

cordingly, there is some justification to assume that the Rh factor may be limited to red blood cells only. However, a comprehensive study of various organs and body fluids is desirable.

The absence of the Rh factor from the tissue cells and body fluids might have been anticipated on the basis of the evidence indicating the importance of the Rh factor in the pathogenesis of erythroblastosis fetalis.<sup>12</sup>

13244 P

**Succinyl Sulfathiazole, a New Bacteriostatic Agent Locally Active in the Gastrointestinal Tract.**

EDGAR J. POTI AND F. LOUIS KNOTTS. (Introduced by W. M. Firor.)

*From the Surgical Hunterian Laboratory, Department of Surgery, Johns Hopkins University School of Medicine, Baltimore, Md.*

Much interest has been aroused during the past year over the prospect of developing therapeutic agents that have antibacterial activity in the bowel.<sup>1, 2, 3</sup> A study covering 20 sulfonamides has unearthed a compound of considerable promise.

Succinyl sulfathiazole.\*  $\text{COOH} \cdot \text{CH}_2 \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{SO}_2 \cdot \text{NH} \cdot \text{C}_8\text{H}_2\text{NS}$ , has been shown to have little toxicity when administered to dogs orally at 4-hour intervals day and night. A dosage of one gram per kilo daily given in 6 equal doses results in a fecal drug content of from 5 to 10%. Under this regimen approximately 5% of the ingested drug is excreted in the urine, and the concentration of the drug in the blood will average 1.5 mg % of sulfathiazole and 2.0 mg % of succinyl sulfathiazole. The sulfathiazole is formed by the hydrolysis of a small portion of the conjugated compound by the animal tissues and by the bacteria in the bowel. Crystals of the drug do not appear in the urine.

The antibacterial action of succinyl sulfathiazole in the bowel as measured by the effect on the coliform organisms is presented graph-

<sup>12</sup> Levine, P., Burnham, L., Katzin, E. M., and Vogel, P., *Am. J. Obst. and Gyn.*, in press.

<sup>1</sup> Marshall, E. K., Jr., Bratton, A. C., White, H. J., and Litchfield, J. T., Jr., *Bull. J. H. H.*, 1940, **67**, 163.

<sup>2</sup> Firor, W. M., and Jonas, A. F., *Ann. Surg.*, 1941, **114**, 19.

<sup>3</sup> Firor, W. M., and Poth, E. J., *Ann. Surg.*, in press.

\*This compound was furnished by Sharp and Dohme of Philadelphia, Pa.

## 130 SUCCINYL SULFATHIAZOLE, A NEW BACTERIOSTATIC AGENT

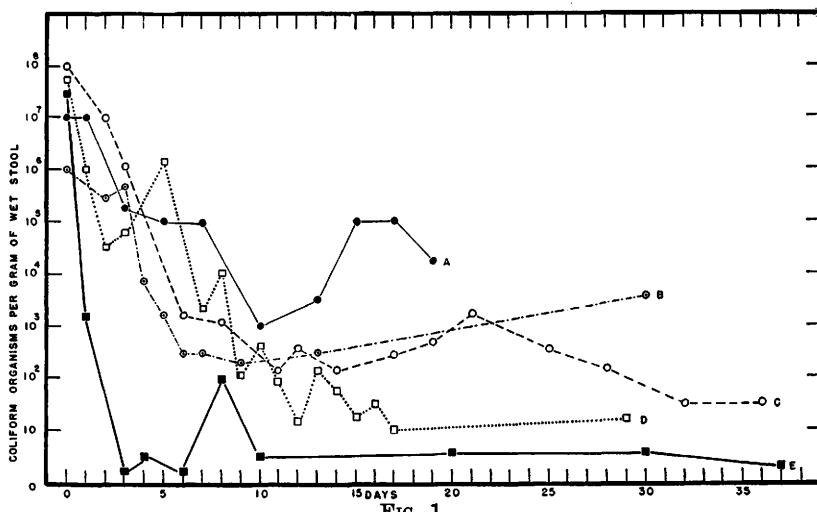


FIG. 1.

The graphic representation of the effect of various dosages of succinyl sulfathiazole on the coliform organisms in the gastrointestinal tract of the dog. Curve A diagrams the results following the oral administration of 0.05 g per kilo per day given in 6 equal doses at 4-hour intervals; B likewise for 0.1 g per kilo; C for 0.25 g per kilo; D for 0.50 g per kilo; and, E for 1.0 g per kilo.

ically. The drug given in therapeutic doses profoundly alters the feces. They become semifluid and practically odorless.

No toxic manifestations have been observed. The animals gain weight and show no gross or microscopic evidence of tissue damage after receiving one gram per kilo of the compound daily in 6 doses for 5 weeks. During this entire period the number of *B. coli* per gram of wet stool averaged less than 100 organisms as compared to an average normal flora of 10,000,000.

Succinyl sulfathiazole has been administered to 40 human beings with various organic lesions and acute intestinal infections without the production of toxic reactions. The stools become semifluid and relatively odorless. The coliform organisms are reduced to such low values that *B. coli* frequently cannot be demonstrated by growth on desoxycholate plates.

The activity of this compound is limited largely to its local effect on the contents of the gastrointestinal tract.