

has been found useful in some cases, but it is not so sensitive as silver nitrate.

It is suggested that the reagent might be of general application wherever a compound forms an insoluble complex with silver. For example, carbobenzoxy- β -alanine thiophenol ester (a derivative employed in peptide synthesis) is not detectable with reagents commonly used, but forms an insoluble complex with silver nitrate and appears as a blue spot on a chromatogram. With the aid of the reagent, the progress of the coupling of this ester with an amino-acid can be followed by paper chromatography, the carbobenzoxy- β -alanine thiophenol ester spot disappearing as the coupling proceeds.

The reagent thus has three distinct fields of application: first, in the detection of halogen ions; secondly, to reveal spots due to compounds forming insoluble complexes with silver; and finally, as a sensitive reagent for certain purine and pyrimidine compounds.

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¹ Reguera, R. M., and Asimov, I., *J. Amer. Chem. Soc.*, **72**, 5781 (1950).
² Geschwind, I. I., and Li, C. H., *J. Amer. Chem. Soc.*, **74**, 834 (1952).

Origin of Penicillin-resistant *Staphylococcus pyogenes*

CLASSIFICATION of strains of staphylococci by their reactions to bacteriophages has been extensively used in epidemiological studies of staphylococcal infection. Thus three main groups of these organisms can be separated, and strains belonging to different groups have been considered to be unrelated. For example, a patient who is infected with a strain of one group, when later found to be infected with a strain belonging to another group, is regarded as having suffered a second infection from a different source.

The present high prevalence of penicillin-resistant staphylococci in the community, associated with the extensive therapeutic use of this antibiotic, is believed to be due largely to their selective spread associated with suppression of the sensitive strains. The fact that the majority of antibiotic-resistant strains belong to phage group III and the majority of sensitive strains to groups I and II might seem to support this view¹.

The alternative view is that antibiotic-resistant strains originate by mutation from sensitive strains under the impact of the antibiotic during treatment. If this is so, one would expect the distribution of resistant strains between the various phage groups to be the same as that of the sensitive strains, that is, the majority would be of groups I and II; but this is not the case. However, Barber and Whitehead² found that antibiotic-sensitive strains of group III tend to become resistant to penicillin more readily than strains of other groups, and this might afford an explanation of their preponderance. Another explanation is suggested by the results of the following experiments involving the production of antibiotic resistance *in vitro*.

These experiments were carried out with cultures of penicillin-sensitive *Staphylococcus pyogenes* derived from single colonies. The cultures were exposed to penicillin by growing them on the surface of

nutrient agar plates containing various concentrations of the antibiotic. After incubation, these plates showed two variant types of colony which were resistant to penicillin. The first, and most frequent, was a relatively slow-growing, unpigmented colony, and cultures from it produced no penicillinase nor did they show any change in phage type. Penicillin-resistant variants of this type have been obtained *in vitro* by many other investigators, but do not appear to occur *in vivo*. The second, less-frequent, type of variant gave colonies which were large, opaque and pigmented; they produced penicillinase, and the majority belonged to phage group III, even when their antibiotic-sensitive parent cultures belonged to groups I and II. A change in phage type thus occurred in association with the acquisition of antibiotic-resistance, and this may explain the preponderance of resistant strains belonging to group III.

If this change can also occur *in vivo*, the development of antibiotic resistance within the individual patient during treatment must be considered as a more frequent occurrence than hitherto believed.

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March 19.

¹ Fusillo, M. H., Roerig, R. N., and Ernst, K. S., *Antibiotics and Chemotherapy*, **4**, 1202 (1954). Gould, J. C., and McKillop, E. J., *J. Hyg. Camb.*, **54**, 486 (1954). Jackson, G. G., *J. Lab. Clin. Med.*, **44**, 317 (1954). Oeding, P., and Vogelsang, T. M., *Acta Path. et Microbiol. Scand.*, **34**, 47 (1954).

² Barber, M., and Whitehead, J. E. M., *Brit. Med. J.*, **ii**, 565 (1949).

Quercetin Glucosiduronic Acid from the French Bean

THE monoglucosiduronic acids of polyhydroxy-flavones, for example, chrysin, baicalein and scutellarein, that have been isolated from plant material, occur chiefly in the genus *Scutellaria*¹. These have been shown to be β -D-glucopyranuronides with a high affinity for animal tissue β -glucuronidase². Recently, a conjugate of apigenin with glucuronic acid has been found in the flowers of *Erigeron annuus*³. French beans (*Phaseolus vulgaris*) have been reported⁴ to contain a glycoside which on acid hydrolysis yielded glucuronic acid and a flavone that appeared to be quercetin; this has been confirmed and the compound has been found to be a substrate for β -glucuronidase.

The beans (var. Prince: other varieties yielded much less product) were cultivated in Aberdeenshire and collected just prior to flowering. Extraction of the leaf by the method previously described yielded quercetin glucosiduronic acid, melting point 190-191° (corr.), $[\alpha]_D^{25} - 50^\circ$ (c, 1 in 50 per cent aqueous pyridine) for the anhydrous product. After being recrystallized from water and dried at 100° *in vacuo*, the product lost 7.2 per cent in weight, corresponding to $C_{21}H_{18}O_{13} \cdot 2H_2O$ (found for the anhydrous product: C, 52.9; H, 3.9; calc. for $C_{21}H_{18}O_{13}$: C, 52.8; H, 3.8 per cent). The yield was 0.25 per cent of the dry weight of leaf.

Hydrolysis with a mouse-liver β -glucuronidase preparation in acetate buffer at pH 5.2, or with hot aqueous sulphuric acid (10 per cent w/v), yielded quercetin, melting points 300-303° and 304-306° (uncorr.) respectively, after recrystallization from