# INTESTINAL OBSTRUCTION.

## I. A Study of a Toxic Substance Produced in Closed Duodenal Loops.*

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Plate 55.

During the past few years a great amount of experimental work has been done in an attempt to solve some of the problems concerned with intestinal obstruction. We shall make no effort toward a critical review of this material, but refer to recent publications by Hartwell and Hoguet, Murphy and Vincent, Clairmont and Ranzi, Albeck, Kukula, and Draper-Maury.

Before we proceed with our own work, it will be well to emphasize two points which seem to be fully established by several workers. Clairmont and Ranzi, followed by Hartwell and Hoguet, have shown that blood cultures, cultures from the viscera, and, most important of all, peritoneal cultures, may be sterile when the experimental obstruction has been carefully performed, yet the animals die in the characteristic manner. This rules out the importance of bacterial growth and activity in the general circulation or in the peritoneal cavity, but does not exclude bacterial activity in the intestinal lumen.

Experiments of Halsted and von Baracz show that the closed loops of ileum and colon may be very slightly toxic, the dogs living for weeks or even months. At autopsy the loops were filled with inspissated, cheesy material. Our few experiments with closed loops of ileum give no evidence of grave intoxication and support the observations just cited.

We felt that experiments (Kukula, Murphy and Vincent, and others) in which intestinal contents were introduced into a normal

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animal (intravenously, intraperitoneally, or subcutaneously) were open to objection because of the complexity of the factors involved; namely, bile, pancreatic and gastric juices, besides the split products of proteid digestion which are known to be more or less toxic when given intravenously.

The use of a closed washed duodenal loop does away with some of these confusing factors and when produced in a dog will usually lead to death in one to three days, the symptoms being similar to those of patients with volvulus or high intestinal obstruction; these are intoxication, low temperature, a fall in blood pressure, and venous congestion. By the use of the closed washed loop we are able to exclude bile, gastric and pancreatic juices, and products of food digestion. This procedure simplifies the problem and limits us to a consideration of substances elaborated by the bacteria which are known to multiply rapidly in these closed loops (McClure) and by the intestinal mucosa which is capable of secretion as well as of absorption.

This closed duodenal loop we may compare with a volvulus in which there are no vascular disturbances and no food products to complicate the picture. We hope to show clearly that in such a duodenal loop there is formed a toxic substance, or substances, which give a characteristic picture when introduced into a normal animal of like species. Further, we believe that the intestinal epithelium is necessary for the production of this toxic substance and that dogs can be immunized against this poison. Immunized in this way they may live six or seven days with a closed duodenal loop, which is three times the average length of life under these conditions. Many experiments on dogs with closed duodenal loops are given because it is important to know the history of the cases and the findings under different conditions and after different intervals of time. The material used for study was obtained in large part from these dogs and references to the protocols will be made constantly in the later experiments.

## METHOD.

The operative detail with illustrations has been given in a previous communication by the writers. The essential feature, however, is the isolation of the greater part of the duodenum by means of heavy ligatures placed just below

the pancreatic duct and just beyond the duodenojejunal junction. These heavy ligatures are buried by mattress sutures and the continuity of the alimentary tract is established by a posterior gastro-enterostomy. Ether was invariably used as an anesthetic in all operations, and morphia was usually not given. All the experiments were performed upon dogs. The material obtained from the closed duodenal loops at autopsy was usually diluted with normal saline or washed into a container with water. Autolysis with toluol and chloroform does not injure the toxic substance and is valuable for making the material more suitable for filtration or extraction. The fluid, unless otherwise stated, was heated at 60° to 70° C. for one half to one hour, centrifuged, and the supernatant fluid filtered through a Gooch crucible or porcelain perforated funnel. The kymograph experiments were always done under ether anesthesia. The carotid artery and jugular vein can be reached by a small incision, and if the operation is done with clean instruments, and with as little handling of the tissues as possible, the wound will heal promptly.

## EXPERIMENTAL OBSERVATIONS.

In the first series of four dogs the isolated loop was not washed out and the intestine was cut across with inversion of the ends. These dogs all died in twenty-four to twenty-eight hours, as described in our previous report, and it is possible that the cut and inverted ends of the intestine favored absorption and the fatal outcome. It may be thought, too, that careful washing out of the duodenal loop before closure in later experiments removed all food elements and great numbers of bacteria, thus retarding the ultimate growth of the bacteria which may be in part essential to the production of the toxic substances. For this reason it will be seen below that in this second series the dogs lived one to three days after operation, or an average of about forty-eight hours

### CLOSED DUODENAL LOOP. DEATH IN TWENTY-SEVEN HOURS.

*Dog S-34.*—Adult mongrel, male; weight, 15 pounds.

April 2, 11 A. M. Operation and isolation of duodenal loop with careful washing.

April 3, A. M. Dog seems very toxic; refuses food. 2 P. M. Dog is moribund. Muscular tremors are very conspicuous. The pupils are dilated. The extremities are cold. Given ether.

*Autopsy.*—Performed at once. The heart continued to beat with a very slow rhythm several minutes after opening the thorax. The lungs are rather voluminous and pale. The spleen, liver, and kidneys are normal. The duodenal loop is of enormous size. Its serous surface shows a fine granular deposit of fibrin, but elsewhere the peritoneal surface is smooth. Purplish patches show through the transparent serosa. It contains 130 c.c. of blood-stained fluid of a

characteristic odor. Flakes of mucus and epithelium can be made out in the fluid, which is rather thin. The stomach is decidedly pale. The duodenum above the loop shows a pinkish mucosa. The jejunum shows a mottled pinkish red mucosa and contains a good deal of fluid. The splanchnic vessels are conspicuous in the mesentery.

*Microscopical Examination.*—The lungs, liver, small intestine, and kidneys are normal except for slight congestion. In places the wall of the duodenum shows necrosis, hemorrhage, and invasion by leucocytes. Bacteria are very numerous throughout the necrotic mucosa. The peritoneum shows a beginning exudate of leucocytes.

CLOSED DUODENAL LOOP WITH RUPTURE. DEATH IN THIRTY-TWO HOURS.

*Dog S-27.*—Large mongrel, male; weight, about 45 pounds.

March 18, 3 P. M. Operation and isolation of closed duodenal loop with washing as usual.

March 19, 11 P. M. Dog found gasping for breath, with marked muscular twitchings. Death followed in a few minutes.

*Autopsy.*—Performed at once. The peritoneal cavity contains turbid, gray fluid similar to that often found in the closed loops. The peritoneal surfaces are injected and specked with ecchymoses. The duodenal loop is contracted and contains a little material. Its wall shows a few areas of subserous hemorrhage about 1 or 2 cm. in diameter. There is obvious necrosis associated with these areas and through one of them rupture had taken place, with escape of duodenal loop fluid into the peritoneum. The mucosa of the loop in general is intact, but shows some superficial erosion, particularly in association with submucous hemorrhage.

