INTESTINAL OBSTRUCTION

THE PROTECTIVE ACTION OF SULFASUXIDINE AND SULFATHALIDINE TO THE ILEUM FOLLOWING VASCULAR DAMAGE*

EDGAR J. POTH, M.D., PH.D.

AND

JOHN N. MCCLURE, JR., M.D.†

GALVESTON, TEXAS

FROM THE SURGICAL RESEARCH LABORATORY, UNIVERSITY OF TEXAS, MEDICAL BRANCH, GALVESTON

INTRODUCTION

INTESTINAL OBSTRUCTION is a complex entity made up of numerous variable factors which cannot be separated and isolated for definitive experimental study. Two important factors are the blood supply of the bowel and the intraluminal bacterial flora. The importance of the former under altered conditions of the latter has been the object of considerable investigative work. Poth and associates[8-13] have shown in numerous publications that the bacterial flora of the intestine can be changed appreciably by the oral administration of sulfasuxidine and sulfathalidine.

While working on the factor of blood supply, Scott and Wangensteen,[17] Foster and Hausler,[3] and Murphy and Vincent[6] found that obstruction of the mesenteric veins produced death in dogs more rapidly and more frequently than other types of mesenteric vascular occlusion. Recently, Sarnoff and Poth[16] and Sarnoff and Fine[15] found approximately 90 per cent of dogs weighing ten kilograms would die within 48 hours from simple interruption of the mesenteric veins to a 50 cm. segment of terminal ileum. Death was consistently due to peritonitis. In the experiments of Sarnoff and Poth,[16] all control animals had large perforations in the loop of bowel under study, while Sarnoff and Fine[15] observed 75 per cent gross perforations.

The same observers also found that by administering sulfasuxidine or sulfathalidine orally for several days before venous ligation only 25 to 30 per cent of the animals died within 48 hours and 70 to 75 per cent survived indefinitely. This difference of survival is significant.

If sulfa drugs were given at the time of operation or immediately after, protection was afforded to a smaller number of animals. Sarnoff and Fine injected, by means of a needle and syringe, 1 Gm. per Kg. of body weight of sulfasuxidine into the lumen of the proximal bowel at the time of operation. In this group 34 per cent of the animals survived. They gave another group of dogs parenteral sodium sulfathiazole for two days after the operation. This procedure resulted in the survival of four out of eight animals. The number

* Submitted for publication November, 1948.

† Now Research Fellow, Whitehead Laboratory of Surgical Investigation Emory University Hospital, Emory University, Georgia.

of animals is small and the differences observed in the survival rate may well be insignificant.

Subsequently, Blain[1] demonstrated that parenteral penicillin would protect, for a limited period of time, dogs which had been subjected to mesenteric venous ligation. The experiment was different in that the terminal ileum was divided and the ends inverted so as to produce a complete obstruction. The veins in the proximal 60 cm. segment were then ligated. Death overcame all control animals in less than 36 hours, even though they were treated for shock, hemorrhage, and fluid loss. Perforation was "often" observed in the controls and all showed massive bacterial invasion of the infarcted walls of intestine. The percentage of perforations in treated animals is not reported. On the other hand, most of the animals given massive doses of penicillin survived three to four times as long, and some were cured after resecting the infarcted bowel 72 hours following ligation. The important role of bacterial infection in cases of intestinal obstruction was re-emphasized.

The visible changes in a loop of bowel after venous ligation are very interesting. The normal color is replaced by cyanosis, which progresses to a deep reddish purple within 20 to 30 minutes. The involved segment is sharply demarcated from the normal. Engorgement of the bowel wall and the mesenteric veins continues until the pressure within them equals the arterial capillary blood pressure. Shortly thereafter arterial pulsations cease. If the infarcted segment is incised there is practically no bleeding, indicating that early thrombosis has occurred. Histologic sections of the bowel taken at different intervals postoperatively confirm these observations. There is widespread thrombosis in veins of untreated animals, while thrombosis in the veins of surviving treated dogs is minimal.

In a further investigation of this subject, the influence of ligating the arteries to a corresponding segment of ileum, as well as that of the simultaneous ligation of arteries and veins, is studied and reported in this communication.

