

were obtained. *Anal.* Calcd. for $C_6H_8N_2Cl_2$: Cl, 42.47. Found: Cl, 42.34, 42.54. Mixed with a sample of β -aminopyridine dihydrochloride kindly sent to us by Dr. Y. Subbarow, the melting point was 173–175°. There thus seems to be no question but that the compound assayed in each laboratory was actually β -aminopyridine.

The following results were obtained when the compound was administered to dogs suffering from blacktongue. The method of producing blacktongue has been described.³

1. On 6/13 a 6800-g. dog showing slight symptoms of blacktongue was given 23 mg. of β -aminopyridine orally, and on the next day a further oral dose of 23 mg. was given. During the next two days the symptoms became progressively worse, and the weight dropped 100 g. On 6/15 two 30-mg. doses of nicotinic acid were fed. Two days later the symptoms were much improved and the dog weighed 7200 g. On 6/22 the weight was 8000 g. and the dog was completely cured.

2. On 6/21, 100 mg. of β -aminopyridine was given orally to a 5400-g. dog suffering from severe blacktongue. Two days later the symptoms were slightly worse, and the weight had dropped to 4900 g. One hundred mg. of nicotinic acid was then fed. Four days later the dog weighed 5500 g. and was completely cured.

3. An aqueous solution of β -aminopyridine dihydrochloride containing 6.67 mg. per cc. was adjusted to pH 4.4 with sodium hydroxide. A dog which had been kept on the blacktongue-producing diet until its weight had dropped from 5600 g. to 4800 g., but in which symptoms of blacktongue had not yet appeared, was given daily doses of 20, 20, 20, 15 and 15 mg., respectively, of the dihydrochloride by subcutaneous injection of the above solution. During this six-day period (7/7–13) the weight remained at 5000 g., and no symptoms of blacktongue appeared. On each of the four succeeding days (7/13–16) 15 mg. of nicotinic acid were administered by subcutaneous injection. After four days of this treatment the animal's weight had increased to 5600 g., and three days later (7/19) to 6200 g.

4. A 4250-g. dog suffering from rather severe blacktongue was given three 20-mg. doses of β -aminopyridine dihydrochloride on three successive days. Administration was by subcutaneous injection of the above described solution, which had been readjusted to pH 1.8 (approximately the pH of a solution of 6.67 mg. of the pure dihydrochloride in 1 cc. distilled water). Since the dog weighed only 3800 g. and was much worse on the third day, the dose for the fourth day was increased to 40 mg. On the fifth day of the assay the dog weighed 3400 g., and was in such bad condition that death ensued, despite the injection of 30 mg. of nicotinic acid.

5. A 10-kg. dog was given 100 mg. of β -aminopyridine dihydrochloride daily for three days (7/29–31). The substance was injected subcutaneously in the form of a solution containing 12.3 mg. per cc., pH 1.25. The β -aminopyridine used in this case was obtained from Dr. T. Spies,

(3) Woolley, Strong, Madden and Elvehjem, *J. Biol. Chem.*, **124**, 715 (1938).

University of Cincinnati. The symptoms of blacktongue which were slight at first had become worse at the end of the third day, and the weight had dropped to 9600 g. The dog was allowed to remain untreated for two more days and the weight dropped to 9100 g., while the symptoms became very severe. One hundred mg. nicotinic acid was then injected (8/2) and after two days the dog weighed 9600 g. and showed definite improvement. On 8/5 50 mg. of nicotinic acid was injected and on 8/8 the weight was 10,100, and the animal was completely cured.

6. A 9200-g. dog was given 100 mg. of β -aminopyridine dihydrochloride daily for three days (8/19–21). The substance was injected subcutaneously in the form of a solution containing 12.3 mg. per cc., pH 1.25. The β -aminopyridine dihydrochloride used in this case was obtained from Dr. Y. Subbarow, Harvard University. The symptoms of blacktongue which were slight at first remained unchanged but the weight dropped to 8900 g. The dog was allowed to remain untreated for one more day and the weight dropped to 8400, while the symptoms remained the same. One hundred mg. of nicotinic acid was then injected (8/23) and after two days the dog weighed 9200 g. and the symptoms of blacktongue were markedly improved. On 8/25 100 mg. of nicotinic acid was injected and on 8/29 the animal weighed 10,400 g. and was completely cured.

In this connection it has been found in this Laboratory (unpublished data) that β -aminopyridine cannot replace nicotinic acid as a growth essential for *Staph. aureus*.

It is evident from these results that β -aminopyridine as tested in our laboratory has no activity as compared to nicotinic acid in the treatment of blacktongue.

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The Inactivity of β -Aminopyridine in Blacktongue

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Dr. Elvehjem has informed us privately of his findings as reported in the preceding communication and as a result we have re-examined the question of the activity of β -aminopyridine in blacktongue. We have been unable to repeat our earlier observation that small doses of this substance will cure blacktongue, or to account for the cures then obtained. It is, however, clear that our earlier conclusion is incorrect and that β -aminopyridine is not a blacktongue preventive factor.

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