CLOSED DUODENAL LOOP. DEATH IN FORTY-EIGHT HOURS.

*Dog S-20.*— Large male; weight, about 50 pounds.

February 25, 11 A. M. Operation and isolation of duodenal loop with washing in the usual way. 4 P. M. Dog walks about normally.

February 26. Dog appears sick and has diarrhea with blood in stools.

February 27, 10 A. M. Same, and much vomiting. 11.30 A. M. Death preceded by slow deep gasping respirations; wide pupils and muscular tremors.

*Autopsy.*—Performed at once. The heart, lungs, and thorax are negative. The peritoneal cavity shows a very slight amount of fibrinous exudate and a few ecchymoses about the area of operation. There is no fluid in the peritoneum. The liver is congested and deep purple in color. The spleen, pancreas, and kidneys show congestion. The stomach contains some peculiar black fluid much like that in the closed loop, and it is probable that the upper ligature was not tight and some of the duodenal fluid has escaped into the stomach. The small intestine shows a diffuse reddening of the mucosa, which is specked with ecchymoses.

The duodenal loop contains 100 c.c. of dark, slaty, slimy fluid. The closed loop mucosa is pinkish and a little swollen, but no ulcers are present.

CLOSED DUODENAL AND JEJUNAL LOOPS. DEATH IN FIFTY-FIVE HOURS.

*Dog 56.*—Strong, adult male hound; weight, about 45 pounds.

May 22, 3 P. M. Operation and isolation of a loop much longer than usual,

including the duodenum below the pancreatic duct and about six inches of the jejunum. The loop was washed out thoroughly before closure.

May 23. Dog seems well, but has had some diarrhea.

May 24, A. M. Dog vomits bile-stained fluid repeatedly; this vomiting is much more conspicuous than in the usual closed duodenal loop. Dog drinks much water. Rectal temperature, 38° C. 4 P. M. Vomiting continues; marked bloody diarrhea. 11 P. M. Found dead but quite warm.

*Autopsy.*—Performed at once. The abdominal cavity is clear, except for slight granular peritonitis about the loop and area of operation. The gastro-enterostomy is patent. The stomach contains bile-stained, watery fluid. The small intestine below the loop contains blood-stained mucus, and its mucosa has a mottled appearance with large areas of deep red color, where the capillary injection is quite marked.

The duodenal loop is rather flabby and not greatly distended. It contains about 50 c.c. of a thin, soup-like, faintly blood-tinged fluid. The loop mucosa is quite intact, but of a delicate pinkish tinge.

CLOSED DUODENAL LOOP. DEATH IN THREE DAYS.

*Dog S–53.*—Mongrel, male; weight, 17 pounds.

May 14, 3 P. M. Operation and isolation of duodenal loop after careful washing.

May 15, A. M. Dog seems normal. 5.30 P.M. Dog lies on side and is quite sick. Temperature, 38° C. Pulse is normal. 8.30 P. M. Dog vomited turbid brown fluid. Pulse is weak. Temperature, 37.5° C.

May 16, 10.30 A. M. Dog is quiet. Temperature, 37° C. 12.30 P. M. Temperature, 36.5° C. Muscular tremors; respirations becoming slow and deep. 5 P. M. Temperature, 38.2° C. Pulse fair. Drinks water and does not vomit. Muscular tremors still present.

May 17, 9 A. M. Vomited during night, and vomits immediately after drinking water. Pulse weak and slow. Temperature, 35.5° C. 10 A. M. Moribund; etherized.

*Autopsy.*—Performed at once. Blood showed delayed coagulation. The thorax is normal. The peritoneal cavity is normal. The liver, spleen, and mesenteric vessels are congested. The stomach contains a little bile-stained fluid; pyloric portion pale, and cardiac mucosa deep pinkish.

The duodenal loop contains a dark slaty paste, about the consistence of butter, which scrapes off very easily from the pink duodenal mucosa which is intact.

The duodenum just below the pylorus shows definite congestion of the mucosa giving a red mottled appearance. There are no ecchymoses. The injection begins 1 cm. below the pyloric ring and suggests the picture following injection of duodenal fluid in the normal dog. The jejunum below the gastro-enterostomy shows considerable injection of its mucosa, presenting a reddish mottled appearance fading to normal mucosa in the ileum. The intestinal contents are thin, watery, and bile-stained.

This group shows the characteristic picture following the production of a closed washed duodenal loop in a normal dog. The

last case illustrates the drop in temperature. Loss of fluid by diarrhea or vomiting may be conspicuous and is usually obvious. Muscular tremors, twitching, and irritability are usually present. A weak pulse with low blood pressure is present in the last stages. The autopsy shows splanchnic congestion and, usually, dilatation of the closed loop, but this last may not always occur. The intestinal mucosa usually shows the splanchnic congestion to best advantage and is similar to, though much less striking than the extreme engorgement of the intestinal mucosa which may follow the intravenous injection of large amounts of duodenal loop fluid. The duodenal loop may show a normal intact mucosa in gross and microscopically, except for a little diffuse injection. Again it may show necrosis, ulceration, and hemorrhage, and the contained fluid may vary correspondingly in characteristics, but it always contains a toxic substance.

ECK FISTULA AND CLOSED DUODENAL LOOP. DEATH IN THREE DAYS.

*Dog C–39.*—Large mongrel, male; weight, 37 pounds.

March 2. Operation with production of Eck fistula below the splenic vein, allowing the greater part of the intestinal venous blood to pour directly into the vena cava. A ligature was placed on the portal vein just below the splenic vein.

March 30. Animal in good condition. Operation and ligation of hepatic artery in the usual way.

April 23, 2 P. M. Dog in excellent condition. A closed duodenal loop was made in the usual way, with careful washing out of the intestinal contents. There was some difficulty on account of old adhesions.

April 24. Dog appears active and practically normal.

April 25. Dog is quite sick and refuses food; vomits bile-stained material.

April 26, 10 A. M. Dog is very sick. Pulse weak. Rectal temperature, 38.8° C. Etherized; bled from the carotid which showed very low arterial pressure.

*Autopsy.*—Performed at once. The abdominal wound shows some infection, but the peritoneal cavity is clear. The lungs show a few tiny patches of bronchopneumonia. The heart, spleen, pancreas, and kidneys are normal. Eck fistula is widely open, and the hepatic artery is completely cut off by the ligatures. The liver is slightly decreased in size as is usual, but is normal except for some capsular adhesions. The stomach contains a little bile-stained fluid and mucus. The small intestine is negative.

