# Protection of Colonic Anastomoses with Antibiotics *

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IN AN ATTEMPT to evaluate the importance of antibiotics in surgery of the colon a procedure was devised to test the efficacy of antibiotics under conditions of extreme duress. Devascularization of one side of an anastomosis in an unprepared colon provided the desired stress.[4] While this severe test indicated that postoperative antibiotics have a role in colonic surgery, it did not adequately evaluate the role of antibiotics under conditions more closely simulating those encountered clinically. This report is a continuation of the study of the role of antibiotics in various phases of surgery of the colon.

Few surgeons do elective colonic surgery in a totally unprepared colon. However, the original work had to be done under the most unfavorable conditions to evaluate properly the use of postoperative antibiotics in surgery of the colon. After the value of postoperative antibiotics was established it became necessary to study the role of mechanical cleansing and of mechanical cleansing combined with preoperative antibiotic preparation under similar conditions. The results continue to emphasize the value of antibiotics in colonic surgery and prompted us to institute clinical studies with intraluminal antibiotics.

## METHODS

Dogs weighing between 7.4 Kg. and 20.4 Kg. were used after they had been in the animal colony a minimum of two weeks.

Operations were performed under intravenous Nembutal® anesthesia and utilized aseptic technics. The abdomen was opened through a mid-line incision. The omentum was removed in all experiments to prevent its serving as a source of revascularization or protection for the devascularized segment. In the latter half of the experiments, the spleen was routinely removed to prevent it from protecting the devascularized segment.

The colon was completely divided between non-crushing clamps (Fig. 1). Specimens from the lumen of the colon were sent immediately for aerobic and anaerobic cultures. Qualitative studies were done in all experiments, and quantitative studies were done in the latter half of the study. An end-to-end one layer anastomosis was performed with a continuous #3–0 silk suture.

In each treated group, a plastic tube was inserted through a #14 needle in normal bowel and threaded towards the anastomosis. A purse string suture prevented leakage about the tube and also prevented the tube from slipping out of the bowel. The tube was exteriorized through a stab wound so that antibiotics could be in-

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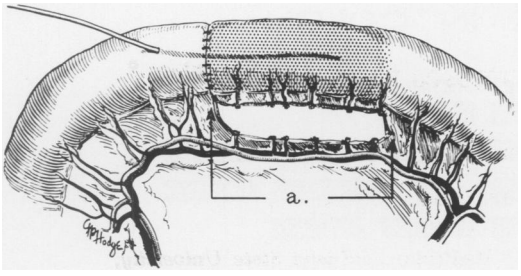



FIG. 1. Diagram of operative procedure. End-to-end colon anastomosis. Insertion of plastic tube proximal to anastomosis. Tube threaded into devascularized area. Division of mesentery and all vessels in mesentery to segment "A." "A" is 5 cm. in Series I, 7 cm. in Series II, and 10 cm. in Series III.

jected into the colon after operation. After the original series, the tube was routinely inserted proximal to the anastomosis. This eliminated the possibility of peristalsis causing a kink in the tube or forcing something into the tube which could block it. The tip of the plastic tube was placed at, or proximal to, the anastomosis to provide maximum protection to this vital area.

Beginning at the anastomosis and proceeding a given distance, all vessels to the colon were doubly clamped, divided, and ligated to achieve complete extramural devascularization of a segment of known length.

During operation and on the first postoperative day intravenous fluids were administered to take care of all fluid requirements, and nothing was allowed by mouth. On successive days water, water and milk, dog biscuits, and finally regular kennel ration was allowed. Generally if anorexia or vomiting were noted no attempt was made to supplement the intake after the first postoperative day.

The three series of experiments differed mainly in the type of preoperative preparation and the length of segment devascularized. Within each series the control and treated animals were subjected to identical procedures except for the use of antibiotics in the postoperative period in the treated series. As the preoperative preparation improved, it was obvious that longer segments of bowel had to be devascularized to subject the anastomosis to greater stress.

The experiments were divided as follows:

Series I No preoperative preparation.
Devascularization of a 5 cm. segment.

Series II Preoperative mechanical cleansing.
Devascularization of a 7 cm. segment.

Series III Preoperative antibiotics and mechanical cleansing.
Devascularization of a 10 cm. segment.

Autopsy was performed as soon as possible on all animals that died. Histologic studies were not done if the autopsy was more than one hour after death. Animals that survived were re-explored after a sufficient time interval to permit re-examination of the devascularized area, or were sacrificed at appropriate intervals for histologic study of the involved area.

### SERIES I.

These animals had no preoperative preparation except two days of starvation.[4] At operation a 5 cm. segment of bowel was devascularized, either proximal or distal to the anastomosis. The controls received no antibiotics postoperatively. The treated group received postoperative antibiotics as outlined in Table I.

TABLE I. *Postoperative Antibiotic Therapy—Series I*

| Achromycin ® | Operation | 0–24 Hours | 24–72 Hours | 72–168 Hours |
|---|---|---|---|---|
| Into Bowel | 1.0 Gm. | 500 mg. q. 6 h. | 500 mg. q. 6 h. | |
| Orally | | | 500 mg. q. 6 h. | 500 mg. q. 8 h. |
| Penicillin | 600,000 u. B.I.D., I.M. | | | |

*Bacteriology. Cl. welchii* and streptococci were found in all animals. *E. coli*, staphylococci, proteus, and *Aerobacter aero-*

