there are protoplasmic extensions connecting the cells and that these filaments are surrounded by clearly demonstrable cell walls. In mammalian smooth muscle this particular situation does not exist insofar as could be ascertained. The tissue spaces are extremely small and difficult to locate. One of the striking features in mammalian muscle is the clearness with which cell boundaries can be determined. Yet Ca and Mg were by no means, either in frog or mammalian smooth muscle, limited to the periphery of the cell.

These findings do not imply that there is no Ca or Mg in the tissue spaces. The conclusion is apparent, however, that under conditions of normal existence the Ca and Mg concentration is many times greater within the smooth muscle cells of the forms studied than in their surrounding tissue fluid environment.

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Protective Effect of Sulfamethylthiazol* on Experimental *Salmonella enteritidis* Infection in Mice.

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In a previous report[1] the effect of sulfamethylthiazol upon the course of experimental staphylococcus infection in mice was presented. In further studies of the protective effect of this drug against experimental infections in mice a series of experiments have been made wherein the infecting organism was a strain of *Salmonella enteritidis*.† The organism had been previously recovered as the etiological agent in an epizootic disease among the mice of our colony.

Preliminary studies regarding the pathogenicity of this organism for mice of a selected strain, known to be free from Salmonella organisms, indicated that animals succumbed to the organism as a result of a progressive infection rather than to the presence of pre-formed toxin factors present in the inoculum. A dose of one million cells, injected intraperitoneally, brought about the death of a majority of

* Supplied through the courtesy of the Department of Medical Research of the Winthrop Chemical Co., New York.

1 Carroll, G., Kappel, L., Jones, L., Gallagher, F. W., and DiRocco, F. W., *South. Med. J.*, 1940, **33**, 83.

† We are indebted to Dr. P. R. Edwards for determining the serological character of this organism.

the animals within 7 days. A similar inoculation of from 75 to 100 million organisms consistently killed mice within 24 hours. Attempts to produce infection *per os* were unsuccessful.

Methods. A number of experiments were carried out in order to ascertain the possible effect of sulfamethylthiazol on the course of experimental infection in mice. The drug was administered on a dosage basis of 4 g per kilo of body weight per day, half of the required amount being given in the morning and the remainder 10 to 12 hours later. Because of its insolubility, the drug was suspended in milk so that the desired dose was contained in 0.2 cc of the suspension, and this amount was placed directly into the stomach of the animal by means of a specially prepared 18-gauge hypodermic needle having a solid blunt end and an opening along the side. In control experiments it was found that milk *per se* was without effect in altering the survival time of infected mice. Control animals were always maintained which were infected but not medicated.

Mice were experimentally infected by the intraperitoneal injection of 0.1 cc of a cell suspension which was derived from 24-hour broth cultures of the organism. The numbers of viable organisms in these suspensions were determined by plate counts.

Results. The data incorporated in Table I indicate a significant protective effect of sulfamethylthiazol. This was further confirmed in another experiment involving the administration of 90 million *Salmonella enteritidis* cells per mouse, the average survival time being 14 hours for the control group and 92 hours for the medicated group. In a third experimental series wherein 87 million organisms were injected, the survival times were 15.4 hours and 95.6 hours respectively.

TABLE I.
Protective Effect of Sulfamethylthiazol in Mice Infected with *Salmonella enteritidis.*
Hours of Survival Following Injection of 85 Million Cells.

Control animals (non-medicated)	Medicated animals
13.5	13.5
13.5	20.5
14.5	38.5
14.5	49.5
16.5	74.5
16.5	92.5
16.5	115.5
18.5	117.5
18.5	181.5
20.0	181.5
Avg survival time 16.25 hr	88.5 hr

In the above experiments, the drug was first administered 2 hours prior to the injection of the organisms. In another group of experiments we compared the effectiveness of sulfamethylthiazol in protecting mice against experimental Salmonella infections when the initial administration of the drug was (1) at the time of injection of the organisms, and (2) 14 hours previous to the injection of the organisms. The non-medicated control animals survived, on the average, 15 hours. The animals first medicated at the time of the injection of the organisms had an average survival time of 96 hours, thus living more than 6 times as long as the untreated animals. Those which were first medicated 14 hours before and again 1 hour before injection and subsequently medicated according to the usual scheme, survived an average of 110 hours, or more than 7 times as long as the controls. Thus it becomes apparent that pre-medication, which conceivably leads to the development of a certain concentration of the drug in the blood at the time of injection, increases the protection afforded the animals.

The adequacy of dosage was partially investigated by administering to a series of experimental animals only one-half (2 g per kg per day) of the usual amount of drug, starting the medication program at the time of injection. These mice showed an average survival time of 51 hours, or more than 3 times that of the control group. Accordingly, it would seem that when the posology scheme is quantitatively reduced by one-half there is a significant decrease in the protective effect of the drug.

Conclusions. Sulfamethylthiazol apparently exerts a definite protective effect in mice which have been experimentally infected with a virulent strain of *Salmonella enteritidis.* This protective effect is manifested only by an increase in average survival time of medicated animals. Eventually all of the medicated animals succumb to the *Salmonella enteritidis* infection.