The duodenal loop is moderately distended with fluid. The serous surface is quite normal. The fluid is turbid gray in color and of the consistence of pea soup. The duodenal loop mucosa is a diffuse pink, and there is obvious engorgement of the vessels in the mucosa. There are no ulcers nor subcutaneous ecchymoses. The mucosa is intact throughout.

*Microscopical Examination.*—The mucosa of the duodenal loop is normal

except for a trifling congestion of the capillaries in the villi. The epithelium is normal and intact. The mucus covering the surface is extremely rich in bacteria, and this material contains a good deal of desquamated epithelium. The liver cells appear normal. There is no increase in connective tissue. The presence of the Eck fistula seemed to affect in no important way the general progress of the intoxication.

If the liver exerts a detoxifying action against this poison one might expect a more rapid intoxication in a dog with a closed loop when the intestinal blood is shunted directly into the vena cava (Eck fistula), or less intoxication when the toxic substance is introduced into the portal vein of a normal dog. The preceding experiment speaks against any such protective action of the liver, for the dog with a closed loop and with an Eck fistula survived longer than the average dog with a closed loop alone. Experiments given below show that the duodenal loop material is just as toxic whether injected into the portal vein or into the systemic veins.

CLOSED DUODENAL LOOP AND INTESTINAL OBSTRUCTION. KYMOGRAPH.

*Dog C–19.*—Mongrel pup, female; weight, 17 pounds.

March 27. Usual operation and isolation of washed duodenal loop.

March 29, 9 A. M. Dog is cold and toxic; would probably die in a few hours. Etherized, and kymographic tracings taken from the carotid. Blood pressure is low, averaging between 70 and 80 mm. of mercury. The pulse rate is very slow, averaging between 60 and 80 per minute, becoming slowed to even 30 or 40 per minute with occasional missed beats. Respiration is slow, about 5 or 6 to the minute, and the tracings showed conspicuous muscular tremors. The dog has cold, livid extremities, and seems in the last stages of surgical shock.

*Autopsy.*—Performed at once. The peritoneal cavity is clear. The stomach contains about two quarts of bile-stained fluid, caused by a twist in the jejunum just below the gastro-enterostomy, producing considerable intestinal obstruction. The duodenal loop is flaccid and its walls appear normal. It contains a little blood-stained pasty mucoid material in which are found a few small particles of food, showing that the washing had not been sufficiently prolonged. The mucosa is intact and, except for a slight injection, normal. The heart continued to beat for several minutes after the thorax was opened. It is normal. The lungs show a small patch of bronchopneumonia. The other viscera are normal. Since dogs with an intestinal obstruction in this location will live from seven to ten days, it is fair to suppose that the obstruction and especially the duodenal loop were responsible for death.

CLOSED DUODENAL LOOP. KILLED AFTER TWENTY-FOUR HOURS.

*Dog S–4.*—Adult mongrel, male; weight, 20 pounds.

January 19, 3 P. M. Operation and isolation of duodenal loop with careful

washing. January 20. Somewhat dull but not very toxic. 3 P. M. Ether anesthesia and bleeding from carotid.

*Autopsy.*—Performed at once. The serous surfaces and viscera are normal. The stomach contains bile-stained fluid and food. The intestine is normal. The duodenal loop is slightly dilated and contains 20 c.c. of slimy fluid which is slightly blood-tinged, due to inversion of the duodenal mucosa. The mucosa throughout the loop is intact, but slightly swollen and of a pinkish color. There are no ecchymoses to be seen.

*Microscopical Examination.*—The liver and kidneys are normal. The mucosa of the duodenal loop is practically normal. The tips of a few of the villi are slightly swollen and contain a few polymorphonuclear leucocytes. The epithelium is normal throughout.

CLOSED DUODENAL LOOP. KILLED AFTER TWENTY-FOUR HOURS.

Dog *S–28.* March 20, 3 P. M. Operation and isolation of duodenal loop as usual with washing.

March 21, 3.30 P. M. Dog is dull and sick. Ether anesthesia and bleeding from carotid.

*Autopsy.*—Performed at once. The stomach contains fluid and food. The intestine contains a moderate amount of fluid and shows a rather pale mucosa. The other viscera are negative. The closed duodenal loop contains only 2 to 3 c.c. of pasty, tenacious material. The mucosa shows a definite pinkish tinge, due to injection of the vessels, and is intact everywhere.

CLOSED DUODENAL LOOP. KILLED AFTER TWENTY-SIX HOURS.

*Dog S–2.*—Mongrel terrier, male; weight, 10 pounds.

January 10, 1 P. M. Operation and isolation of duodenal loop without washing.

January 11, 10 A. M. Dull and drowsy; no vomiting. 3 P. M. Weak. Ether anesthesia and bleeding from carotid which shows low blood pressure.

*Autopsy.*—Performed at once. The serous cavities and viscera are normal. The stomach contains bile-stained, blood-tinged fluid. The small intestine is normal. The duodenal loop contains 35 c.c. of blood-tinged thick fluid. The mucosa is intact, but seems somewhat swollen. There are a few subserous hemorrhages.

*Microscopical Examination.*—The liver and kidneys are normal. The duodenal loop in places shows some areas of necrosis with hemorrhage and invasion by pus cells, involving mucosa and submucosa.

CLOSED DUODENAL LOOP. KILLED AFTER TWENTY-EIGHT HOURS.

*Dog S–29.*—Large mongrel bull, male; weight, 25 pounds.

March 22, 12 M. Operation and washed duodenal loop isolated.

March 23, 4 P. M. Dog appears sick; muscular tremors present. Pulse is strong. Ether and bleeding from carotid.

*Autopsy.*—Performed at once. The organs are all negative except the duodenal loop which is flabby and collapsed. The serous surface is normal. It contains about 5 to 10 c.c. of thick, viscid, dark brown, mucoid material. The duodenal mucosa appears normal, and shows no injection, ecchymoses, or ulceration.

CLOSED DUODENAL LOOP. KILLED AFTER TWENTY-EIGHT HOURS.

*Dog S–5.*—Mongrel, male; weight, 14 pounds.

January 22, 11 A. M. Operation and isolation of washed duodenal loop.

January 23, 3 P. M. Animal rather dull and lies on its side. Pulse pretty strong. Ether anesthesia and bleeding from carotid.

*Autopsy.*—Performed at once. The serous cavities and viscera are normal, except the duodenal loop. It contains 16 c.c. of slightly blood-stained soup-like material. The duodenal mucosa loop is quite intact and of a pinkish color. No hemorrhages.