EXPERIMENTAL PROCEDURE

In the experiment, healthy mongrel dogs were divided into two groups. One, the controls, received only horse meat for ten to 16 days before operation; the other, treated animals, received 1 Gm. per Kg. of body weight per day of sulfasuxidine, or ½ Gm. per Kg. per day of sulfathalidine, mixed with the horse meat given every four hours for the same length of time. The dogs were in a weight range of seven to 12 Kg., most of them weighing approximately 10 Kg. After operation, the animals were offered water but no food for the first two days, then they were fed for ten days in the same manner as before operation. While on a diet of horse meat, the control dogs often developed a diarrhea with very foul stools. However, the dogs receiving horse meat plus sulfasuxidine rarely developed diarrhea and frequently would go seven to ten days without a bowel movement. Their feces were soft and devoid of the unpleasant odor always found in those not receiving the drug.

The operative procedure, done under ether anesthesia and aseptic technic, is briefly as follows. The peritoneal cavity is entered and the terminal ileum located. A segment of ileum 50 cm. in length is selected 10 cm. proximal to the termination of the antimesenteric artery (Fig. 1) so as to avoid collateral circulation from this vessel. Occasionally, when a dog weighed less than 10 Kg., a length of 5 cm. of bowel per Kg. of body weight was similarly isolated. At either end of the segments the mesentery is divided down to its root and includes the careful ligation of the arteries and veins running parallel to the bowel in its mesenteric border. Near the base of the mesentery, the arteries

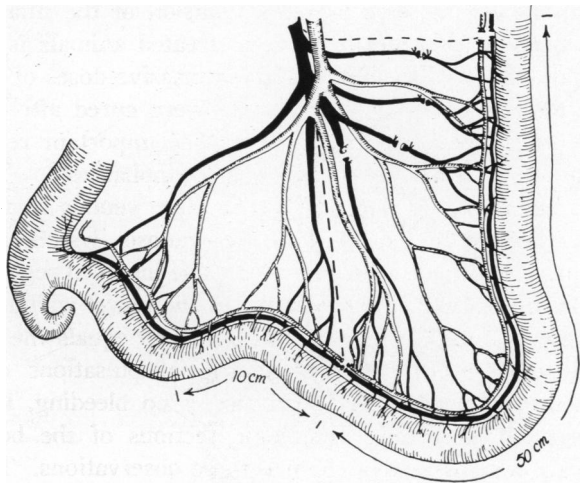


FIG. 1.—A schematic representation of the segment of ileum 50 cm. long and located 10 cm. proximal to the termination of the antimesenteric artery. In this instance the division and ligation of the veins is indicated.

or arteries and veins are isolated. If arteries alone are divided and ligated, care is taken to avoid injury to the veins which are left intact. The changes which occur after such a procedure are quite striking. Immediately upon interruption of the arterial blood supply, the vessels collapse distal to the ligature. The bowel undergoes violent peristaltic and spastic contractions, causing it to become nodular, blanched, and one-half its original length. Cyanosis develops within a few minutes and the veins become distended with dark blood. If arteries and veins are ligated simultaneously, there is a similar immediate reaction, but the vessels and bowel become engorged and cyanotic much more rapidly.

Among control animals, there is a very high mortality during the first three days after operation. These animals die of a massive acute fulminating peritonitis. The peritoneal cavity is distended with bloody purulent fluid. All peritoneal surfaces are intensely inflamed. The limits of the ligated segments are sharply demarcated and deep bluish-red in color. The midportion of the segment is autolysed, sometimes completely destroyed or containing very large perforations with only portions of the serosa and the muscularis

remaining attached to the mesentery (Fig. 2). In the mesentery there is dilatation and engorgement of smaller vessels with thrombosis and extravasation of blood along the larger ones. On the surface, and sometimes between the leaves of the mesentery, there is a fibrinous exudate. In the majority of

