4. It acts as a temporary ringing compound. (Although it does not replace standard ringing compounds, it forms a temporary protection for the specimen.)

5. Specimens may be mounted from xylene, toluene, water, alcohol, cellusolve, lactic acid, lactophenol, or a number of other preservatives and clearing agents, or specimens may be placed in the mounting medium alive.

6. It does not crystallize (there were no signs of crystallization after slides were held at 55° C for six months).

Enhancement of the Action of Streptomycin

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Various attempts have been made to enhance the action of streptomycin, either by combining it with other drugs such as potassium iodide (*1*) and *p*-aminosalicylic acid, (*2*, *3*) or by making a compound with *p*-aminosalicylic acid ([*4*], intracerebral method). In the present investigation we have used the rabbit and mouse corneal methods (*5*, *6*) in order to determine the activity of such combinations.

Combination of streptomycin and potassium iodide. In the first of two experiments 12 rabbits were used; 6 were infected in both eyes and 6 in the right eye only. Treatment was started on the 7th day, when all inoculated animals had developed very early lesions. In the group of 6 animals bilaterally infected, the right eyes received streptomycin and potassium iodide, and the left eyes received streptomycin only. Ten mg of streptomycin was given twice weekly, and 10 mg of potassium iodide was given thrice weekly, all by intravitreous injection. Of the 6 animals in which only the left eyes were infected 3 received thrice weekly injections of potassium iodide and the other 3 were untreated controls. Treatment was continued until the 60th day. The results are shown in Fig. 1, in which the size of the corneal lesion is plotted against time.

In the second experiment 10 rabbits were used, 8 of which were infected in both eyes and the other 2 in the right eyes only. Treatment was withheld until the 16th day, when all inoculated eyes had developed more advanced lesions, with early caseation. The treated group consisted of the 8 animals with bilateral corneal infection; the right eyes received streptomycin and potassium iodide, and the left eyes streptomycin only. The remaining 2 animals served as untreated controls. Treatment was as in the first experiment but was continued for 72 days, and the experiment was finally terminated on the 147th day. The results are shown in Fig. 2.

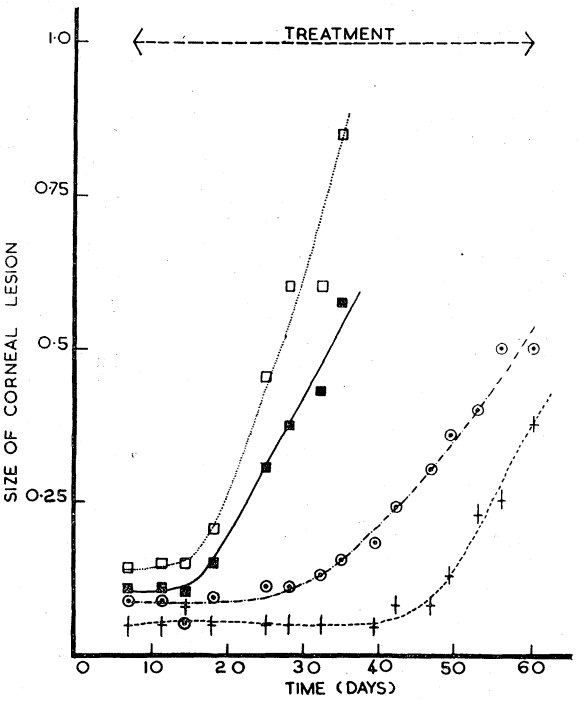

FIG. 1. Effect of combined streptomycin and potassium iodine in early tuberculous corneal lesions in rabbits.

——■—— = control group

···· □ ···· = potassium iodide group

- - - - - ⊙ - - - - - = streptomycin group

- - - - - + - - - - - = streptomycin and potassium iodide group

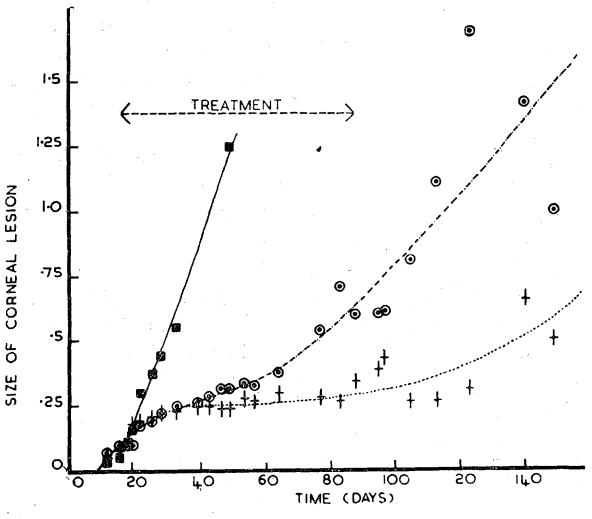

FIG. 2. Effect of combined streptomycin and potassium iodide in later tuberculous corneal lesions in rabbits. (Legends as in Fig. 1.)

[1] At present on the scientific staff of the Medical Research Council.

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The corneal test was used in a similar experiment with streptomycin and potassium iodide in mice in which only one eye was infected. The results were assessed both on the incubation period and on the subsequent progress of the corneal lesions. There were 6 untreated control mice, 7 mice on potassium iodide (400 mg/k of the diet), 14 mice on potassium iodide combined with streptomycin (4 mg daily subcutaneously) and 12 mice on streptomycin (4 mg daily). Treatment was started on the day of infection and maintained for 28 days (Fig. 3).