*Microscopical Examination.*—The liver shows a little fatty degeneration, but is otherwise normal. The duodenal loop is quite normal except for hookworms buried in the mucosa.

The presence of a closed duodenal loop for twenty-four hours may not bring about any marked anatomical change. The viscera are normal and the loop usually shows an intact mucosa of pinkish color and contains a few cubic centimeters of mucoid material. At this time, however, the toxic material can be easily demonstrated in the contents and mucosa of the closed loop.

CLOSED DUODENAL LOOP. KILLED AFTER FORTY-FOUR HOURS.

*Dog S–12.*—February 6, 1912, 3 P. M. Operation with isolation of duodenal loop after careful washing.

February 7. Dog will not eat.

February 8. Vomits frothy mucus. Muscular tremors marked. 11 A. M. Ether anesthesia and bleeding from carotid. Autopsy at once. All the viscera are normal. The duodenum is greatly dilated and quite tense. The serous coat shows a few grains of fibrin, but the peritoneum elsewhere is clear. The loop contains 100 c.c. of turbid dark brown fluid. The mucosa of the loop, except for a little injection, is quite normal and intact. There are no ecchymoses or ulcers.

*Microscopical Examination.*—The mucosa of the duodenal loop is quite normal. There are no polymorphonuclear leucocytes seen anywhere. The liver and kidneys are likewise normal.

CLOSED DUODENAL LOOP. KYMOGRAPH. KILLED AFTER FORTY-FOUR HOURS.

*Dog S–9.*—Large mongrel; weight, 22 pounds.

February 3, 4 P. M. Operation with isolation of closed duodenal loop after careful washing.

February 4. Dog quiet and refuses food.

February 5, 11 A. M. Dog sick. Ether anesthesia and kymograph record from carotid. Blood pressure 100 to 110 mm. of mercury, with almost normal pulsation. Dog killed by bleeding.

*Autopsy.*—Performed at once. The viscera are negative, except the duodenal loop, which contains only 3 to 4 c.c. of concentrated dark colored material of buttery consistence. The mucosa is intact.

*Microscopical Examination.*—Liver: the cells show some fatty degeneration of a moderate grade and a little increase in cell pigment. The duodenal loop mucosa is normal.

CLOSED DUODENAL LOOP. KYMOGRAPH. KILLED AFTER FORTY-EIGHT HOURS.

*Dog S–38.*—Mongrel, male; weight, 17 pounds.

April 16, 3 P. M. Operation and isolation of duodenal loop after careful washing.

April 18. Dog is somewhat toxic and has vomited once. Rectal temperature, 39° C. 2 P. M. Ether anesthesia and kymographic tracings from carotid. The blood pressure was practically normal and the pulse regular. The dog was killed at the end of the observation. The thorax and viscera are negative. The peritoneal cavity is clean. The duodenal loop contains 20 to 30 c.c. of a strawberry colored thick fluid. The loop shows a diffuse pinkish mucosa, no ecchymoses, and no ulcers.

DUODENAL LOOP DRAINED. DEATH IN THIRTY DAYS.

*Dog S–17.*—Mongrel fox terrier, male; weight, 17 pounds.

February 16. Operation and isolation of duodenal loop, a rubber tube being sewn into one end of the duodenal loop which was fixed to the abdominal wall.

February 17 to 18. Animal appears toxic. The loop is rinsed out repeatedly by inserting a catheter.

February 19. The rubber tube has sloughed out from the end of the duodenum. Dog seems less toxic.

February 20. White mucus flakes escaping from the fistula. Dog seems slightly toxic. Duodenal washings contain a good deal of mucus.

February 24. Duodenal loop rinsed out thoroughly with catheter. Animal is improving and eats well.

March 9. Duodenal loop rinsed out thoroughly. Dog has lost a little weight but seems strong.

March 17. Dog is sick with distemper and killed with ether.

*Autopsy.*—Performed at once. The heart is normal. The lungs show a few patches of bronchopneumonia. The pancreas, liver, and kidneys are normal. The stomach shows a large gastro-enterostomy wound and no ulceration. The intestines are normal except for adhesions about the site of the duodenal loop. The drained loop is quite empty. Its mucosa is pale and normal.

*Microscopical Examination.*—The liver and kidneys are normal. The mucosa of the drained loop is normal in all respects.

DUODENAL LOOP DRAINED. DEATH IN ELEVEN DAYS.

*Dog S–35.*—Large mongrel collie.

March 11, 4 P. M. Operation with isolation and drainage of the duodenal loop. A rubber tube was fixed in the end of the duodenal loop.

March 12. The duodenal loop was washed out with a catheter. The washing is tinged with blood and contains much mucus. Dog not toxic.

March 13. Duodenal loop washed again.

March 14. Drainage tube has sloughed away. Dog fairly well except for a little vomiting.

March 17. Dog seems normal.

March 22. Dog in poor condition; has lost weight; some digestion of skin of abdomen. Ether anesthesia, and bled from carotid.

*Autopsy.*—Performed at once. All the viscera are normal. The loop of jejunum just below the gastro-enterostomy wound had opened into the abdominal wound discharging gastric and pancreatic juices, explaining the skin digestion and rapid loss of weight. The duodenal loop contains about 2 c.c. of slimy mucus. The mucosa is intact, but slightly pinkish. No ulcers and no submucous hemorrhages.

DUODENAL LOOP DRAINED. DEATH IN FIVE DAYS.

*Dog S-49.*—Strong mongrel bull, male; weight, 16 pounds.

May 11, 2 P. M. Operation and isolation with drainage of duodenal loop in the usual way.

May 12. Dog toxic. Duodenal loop washed out carefully.

May 13. Dog active and shows no signs of intoxication.

May 14. Duodenal loop washed out. Dog toxic and refuses food.

May 15. Wound breaking down. Duodenal loop washed out. Dog refuses food.

May 16. Dog is very cold and toxic and has lost considerable weight. Killed with ether and bleeding from carotid. Viscera in general are negative. The peritoneal cavity is clear except for firm adhesions about the drained loop. The stomach is full of bile-stained fluid. The small intestine is normal.

Duodenal loop is empty and collapsed. Its mucosa is pinkish but intact.

DUODENAL LOOP DRAINED. DEATH IN FIVE DAYS.

*Dog S-46.*—Fox terrier, male; weight, 15 pounds.

May 1, 3 P. M. Operation with isolation and drainage of duodenal loop as usual.

May 2, 11 A. M. Dog toxic. The duodenal loop was washed out by means of a catheter; the washings contained blood and mucus. They resemble closely the material found in some of the closed loops.

May 3. Duodenal loop again washed out thoroughly. Dog improving.

May 4. Duodenal loop washed out thoroughly; washings contain mucus.