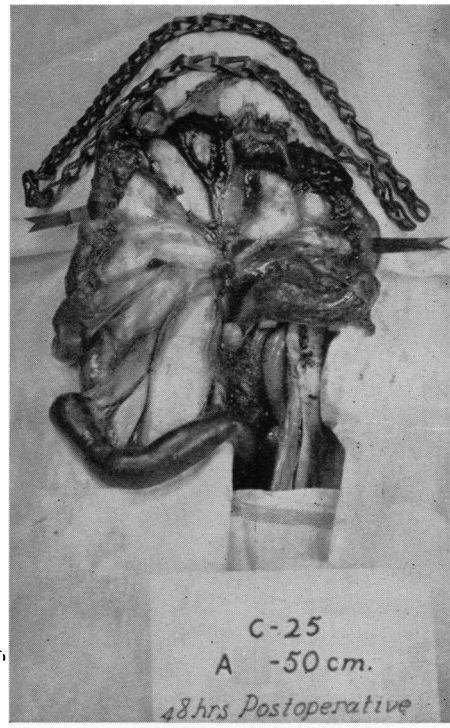


FIG. 2

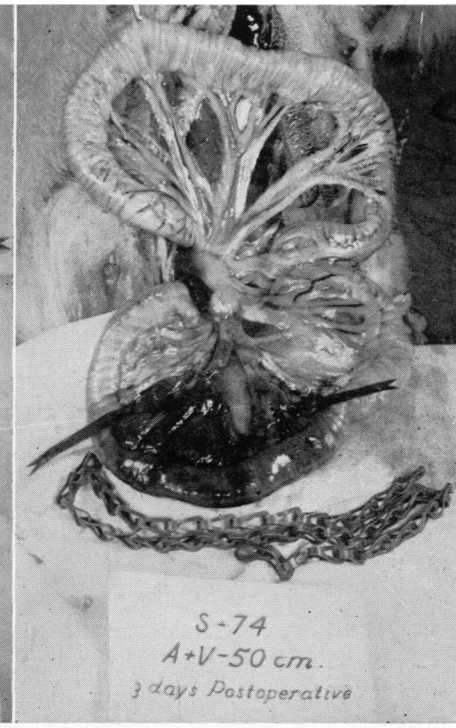


FIG. 3

FIG. 2.—(Experiment C-25). This animal had not received sulfasuxidine before arterial interruption. Death occurred 48 hours postoperatively with nearly complete autolysis of the segment. The chain shown is 50 cm. long and represents the initial length of the segment of ileum which has become shortened to approximately half its length at time of ligation. This extent of destruction is the usual result in the control animals.

FIG. 3.—(Experiment S-74). This animal received sulfasuxidine before the simultaneous ligation of the arteries and veins to a 50 cm. segment of ileum. The animal was alert and active on the third postoperative day when sacrificed. There was some discoloration of the segment which had become shortened to 20 cm. There were no perforations, no peritonitis. This animal would have survived. The mesentery is not yet shortened.

cases, the intestines are massed together and enveloped by the omentum. When there is almost complete destruction of the bowel, however, there may be no adhesions.

Among the four control dogs which survived the immediate postoperative period, one died of intestinal obstruction from adhesions and volvulus after ten days. Another died from an undetermined cause at two weeks; the peri-

toneal cavity was not remarkable. The other two were sacrificed at different intervals. This phenomenon of late obstruction was observed in only three of the treated animals, although the number of animals surviving the acute phase was much greater.

When dogs are given sulfasuxidine or sulfathalidine preoperatively and are subjected to the same operation, there is a comparatively low mortality and most of them survive and appear normal. In order to follow the immediate recovery and eventual healing after operation, dogs were sacrificed for colored still and motion pictures at daily intervals for seven days, then at ten, 15, 20, 30, 50, 75, and 100 days, six months, and nine months.

Although there was considerable variation in the intensity of the inflammatory reaction among the treated survivors, the protective mechanism was in general the same. There was no free fluid found in the peritoneal cavity after the first week; some animals had none even on the second and third days. When present it was small in volume and serosanguineous in character.

The involved segment was frequently folded upon itself with the adjacent loops of bowel coiled in a mass closely enveloped by the omentum. There were numerous fibrinous adhesions between loops of bowel as well as with the omentum. These adhesions vascularized early and bled freely when separated five to ten days postoperatively. During the first week, the inflammatory reaction was usually conspicuous. In some instances the segment was sharply demarcated from the normal intestine at either end (Fig. 3); in others there was little discoloration except for small areas in the center of the loop. In the mesentery, there was dilatation and engorgement of blood vessels with extravasation and exudation along the larger mesenteric vascular trunks as well as on the surface. Thrombosis was not conspicuous. From the period immediately after ligation of the vessels, the loop of bowel was always found to be shortened ½ to ⅓ its original length. After two to four weeks the inflammatory reaction had largely subsided and the bowel was normal in color, although some thickening of the bowel wall persisted. After several weeks or months, there was no demonstrable scar contracture of the bowel wall, and in only one case, 11 months postoperatively, was an annular fibrosis found which reduced the size of the lumen. In this case it was not significant. There was no obstruction. The dog had grown and doubled in weight since operation.