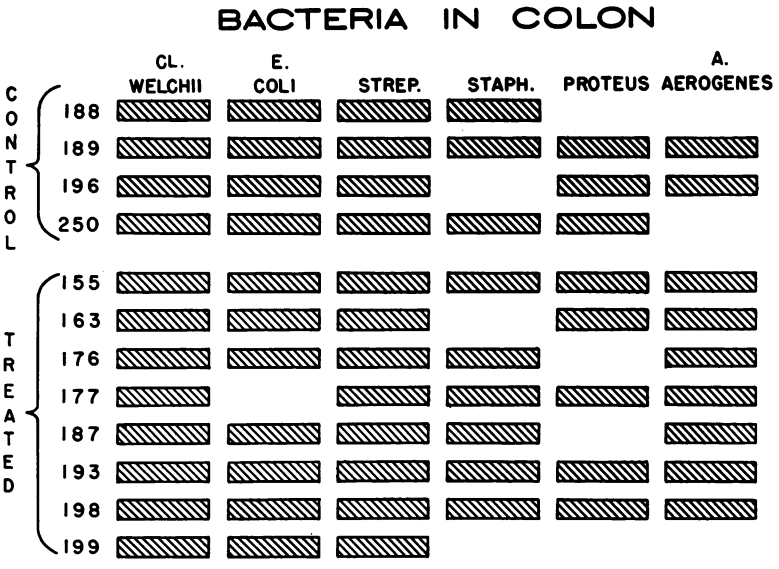



FIG. 2. Bacteria in colon, Series I. (Reproduced from *Annals of Surgery.*)

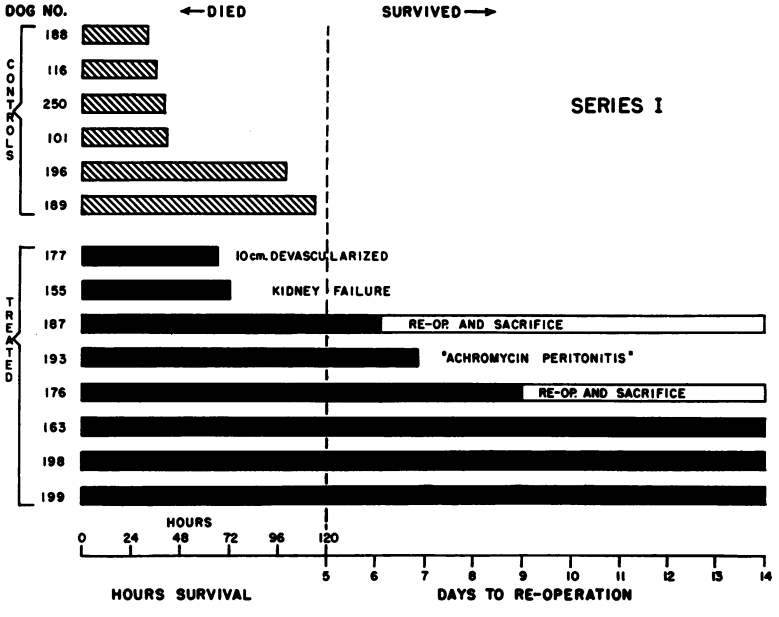



FIG. 3. Survival in Series I.

*genes* were found next in order of frequency, and diphtheroids and yeasts only rarely (Fig. 2). Since there was no significant difference between the bacterial flora of the bowel in the control and treated groups the original bacterial content of the bowel could hardly have contributed to the ultimate results.

*Control.* Six dogs subjected to the control procedure demonstrated that this procedure was uniformly fatal (Fig. 3). Survival times ranged from 32 to 114 hours following operation. Autopsy revealed massive peritonitis and perforation in all experiments. Perforation occurred in the necrotic gangrenous area of devasculariza-

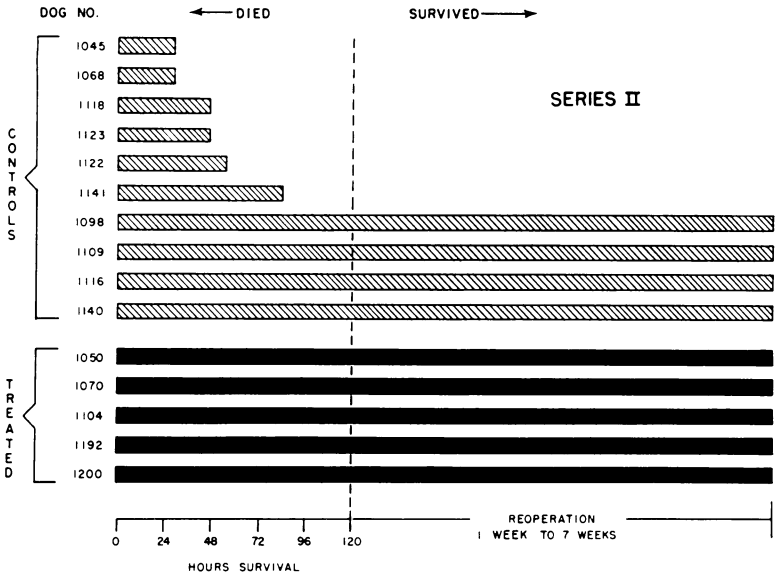



FIG. 4. Survival in Series II.

tion, and not at the suture line. The peritoneal cavity contained a foul-smelling, purulent, fecal fluid. The devascularized segment exhibited varying stages of gangrene. In five of the six experiments there was complete separation of the two segments of bowel. The suture remained intact throughout, eliminating breakage of the suture as the cause of separation of the bowel.

*Treated.* Eight dogs received postoperative antibiotic protection (Fig. 3). Six dogs maintained a functioning and viable colonic anastomosis, and thus demonstrated satisfactory protection by the type of antibiotic therapy chosen. One dog died with what appeared to be a healing anastomosis, but was found to have only one kidney. The other dog was a failure of antibiotic protection, but inadvertently had a 10 cm. segment of devascularization. It was postulated that there would be a limit to the length of colon that could be devascularized under these circumstances.