May 6. Found dead in cage.

*Autopsy.*—Performed at once. The heart, lungs, and serous surfaces are normal. The spleen, pancreas, and liver are normal. The stomach contains brownish fluid much like that found in intestinal obstruction. The small intestine shows a pink and purple mottled mucosa like that found in some of the dogs poisoned by injection of toxic duodenal contents. The duodenal loop contains a few cubic centimeters of thick buttery material. The mucosa is quite intact and of a pinkish color.

Dogs with drained duodenal loops may live for months, and the first animal of this series lived for one month and died of distemper and bronchopneumonia. The second dog was in good condition until the jejunum opened into the abdominal wound.

The last two cases, however, are so interesting that they will be referred to later. Several other dogs showed an identical picture, and the reason for the intoxication is obscure. The drainage appeared to be perfect, and daily washings of the loop seemed to insure this, yet the dogs died after signs of intoxication similar to the closed-loop dogs. The mucosa of the drained loop dog shows the presence of a toxic substance (dog S–45[1]), and absorption obviously takes place from the epithelium and not the lumen which is empty.

DUODENAL LOOP EXCISED. KILLED AFTER FIFTY-THREE DAYS.

*Dog S–15.*—Old mongrel, male; weight, 20 pounds.

February 10. Operation and excision of the portion of the duodenum commonly isolated in the duodenal loop.

February 12 to 15. Quiet but eats. Some diarrhea.

February 18 to March 10. Dog seems wholly normal.

April 3. There has been trifling emaciation, but the animal is strong and in good health. Ether and bleeding from the carotid.

*Autopsy.*—Performed at once. The heart, lungs, and thorax are quite normal. The spleen is small and fibrous. The liver is pale, but otherwise normal. The kidneys, pancreas, and intestinal tract are normal. The area of operation is perfectly normal; gastro-enterostomy is functioning perfectly. There are no ulcers in the intestinal tract.

*Microscopical Examination.*—The kidneys and liver are normal. The spleen is of senile type. The duodenum and jejunum show a perfectly normal mucosa.

The experiments so far reported show clearly that this particular portion of the duodenum is not essential to life and that drainage of a duodenal loop under certain conditions may be perfectly compatible with life for months. Complete closure of this duodenal loop is always associated with severe intoxication and is followed by death in one to three days with a characteristic picture much like that of volvulus in human cases. There seems to be no escape from the assumption that some toxin is being formed in the closed duodenal loop and absorbed from it.

DUODENAL LOOP FLUID INTRAVENOUSLY. DEATH IN FOUR HOURS.

*Dog S–37.*—Mongrel, male; weight, 13.5 pounds.

April 13, 5 P. M. Ether anesthesia and kymograph record from carotid. Duodenal loop fluid from dog S–30 (closed duodenal loop; killed after forty-eight hours). Duodenal loop flaccid; contained 5 to 7 c.c. of strawberry colored thick fluid. This material was washed into a beaker with distilled water and allowed

[1] Whipple, G. H., Stone, H. B., and Bernheim, B. M., *Jour. Exper. Med.*, 1913, xvii, 307.

to undergo autolysis at 38° C. under toluol and chloroform for a period of ten days. The supernatant fluid was poured off, heated to 60° C. for thirty minutes, centrifuged, and filtered. 40 c.c. of the clear broth-like fluid obtained were injected intravenously in small divided doses; an initial drop in blood pressure from the normal 180 mm. of mercury to 140 mm. occurred with rapid return to normal. During ten minutes following the last injections, a slow fall in blood pressure began, reaching 110 mm., and at the end of forty minutes, 65 mm. of mercury. During this fall there was considerable slowing of the pulse rate and variation in force and volume of heart beat. 5.45 P. M. Dog removed from kymograph; appears to be greatly shocked. 9 P. M. Dog found dead but quite warm. Abundant bloody mucus and fluid feces were passed, and blood-stained feces are oozing from the rectum.

*Autopsy.*—Performed at once. Blood removed from the heart shows no sign of clotting in thirty minutes; a flabby clot in twelve hours; and a firm clot in forty-eight hours. This is due to a great excess of antithrombin. The blood after centrifugalization shows only one fourth to one fifth plasma by volume, the normal plasma volume being one half of the whole blood. This condition results from great concentration of the plasma and loss of fluid from the blood. The heart, lungs, and kidneys are normal. The liver and spleen are greatly congested. The stomach contains a little fluid and shows a pink and red mottled mucosa over its cardiac portion. The pyloric portion is pale. The duodenum beginning sharply 1 cm. below the pylorus shows a swollen, deep purple, velvety mucosa (figure 1). The mucosa is coated with thick, creamy mucus which is loosely adherent. On removing this one sees the engorged villi as tiny red specks. The jejunum shows the same condition. The ileum shows a deep red mucosa fading gradually to the region of the ileocecal valve. The large intestine shows the same deep red mucosa and contains large amounts of blood-tinged fluid.

DUODENAL LOOP FLUID INTRAVENOUSLY. DEATH IN THREE HOURS.

*Dog S-32.*—Strong fox terrier, male; weight, 15 pounds.

March 28, 4 P. M. Ether anesthesia and kymograph record from carotid. Intravenous injection of duodenal loop fluid from dog S–21 (closed duodenal loop; killed after forty-four hours). The duodenal loop contained 5 c.c. of thick, dark paste which was washed into a beaker with distilled water and diluted to 60 c.c. with salt solution. The material was mixed thoroughly and allowed to stand at room temperature for four hours, was then heated at 60° C. for twenty minutes, centrifuged, and filtered through a Gooch crucible, centrifuged again, and the supernatant fluid used. The resulting opalescent broth-like fluid was injected in small doses intravenously. Blood pressure at the beginning, 190 mm. of mercury. 20 c.c. of duodenal loop fluid caused a prolonged drop in blood pressure to 80 mm. of mercury after a period of five minutes. Repeated small injections brought the blood pressure down to 60 mm. during the next twenty minutes. At the end of forty minutes the blood pressure was 100 mm. There was moderate slowing of the heart beat during this period of low blood pressure. 4.45 P. M. Dog removed from kymograph. 6.50 P. M. Cold extremities; death. Eyes show widely dilated pupils.

*Autopsy.*—Performed at once. Blood removed from the heart was fluid, and

there was no clot for thirty minutes. The next day the blood showed flabby clots. The lungs are normal. The spleen, liver, and kidneys show greatly engorged vessels. The mesenteric vessels in the abdominal cavity are much dilated and quite conspicuous. The stomach contains a little bile-stained mucus. The cardiac portion is reddish, the mucosa pinkish, while the pyloric portion is quite pale. There are no hemorrhages.

