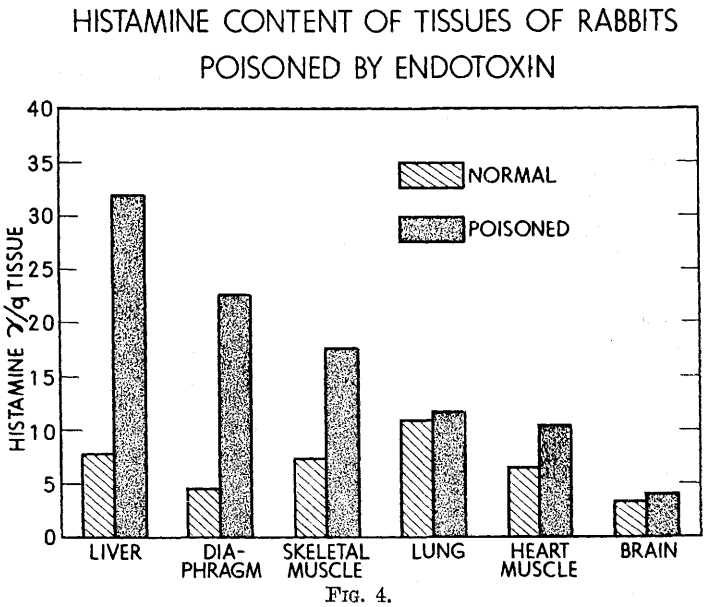

FIG. 4.

clusive proof of this supposition.

Summary. Meningococcal endotoxin injected intravenously into rabbits caused a rapid decrease in the histamine content of the blood and an increase in the histamine content of liver and muscle.

The decrease in histamine in the blood was not prevented by the intravenous injection of histamine along with the endotoxin.

The survival time of rabbits injected intravenously with meningococcal endotoxin was markedly shortened by a simultaneous injection of a small dose of histamine.

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Effect of Oral Streptomycin on the Intestinal Flora.

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The majority of evidence seems to indicate that *E. coli* plays a predominant role in the pathogenesis of peritonitis following large bowel surgery.[1] Among the other microorganisms most frequently encountered are the fecal streptococci (Lancefield Group D streptococci), and *Clostridium welchii*.[1] With these facts in mind, it seems logical to suppose that the incidence of post-operative peritonitis would be reduced if the *E. coli* present in the bowel were eliminated. The less readily absorbable sulfonamides such as sulfaguanadine, sulfasuxidine and sulfathaladine have been used in an endeavour to accomplish this.

[1] Meleney, F. L., Harney, H. D., and Jern, H. Q., *Arch. Surg.*, 1931, **22**, 1.

Streptomycin as an antibacterial agent in the intestine, has the following properties: (1) soluble in water, (2) non-absorbable through the intestine, (3) non-toxic, (4) active in the presence of intestinal contents. Six cases were selected for study. Three of these had ulcerative colitis and 2 were pre-operative cases—a uretero-enterostomy and a large bowel resection. One was a normal individual. The 2 cases of ulcerative colitis, one pre-operative large bowel resection, and one normal individual were each administered 1.0 g of streptomycin *per os* daily, in 2 divided doses (0.5 g dissolved in a half-glass of water, morning and evening). The pre-operative uretero-enterostomy received 0.4 g of streptomycin *per os* 5 times daily. The third case of ulcerative colitis received streptomycin as a lavage per rectum; 20 ml containing 0.005 g streptomycin per ml was administered twice daily in an attempt to rid the distal segment of an old colostomy of *E. coli*.

Aerobic and anaerobic cultures were planted daily with a generous amount (approximately 0.5 g) of fresh stool collected from each patient. Bacterial counts per gram of wet stool were estimated from duplicate horse blood agar plates streaked with 0.05 ml of a 1:1,000,000 dilution of stool. In the 2 pre-operative cases who received streptomycin, swabs taken directly from the mucosa of the colon at operation were planted in aerobic and anaerobic cultures.

The results obtained in all 6 cases were essentially similar. A representative case is summarized in Table I. As can be seen in the Table, *E. coli* disappeared from the stool after streptomycin had been administered for 2 days. In one case, a normal individual, *E. coli* disappeared in one day, and in the remaining 4 cases, these microorganisms could not be cultured after 2 days on streptomycin.