Concomitant with contraction of the length of the bowel there is a shortening of the mesentery. The process continues along with thickening and fibroplastic proliferation around the severed ends of the vessels, and by two weeks to one month it will have shortened one-half to one-third its original length (Fig. 4). Later, when the scar tissue contracts, there is further decrease in length so that the intestine may be resting almost on the mesenteric lymph nodes.

Retractile mesenteritis was first produced experimentally by Jura[5] in 1924 by injecting intestinal bacteria into the mesentery of the ileum. Stropeni[18] (1933) produced the condition by ligating or injecting the mesenteric veins but not following ligation of the arteries. Reichert, Gerbode and Halford[14]

(1939) concluded that retractile mesenteritis could be produced by ligation of all vessels in the mesentery, by ligation of the lymphatics alone, and by irritation or trauma of the leaves of the mesentery. In the ligations of the vessels to the long segments of ileum as practiced in this study, shortening of the mesentery as well as of the bowel itself occurred regularly, regardless of whether arteries, veins, or arteries and veins were ligated. The factor of bacterial infiltration of the bowel wall and tissues of the mesentery was undoubtedly always present and was likely the most important factor in these studies. Dilatation of lymphatics was not observed, and, in all probability, the

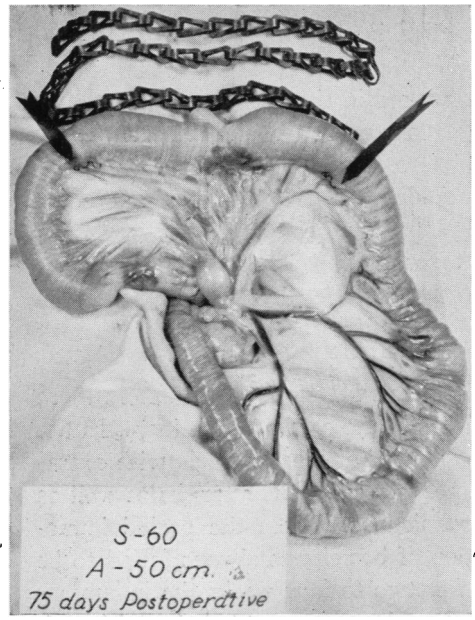


FIG. 4.—(Experiment S-60). Arterial ligation after sulfasuxidine administration. The animal was sacrificed 75 days postoperatively. Normal peristalsis had been restored. The segment is contracted to 1/3 its original length, but its diameter is not reduced. The corresponding mesentery is strikingly shortened. Adhesions were minimal.

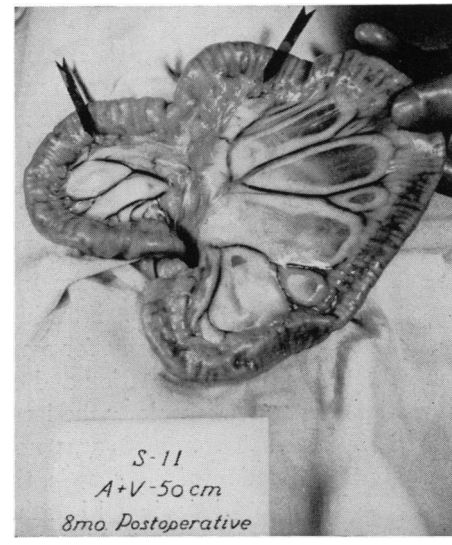


FIG. 5.—(Experiment S-11). Simultaneous ligation of arteries and veins after sulfasuxidine administration. The animal was sacrificed eight months postoperatively. This shows essentially the same findings as S-60 in Figure 4. The arrows indicate the ends of the segment.

lymphatics were not completely interrupted. The characteristic thickening and fibrosis of the wall of the bowel seen in regional enteritis was not produced in these experiments.

If the mesentery is examined closely after the acute phase, small blood vessels can be seen bridging the gap around the severed ends of the large mesenteric arteries and veins, so that through these small collaterals the original vessels re-establish function. This finding is demonstrated in Figure 6. Roentgenographic examination of specimens injected with radiopaque material demonstrates the manner in which revascularization occurs (Figs. 6 and 7).