The duodenum beginning sharply 1 cm. below the pylorus shows a deep purple velvety mucosa. There is a thick, loosely adherent coat of mucus all over the surface. The villi stand out conspicuously as tiny bright red specks. The upper half of the small intestine shows a similar condition and the last foot of the ileum a pinkish mucosa. The large intestine is slightly reddened in its lower portion.

*Microscopical Examination.*—Duodenum: the villi show enormous engorgement of all their vessels. The deeper parts of the mucosa show only a trifling congestion, and the surface is coated with a thick layer of mucus. The epithelium appears normal. There is a trifling edema of the mucosa of the stomach. No acute inflammatory exudate is present. The kidneys and spleen, and the liver especially, show great congestion.

DUODENAL LOOP FLUID INTRAVENOUSLY. DEATH IN FOUR HOURS.

*Dog S-71.*—Small pup; weight, 10 pounds.

June 21 and 24. Dog injected with extracts of normal intestinal mucosa and the alcoholic extracts of duodenal fluid with negative result.

July 8, 5.30 P. M. Dog in excellent condition; weight, 11 pounds. Ether anesthesia and kymograph record from carotid. Intravenous injection of duodenal loop fluid from dog S-69 (closed duodenal loop; death after two and one half days). Duodenal loop fluid, autolysis for three days at 38° C. under toluol and chloroform. Heated at 60° C., centrifuged, and filtered. 55 c.c. of filtrate were injected slowly. Blood pressure before injection, 145 mm. of mercury; after injection, 70 mm.; and at the end of twenty minutes, 80 mm. There was marked slowing of the pulse during this period of low blood pressure. Feces were passed at the end of fifteen minutes following the injection. Muscular twitchings occurred.

9.30 P. M. Found dead.

*Autopsy.*—Performed next morning. The viscera are negative, except the intestinal tract. The cardiac portion of the stomach shows some congestion. The small intestine is greatly relaxed and contains large amounts of thin, blood-stained fluid. The mucosa beginning just below the pylorus is of a dull pink or red with considerable post-mortem digestion.

CLOSED DUODENAL LOOP FLUID INTRAVENOUSLY. ADRENALIN.

*Dog S-27.*—Fox terrier, male; weight, 12 pounds.

June 15, 12 M. Kymograph records from carotid. Duodenal fluid from dog S-53 (closed duodenal loop; death after sixty-six hours). The duodenal loop contained a little pasty material which was scraped out of the loop together with the mucosa, diluted with a little water, and allowed to undergo autolysis under toluol at 38° C. (May 16). Autolysis for one month at 38° C. Fluid heated to 60° C. for one hour, centrifuged, and filtered. 17 c.c. of filtrate given intrave-

nously. This caused a fall from 130 mm. of mercury to 60 mm., with a rapid rise above normal to 160 and return to normal. The second fraction of duodenal loop fluid gave a similar result, followed by a slow secondary fall during the next five to ten minutes, reaching a level of 80 mm. of mercury. A small amount of adrenalin, 2 c.c. of a 1 : 10,000 solution, gave the usual result with a rise to 240 mm. of mercury. At the end of one hour the intestine was opened and the mucosa of the jejunum presented a deep red velvety appearance. This did not bleach on giving adrenalin intravenously nor on adding a solution of adrenalin directly to the mucosa. The dog was killed at the end of one and one half hours.

*Autopsy.*—Performed at once. The usual congested intestinal mucosa was seen, beginning just below the pyloric ring. The viscera were negative, except for congestion.

The preceding experiments show that the material which accumulates in a closed duodenal loop is highly toxic when introduced intravenously. This material in the loop may be thin and soup-like or thick and pasty, but in all cases the toxic material can be demonstrated. Only a few cubic centimeters of this material (dogs S–37 and 32) may be diluted, incubated at 38° C. under toluol for days, then heated at 60° C. for thirty minutes, and filtered without removing or destroying the toxic substance. Intravenous injection of this broth-like substance will cause an initial drop in blood pressure followed by a rise to normal and a prolonged secondary fall to one half or one third of normal. The heart beat is slowed and may become irregular at this time. The dog is then in a condition of severe shock and the temperature falls; the pulse is scarcely palpable and muscular tremors are conspicuous. Vomiting and profuse diarrhea occur in the fatal cases and blood streaks appear in the watery stools. Respiration becomes slow and very deep some time before death. In these dogs it is to be remembered that a large amount of toxic material was given even though a small amount of concentrated duodenal loop material was used. It is probable that at least double the lethal dose was given in these first experiments, and it is possible to give a sufficient amount of poison to kill a normal dog in twelve to twenty hours. The anatomical findings in the dogs poisoned less acutely may not be as striking, but in general are quite similar. The acutely poisoned dogs here described present characteristic anatomical lesions. The blood remains fluid much longer than is normal, and clots form slowly, but can be accelerated by tissue extracts, showing the pres-

ence of an excess of antithrombin. The blood plasma becomes concentrated and the dried weight of the blood is above normal, as would be expected when the great loss of fluids by the alimentary tract is recalled. The thorax, heart, and lungs are normal. The liver, spleen, and mesenteric vessels show great engorgement, and the liver may be very tense and elastic. The gastro-intestinal tract shows the most striking changes (figure 1). The stomach contains bile-stained fluid, and the cardiac portion shows a moderate congestion of the mucosa, but the pyloric end is quite pale. About one centimeter below the pylorus there is a sharp line of demarcation separating the pale mucosa from the deep purple velvety mucosa of the duodenum. The duodenum is relaxed, usually contains fluid, and its engorged mucosa is coated with thick mucus. The intestinal contents are blood-tinged and rich in mucus. The jejunum presents a similar picture, but the intensity of the color usually fades to pink in the lower ileum. The large intestine shows congestion of its mucosa and ecchymoses are not infrequent.

*Microscopical Examination.*—There is great engorgement of all capillaries in the villi and no other change except occasionally some escape of red blood cells into the tissue.

Adrenalin given during the period of low blood pressure causes the usual reaction, but does not effect any bleaching of the intestinal mucosa whether given intravenously or applied directly to the surface.

Secretin can be prepared from the jejunum of a closed-loop dog and acts in the usual manner, but the material from the closed duodenal loop in the same dog will cause no pancreatic reaction when given intravenously.

DUODENAL LOOP FLUID INTRAVENOUSLY. DEATH IN FOUR HOURS. SECRETIN ABSENT.

*Dog S–13.*—Strong adult male; weight, 24 pounds.

