FIG. 3. Mature fiber of *G. klotzschianum* var. *davidsonii* showing a cross wall (× 4,850).

cell. Binuclear epidermal cells and, at a later stage, binuclear lint hairs were seen (Fig. 1). Subsequently, one nucleus degenerates, at a time apparently dependent on the rate of cell growth.

(4) The seed hairs of a wild species, *G. klotzschianum* var. *davidsonii*, are *multicellular* both in young and older stages (Figs. 2 and 3). In mature fibers the cross

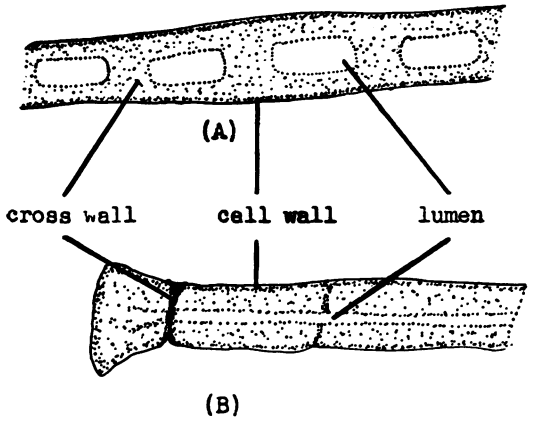

FIG. 4. Diagrammatic illustrations to show the mature fiber of *G. thurberi* (A) and *G. klotzschianum* var. *davidsonii* (B), suggesting the multicellular structure of the fiber.

walls are less thickened than the longitudinal walls, but are clearly visible toward the terminal end of the hair. Previously published illustrations (*5*) of the mature seed hair of another wild species, *G. thurberi*, suggest a similar basic structure in which the cross walls have been thickened to a greater degree. Thus, the lumen appears as a chain of "vacuoles" in an otherwise solid fiber (Fig. 4).

These results indicate that the unicellular lint hairs of cultivated cottons may be developmentally derived from multicellular wild type seed hairs through an evolutionary process that progressively reduced a primitive, strongly thickened, multicellular structure to a unicellular, partly thickened, long hair (lint) and a unicellular, strongly thickened, short hair (fuzz). From the standpoint of differentiation, the seed hairs of *Gossypium* can therefore be grouped as follows: (1) multicellular type, e.g. the seed hairs of *G. thurberi* and *G. klotzschianum*; (2) binuclear type (one nucleus subsequently degenerating), e.g. the lint hairs of cultivated cottons; and (3) uninucleate type, e.g. the fuzz hairs of cultivated cottons. It is possible that the seed hairs of the wild species, *G. anomalum* and *G. raimondii*, represent an intermediate stage between the multicellular and binuclear types shown above.

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The Relation of Backscattering to Self-Absorption in Routine Beta-Ray Measurements

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The enhancement of observable activity caused by reflection processes is said to be due to "backscattering." The intrinsic activity of a thin sample is increased by "exterior reflection" from the sample mount; that of a thick sample is further raised by "interior reflection" due to multiple scattering processes taking place within the sample itself. The latter effect is always observed as part of self-absorption, and therefore one compensates for it automatically when self-absorption corrections are derived from data obtained experimentally under conditions identical with those used in routine counting.

Beta radiations subjected to interior reflection can be divided arbitrarily into two groups: (a) some particles which start toward the counter are *deflected* away from

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the sensitive volume; (b) others start away from the detector but are *reflected* back into the counter from some point in the sample. These two processes differ only in direction. *Deflection* has always been measured as part of the complex beta-ray absorption phenomenon; *reflection*, on the other hand, effectively adds more particles to the measurable flux and thus enhances the observed activity. At the surface of a thick sample the enhancement of the activity is due entirely to internal reflection, since deflection is negligible in the short air path between sample and counter. It can be shown that in deeper-lying layers of the sample this net enhancement is maintained despite the increasing importance of deflection processes.

The magnitude of the backscattering effect depends upon the nature of the sample and mounting and upon the energy of the radiations involved. When thick samples or mounts are used, the effect increases with their atomic numbers and with increasing beta-particle energy. The activity increase due to the mount is kept small by using backings which contain only the lighter elements, such as paper, Cellophane, Nylon, etc. (Accurate determinations of backscattering factors as functions of the solid angle subtended by the detector at the source have not been made. It is known that the size of the effect observed is dependent upon the geometry of the detection system, increasing with increasing geometric efficiency.) In order to gain information on the effect of backscattering upon self-absorption data, some experiments were performed which were designed to yield information concerning the relative backscattering powers of a number of substances at two different detection geometries.