TABLE I.—*Tabulation of Results of the Division of the Arteries to Segments of Distal Ileum of a Group of Control Animals.*

Animal No.	Weight in Kg.	Length of Segment	Lived	Comments
1	10	50 cm	14 hrs.	Died. Large perforation with massive peritonitis.
6	10	50 cm	30 hrs.	Died. Large perforation with much free fluid in peritoneal cavity. Diffuse crepitus in viscera and walls.
7	9	25 cm	48 hrs.	Sacrificed. Was very ill. Large walled off perforation; much free fluid in cavity.
10	10	40 cm	50 hrs.	Sacrificed. Large perforation of gut. Would have died shortly. Massive peritonitis; much free fluid.
11	11	35 cm	3 days	Sacrificed. Large perforation of gut, walled off, much free fluid. Would have died.
13	10.5	25 cm	1 week	Sacrificed. Was doing well. Reaction subsiding, would have recovered.
16	18.5	50 cm	36 hrs.	Died. No perforation; much free fluid, massive peritonitis.
18	11	50 cm	4 days	Died. Large perforation. Much free fluid; massive peritonitis.
20	10	50 cm	3 days	Died. Much free fluid; large perforation; massive peritonitis.
22	13.5	50 cm	48 hrs.	Died. Much free fluid; autolysis with large perforation; massive peritonitis.
24	9	40 cm	36 hrs.	Died. Much free fluid; autolysis with large perforation; massive peritonitis. Photographed.
23	11	50 cm	10 hrs.	Died. Much free fluid; complete obstruction adhesions and volvulus. No perforation.

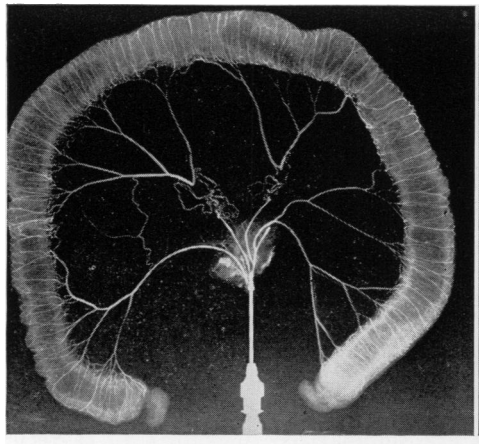


FIG. 6

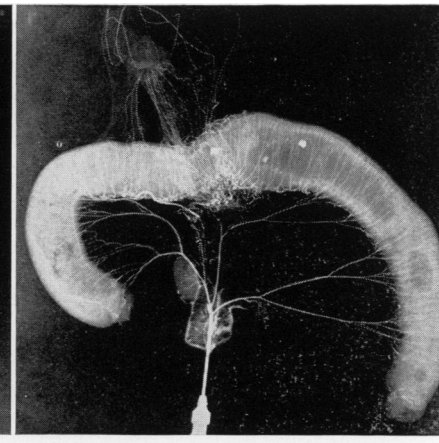


FIG. 7

FIG. 6.—(Experiment S-29). This dog was sacrificed 5½ months after the simultaneous ligation of both arteries and veins following sulfasuxidine administration, and injected with BiOCl suspension (Poth[7]). Roentgen ray film shows development of collaterals between ends of severed arteries, across the mesentery from an adjoining artery, and a definite increase of vascularity in the wall of the bowel at either end of the segment. This latter is the only available circulation immediately following operation, and serves to sustain the bowel for a considerable period until other vessels can become established.

FIG. 7.—(Experiment S-24). This dog was sacrificed eight months after the simultaneous ligation of arteries and veins to a 50 cm. segment of distal ileum following sulfasuxidine administration and then injected with BiOCl suspension. Roentgenogram shows the collaterals, especially in the wall of the bowel and through an omental adhesion. This segment is obviously greatly shortened.

During the first several days after operation the mucosal layer is usually edematous and hemorrhagic. However, within one to two weeks, it regains its normal color and consistency, and the folds resume their usual pattern without evidence of deformity by scar formation.