The colon was grossly normal in the animals that survived. Both serosal and mucosal surfaces were indistinguishable from immediately adjacent normal structures.

The postoperative course of the treated animals differed from that of the control group in that the anorexia, listlessness, and malaise exhibited by the control animals were not observed in the treated group. The treated animals were hungry and ate well as soon as food was given to them.

Histologic examination of the 'devascularized' segment of colon removed from animals that survived confirmed the gross impression of its normal character.

SERIES II.

These animals had preoperative mechanical cleansing as follows: three days of starvation, 50 ml. castor oil the first day of starvation, and two soap suds enemas daily

TABLE II. *Postoperative Antibiotic Therapy—Series II*

| Achromycin ® Neomycin ® | Operation | 0–24 Hours | 24–72 Hours | 72–120 Hours |
|---|---|---|---|---|
| Into Bowel | 1.0 Gm. | 500 mg. q. 6 h. | 500 mg. q. 6 h. | |
| Orally | | | 500 mg. q. 6 h. | 500 mg. q. 8 h. |
| Penicillin | 600,000 u. B.I.D., I.M. | | | |

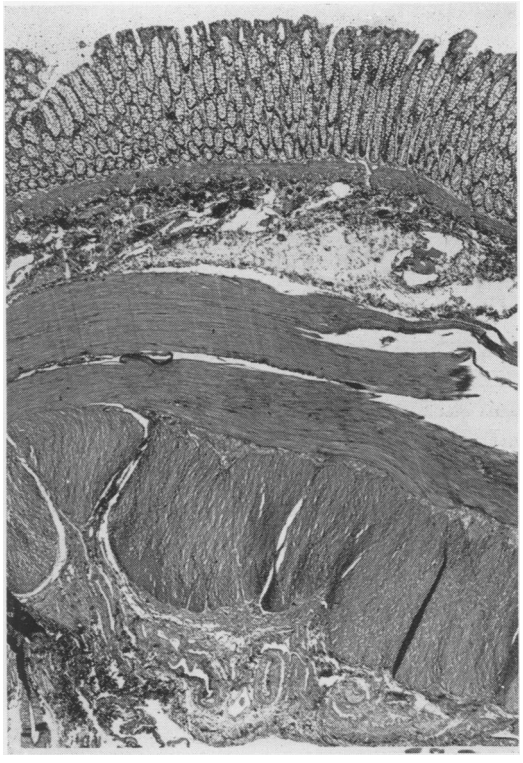


FIG. 5. Photomicrograph of 'devascularized' segment three weeks after devascularization. Note normal condition of bowel wall and the preservation of mucosal structure.

for these three days.[1] At operation a 7 cm. segment of bowel was devascularized on the distal side of the anastomosis. Controls received on antibiotics postoperatively. The treated animals received antibiotics postoperatively as listed in Table II.

*Bacteriology.* The control and the treated groups were similar to each other and to the animals that had no preoperative preparation. These studies demonstrated that mechanical cleansing did not decrease the variety of organisms present in the colon.

*Control.* Ten dogs were subjected to the control procedure (Fig. 4). Six died between 28 and 48 hours. Four survived to be re-explored at a later date. The six animals that died all had severe peritonitis, with necrosis and perforation of the devascularized segment and fecal material pouring into the peritoneal cavity. The suture line was intact in all experiments. Re-exploration of the surviving animals revealed no detectable difference between the normal and devascularized sides of the anastomosis.

*Treated.* Five dogs received postoperative antibiotic protection (Fig. 4). *All* survived to be re-explored from one to ten weeks following the original operation. The colon anastomosis was viable and functioning in all. There was no difference between the devascularized and the immediately adjacent normal serosal surface of the bowel in these experiments.

The mucosal surface presented some interesting findings in the animals that were re-explored at the shortest intervals. Each had a circumferential mucosal ulceration immediately adjacent to the suture line on the devascularized side. The underlying submucosa and muscularis were normal. The mucosa in the animals explored at the longer intervals showed no difference from the normal.

Histologic study of the 'devascularized' segment of bowel revealed that it had returned to normal much as in the surviving animals in Series I (Fig. 5).

### SERIES III.

These animals had preoperative antibiotics and mechanical cleansing. The mechanical cleansing program used in Series II was combined with Achromycin®-neomycin for preoperative reduction of the bacterial content of the colon. The antibiotic schedule was: Achromycin® 200 mg., neomycin 1.0 Gm. every hour for four hours, then three times a day until operation. At operation, a 10 cm. segment was devascularized on the distal side of the anastomosis. Controls received no antibiotics postoperatively. The treated animals received postoperative antibiotics as listed in Table III.

*Bacteriology.* The value of preoperative antibiotics is shown in the quantitative aerobic and anaerobic studies in Figure 6. No bacterial growth was obtained in 16

TABLE III. *Postoperative Antibiotic Therapy—Series III*

| Route | Drug | Operation | 0–24 Hours | 24–72 Hours | 72–120 Hours |
|---|---|---|---|---|---|
| Into bowel | Achromycin® | 750 mg. | 500 mg. | 500 mg. | |
| | Neomycin | 1.25 Gm. | 750 mg. q. 6 h. | 750 mg. q. 6 h. | |
| Orally | Achromycin® | | | 200 mg. | 200 mg. |
| | Neomycin | | | 1.0 Gm. q. 6 h. | 1.0 Gm. q. 8 h. |
| I.M. | Penicillin | 600,000 u. B.I.D. | | | |

experiments, the majority of both the control and the treated groups. Yeasts were found in most experiments, as could be expected in the absence of bacterial growth.[2, 3] An occasional clostridium, coliform, or miscellaneous other organism was recovered. There was no significant difference between the bacterial flora of the control and the treated groups.

