As shown in Table I, the *in vitro* activity of p-(2,4-diamino-s-triazinyl-6)-aminophenyl p'-aminophenyl sulfone is of the same order as that of 4,4'-diaminodiphenyl sulfone. Since p-aminobenzoic acid (5×10^{-5} molar) was found to reverse completely the antibacterial action of the heterocyclic sulfone (5×10^{-4} molar), the latter presumably acts through a mechanism similar to that reported for 4,4'-diaminodiphenyl sulfone(4).

Summary. p-(2,4-Diamino-s-triazinyl-6)-aminophenyl p'-aminophenyl sulfone has been synthesized and shown to inhibit the growth of *M. tuberculosis* and *E. coli in vitro* at a concentration of 1.2×10^{-4} moles per liter, the inhibition being reversed by p-aminobenzoic acid.

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Production of Acrodynia in Mice Fed Diets Low in Pyridoxine.* (18949)

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During the course of an investigation on the influence of vitamins of the B complex on the induction of tumors in mice, a fortuitous observation of an acrodynia was made. This condition was cured by the injection of pyridoxine(1). However the diet fed to these mice was low in several of the B vitamins.

The present report describes further studies on the production of acrodynia in mice. The results are of interest because it has been reported that the pyridoxine deficient mouse, in contrast to the rat, does not develop acrodynia(2-5) except with the aid of desoxypyridoxine(6).

Methods and results. Since the original observation of acrodynia was made on female albino mice that were 2-3 months of age at the start of the experiment(1), similar mice were used in the present study. Weanling male mice, capable of rapid growth on a complete diet, were also used. These mice were obtained from a commercial source,† and upon arrival were immediately placed in screen bottom cages and were given water and the experimental diets *ad libitum*.

The following 4 diets were used: *Diet A*, a semi-purified diet plus pyridoxine: Glucose monohydrate (Cerelose), 78; ordinary commercial casein, 15; corn oil (Mazola), 2; liver concentrate (Wilson Laboratories 1-20 liver powder), 1; salt mixture (modified Phillips-Hart), 4. This was supplemented with the following vitamins per kg of diet: pyridoxine-HCl, 30 mg; thiamine-HCl, 1.55 mg; biotin, 0.1 mg; inositol, 20 mg; para aminobenzoic acid, 20 mg; choline-Cl, 20 mg; and 6 drops of halibut liver oil premixed with the corn oil. *Diet B*, a semi-purified diet without added pyridoxine: This diet was the same as diet A except that no pyridoxine was added. *Diet C*, a purified diet with low pyridoxine: This diet differed from diet A as follows. The crude casein was replaced by purified casein (Smaco) and the liver concentrate was replaced by an equivalent weight of glucose. The following vitamins were added per kg: pyridoxine-HCl,

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† Arthur Sutter, Springfield, Mo. The mice were described as "Rockland Strain."

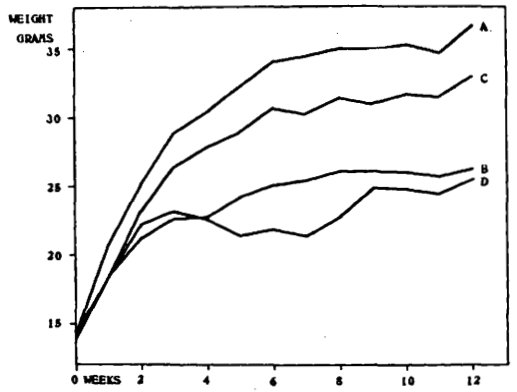

FIG. 1. Growth curves showing the effects of various diets on the growth of weanling male mice.‡ A. Growth curve of mice fed the non-purified diet plus pyridoxine. B. Growth curve of mice fed the non-purified diet without added pyridoxine. C. Growth curve of mice fed the purified diet with low pyridoxine. D. Growth curve of mice fed the purified diet without added pyridoxine.

0.166 mg; thiamine-HCl, 3 mg; riboflavin, 3 mg; niacinamide, 5 mg; calcium pantothenate, 20 mg; folic acid, 1 mg; para aminobenzoic acid, 250 mg; inositol, 250 mg; choline-Cl, 500 mg; biotin, 0.1 mg; and 6 drops of halibut liver oil. *Diet D,* a purified diet without pyridoxine: This diet was the same as diet C except that no pyridoxine was added. Each of the 4 diets was fed to a group of 8 weanling male mice and to a group of 8 females about 2 months of age, making 8 groups in all.

