icthyosmius members of the genus Proteus because of their mannitol fermenting property and we would also exclude these strains from the genus because of their inability to attack urea. A similar conclusion can be drawn with regard to *bombycis* since it also failed to attack urea. The 2 strains of *Proteus pseudovaleriei** which decomposed urea did not conform to the description of Bergey and of St. John-Brooks and Rhodes. One strain appeared to be *Proteus vulgaris* and the other *Proteus mirabilis*. On the other hand, we do not agree with St. John-Brooks and Rhodes that the names *vulgaris* and *mirabilis* should be changed.

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Selective Action of Sulfanilyl-Guanidine on Different Salmonella Types and Its Practical Importance.*

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Marshall and coworkers[1] have produced a new sulfa-compound, sulfanilyl-guanidine, and studied its bacteriostatic effect. The solubility of this substance in water at 37.5°C is 220 mg %, its absorption from the intestines comparatively poor. These properties make the drug particularly fit for use in intestinal infections.

In order to study the action of sulfanilyl-guanidine† on different organisms of the Salmonella group, we tested 74 types listed in the latest edition of the Kauffmann-White schema[2] and 13 types which were described since. Fifteen strains of *E. coli* isolated from human feces, urine and blood, 4 strains of Shigella (2 Flexner, 1 Sonne, 1 Shiga type) and a strain of Aerobacter were also tested.

For preliminary information on differences in susceptibility the agar strip method was used. Strips 1 cm wide were cut out of agar plates and filled in with a suspension of 1% sulfanilyl-guanidine in agar. The cultures were streaked out across the inlaid strips.

* Aided by a grant from the Ella Sachs Plotz Foundation.

1 Marshall, E. K., Jr., Bratton, A. C., White, H. K., and Litchfield, J. T., Jr., *Bull. Johns Hopkins Hosp.*, 1940, **67**, 163.

† We received the sulfanilyl-guanidine through the courtesy of the research department of E. R. Squibb & Sons.

2 *J. Hyg.*, 1934, **34**, 33; Report of the Salmonella Subcommittee of the Nomenclature Committee of the International Association of Microbiologists, June, 1939.

Of all the Salmonella organisms tested, only the typhoid bacillus *(S. typhi), S. paratyphi A* and *S. cholerae suis* showed any marked degree of inhibition. Very slight inhibitory action was noted on *S. paratyphi C, S. abortus equi, S. sendai, S. gallinarum, S. muenster* and *S. newington.*

While Aerobacter was resistant and all 4 dysentery strains were strongly inhibited, the 15 strains of *E. coli* showed individual differences. In Salmonella organisms, however, no marked differences between strains of the same type were noticed, when 2 strains of *S. paratyphi A,* 7 strains of *S. cholerae suis,* 6 strains of *S. typhi* and 10 strains each of *S. paratyphi B* and *S. typhi murium* were tested.

Test tube experiments were then carried out to determine more accurately the bacteriostatic action of sulfanilyl-guanidine on representative Salmonella types and control organisms, 30 in all. Test tubes containing 4 cc of beef infusion broth with the drug in decreasing concentrations were inoculated with 0.1 cc of 24-hour broth cultures in serial dilutions, and incubated at 37.5°C for 24 hours. The results confirmed the findings by the agar strip method.

The differences between individual strains of *E. coli* were of minor degree in the test tube experiment, especially so with small inocula. The 2 extreme results are shown in Table II.

It was concluded that sulfanilyl-guanidine which has a marked bacteriostatic action on *E. coli* and *S. typhi,* and acts very strongly on Shigella, is practically without effect on other Salmonella types

TABLE I.
Bacteriostatic Effect of Sulfanilyl-guanidine. Medium: Beef-infusion Broth.

Strain	Inoculum No. organisms	Conc. of sulfanilyl-guanidine, mg% 200	100	50	25	10	—
S. paratyphi A No. C2	10	—	—	—	—	+	+
S. paratyphi B No. C3	10	+	+	+	+	+	+
S. typhi murium No. C9	7	+	+	+	+	+	+
S. choleræ suis No. 36	10	—	—	—	—	—	+
S. thompson No. C39	2	—	+	+	+	+	+
S. newport No. 50	18	+	+	+	+	+	+
S. typhi H-901 No. C57	10	—	—	+	+	+	+
S. gallinarum No. C74	13	—	+	+	+	+	+
S. enteritidis No. C64	10	+	+	+	+	+	+
E. coli No. 3648	10	—	—	—	+	+	+
Shigella Flexner (D.I.)	30	—	—	—	—	—	+

+, macroscopic growth after 24 hr; —, culture tube clear after 24 hr.