The paucity of bacteria in spite of the fact that the colon was frankly dirty in all but one experiment, and in spite of the large mass of feces that had to be removed from the colon at operation was surprising. Thus a mechanically unclean colon may be bacteriologically clean.

*Control.* Eleven dogs were subjected to the control procedure (Fig. 7). Nine died between 52 and 192 hours. One died two weeks after operation, and autopsy did not reveal the cause of death, so this one was considered to have survived the experimental procedure even though the devascularized segment was somewhat discolored. Another animal survived to be re-explored two months after the initial procedure, at which time the colon was found to be normal except for stenosis limited to the anastomotic site.

Seven animals had a frank peritonitis, with feces pouring into the peritoneal cavity from perforations ranging up to 7 cm. in size in the devascularized segment (Fig. 8). The peritoneal fluid was foul-smelling, even when autopsy was performed immediately. In one the perforation extended to the mesenteric side of the colon, the only involvement of the mesenteric side in the entire study. Discoloration usually extended only one-half to two-thirds the length of the devascularized segment. The mucosal surface usually showed the demarcation between normal and devascularized bowel more sharply than did the serosal surface.

Two animals that died at 52 and 90 hours presented slightly different pictures from the remainder. The animal dying at 52 hours appeared moribund from 12 hours after operation until death, and the other animal appeared moribund for 24 hours prior to death. At autopsy neither had a perforation in the bowel. The peritoneum was clean, smooth, shiny, and was devoid of free fluid in both experiments. In both experiments normal and necrotic mucosa were easily distinguished, but serosal differences were not as marked as in other experiments.

*Treated.* Ten dogs received postoperative antibiotic protection (Fig. 7). Seven dogs died between 37 hours and nine and a half days. The average and median survival times were longer than those achieved by the non-surviving animals in the control group. Three animals survived two weeks or longer to indicate that antibiotics can sometimes protect a colonic anastomosis with a 10 cm. segment of devascularization.

Autopsy failed to reveal the cause of death in the animal that died at 37 hours

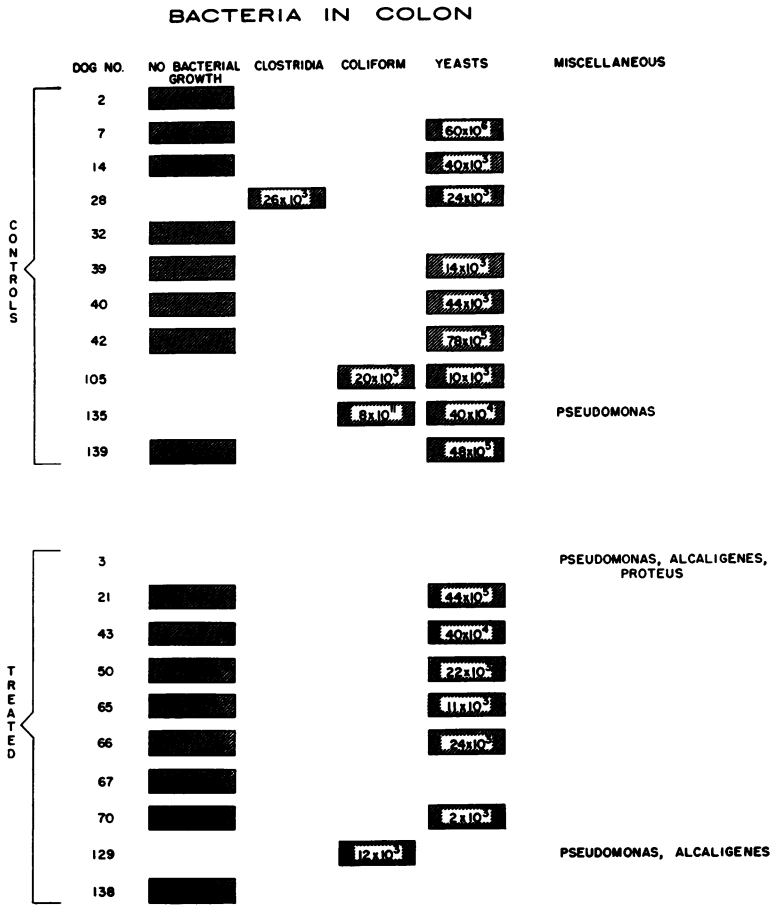



FIG. 6. Bacteria in colon, Series III.

and one that died at 91 hours. There were no perforations, no free peritoneal fluid, and no intra-abdominal adhesions. The animal that died at 37 hours had a devascularized segment which measured 15 cm., with discoloration limited to 11.5 cm. on the mucosal surface only. Even though the cause of death was not found, the rapid demise implicated the experimental procedure. The animal that died at 91 hours was found to have the plastic tube almost at the rectum which probably explained the diarrheal stool following each intraluminal antibiotic injection. The rapid elimination of drug and its possible injection beyond the devascularized portion of the bowel may have prevented the drug's effectiveness. Thus, these two animals do not strictly meet the requirements of the experimental procedure but were included because an adequate explanation for the findings is not available.