In order to compare the concentrations of potassium iodide produced in the present experiments with those used by Woody and Avery, experiments were done with radioactive iodine. Guinea pigs (as used by Woody and Avery) were given sodium iodide (containing I^{131}) by stomach tube in doses of 80 mg/k. Rabbits and mice

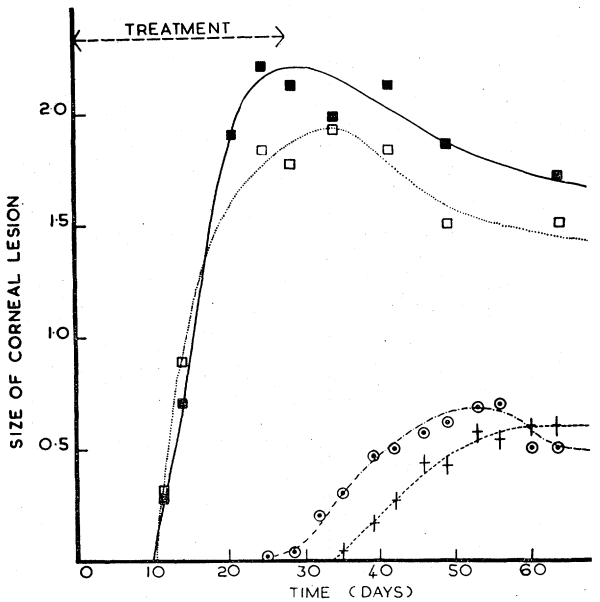

FIG. 3. Effect of combined streptomycin and potassium iodide on the development of tuberculous corneal lesions in mice. (Legends as in Fig. 1.)

were treated with I^{131} as described above. The results show that the concentrations of iodine in the guinea pig and mouse were of the same order, but that the iodine in the aqueous of the rabbit's eye was considerably higher.

Our results with combined streptomycin and potassium iodide confirm those of Woody and Avery. The enhancement of the action of streptomycin, though not marked, is most definite in established caseous tuberculosis (Experiment 2 on rabbits) and becomes more evident only after prolonged treatment. The effect in very early lesions (first experiment on rabbits and mice) is much less definite, and this probably explains the negative results recently described by Levaditi and his co-workers (*7*) in acute tuberculosis in the mouse.

An experiment on mice using a combination of potassium iodide and *p*-aminosalicylic acid (2% in the diet) showed no enhancement of the effect of *p*-aminosalicylic acid, thus confirming the work of Bavin (*8*).

Streptomycin p-aminosalicylate compound. In this experiment 33 mice were infected intracorneally and divided into four groups. Streptomycin was given in a dose of 4 mg/day and the streptomycin *p*-aminosalicylate compound in daily doses containing 4 mg of streptomycin. *p*-Aminosalicylic acid was given as 2% in the diet. The treatment was begun within a few hours of infection and maintained for 28 days. The results, as judged by prolongation of the incubation period and by the number of eyes remaining free from tuberculosis at the end of the experiment, show clearly that all three forms of treatment had produced a beneficial effect, but of the three treatments the streptomycin *p*-aminosalicylate was the least effective. Hence, even if streptomycin salicylates reduced the development of resistant strains of tubercle bacilli in man, combined streptomycin and PAS treatment definitely can (*9*), and at the same time it has greater chemotherapeutic activities.

References

1. WOODY, E., and AVERY, R. C. *Science,* **108**, 501 (1948).
2. SWEDBERG. B., and WIDSTRÖM, G. *Acta Med. Scand.,* **131**, 116 (1949).
3. KARLSON, A. G., and FELDMAN, W. H. *Proc. Mayo Clin.,* **24**, 510 (1949).
4. HOBBY, G., REGNA, P., and LENERT, T. *Am. Rev. Tuberc.,* **60**, 808 (1949).
5. GARDINER, P. A., REES, R. J. W., and ROBSON, J. M. *Brit. J. Pharmacol.,* **4**, 209 (1949).
6. REES, R. J. W., and ROBSON, J. M. *Brit. J. Pharmacol.,* **5**, 77 (1950).
7. LEVADITI, C., VAISMAN, A., and LEVY, P. *Compt. rend. Soc. Biol.,* **143**, 1324 (1949).
8. BAVIN, E. M. *J. Pharm. Pharmacol.,* **1**, 790 (1949).
9. MEDICAL RESEARCH COUNCIL. *Lancet,* **2**, 1237 (1949).

Use of Selective Fluorescent Stains to Detect Insect Egg Plugs on Grain Kernels[1]

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A major need in the cereal-processing industries is a method for the detection and elimination of grain which contains insects at various stages of development within the kernels. Methods yielding presumptive evidence of internal infestation have been proposed. These involve staining the gelatinous insect egg plug of the granary weevil, *Sitophilus granarius* L., and the rice weevil, *S. oryzae* L., with Lugol's solution (*1*), acid fuchsin (*1*), or gentian violet (*2*) in order to render them visible. Such procedures have not proved entirely satisfactory, since these reagents usually stain the starchy endosperm and frequently other tissues of the grain as well, and thus render difficult the adequate differentiation of infested kernels from those that are only mechanically injured. A selective stain specific for the egg plug is highly desirable.

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