basal diet alone.

Diet B, the basal diet minus pyridoxine.

Diet C, the basal diet containing 5 mg of TXP per 100 g.

Diet D, the basal diet containing both 5 mg of TXP and 6.6 mg of pyridoxine per 100 g.

Diet E, the basal diet plus 5 mg of TXP per 100 g minus pyridoxine.

Results

1. Effect of TXP on the Growth of Mice.

TABLE I
Clinical Symptoms of the Deficiency in Test Animals

Symptoms	Group 1. Fed with diet B	Fed with diet D	Group 2.	Group 3.	Group 4.	Fed with diet E
Bristling up or lying of hair	—	—	+	—	++	++
Dermatitis	—	—	—	—	—	—
Ears covered by a scaly encrustation	—	—	—	—	—	—
Loss of hair in encrusted areas over the forehead	—	—	—	—	—	—
Adhesion of the eye lids	—	—	—	—	—	—
Loss of hair around the nostril	—	—	+	—	++	++
Loss of hair on the ventral side of the neck	—	—	+	—	++	++
Loss of hair of the shoulders	—	—	—	—	—	—
Loss of hair of the abdomen	—	—	+	—	++	++
Loss of glossiness and drying of the tail skin	—	—	+	—	++	++
Necrotic tails	—	—	—	—	—	—
Reddishness and swelling of the hind legs	—	—	++	+	++	++
Paralysis in the hind legs	—	—	—	—	—	—

died in 21 days during the experiment (Fig. 1, C).

In mice fed with diet *B*, increase in body weight was stopped within 18 days, but no apparent symptoms of deficiency were seen till the 21st day (Fig. 1, *B*).

2. Antagonistic Action of Pyridoxine to TXP on the Growth of Mice.

In the next series of experiments, the animals were fed with diets *A*, *C*, and *D*, respectively, for 21 days. Mice fed with diet *D* showed neither loss in weight nor deficiency symptoms as shown in Fig. 2.

Then, the diets of the group fed with diet *C* or *D* were exchanged after 21 days, and the second diets were given for 28 days as follows: Mice fed with diet *A* were given the same diet (Group 1); mice fed with diet *D* were switched to diet *C* (Group 2); mice first fed with diet *C* were divided into 2 groups: one group received then diet *D* (Group 3), and another group successively received diet *C* (Group 4). Mice in Group 2 showed a rapid loss in weight, and symptoms of deficiency appeared within 15–20 days (Fig. 2, curve 2). Mice in Group 3 showed a very rapid restoration of lost weight, and deficiency symptoms disappeared in 7 days after the change in diet (Fig. 2, curve 3). On the contrary, mice in Group 4 died in 37 days (Fig. 2, curve 4).

SUMMARY

In mice reared on a basal ration containing 5 mg of TXP per 100 g, increase in body weight was considerably suppressed.

When the animals were fed with vitamin B₆ deficient diet containing TXP, they gradually lost weight and died within 13–15 days.

The symptoms of vitamin B₆ deficiency could be prohibited to some extent by administering the basal ration containing 0.1 mg pyridoxine per 100 g but not sufficient. When basal ration containing 6.6 mg of pyridoxine per 100 g was given, the weight loss and vitamin B₆ deficiency symptoms caused by TXP were thoroughly prevented, and the animals manifesting the symptoms recovered.

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