The five other animals each had perforation in the devascularized segment of bowel and frank peritonitis. The prolonged survival time in the face of this massive insult to the peritoneal cavity and the odorless character of the peritoneal fluid were unusual. The appearance of the devascularized segment of bowel was of interest. The length of the divided mesentery was the only way to identify the ends of the devascularized segment since it was not otherwise different from the adjacent

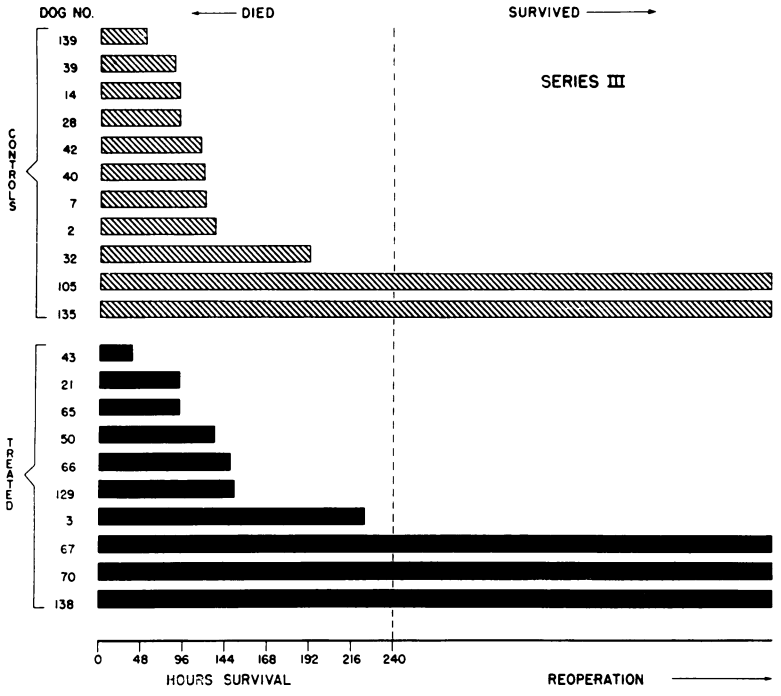



FIG. 7. Survival in Series III.

normal colon (Fig. 9). The discolored and obviously damaged portion of the bowel extended only one-half to two-thirds the length of the devascularized area, and the demarcation was sharper on the mucosal than on the serosal surface (Fig. 10). The perforation was in the discolored, necrotic portion of the devascularized segment, and usually on the antimesenteric side of the colon.

One animal died from distemper two weeks after operation but had no abnormal findings in the peritoneal cavity, and represented a successful application of antibiotic protection of the colon anastomosis. One animal was sacrificed after two weeks and the colon was found to be indistinguishable from adjacent normal colon (Figs. 11 and 12). The final animal is still kept living in order to study the long-term effects of the procedure.

## DISCUSSION

The experiments described in Series I indicate the value of antibiotics in surgery of the colon. However, clinical applications of this work are limited, since few surgeons today perform elective colonic surgery on an unprepared bowel. Clinical applications would be limited to emergency conditions which sometimes force operations upon an unprepared colon, to certain conditions in military surgery, or to those cases in which partial obstruction made the preoperative preparation ineffective.

It remained, therefore, to evaluate whether or not postoperative antibiotics would be of value in a clean colon, and what further aid preoperative antibiotics would provide. Since many surgeons still favor mechanical cleansing alone, this was evaluated first. Adequate cleansing was not obtained by mechanical means in the dog in contrast to the success which this technic usually obtains in humans. It is not known why so much difficulty was encountered in cleansing the dog's colon but it suggests that clinically it would be worthwhile to check each patient individually prior to colonic surgery rather than to rely upon a

FIG. 8.

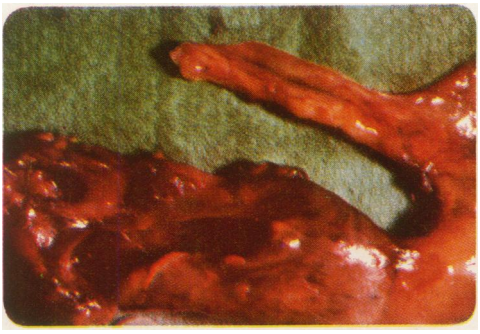
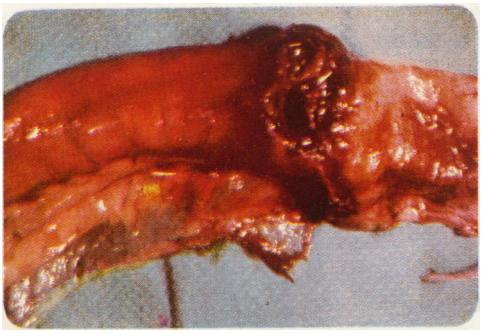


FIG. 9.



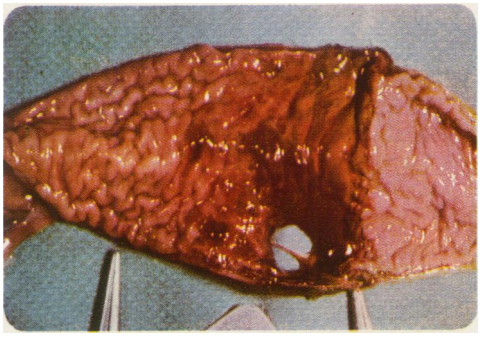


FIG. 10.

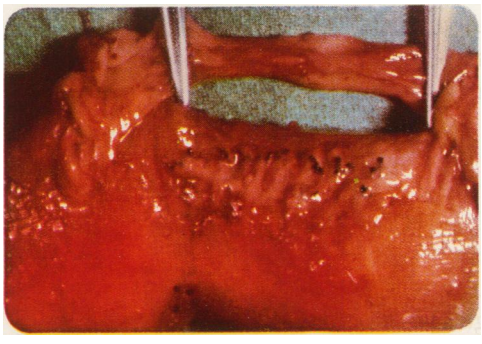


FIG. 11.

