[4] Since the preparation of this manuscript Williams has called our attention to the fact that vitamin B_1 is sparingly soluble in absolute alcohol and is not extracted from yeast and foodstuffs by this solvent unless an excess of mineral acid is present. This explains our failure to secure a beneficial effect with extracts of yeast made with absolute alcohol.

[5] R. Gautheret, *Compt. Rend. Acad. Sci. Paris*, **197**, 85-87 (1934).

[6] R. R. Williams and J. K. Cline, *Jour. Am. Chem. Soc.*, **58**, 1504-1505 (1936).

PYRIMIDINE AND THIAZOLE INTERMEDIATES AS SUBSTITUTES FOR VITAMIN B_1

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In studying the nutrient requirements of excised tomato roots two of the authors (Robbins and Bartley) have found that the roots do not grow in a liquid medium containing mineral salts and pure cane sugar but grow in the same medium to which a small amount of crystalline vitamin B_1 has been added.[1] They have found, further, that 4-methyl-5-β-hydroxyethylthiazole will replace vitamin B_1 in a synthetic liquid medium for the growth of excised tomato roots but that 2-methyl-5-bromomethyl-6-aminopyrimidine is not effective.[2] Williams and Cline[3] synthesized vitamin B_1 by combining these two compounds. It appears from these results that the thiazole radical of the vitamin is the effective agent so far as the growth of tomato roots is concerned.

If thiazole can be substituted for vitamin B_1 in a nutrient medium suitable for the growth of tomato roots, can it be used to replace vitamin B_1 for other organisms?

Our results indicate that neither the thiazole nor the brompyrimidine relieve vitamin B_1 deficiency in pigeons, but that sufficient quantities of the pyrimidine and the thiazole given together by mouth are effective. The pyrimidine and the thiazole used in these experiments were secured through the courtesy of R. R. Williams and of Merck and Company. The pigeons used were maintained on ration No. 1669 containing sucrose, casein (treated with alcohol), the Osborne and Mendel salt mixture, celluflour and cod liver oil until they showed symptoms of polyneuritis, at which time they were given the thiazole or pyrimidine in capsules by mouth. Our results follow.

Pigeon No. 1602. Showed definite signs of polyneuritis. Given 100 gamma of thiazole. Little or no improvement noted the next day. Given

100 gamma of thiazole. Little or no improvement noted during next two days. Given 100 gamma of thiazole. On the following day violent symptoms of polyneuritis developed. Given 10 mgm. of thiazole. No improvement on the following day. Given 20 gamma vitamin B_1 crystals. Complete recovery.

Pigeon No. 1583. Showed violent symptoms of polyneuritis. Given 10 mgm. thiazole and 10 mgm. of brompyrimidine in afternoon. Recovery noted next day. Additional dose 1 + mgm. of thiazole and pyrimidine given. Still normal at end of 11 days.

Pigeon No. 1542. Developed violent polyneuritis. Given 100 gamma of brompyrimidine and 100 gamma of thiazole. No improvement next morning. Given 5 mgm. of each. Normal when examined seven hours later. Still normal after 11 days.

Pigeon No. 1503. Developed violent symptoms of polyneuritis. Given 100 gamma brompyrimidine. Later in the day symptoms still violent. Given 10 mgm. of the brompyrimidine. The following day still showed violent symptoms; given 10 mgm. thiazole. Condition very bad next morning. Given 5 mgm. brompyrimidine and 5 mgm. thiazole. Recovery by afternoon and still normal after 10 days.

While the number of pigeons available for experiment thus far has been limited our results strongly suggest that polyneuritis in pigeons may be cured by doses of 5 milligrams each of 2-methyl-5-bromomethyl-6-aminopyrimidine and 4-methyl-5-β-hydroxyethylthiazole, the two intermediates used by Williams and Cline in synthesizing vitamin B_1. It would appear that a dose of 0.1 mgm. of each of these two compounds is insufficient; and further that the curative action does not occur if the two compounds are given separately, 24 hours apart.

Our results suggest that vitamin B_1 is synthesized from the two intermediates, either in the crop or in the tissues. In reply to the inquiry as to whether the thiazole and pyrimidine would react at room temperature in acid solution Williams[4] states: "Theoretically one would expect such a combination of the pyrimidine and the thiazole to occur, though perhaps at a very slow rate unless catalyzed. We have not succeeded in demonstrating such a synthesis *in vitro* but think it not at all unlikely, especially *in vivo*."

[1] William J. Robbins and Mary A. Bartley, *Science*, **85**, 246–247 (1937).

[2] William J. Robbins and Mary A. Bartley, *Proc. Nat. Acad. Sci.*, **23**, 385–388 (1937).

[3] R. R. Williams and J. K. Cline, *Jour. Am. Chem. Soc.*, **58**, 1504–1505 (1936).

[4] Letter from R. R. W. to W. J. R.