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Use of Synthetic Medium in Study of Antibacterial Effect of Sulfathiazole.*

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In the present study we have employed the synthetic medium previously reported as being valuable for the study of the antibacterial effect of the thiazole compounds against *Salmonella enteritidis* and, as originally employed in demonstrating the inhibiting effect of p-aminobenzoic acid upon these drugs.¹ This liquid medium contains the same nutritive materials as are present in Simmon's citrate agar and is quite suitable for the cultivation of this organism even though very small inocula are employed.

This synthetic medium possesses definite advantages over ordinary broth containing meat extractives and peptone, since it is invariably uniform in composition, devoid of growth factors, essential metabolites, and of such substances as are known to interfere with the activity of the sulfonamide drugs. That this synthetic medium is superior to ordinary broth is further revealed by our experimental observations wherein 0.3 mg % of sulfathiazole prevents growth

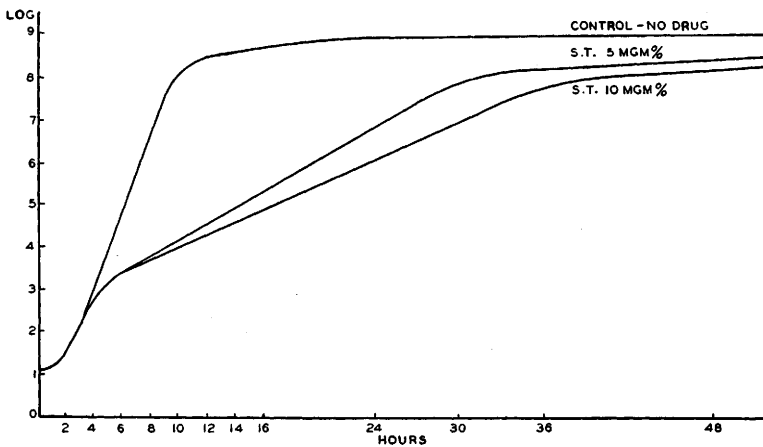


FIG. 1.

Viable cell counts of *S. enteritidis* in meat extract-peptone-broth with and without sulfathiazole.

* Aided by a grant from the Department of Medical Research of the Winthrop Chemical Company.

¹ Muir, R. D., Shamleffer, V. J., and Jones, L. R., *J. Bact.*, 1941, **41**, 84.

(as judged by visible turbidity) of *S. enteritidis* in the former whereas 20 mg % does not prevent growth in the latter medium.

Recognizing this superiority, it was deemed of interest to ascertain the relative effects of sulfathiazole upon *S. enteritidis* in each of these media as would be elicited by a comparison of viable population curves. In Fig. 1 are recorded the growth curves of the organism in meat extract-peptone broth, without drug, and with 5 and 10 mg % sulfathiazole. One of the effects of sulfathiazole is seen as a delay in the inception of the logarithmic phase of multiplication. During this phase, the drug (5 mg %) serves to increase the generation time by about five-fold as is reflected in the slope of the curve. The stationary phase is reached much earlier in control cultures. However, the ultimate number of cells developing in the drug-containing media is about one-fourth the number found in the control.

In Fig. 2 are recorded curves, similarly developed from cultures in synthetic medium. In a comparison of the control cultures and sulfathiazole cultures, it will be noted that the rate of multiplication does not appear to be markedly inhibited during the first 6 or 8 hours, whereas subsequent to that time while the control culture continues to increase logarithmically for the next 24 hours, the sulfathiazole cultures tend to remain stationary for an extended period. In the sulfathiazole cultures, during the interval from the 4th to the 8th hour there is an ill-defined period of probable logarithmic increase. In the stationary phases the control culture populations were about 150,000 times those observed in the sulfathiazole cultures.

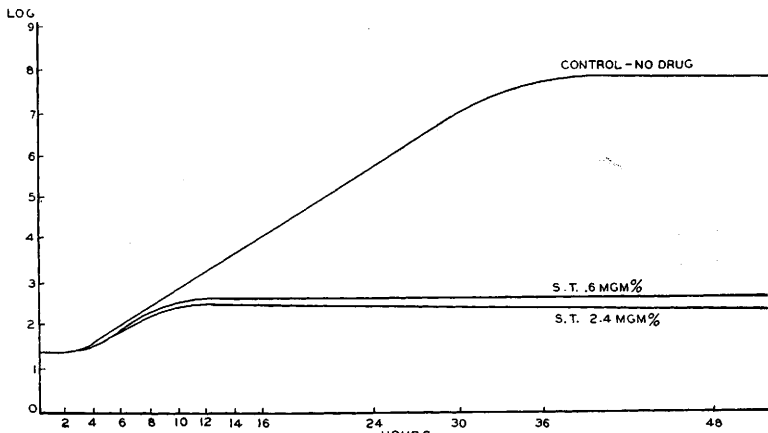


FIG. 2.

Viable cell counts of *S. enteritidis* in synthetic medium cultures with and without sulfathiazole.

In a comparison of Fig. 1 with Fig. 2, it will be noted that with peptone broth 5 and 10 mg % were employed whereas 0.6 and 2.4 mg % were used in the synthetic medium. In peptone broth sulfathiazole serves to reduce bacterial proliferation by about 75% whereas a much smaller quantity of sulfathiazole in synthetic medium serves to reduce bacterial multiplication by more than 99.9%. From these figures it becomes evident that sulfathiazole is approximately ten times as effective in the synthetic medium as it is in meat-extract peptone broth.

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Histopathology of CNS of Mice Infected with Virus of Theiler's Disease (Spontaneous Encephalomyelitis.)*

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Since 1937, when Theiler¹ first described spontaneous encephalomyelitis of albino mice (Theiler's disease; "mouse poliomyelitis") and the virus causing it, two major developments have given this disease renewed importance because they confirm the impression that one is dealing here with an infection more closely related to human poliomyelitis than is any other known disease. In the first place, the finding by Olitsky² and by Theiler and Gard³ of Theiler's virus in the intestinal contents and feces not only of mice showing the signs of the spontaneous or experimental malady but also of normal, young adult or mature animals, recalls similar results obtained in studies on human poliomyelitis.^{4, 5} Again another epidemiological feature is shown commonly by the two diseases, *i. e.*, the analogous incidence of paralytic cases of one in more than 5000.

The second recent development under consideration concerns the successful transmission by Armstrong⁶ of one strain (Lansing)

* The writers wish to thank Dr. M. Theiler for his coöperation and for Lansing-strain infected mice, and Mr. P. Haselbauer for his technical assistance.

¹ Theiler, M., *J. Exp. Med.*, 1937, **65**, 705.

² Olitsky, P. K., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **41**, 434; *J. Exp. Med.*, 1940, **72**, 113.

³ Theiler, M., and Gard, S., *J. Exp. Med.*, 1940, **72**, 49, 79.

⁴ For literature see Trask, J. D., and Paul, J. R., *Am. J. Public Health*, 1941, **31**, 239.

⁵ Sabin, A. B., and Ward, R., *J. Bact.*, 1941, **41**, 49.

⁶ Armstrong, C., *Public Health Rep.*, 1939, **54**, 1719.