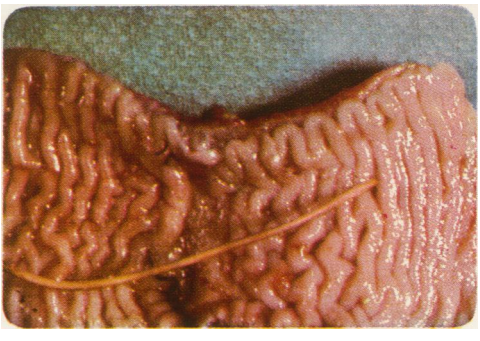


FIG. 12.

FIG. 8. Autopsy appearance of massive perforation in devascularized segment in control group.

FIG. 9. Autopsy appearance of serosal surface of bowel in treated animal that did not survive. Necrosis and discoloration in devascularized segment not as extensive as in control.

FIG. 10. Mucosal surface of colon of treated animal that did not survive. Note sharp demarcation between normal and necrotic portions. Devascularized area extends to pointers.

FIG. 11. Reoperation on treated animal that survived, showing normal appearance on both sides of anastomosis.

FIG. 12. Mucosal surface of colon in treated animal that survived, showing identical appearance of two sides of anastomosis.

pre-set routine. Since postoperative antibiotics provided survivals in animals that had no preoperative cleansing it was obvious that it would be necessary to increase the stress placed upon animals that had preoperative mechanical cleansing. This was done by increasing the length of segment devascularized at operation. That this was necessary can be seen from the survival of four of the control group in Series II. Thus, while mechanical cleansing may eliminate the majority of the fecal matter in the colon, it does not change the variety of bacterial flora present, nor does it adequately reduce the bacterial flora. In spite of the inadequate cleansing, survival was improved over that obtained in the series without any preparation. The importance of the remaining flora is shown by the improved survival percentage in the treated group, which received the additional benefit of postoperative antibiotics.

Just as it was necessary to increase the length of the devascularized segment in the series that had preoperative mechanical cleansing, so it was necessary to further increase the length of this segment in the animals that had both mechanical cleansing and preoperative antibiotics. A clean colon was still not obtained, but two differences were noted in the feces in these animals. There was no odor when the colon was opened in contrast to the penetrating odor usually observed in dogs, and cultures of the large amount of fecal material present yielded almost no bacteria. This meant that the bulk of fecal material present would be considerably less dangerous than a similar quantity of bacteria-laden feces. In addition, the treated animals that died with a fecal peritonitis had odorless fluid in the peritoneal cavity.

The differences in survival time and mortality percentage were not as striking in Series III as in the preceding experiments, even though both median and average survival times favored the treated group. The differences in the pathologic observations in the treated and control groups were more impressive than the differences in mortality. The contrast at autopsy between the odorless peritoneal fluid in the treated group and the foul-smelling fluid in the control group, and the differences in degree of involvement of the devascularized segment in the two groups both indicated the additional value of postoperative antibiotic protection. It was postulated that there would be some length of colon beyond which further devascularization would lead to such severe damage that survival would not be possible. It is thought that the ten centimeter segment selected for this series either approaches or reaches this limit. The unfortunate choice of a segment that was too long to permit survival does not detract from the value of the technic or invalidate the importance of the basic ideas for clinical application. Further work with a slightly shorter segment is indicated to study other phases of this problem.

It was usually possible to predict within the first 72 hours whether or not a given animal would survive. The animals that succumbed were listless, not interested in water or food, vomited or retched frequently, and in general looked quite ill. In contrast, those that survived were usually quite alert by this time, took water or food quickly, and had little or no vomiting. The same distinctions could be made by 120 hours for the animals in Series III. This is an indication of the critical importance of the first few days in the survival or nonsurvival of a colon anastomosis.

The importance of this time interval is further indicated by the duration of antibiotic therapy in different series. In all treated series there were some animals that reacted to the antibiotic therapy by nausea, retching, vomiting, diarrhea, or a combination of these factors, and thus made it necessary to discontinue therapy before the projected time. In no instance was it noted that discontinuance of therapy before the

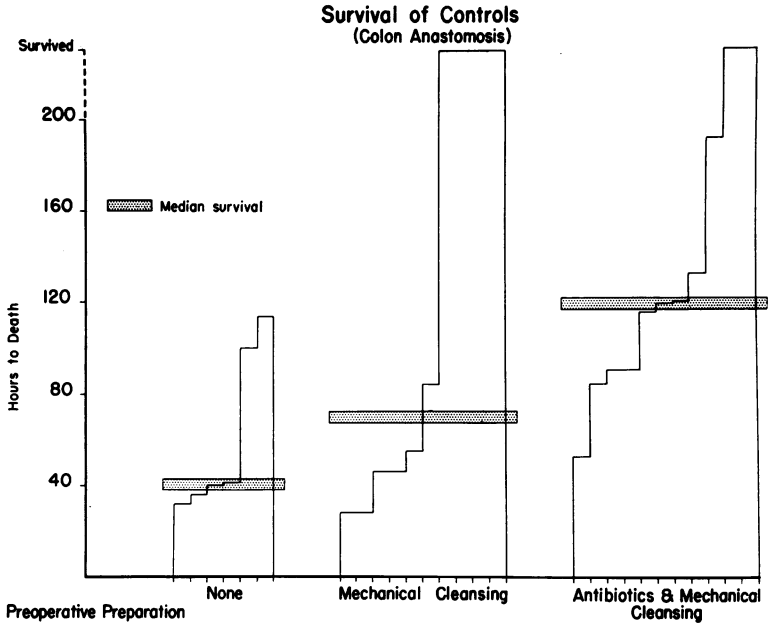



FIG. 13. Survival of control group in each series and comparison of median survival in control groups.

completion of the proposed time changed the results. Thus, the first three days after a colonic anastomosis would appear to be the most important time for antibacterial control. The frequency of gastrointestinal side-effects with this combination of drugs should not be taken as an index of their expected clinical frequency since the animals were given the normal human dosage because the devascularization technic put such an abnormal stress upon the animal that excessive protection seemed to be indicated.

