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Bacteriostatic Effect of Sulfanilamide in Spinal Fluid of Convalescent Cases of Streptococcal Meningitis.

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During the latter part of August, 1936, and the first week of September, we treated successfully with sulfanilamide what appears to be the first critically studied case on record of streptococcal meningitis. Our second case, one of highest severity, was treated in December. It also recovered. The spinal fluid in each was characterized by a remarkable bacteriostatic effect of the drug, manifesting itself in the first case in 72 hours, and in the second in 48 hours.

In the latter case there were 3,000 white cells per cmm., of spinal fluid, and 8 chains of streptococci per high-power field. One loop of spinal fluid yielded countless numbers of colonies on a blood agar plate; yet after 48 hours' treatment, seeding of ½ cc., of spinal fluid under the same conditions gave no growth, even after 5 days' incubation at 37°C.

When contrasted with the normal serum of a healthy adult, the following results obtain: Both fluids were seeded with 100 streptococci and incubated at 37° for 24 hours. No growth was obtained from the spinal fluid, while the serum showed slightly over 1,000 colonies. A complete clinical report[1] of these cases has been in press for some months.

In a case of brain abscess[2] with a Type V pneumococcus, which was successfully treated, a question arose with the surgeon relative to the accessibility of the spinal fluid to the drug, which was administered para-spinally. A quantitative test for sulfanilamide, devised by one of us (Bambas), proved to be essentially the same as the one later reported by Fuller,[3] except that H acid (1-amino-8-naphthol-3.6-disulfonic acid) was used as the coupling compound.

In 72 hours the patient had received 10 cc. of Prontosil in 2 doses of 5 cc. each, and a total of 40 grains of sulfanilamide in 5 doses. The concentration of the drug in the ventricular fluid was 1:25,000, or 4 mg. per 100 cc. of fluid.

The patient continued to receive 20 grains of sulfanilamide per day for 3 more days. The concentration at this time was 1:35,000

[1] Weinberg, M. H., Mellon, R. R., and Shinn, L. E., *J. Am. Med. Assn.*, 1937, **108**, 1948.

[2] Rowe, N. S., to be published.

[3] Fuller, A. T., *Lancet*, 1937, **232**, 194.

in both blood and spinal fluid, showing the interesting fact that no partition-coefficient between the 2 fluids existed.

Curiosity as to the mechanism of the bacteriostatic and killing action of the drug led to experiments on its possible effect on the dehydrogenases of the pneumococcus. Sulfanilamide was studied comparatively with other well-known bactericidal agents, and the results follow. We used Type I Neufeld strain, and glucose was employed as a metabolite.

In these experiments the Thunberg technic was employed: one cc. of 1:5,000 methylene blue; one cc. of 0.01 M glucose; one cc. of pH 7.4 phosphate buffer; one cc. of washed cells of Type I Neufeld, mucoid, pneumococcus; and one cc. of the inhibitor were placed in a Thunberg tube. The tubes were exhausted, placed in a water-bath, and the rate of reduction of the methylene blue was noted.

With sodium glycocholate the inhibiting molarity of its concentrations was M/5,000 to M/2,000; with optochin hydrochloride, M/1,500 to M/1,000; with apoquinine hydrochloride, M/750 to M/250; with quinine acetate, M/1,000 to M/200; but with sulfanilamide, M/100 (0.17%). No inhibition of reducing power of Type I Neufeld pneumococcus in the presence of glucose at M/100 (0.17%), the highest concentration obtainable was shown with this technic.

The results show that whereas the ordinary bacteriostatic compounds inhibit the dehydrogenases (a part of the respiratory mechanism), the sulfanilamide does not affect these enzymes. This rules out an effect that the drug might have on the organisms.

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A Virus Disease of Swiss Mice Transmissible by Intranasal Inoculation.

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Mice have been extensively employed in the study of the virus of human influenza since the discovery by Andrewes, Laidlaw, and Smith,[1] and by Francis[2] that these animals are susceptible to intra-

[1] Andrewes, C. H., Laidlaw, P. P., and Smith, W., *Lancet*, 1934, **2**, 859.

[2] Francis, T., Jr., *Science*, 1934, **80**, 457.