In Fig. 1 are shown the growth curves of the 4 groups of weanling male mice. Excellent growth was shown by the mice fed the semi-purified diet plus pyridoxine (diet A), and the purified diet containing a presumed suboptimum level of pyridoxine (Diet C) allowed good growth. However growth was inferior in mice fed either diet without added pyridoxine (Diets B and D). Since the young adult female mice were nearly full-grown and therefore showed less growth, their weight curves are not shown. The initial weights averaged 23 g and 12 weeks later the average of each of the 4 groups ranged from 26 to 33 g, and the curves of the averages followed the same pattern as was the case for the young growing male mice.

Both groups of mice fed diet A were in good health throughout the experiment and no definite signs of deficiency were noted in the two groups fed the purified diet with a trace amount of pyridoxine, diet C. However, acrodynia was observed between the 8th and 9th weeks in each age-sex group fed diets B and D. The acrodynia affected a greater proportion of the young adult female mice fed the purified diet without pyridoxine (5 of 8 mice) than in the other 3 groups (2 of 8 in each). Furthermore 3 of the 8 weanling mice fed the purified diet without added pyridoxine died between the 7th and 12th weeks.

At the 12th week, pyridoxine therapy was begun on 3 female mice with severe acrodynia that had been fed the purified diet without added pyridoxine. The appearance of these mice became normal within one week by the addition of 30 mg/kg of pyridoxine-HCl to the diet.

Discussion. The acrodynia displayed by the mice in these experiments resembled that described by Birch, Gyorgy, and Harris(7) in the rat. The ears of these mice were red and swollen, and the paws were scaly and even raw. There was dermatitis of the nose which often extended beyond the eyes. The tail was not affected, although scaliness sometimes appeared at the base. An ataxic gait involving the hind legs was also observed. The mice appeared anemic but the hemoglobin was not determined.

This syndrome was related specifically to a low dietary level of pyridoxine. As little as 0.166 mg of added crystalline pyridoxine-HCl per kg of the purified diet protected the mice from acrodynia and resulted in a good growth response. In contrast, mice fed the semi-purified diet without added pyridoxine developed acrodynia, yet this diet has been calculated to contain over three times as much pyridoxine-HCl as the purified diet, namely 0.51 mg/kg. Perhaps the pyridoxine of the liver powder and casein as determined micro-

‡ The increase in the average weight of the surviving mice of group D between the 7th and 8th, the 8th and 9th, and the 11th and 12th weeks is accounted for by the death of one mouse during each of these weeks.

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biologically is not all available to the mouse.

No explanation is offered for the appearance of acrodynia in our experiments in contrast to the usual freedom in mice from acrodynia during pyridoxine deprivation. By inspection of the conditions of previous studies of B_6 deficient mice together with the variables introduced in our experiments, no definite correlation could be established relating the composition of the diet, age or sex of the mice, the probable pyridoxine content of the diet, levels of other vitamins, etc., to the protection from, or appearance of, acrodynia. The syndrome has appeared in the mice without fail on 3 different occasions that were so spaced in time (February, May, and September) that such factors as season and humidity were probably not involved. Only one strain of mice was tested, and it may be that strain differences play an important role in the appearance of acrodynia.

Summary. 1. Pyridoxine deficiency was produced in weanling male and in young adult female mice fed (a) a purified diet containing 9 other crystalline B vitamins, and (b) a semipurified diet containing a low level of liver powder. 2. Acrodynia appeared among both the weanling and young adult mice fed these 2 diets. 3. As little as 0.166 mg of added crystalline pyridoxine-HCl per kg of the purified diet protected the mice from acrodynia and resulted in a good growth response by the weanling mice.

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Role of Bile and Pancreatic Juice in Production of Esophageal Erosions and Anemia.* (18950)

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Numerous studies have been carried out on the ability by trypsin to digest living tissues and on the toxic effect of bile salts on certain tissues. Claude Bernard(1) showed that the leg of a living frog was digested away when introduced into the stomach of a dog. Rosenbach(2) produced hemorrhages on the tongue of a frog by the local application of a solution of active trypsin. Langenskjöld(3) found he could cause ulceration and necrosis of urinary bladder mucosa in the dog by perfusing it with pancreatic juice, but not to the degree produced by gastric juice. Kirchheim and Böttner(4) found no changes in the mucous membrane of the urinary bladder, esophagus or intestine after exposure to active trypsin solution for 10 hours. Necheles and associates(5) and Dragstedt and associates(6) implanted various organs such as pancreas, kidney, liver and omentum into the duodenum exposed to active pancreatic ferments and found in most cases no digestion of these organs. Rywosch(7) was one of the first investigators to point out the toxic effect of bile salts on various tissues. Opie(8) and Flexner(9) showed the destructive effect of bile

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