The differences in mortality in control and treated groups of each series (Figs. 3, 4, and 7) indicate the value of postoperative antibiotic therapy under each set of circumstances. The difference is most marked in Series I. The 100 per cent mortality in the control group suggests the dangers in primary anastomosis in an unprepared colon. The differences are less striking in Series II, and indicate the value of preoperative mechanical cleansing. The lower mortality in both the control and treated groups suggest that the devascularized segment was not quite as long as it might have been to make test conditions more severe. In contrast, the closely comparable mortality in the control and treated groups in Series III indicates that this devascularized segment was too long. In spite of the unfortunate choice of too long a segment, the value of preoperative antibiotic therapy in addition to mechanical cleansing for elective surgery of the colon is demonstrated by contrasting the survival times and the pathologic changes in this and preceding series.

A critical evaluation of the importance of each type of preoperative preparation is given by Figure 13 which shows the survival times of each animal and the median survival in each control group. The increasing median survival argues for the importance of each of the types of preoperative preparation for elective surgery of the colon. It should be remembered that this increasing survival time was achieved in the face of longer segments of devascularization for each type of preoperative preparation.

The function of antibiotics under the circumstances of these experiments may be summarized by a correlation of the ability of the bowel to survive a devascularized anastomosis with the bacterial population of the colon at the time of anastomosis and devascularization. Adequate reduction of the bacterial population prior to operation improved the chances for survival of the colonic anastomosis. Contrariwise, if the bacterial count is too high at the time of anastomosis and devascularization, bacteria may destroy the bowel wall before revascularization can occur, and necrosis, slough, perforation, and fecal peritonitis can be expected. If the bacterial population can be controlled during the critical first 48 to 72 hours after devascularization, sufficient revascularization can occur to permit the bowel to survive.

Since studies of the bacterial population of the stool show it to return to pre-therapy status within 24 hours after antibacterial therapy is discontinued, preoperative antibiotics will not suffice to control the bacterial flora in the critical postoperative period.[2, 3] Preoperative antibacterial agents suffice as long as an ileus is present, but when peristalsis begins, this protection is carried away. The parenteral route does not provide sufficient antibiotic concentration in the lumen of the bowel where it is most needed. The oral route is contraindicated and usually impractical postoperatively in surgery of the bowel. Therefore we have advocated the use of the plastic tube inserted at the time of operation to afford postoperative antibacterial protection.

*Clinical.* On the basis of this and other experimental work,[2, 3] a routine for patients undergoing colonic surgery was established. The three day preoperative preparation consists of a low residue diet, a cathartic the first day of preparation, daily enemas, and antibiotics. The combination of Achromycin® 200 mg. and neomycin 1 Gm. is given every hour for four hours, then every six hours for a total of 72 hours. At operation 5 Gm. of sterile Achromycin®-neomycin surgical powder, containing Achromycin® 250 mg. and neomycin 1.25 Gm., are inserted in the bowel to provide an immediate level of antibiotic at the anastomosis or colotomy site, where the experimental work indicated it was most needed. A plastic tube is inserted in the colon through a #14 needle proximal to the anastomosis or colotomy site to permit postoperative intraluminal antibiotic administration. The tube is brought out through a stab wound rather than through the incision. One vial of Achromycin® 150 mg. and neomycin 750 mg. is dissolved in 10–15 ml. sterile saline and injected through the tube three times a day for five days postoperatively.

Between July 1, 1955 and March 1, 1956 33 patients were prepared for a variety of colonic procedures with the Achromycin®-neomycin routine. There were no side effects in 23 patients. The remaining ten patients complained of nausea nine times, vomiting three times, and weakness and stomach cramps once each. In no case were these symptoms severe enough to warrant discontinuance of the drug.

In 13 patients 5 Gm. of sterile Achromycin®-neomycin surgical powder were inserted in the bowel when the colon was opened.

The plastic tube was inserted in the colon in 21 patients (Table IV) and the antibiotic mixture injected for the five day postoperative period. In only three patients was it thought that the use of the drug through the tube might have caused some

TABLE IV. *Postoperative Intraluminal Antibiotics*

| | |
|---|---|
| Colostomy closure | 5 |
| Polypectomy | 5 |
| Sigmoid colectomy | 4 |
| Transverse colectomy | 2 |
| Right hemicolectomy | 2 |
| Left colectomy | 2 |
| Splenic flexure colectomy | 1 |

difficulty, and in two of these this decision could not be made with certainty.

There were two postoperative deaths in the series. One occurred three weeks after operation and could not be correlated in any way with the tube use. Autopsy failed to reveal the cause of death in this patient. The other patient was an 85-year-old male who was submitted to a right hemicolectomy, segmental sigmoid colectomy, ileotransverse colostomy, and end-to-end sigmoid anastomosis for an adenocarcinoma of the cecum which had invaded an adherent loop of sigmoid. On the second postoperative day temperature elevation and clinical shock were noted. Poor urinary output was observed the next day, and a diagnosis of lower-nephron syndrome was made on the fourth postoperative day. Diarrhea was noted on the fifth day, and intravenous nor-epinephrine was begun. From this time until death on the eighth postoperative day the course was downhill with poor renal output and continuing diarrhea. Autopsy was not obtained. Intraluminal antibiotic therapy might have contributed to the diarrhea and increased the difficulties in maintaining fluid balance. The onset of the other problems prior to the diarrhea make it seem unlikely that the antibiotic could have been the ultimate cause of death.