As mentioned before, there were only three intestinal obstructions in the animals receiving drug, even though there were always numerous adhesions and kinks in the bowel. With the eventual establishment of adequate collateral circulation through the mesentery and through the bridges around the severed

TABLE II.—*Tabulation of Results of the Simultaneous Interruption of Both Arteries and Veins to Segments of Distal Ileum of a Group of Control Animals. Animal 3 Had Only the Vein Divided.*

Animal No.	Weight in Kg.	Length of Segment	Lived	Comments
2	9.5	50 cm	36 hrs.	Sacrificed. Autolysis of segment with perforation and massive peritonitis.
4	10	50 cm	30 hrs.	Sacrificed. Necrosis but no gross perforation. Crepitus extensive in peritoneal cavity and abdominal wall.
5	6.5	50 cm	30 hrs.	Sacrificed. Large perforation with massive peritonitis.
8	10	25 cm	50 hrs.	Sacrificed. Might have lived. No perforation, little free fluid. Mass well walled off.
9	14	30 cm	36 hrs.	Sacrificed. Very large dog. Autolysis of segment. Massive peritonitis with crepitus.
12	8	40 cm	36 hrs.	Sacrificed. Much free fluid; large perforation walled off.
14	11	25 cm	2 weeks	Sacrificed. Was doing well. Peritoneum clean, healing well.
15	16	50 cm	7.5 mo.	Sacrificed for photograph. Only control dog to live. Well healed; omentum adherent to bowel.
17	8	40 cm	2 weeks	Died. Cause unknown. Peritoneum clean—some adhesions, no obstruction.
19	9	50 cm	48 hrs.	Sacrificed. Much free fluid; massive peritonitis; segment very dark and soft; no perforation.
21	10	50 cm	3 days	Sacrificed. Much free fluid; autolysis with large perforation; massive peritonitis.
25	10	50 cm	36 hrs.	Sacrificed. Much free fluid; autolysis with large perforation and massive peritonitis.
3	11	50 cm	18 hrs.	Sacrificed. Much free fluid; autolysis with large perforation and massive peritonitis.

ends of the parallel vessels many of the adhesions resolve, and the number of adhesions persisting after six months was much fewer than within a month of the procedure. The omentum usually remains attached to the segment, but occasionally the loop lies free in the peritoneal cavity.

The results of these experiments are summarized in Tables I, II, III, and IV.

The difference in survival rates between control and treated animals is readily presented in graphic form, (Figs. 8, 9, 10 and 11). In the control series the mortality rate during the first four days ranged from 80 to 100 per cent. Among the treated animals 30 to 35 per cent died within this four-day period with a final survival rate of approximately 50 per cent.

DISCUSSION

The rôle played by the blood supply and the importance of its preservation in the final outcome of obstruction of the bowel are again emphasized in these

FIG. 8

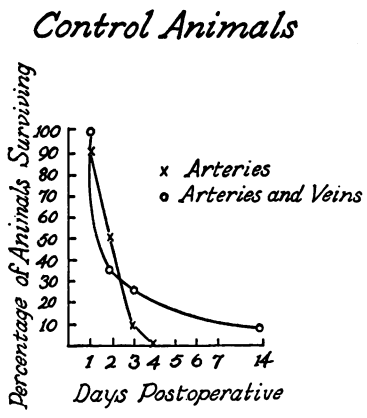
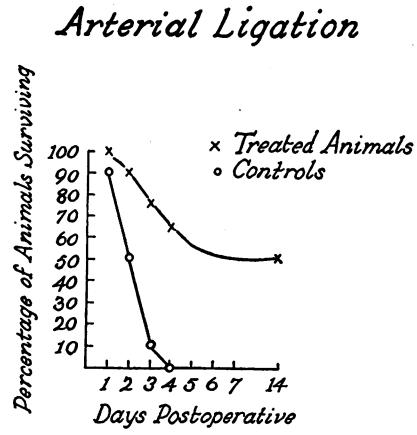
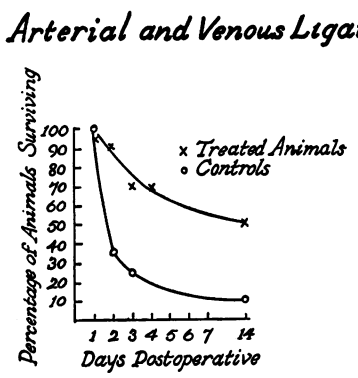


FIG. 9





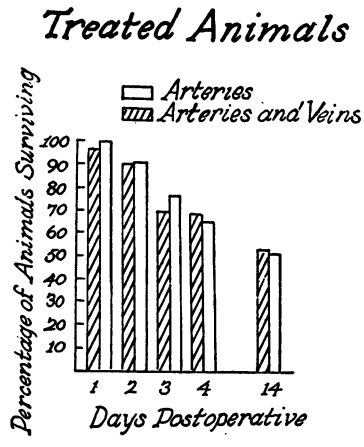


FIG. 10

FIG. 11

FIG. 8.—A plot of survival of control animals following the ligation of arteries and arteries and veins to 50 cm. segments of distal ileum. Within the limits of the experiment, they are identical.