A 4-μg sample of C^{14}-active barium carbonate was mounted over an area of 0.040 cm² in the center of a plastic film circle 20 cm in diameter and 0.07 mg/cm² thick; the sample layer was not thicker than 0.15 mg/cm². The aluminum equivalent thickness of the counter window and air path was 3.4 mg/cm² at the lower geometry (12%) and 2.3 mg/cm² at the higher (36%). The sample was first counted over 25 cm of air; then thick layers of various materials were maneuvered to within 0.05 mm of the back of the sample spot and the activity again measured. This enhanced activity, divided by that first observed, is taken as being equal to the backscattering factor of the substance in the thick backing layer at the geometric efficiency with which detection was carried out. The data are collected in Table 1.

From these data it is possible to make certain statements about interior reflection in samples of various thicknesses. Consider, first, a sample of radioactive barium carbonate mounted on aluminum and counted at 36% geometry. If one envisions the sample as made up of many thin layers, it is apparent that the observed activity of the first lamina (counting from the mount) is 1.16 times the intrinsic activity because the aluminum mount contributes an additional radiation flux to the measurement by exterior reflection. The activity observable from the next lamina is increased by slightly more than 1.16, for although fewer radiations can reach the backing, they are more powerfully reflected from the first barium carbonate lamina. Thus, as the sample thickness is increased, the activity rises from 1.16 to 1.35 times that observed when all reflection effects are neglected. If samples of active wax were used, the activity observable would fall from 1.16 to 1.07 times the "no-reflection" strength because the interior reflecting power of wax is less than the exterior reflecting power of aluminum.

TABLE 1

BACKSCATTERING OF C^{14} BETA-PARTICLES

Scatterer	Relative observed activity	
	12% geometry	30% geometry
Air	1.00	1.00
Platinum	1.43 ± 0.02	1.51 ± 0.02
Barium carbonate	1.30 ± .01	1.35 ± .01
Glass	1.16 ± .01	1.17 ± .01
Aluminum	1.15 ± .01	1.16 ± .01*
Paper (unsized)	1.04 ± .015	1.07 ± .015
Wax (artificial ceresin)	1.04 ± .015	1.07 ± .015

* Compare with L. D. Norris and M. G. Inghram. *Phys. Rev.*, 1948, **73**, 350.

Backscattering effects saturate very rapidly because they involve double transit of radiations through absorbing layers. The maximum penetration thickness of C^{14} beta-particles is about 28 mg/cm²; yet the reflection effects reach 80% of their maximum at a sample thickness of 6 mg/cm² and 97% at 12 mg/cm².

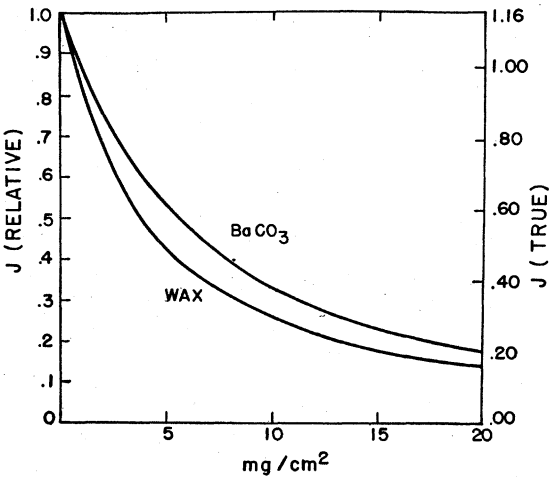

FIG. 1. Self-absorption correction curves for barium carbonate and wax samples, mounted on aluminum, as functions of sample thickness. (Data obtained at 30% geometry.) J is fraction of maximum specific activity.

It has been assumed by many investigators that the effective self-absorption corrections for several sample substances are very nearly the same as those for barium carbonate, for which most such determinations have been made. That this is not the case can be seen by reference to Fig. 1, where data for wax and barium carbonate samples, all mounted on aluminum, are graphed. (The active wax was prepared by dissolving in a large amount

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.

[1] The authors wish to thank the Lederle Laboratories Division, American Cyanamid Company, for a research grant which has aided greatly in this work. The authors also wish to acknowledge the kindness of Parke, Davis and Company in placing at our disposal a supply of S-benzyl-DL-penicillamine, which served partially as a source of the penicillamine used in this investigation.

[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.