Kymograph experiment with tracings from the carotid, and injection of material into the jugular vein. The cannula was placed in the pancreatic duct and the flow was recorded by a Marey tambour. Anesthesia with ether and 0.25 of a grain of morphia. Duodenal fluid obtained from dog S–12 (closed duodenal loop; killed after forty-four hours), centrifuged at high speed, and filtered through a thick Gooch crucible. Fluid very faintly acid to litmus. Duodenal fluid (10 c.c.) given intravenously caused a slight drop in blood pressure, but

there was no flow from the pancreatic duct. Blood pressure before injection, 140 mm.; five minutes after injection, 130 mm. of mercury.

Secretin was made from the normal duodenal and upper jejunal mucosa (dog S–12), by the method of Bayliss and Starling. Secretin (10 c.c.) produced a great drop in blood pressure; namely, from 140 to 60 mm. of mercury. There was prompt and striking pancreatic secretion within about fifteen seconds, lasting several minutes, during which time the blood pressure came back nearly to normal. Duodenal loop fluid (8 c.c.) was again injected, followed by a slight drop in blood pressure, but no pancreatic flow. After an interval of a few moments a third injection of acidified duodenal loop fluid (10 c.c.) was given. This caused no influence upon the pancreatic flow, but caused a slow drop in blood pressure, reaching 60 mm. of mercury. There was some slowing in the pulse rate. Blood removed at the end of the kymograph observation clotted very slowly, requiring about four times the normal time to clot. 1 P. M. Dog removed from kymograph and abdomen closed. 2.30 P. M. Slow deep respiration and very weak pulse. 4 P. M. Death occurred in the condition of shock with slow deep respiration and cold extremities.

*Autopsy.*—Performed at once. Blood taken from the heart required two hours for the formation of soft clots. The heart is negative. The lungs are slightly dilated. The spleen, liver, and kidneys show congestion. The stomach contains a little blood-tinged mucus, and its mucosa is pale. The duodenum beginning 1 cm. below the pyloric ring shows a deep purple and velvety mucosa coated with mucus. This picture is most intense throughout the duodenal loop, but there is a deep red mucosa throughout the jejunum fading to a pink color in the ileum. The large intestine shows a deep red mucosa. The intestine contains fluid which is slightly blood-stained.

*Microscopical Examination.*—The kidneys are practically normal. The liver shows a good deal of congestion. The gastric mucosa shows a little congestion, but the villi of the duodenum show enormous engorgement of all their capillaries. There is no inflammatory reaction, simply great widening of the capillaries in the ends of the villi and engorgement with red blood cells. No thrombi are seen, and no escape of blood into the tissue.

DUODENAL LOOP FLUID INTRAPORTALLY. DEATH IN THREE HOURS.

*Dog S–40.*—Fox terrier, male; weight, 13 pounds.

April 20, 11.30 A. M. Kymograph records taken from the carotid. Ether anesthesia and abdominal incision with aseptic precautions. A cannula was tied in a branch of the portal vein, and duodenal loop fluid from dog S–30 was given at intervals; the total amount was 20 c.c. The same fluid was used in dog S–37 with fatal intoxication. There was a fairly rapid drop in blood pressure from the normal 155 mm. of mercury to 60 mm. Then followed a slow return to about 110 mm. during the next five or ten minutes. The curve was similar to that produced after intravenous injection. A marked secondary fall occurred during the next twenty minutes to 60 mm. At the end of thirty minutes a loop of the jejunum was opened and showed a deep pink mucosa which became more and more engorged during the following fifteen minutes. There was a marked secretion of mucus and clear fluid. At the end of the observation the mucosa had the characteristic purple appearance found at autopsy. The

mesenteric vessels were very conspicuous. The intestine and abdomen were closed in the usual way. 12.30 P. M. Blood drawn from the jugular vein. Dry weight 24.1 per cent. in two parallel determinations. Rectal temperature 34.5° C., in spite of artificial heat applied by an electric pad. 1 P. M.. Slow, deep respiration. Involuntary passage of thin, yellow, faintly blood-streaked stools. 2.30 P. M. Death. Muscular tremors were conspicuous, and the pupils dilated.

*Autopsy.*—Performed at once. The heart was found beating slowly and continued to beat many minutes after opening the thorax. The lungs were normal. The spleen, liver, and kidneys were greatly engorged with blood. Blood obtained from the heart did not clot in thirty minutes. Flabby clots formed in eighteen hours, and solid clots in forty-eight hours. Dried weight of blood, 24.8 per cent. and 24.9 per cent. in parallel determinations. The stomach shows a pale mucosa about the pylorus and a deep pink in the cardia. The duodenum one centimeter below the pylorus shows a deep purple velvety mucosa covered with thick adherent mucus. The jejunum shows the same picture. The ileum shows a deep red mucosa and contains large amounts of thin, blood-stained fluid. Some tiny specks of hemorrhage are seen in the submucosa in the ileum.

DUODENAL LOOP FLUID INTRAPERITONEALLY. DEATH IN TWELVE HOURS.

*Dog S–52.*—Small mongrel, female.

May 15, 12 M. Ether anesthesia and kymograph tracings from carotid. Blood pressure at start, 160 mm. of mercury. Duodenal loop fluid from dog S–11 (closed duodenal loop; killed after twenty-four hours). The closed-loop (dog S–11) contained only 5 c.c. of a pinkish, thin soup-like material which was washed out into a beaker with distilled water. The mucosa of the loop was scraped off and added to the loop fluid with a little toluol and chloroform in a closed flask. After autolysis at 38° C. for twelve days the fluid was heated at 60° C. for one half hour, centrifuged, and filtered. The total filtrate (60 c.c.) was injected intraperitoneally. 1 P. M. Blood pressure was 120 mm. of mercury. Dog was removed from the kymograph. 2.30 P. M. Dog is much shocked. Pulse is very feeble. No diarrhea, some vomitus, and salivation. Rectal temperature, 37° C. 4.30 P. M. Repeated vomiting; then watery diarrhea. Rectal temperature, 39° C. 5.30 P. M. Diarrhea continued. Pulse weak and scarcely palpable. Respirations slow and deep. Pupils widely dilated. 8.30 P. M. Rectal temperature, 37° C. Diarrhea continued. May 6, 10 A. M. Found dead and cold.

*Autopsy.*—The heart is dilated with flabby clots. The lungs are negative. The spleen and liver are deeply congested. The stomach contains watery bile-stained fluid. The mucosa over the cardiac portion is reddish and mottled. The pylorus is pale. The duodenum shows a mottled mucosa, purplish areas 1 to 3 cm. in diameter being thickly scattered over the reddish mucosa. The same condition is found in the jejunum. The ileum is relatively pale. The large intestine shows considerable injection of the mucosa. The intestine contains thin, fluid, blood-stained material. This picture is almost identical with the findings in some of the dogs dying with closed duodenal loops. In both instances we may assume a relatively slow absorption of the toxic substance (compare dog S–53).