FIG. 9.—A plot of survival of control and treated animals following interruption of arteries to 50 cm. segments of distal ileum.

FIG. 10.—A plot of survival of control and treated animals following the simultaneous division of both arteries and veins to 50 cm. segments of distal ileum.

FIG. 11.—A plot of survival of treated animals following the ligation of arteries in the one instance and the simultaneous interruption of arteries and veins in the other to 50 cm. segments of distal ileum. Within the limits of error of these experiments there is no difference.

studies. It would appear that the value of sulfasuxidine or sulfathalidine resides in their ability to alter the bacterial flora in the lumen of the bowel and thereby reduce the bacterial invasion and impregnation of the tissues of the bowel by toxic substances, which in turn cause thrombosis of the blood

TABLE III.—*Summation of Results Following the Division of the Arteries to 50 cm. Segments of Distal Ileum of 35 Dogs Which Had Received Oral Sulfasuxidine or Sulfathalidine Preoperatively and Postoperatively.**

Animals living 5 days or less		17
Died	2	
Sacrificed†	15	
Peritonitis	12	
Perforation of ileal loop	8	
Animals living 7 days to 9 months		18
Died	0	
Sacrificed	18	
Peritonitis	0	
Perforations of ileal loop	0	
Total		35

* The detailed tabulation of these data is being published in *Texas Reports on Biology and Medicine.*
† Ten of these 15 animals had peritonitis with perforation of the ileal loop in 8 instances.

vessels in the bowel wall, especially the terminal arterioles and capillaries. The preservation of the blood supply by preventing thrombosis and the reduction of toxic bacterial products are sufficient to protect the tissues of the bowel from necrosis and perforation.

The preservation of adequate blood supply is, however, dependent upon factors other than prevention of vascular thrombosis. In addition it is influ-

TABLE IV.—*Summation of Results Following the Division of Both Arteries and Veins to 50 cm. Segments of Distal Ileum of 37 Dogs Which Had Received Oral Sulfasuxidine or Sulfathalidine Preoperatively and Postoperatively.**

Animals living 5 days or less		16
Died	0	
Sacrificed	16	
Peritonitis	14	
Perforation of ileal loop	9	
Animals living 6 days to 9 months		21
Died	0	
Sacrificed	21	
Peritonitis	0	
Perforation of ileal loop	0	
Total		37

* The detailed tabulation of these data is being published in *Texas Reports on Biology and Medicine.*

enced by maintenance of the circulating blood volume. When the survival rates at 48 hours following ligation of veins, arteries, and arteries and veins simultaneously are analyzed, it is found that, both among the control experiments and those animals receiving sulfonamide treatment, the mortality is greatest among those where only the veins are divided.

Mortality Rates Within 48 Hours of Operation

	Venous Ligation	Arterial Ligation	Arterial and Venous Ligation
Control animals — Per cent mortality.....	95	50	64
Treated animals — Per cent mortality.....	27	9	9

Following venous ligation death usually occurs within the first 48 hour postoperative period. There is rapid loss of blood into the wall and lumen of the bowel when the veins alone are interrupted, reducing the circulating blood volume, inducing a greater degree of shock, and augmenting the mortality during the early postoperative period. This is true, although eventually the survival rate of the treated animals is greater following venous ligation than after arterial or simultaneous arterial and venous ligation.

A comparison of the results following arterial ligation alone with the simultaneous division of both arteries and veins to segments of ileum fails to show the beneficial effect of accompanying the arterial interruption with venous ligation as observed by Brooks and Martin[2] and Holman[4] in prevention of gangrene of the leg of the dog following ligation of the iliac artery. The situation here might, however, be different in that bacterial invasion of the wall of the bowel with liberation of toxic substances may be the predominating factor overshadowing all others, while infection would be insignificant following interruption of the iliac artery.

Sulfasuxidine and sulfathalidine have been given in cases of mesenteric infarction in the hope of preventing progression of the intravascular clot or to protect the bowel should there be further mesenteric embolism. Our limited experience with this therapeutic application prevents any reasonable evaluation of the measure.