TABLE II.
Difference in Susceptibility of Strains of *E. coli* Against Sulfanilyl-guanidine.

		Mg% Sulfanilyl-guanidine in beef infusion broth					
	No. organisms in inoculum	200	100	50	25	10	—
E. coli No. 8/41	800	—	+	+	+	+	+
	80	—	—	—	+	+	+
	8	—	—	—	—	+	+
E. coli No. 248/41	600	+	+	+	+	+	+
	60	—	+	+	+	+	+
	6	—	—	—	+	+	+

except *S. paratyphi A* and *S. cholerae suis.* Neither mutual antigenic components nor any other mutual characteristic can be cited as an explanation for the fact that just these types are more susceptible to the drug than others. *S. gallinarum* and *S. paratyphi C,* antigenically related to *S. typhi* and *S. cholerae suis,* respectively, showed weak susceptibility to the drug while *S. thompson,* also closely related to *S. cholerae suis,* was completely resistant.

Our findings seem to indicate that sulfanilyl-guanidine treatment of infections with Salmonellas other than the susceptible types may even be harmful. As a result of the selective action of the drug the pathogenic organisms may flourish while the coli flora is suppressed. A small number of animal experiments, carried out so far, support this opinion.

The 24-hour growth of an agar slant was washed off with 3 cc of tap water, pipetted onto a piece of bread and fed to a mouse of about 20 g after the animal was fasting over night. Three groups of mice were thus infected with *S. cholerae suis, S. typhi murium,* and *S. enteritidis,* 8 with each organism. From the second day the mice were fed 5 g per day Rockland mouse diet and water only. Four mice of each series received 1% by weight of sulfanilyl-guanidine well admixed to the solid food. After 3 weeks the drug treatment was discontinued in 2 of the surviving mice and carried on with half doses in the 2 others.

All the mice infected with *S. enteritidis* died within 3 to 8 days. Of the mice infected with *S. typhi murium* only one out of 4 non-treated animals died, but all 4 mice treated with the drug died within 7 to 11 days.

On the other hand, with *S. cholerae suis,* all the non-treated animals died within 16 days, while the treated ones all survived for more than 3 weeks. Only those whose treatment was discontinued died thereafter. Whether these animals were reinfected from their

TABLE III.
Effect of Sulfanilyl-guanidine Treatment on Salmonella Infections in Mice.

Strain	Not treated				Treated			
S. choleræ suis No. C36	6	6	7	16	31*	25*	S†	S†
S. typhi murium No. C9	11	S	S	S	7	7	9	11
S. enteritidis No. 3612	3	4	4	6	3	3	6	8

The numbers indicate the days after which the mice succumbed.
S: survived more than 40 days.
*: drug discontinued after 21 days.
†: drug continued with half the doses after 21 days.

fur, or whether the organisms survived within their bodies remains a matter of doubt.

Our contention that sulfanilyl-guanidine, though promising for the treatment of infections with *S. paratyphi A* and *S. cholerae suis*, is ineffective in other Salmonella infections, is further supported by the few observations available thus far on Salmonella infections in children treated with the drug.

Marshall and coworkers state in their recent paper[3] in which they report on successful treatment of acute bacillary dysentery with sulfanilyl-guanidine: "Two other infants, age 5 and 8 months, respectively, were treated on the third and fourth day of acute gastro-enteritis, without beneficial effect. A variety of *S. enteritidis* was cultured from the stools in one of these children, and the Morgan bacillus and later a variety of *S. enteritidis* from the stools of the other."

Two children who after acute infections with *S. oranienburg* and *S. newport* continued to excrete the organisms in their stools, were treated with the drug in this hospital. Doses of 0.3 g per kg body weight for 8 and 12 days respectively failed to interrupt the series of positive stool cultures. Another child had an acute infection with *S. cholerae suis* and continued to excrete the organism in the stools. Upon our suggestion he was given the drug by Dr. S. Silvers and immediately after institution of the treatment the stool cultures became negative.

In conclusion, it can be said from *in vitro* and *in vivo* experiments, that sulfanilyl-guanidine, a drug which is known to be effective in the treatment of bacillary dysentery, is also effective against *S. cholerae suis* and, to some degree against *S. paratyphi A*, but ineffective against other organisms of the Salmonella group. In fact, in such cases the drug may even be harmful.

[3] Marshall, E. K., Jr., Bratton, A. C., Edwards, L. B., and Walker, E., *Bull. Johns Hopkins Hosp.*, 1941, **68**, 94.