of artificial ceresin wax a small amount of *p*-phenylphenacylacetate prepared from sodium acetate methyl-labeled with C^{14}.)

A consideration of the reflection enhancement of the observed radiation leads one to expect that, at sample thicknesses where the backscattering effects are saturated, the curves for the two sample materials will be related to each other by the quotient of the proper reflection coefficients. The value predicted is $1.35 \pm 0.01/1.07 \pm 0.015 = 1.26 \pm 0.02$; that observed is 1.27.

Work is now in progress on a theoretical treatment of these effects, as well as on experiments designed to elucidate their angular dependence and variation with particle energy. A more complete report will be published elsewhere.

L-Penicillamine as a Metabolic Antagonist[1]

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Because of the structural relationship of penicillamine (β,β-dimethylcysteine) to the biologically important sulfur-containing amino acids, it occurred to us that penicillamine might possess anti-amine acid activity. In investigating this possibility we found that when L-penicillamine was added to the diets of young albino rats[2] growth was inhibited. However, when cystine, cysteine, homocystine, or homocysteine were added to the diet, the effect was not counteracted. In pursuing further the thought that penicillamine was a metabolic antagonist, we encountered the fact that choline was effective in counteracting the toxic action of L-penicillamine.

This relationship of choline and penicillamine was then studied in greater detail, utilizing a choline-free diet.[3] When L-penicillamine hydrochloride hydrate was added in an amount to make 0.35% of this diet, which otherwise permitted good growth, an immediate loss in weight resulted. When 1.6% of choline chloride was subsequently incorporated in the diet, the loss in weight was counteracted. These animals then grew at the same rate as those on the diet to which no penicillamine had been added. Most of the animals receiving penicillamine but no choline died in a few weeks, although in a few cases the loss of weight was partially overcome and the animals lingered on. Apparently some animals are a little more resistant than others to the action of penicillamine, but all animals seem to be susceptible if sufficiently high levels of penicillamine are used.

Increased amounts of methionine in the diet were incapable of overcoming the effects of penicillamine under these dietary conditions. Dimethylaminoethanol and monomethylaminoethanol were next investigated and found to be effective. Aminoethanol itself was then tried and was found to be an even more effective agent than choline against the toxic effect of penicillamine. When any of the methylated derivatives of aminoethanol is added to the diet at the same time that the penicillamine feeding is begun, there is a loss of weight for a few days before growth is resumed. On the other hand, there is no break in the growth curve if aminoethanol (at a level of 0.33% in the diet) is used under these conditions.

The animals given L-penicillamine hydrochloride hydrate (0.35%) in the diet without supplementation with aminoethanol, or with any of the methyl derivatives, generally have peculiar seizures at irregular intervals beginning a few days after the diet is first given. Such animals run rapidly about their cages and then collapse in either a clonic or tetanic convulsion, accompanied by salivation. During the running phase, the animals frequently shriek. The animals usually recover within a few minutes from the onset of the symptoms. However, the administration of a larger amount of L-penicillamine (330 mg/kg) by stomach tube or by subcutaneous or intraperitoneal injection is followed within a few hours by seizures of the type just described, and the animal usually dies after a series of violent convulsions. Cyanosis frequently occurs, suggesting that respiratory failure may be the cause of death. Histological investigation of the tissues of these animals is being undertaken.

It is of particular interest that when D-penicillamine, the enantiomorph derivable from naturally occurring penicillin, was employed under any of the conditions described for the L isomer, no inhibition of the growth rate was observed nor was any other toxic manifestation encountered. Of additional interest is the fact that the disulfide of L-penicillamine did not inhibit growth.

The data suggest that penicillamine may exert its toxic action by blocking either the synthesis or the utilization of aminoethanol. However, the possibility of direct reaction between aminoethanol, or a product derived therefrom, and penicillamine is not excluded. At the present time we are investigating the possible metabolic significance of this unexpected relationship between this series of compounds and penicillamine.

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[2] Young albino rats from Rockland Farms, New City, New York, were used for the experiments reported in this paper.

[3] The basal diet had the following composition: vitamin-free casein, 20.0 gm; sucrose, 55.0 gm; hydrogenated vegetable oil, 19.0 gm; corn oil, 1.0 ml; salt mixture (Osborne and Mendel. *J. biol. Chem.*, 1919, **37**, 572), 4.0 gm; DL-methionine, 0.15 gm; vitamins A and D concentrate (60,000 I.U. of A and 10,000 I.U. of D/gm), 12 mg; α-tocopherol acetate, 4 mg; 2-methyl-1,4-naphthoquinone, 0.1 mg; vitamin mixture, 1.0 gm (thiamine chloride, 1.0 mg; riboflavin, 1.0 mg; pyridoxine hydrochloride, 1.0 mg; nicotinic acid, 1.0 mg; *p*-aminobenzoic acid, 1.0 mg; calcium *d*-pantothenate, 5.0 mg; inositol, 10.0 mg; biotin, 0.01 mg; folic acid, 0.1 mg; sucrose to make 1.0 gm). When other substances were added to the diet, this was done at the expense of an equal weight of sucrose. The following percentage levels of the compounds were used in the work reported: L-penicillamine hydrochloride hydrate, 0.35, + sodium bicarbonate, 0.16; choline chloride, 1.6; dimethylaminoethanol, 1.00; monomethylaminoethanol, 0.45; aminoethanol, 0.33.