The influence of the intestinal flora on bowel necrosis and perforation has been demonstrated, and it has been shown that this effect can be significantly reduced by the antibacterial action of sulfasuxidine and sulfathalidine.

SUMMARY

The importance of the bacterial flora as a factor in bowel necrosis in the presence of vascular damage is studied.

The bacterial flora is altered and attenuated by the administration of sulfasuxidine and sulfathalidine.

Vascular damage is inflicted by division of arteries, veins, and arteries and veins simultaneously to segments of distal ileum and the results with and without sulfonamide therapy are studied.

The pathologic alterations and the mode of repair is described.

It is concluded that the bacterial flora is an important factor in bowel necrosis in intestinal obstruction.

Sulfasuxidine and sulfathalidine have a distinct favorable effect to promote repair of damaged intestinal tissues.

The administration of sulfasuxidine or sulfathalidine is proposed when intestinal infarction is suspected and whenever intestinal surgery is contemplated.

BIBLIOGRAPHY

1 Blain, Alexander, III: Penicillin in Experimental Intestinal Obstruction: A Summary of Observations with Reference to their Clinical Application. Surg., Gynec. & Obst., **84**: 753, 1947.

2 Brooks, Barney, and K. A. Martin: Simultaneous Ligation of Vein and Artery. J. A. M. A., **80**: 1678, 1923.

3 Foster, W. C., and R. W. Hausler: Studies on Acute Intestinal Obstruction: II. Acute Strangulation. Arch. Int. Med., **34**: 697, 1924.

4 Holman, Emile, and Muriel E. Edwards: A New Principle in the Surgery of the Large Vessels. Ligation of Vein Proximal to Site of Ligation of the Artery: An Experimental Study. J. A. M. A., **88**: 909, 1927.

5 Jura, V.: Sulla mesenterite retractile e slerosante: Policlin, Roma, **31**: 575, 1924.

6 Murphy, F. T., and Beth Vincent: An Experimental Study of the Cause of Death in Acute Intestinal Obstruction. Boston Med. & Surg. J., **165**: 684, 1911.

7 Poth, E. J.: Modification of Hill's Radiopaque Mass for the Injection of Lumina. J. Lab. & Clin. Med., **19**: 1241, 1934.

8 Poth, E. J., and F. L. Knotts: Succinylsulfathiazole, A New Bacteriostatic Agent Locally Active in the Gastro-intestinal Tract. Proc. Soc. Exper. Biol. & Med., **48**: 129, 1941.

9 Poth, E. J., F. L. Knotts, J. T. Lee, and F. Inui: Bacteriostatic Properties of Sulfanilamide and Some of its Derivatives. I. Succinylsulfathiazole, A New Chemotherapeutic Agent Locally Active in the Gastro-intestinal Tract. Arch. Surg., **44**: 187, 1942.

10 Poth, E. J., and F. L. Knotts: Clinical Use of Succinylsulfathiazole. Arch. Surg., **44**: 208, 1942.

11 Poth, E. J., and C. A. Ross: Phthalylsulfathiazole, A New Bacteriostatic Agent. Federation Proc., **2**: 89, 1943.

12 ————: Bacteriostatic Properties of Sulfanilamide and Some of its Derivatives: II. Phthalylsulfathiazole, A New Chemotherapeutic Agent Locally Active in the Gastro-intestinal Tract. Texas Rep. Biol. and Med., **1**: 345, 1943.

13 ————: The Clinical Use of Phthalylsulfathiazole. J. Lab. and Clin. Med., **29**: 785, 1944.

14 Reichert, F. L., F. Gerbode and F. J. Halford: Sclerosing or Retractile Mesenteritis. Ann. Surg., **110**: 669, 1939.

15 Sarnoff, S. J., and Jacob Fine: The Effect of Chemotherapy on the Ileum Subjected to Vascular Injury. Ann. Surg., **121**: 74, 1945.

16 Sarnoff, S. J., and E. J. Poth: Intestinal Obstruction. I. The Protective Action of Succinylsulfathiazole Following Simple Venous Occlusion. Surgery, **16**: 927, 1944.

17 Scott, H. G., and O. H. Wangensteen: Length of Life Following Various Types of Strangulation Obstruction in Dogs. Proc. Soc. Exper. Biol. & Med., **29**: 424, 1932.

18 Stropeni, L.: Ricerche sperimentali sulla patogensi della mesenterite retracttile. Boll. e mem, Soc. piemontese di chir., **3**: 668, 1933.