Since microscopic examination of the stool showed an abundance of Gram negative rods even though *E. coli* could not be cultivated in aerobic or anaerobic media, daily motility tests were done on freshly collected stool specimens in order to ascertain whether or not these microorganisms actually were dead. In

TABLE I.
Effect of Oral Streptomycin on the Intestinal Flora.

Day of study	G streptomycin	Stool examination: Microscopic: Bacteria	Microscopic: Motility	Cultural—Aerobic and anaerobic: *E. coli*	Streptococci	Bacteroides	Clostridia	Candida	Aerobic colony count*
0	0	++++	++++	++++	++++	++++	++++	0	—
1	1.0	++++	++++	++++	++++	++++	++++	0	52.4†
2	1.0	++++	±	++	++++	++++	++++	0	6.6‡
3	1.0	++++	0	0	++++	++++	++++	++++	0
4	0.5	++++	0	0	++++	++++	++++	++++	—
5	0	++++	0	±	++++	++++	++++	++++	—
6	0	++++	++++	++++	++++	++++	++++	++++	—

* Per g of wet stool in billions.
† *E. coli* predominant.
‡ Streptococci predominant.

all cases, when *E. coli* could no longer be cultivated from the stool, wet smears made directly from the specimen failed to show motile microorganisms. The failure of *E. coli* to grow in the presence of sodium thioglycollate or under anaerobic conditions, both of which have been reported as opposing the *in vitro* action of streptomycin,[2,3] is further evidence that these microorganisms were nonviable. Since Bacteroides, a common anaerobic saprophyte of the large bowel could be cultivated from most of these cases, even after *E. coli* had disappeared, it is possible that the Gram negative, non-motile, rods observed by direct microscopic examination belonged to this genus.

E. coli reappeared in the stool the day following the last dose of streptomycin. Fecal streptococci, Clostridia, Bacteroides and Candida were unaffected by the streptomycin in the stool. It is noteworthy that Candida appeared in the stool on occasions after *E. coli* had disappeared (Table I). No change in the character of the stool was observed during streptomycin administration. The color, consistency and quantity was the same during therapy as it had been before.

Discussion. The results obtained in this study are similar to those reported by Reimann, Price and Elias,[4] and others,[8] who found that sensitive microorganisms could be eliminated from the stool by oral administration of streptomycin; and that the stool could be kept free of such microorganisms as long as adequate streptomycin levels were maintained. These authors also noted that the anaerobic flora of the stool was unaffected by oral streptomycin.

It is of interest that although *E. coli* was eliminated from the stool in 3 cases of ulcerative colitis, no apparent effect upon the course of the disease was noted. In order to determine whether or not viable *E. coli* were present on the surface of the mucosa of the colon, in the cases who received streptomycin preoperatively, direct swabs were taken at operation. In neither of these cases could *E. coli* be cultivated.

It is known that the non-absorbable sulfonamides will reduce the number of *E. coli* present in the stool. In some cases, however, no reduction has been observed, yet in spite of the failure of these drugs to eliminate *E. coli,* clinical reports indicate that pre-operative administration decreases the incidence of complicating peritonitis and abscess formation following surgical manipulation of the colon.[5,6,7] It would seem on the basis of this study, that streptomycin is more effective than the sulfonamides in ridding the colon of *E. coli.* It has the further advantage of avoiding the risks associated with the use of the sulfonamides. Accordingly, the oral administration of streptomycin in the preoperative preparation of patients who are to undergo surgery of the colon is suggested.

Summary. The oral administration of as little as 1.0 g of streptomycin daily eliminated *E. coli* from the stool of 5 patients within 2 days. The stool could be kept free of these microorganisms as long as adequate streptomycin levels were maintained, but reappeared promptly when it was discontinued. Swabs taken at operation from the mucosa of the colons of two patients who had received preoperative streptomycin did not contain *E. coli.* These microorganisms also were eliminated from the distal segment of a colostomy by streptomycin lavage per rectum. Streptomycin did not affect the anaerobic flora of the stool, and had no appreciable effect on the fecal streptococci.

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