There are too few cases to permit a statistical evaluation of whether antibiotics have contributed to a lowered morbidity and mortality. It is a clinical impression that these patients have done better but a much larger series of cases will be required to establish this as a fact rather than impression.

The clinical studies have shown that the technic is practical and is essentially without danger. The experimental work coupled with the clinical findings have given added assurance to the safety of certain operations, particularly in the face of a colon that cannot be cleaned prior to operation. It is thought that the use of antibiotics introduced through the tube will obviate the need for a proximal decompressive colostomy or cecostomy in many cases where such decompression might otherwise be used. Intraluminal antibiotics should also contribute to the safety of colon repair following trauma. This technic should increase the safety of closing a small single perforation of the colon in civilian practice.

It must be emphasized that this antibiotic protection technic is not introduced as a substitute for good surgery, nor is it advocated to cover up technical errors. It is advocated to improve the already low mortality and morbidity which obtain when other proper surgical principles of surgery of the colon are followed.

## SUMMARY

1. Devascularization of one side of a colonic anastomosis has been utilized for the evaluation of various types of antibiotic therapy in surgery of the colon.

2. Antibiotic therapy limited to postoperative intraluminal administration will protect a devascularized colonic anastomosis.

3. Preoperative mechanical cleansing and preoperative gastro-intestinal antisepsis combined with mechanical cleansing are each improvements in preparation for colonic surgery as evaluated by the procedure described here.

4. The addition of postoperative intraluminal antibiotics to any type of preoperative preparation further improves survival.

5. Limited clinical experience with the preoperative form of antibiotic therapy of choice and with postoperative intraluminal antibiotic therapy has been satisfactory.

6. The ability of antibiotics to maintain viability in a devascularized colonic anastomosis, and the increasing value of the various types of preoperative preparation indicate the important role of bacteria in surgery of the colon.

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DISCUSSION.—DR. HERBERT REID HAWTHORNE, Philadelphia, Pennsylvania: Dr. Cohn has contributed some excellent and careful studies on intestinal obstruction. As a result of this work he has definitely established the role that bacteria play in the cause of death in strangulation obstruction. When an anastomosis may appear somewhat unsafe as a result of edema, etc., in the proximal segment of the bowel, or in routine use, the introduction of antibiotics, according to his technic, should add a most useful safeguard. A local and direct application of the antibiotic to the area of anastomosis is a much safer route when compared to the possible toxic effects of large doses administered intravenously.

DR. WILLIAM A. ALTEMEIER, Cincinnati, Ohio: I think this paper has been very interesting. Undoubtedly many of you have heard previous papers or statements which indicated that the use of antibiotics preoperatively and cleansing of the intestinal tract preliminary to intestinal resections were of questionable value or of no value. In fact, numerous people have told me that they believed preoperative and postoperative antibiotic therapy were useless in the majority of intestinal resections. Possibly this is true; but the selection of the cases in which antibiotic therapy is going to be of definite prophylactic value is too difficult for me to determine with any degree of certainty.

It seems to me that the experiments we have just heard are indicative of the definite value of preoperative and postoperative antibiotic therapy in preventing septic or infectious thrombosis of the vessels within the wall of a "devascularized" segment of bowel. It would appear that the authors have devascularized only partially the blood supply of the bowel by dividing the vessels in its mesentery. As has been pointed out by Noer and others, there is a definite intramural circulation of the bowel itself, and this has remained intact in the authors' experiments.

We all know that the intestinal tract of animals and man has a profuse bacterial flora consisting of aerobes and anaerobes. We know, further, that some of the anaerobes produce enzymes of two types in particular, (1) necrotizing enzymes and (2) coagulating enzymes which can produce thrombosis of the neighboring vessels.

The real value of this experiment has been the demonstration that the bacterial growth within this segment of bowel is minimized to the point that thrombosis of the vessels within the wall is prevented by bacterial enzymes. I think this is a fascinating experiment, and should answer for all of us the question of whether or not pre- and postoperative antibiotic therapy is important. Thank you.

DR. ALFRED BLALOCK, Baltimore, Maryland: When I moved back to Baltimore in 1941 Dr. Poth was working in the surgical laboratories. He had rigged up a beautiful device by which he would place sulfaguanidine or some such agent in meatballs. The dogs would be fed throughout the 24-hour period without Dr. Poth having to lose too much sleep. The surgeons at first would not accept his findings, but I think they do now.

DR. EDGAR J. POTH, Galveston, Texas: I certainly appreciate this presentation by Drs. Rives and Cohn. I should like to make a few remarks with the aid of some slides.

In 1941 Dr. Sarnoff, who was then a senior medical student at Johns Hopkins, showed that sulfasuxidine would protect a 50 cm loop of distal ileum from necrosis after it had been made ischemic by ligation of the blood supply. The protection was demonstrated to be due to the prevention of thrombosis of the small caliber vessels in the wall of the bowel. I should like to support today's report with the following lantern slides.

(Slide) This first slide shows our test object in animals. A 10 cm segment of distal ileum is rendered ischemic by dividing the arteries and veins in the mesentery. The vascular supply to this segment was limited to intramural vessels entering at the two extremities of the segment. This ischemic segment was sectioned in its middle and then sutured. All control animals (dogs) died within 72 hours.

(Slide) This second slide shows the results of the administration of various antibacterial agents by either the parenteral or the oral route. I should like to acknowledge that these observations were made by Dr. Johnson, who is a member of our house staff. The next column shows the result of the parenteral administration of acromycin. There is a considerable degree of protection.

Next is the administration of neomycin, 1 per cent, injected into the bowel at the time of opera-