DUODENAL LOOP FLUID SUBCUTANEOUSLY. DEATH IN EIGHTEEN HOURS.

*Dog O–8.*—Small, adult fox terrier, female; weight, 8 pounds.

November 1, 10.30 A M. Ether anesthesia and subcutaneous injection of duodenal loop fluid obtained from dog S–90 (closed duodenal loop; immunized; killed after four days). The closed loop contained about 10 c.c. of thick pasty material which was diluted with about 100 c.c. of distilled water; chloroform and toluol were added and the mixture was allowed to undergo autolysis for three months. The supernatant fluid was heated at 60° C. for thirty minutes, centrifuged, and filtered. The total filtrate (100 c.c.) was injected subcutaneously over the abdomen and thorax and the areas were massaged. Ether was stopped at the end of fifteen minutes. 11 A. M. Pulse is weak and just palpable. 11.30 A. M. Pulse slightly stronger; respiration rather slow and deep. 5.00 P. M. Dog walks about; one semifluid stool; appears quite sick; ecchymoses numerous over areas of injection.

November 2, 9 A. M. Dog found dead and cold.

*Autopsy.*—The subcutaneous tissue at the sites of injection is edematous and dotted with ecchymoses. The serous surfaces are all normal. The heart contains no clots. The lungs are pink and normal. The spleen and liver are moderately congested. The stomach contains a little bile-stained fluid and shows a pinkish mucosa. The duodenum contains much fluid and mucus. Its mucosa is swollen and mottled red and purple. The jejunum and upper ileum show the same picture. The lower ileum is normal. The large intestine shows red splotches over its mucosa and apparently some hemorrhage into the submucosa.

The three preceding experiments show that the toxic substance causes the characteristic reaction in a normal dog, whether introduced into the portal vein, peritoneal cavity, or subcutaneous tissues. Intraportal injection gives a reaction practically identical with the intravenous. When the duodenal fluid is introduced subcutaneously or intraperitoneally the absorption is relatively slow, and other things being equal, the dogs survive longer.

The same symptoms, however, are noted, and autopsy reveals the same general changes, although less intense in degree. The intestinal tract excretes a large amount of fluid and suffers much congestion of its mucosa, especially in the duodenum. It will be seen that this reaction and the autopsy findings may be practically duplicated in dogs that have died after a closed duodenal loop has been established (compare dog S–53). In both cases we may assume a relatively slow absorption of the toxic fraction of the duodenal loop fluid, in the one case by the subcutaneous tissue, and in the other by the duodenal loop mucosa.

## SUMMARY.

Closed duodenal loops may be made in dogs by ligatures placed

just below the pancreatic duct and just beyond the duodenojejunal junction, together with a posterior gastro-enterostomy.

These closed duodenal loop dogs die with symptoms like those of patients suffering from volvulus or high intestinal obstruction. This duodenal loop may simulate closely a volvulus in which there has been no vascular disturbance.

Dogs with closed duodenal loops which have been washed out carefully survive a little longer on the average than animals with unwashed loops. The duration of life in the first instance is one to three days, with an average of about forty-eight hours.

The dogs usually lose considerable fluid by vomiting and diarrhea. A weak pulse, low blood pressure and temperature are usually conspicuous in the last stages.

Autopsy shows more or less splanchnic congestion which may be most marked in the mucosa of the upper small intestine. The peritoneum is usually clear and the closed loop may be distended with thin fluid, or collapsed, and contain only a small amount of pasty brown material. The mucosa of the loop may show ulceration and even perforation, but in the majority of cases it is intact and exhibits only a moderate congestion.

Simple intestinal obstruction added to a closed duodenal loop does not modify the result in any manner, but it may hasten the fatal outcome.

The liver plays no essential rôle as a protective agent against this poison, for a dog with an Eck fistula may live three days with a closed loop. A normal dog reacts to intraportal injection and to intravenous injection of the toxic substance in an identical manner.

Drainage of this loop under certain conditions may not interfere with the general health over a period of weeks or months.

Excision of the part of the duodenum included in this loop causes no disturbance.

The material from the closed duodenal loops contains no bile, pancreatic juice, gastric juice, or split products from the food. It can be formed in no other way than by the activity of the intestinal mucosa and the growth of the intestinal bacteria.

This material after dilution, autolysis, sterilization, and filtration produces a characteristic effect when introduced intravenously. When in toxic doses it causes a profound drop in blood pressure,

general collapse, drop in temperature, salivation, vomiting, and profuse diarrhea, which is often blood-stained.

Splanchnic congestion is the conspicuous feature at autopsy and shows especially in the villi of the duodenal and jejunal mucosæ.

Adrenalin, during this period of low blood pressure and splanchnic congestion, will cause the usual reaction when given intravenously, but applied locally or given intravenously it causes no bleaching of the engorged intestinal mucosa.

Secretin is not found in the duodenal loop fluid, and the loop material does not influence the pancreatic secretion.

Intraportal injection of the toxic material gives a reaction similar to intravenous injection.

Intraperitoneal and subcutaneous injections produce a relatively slow reaction which closely resembles the picture seen in the closed duodenal loop dog. In both cases there is a relatively slow absorption, but the splanchnic congestion and other findings, though less intense, are present in both groups.

There seems, therefore, to be no escape from the conclusion that a poisonous substance is formed in this closed duodenal loop which is absorbed from it and causes intoxication and death. Injection of this toxic substance into a normal dog gives intoxication and a reaction more intense but similar to that developing in a closed-loop dog.

## BIBLIOGRAPHY.

Albeck, V., *Arch. f. klin. Chir.*, 1902, lxv, 569.
von Baracz, R., *Arch. f. klin. Chir.*, 1899, lviii, 120.
Bayliss, W. M., and Starling, E. H., *Jour. Physiol.*, 1902, xxviii, 325.
Clairmont, P., and Ranzi, E., *Arch. f. klin. Chir.*, 1904, lxxiii, 696.
Draper-Maury, J. W., *Am. Jour. Med. Sc.*, 1909, cxxxvii, 725.
Halsted, W. S., *Am. Jour. Med. Sc.*, 1887, xciv, 436.
Hartwell, J. A., and Hoguet, J. P., *Am. Jour. Med. Sc.*, 1912, cxliii, 357.
Hartwell, J. A., and Hoguet, J. P., *Jour. Am. Med. Assn.*, 1912, lix, 82.
Kukula, *Arch. f. klin. Chir.*, 1901, lxiii, 773.
McClure, R. D., *Jour. Am. Med. Assn.*, 1907, xlix, 1003.
Murphy, F. T., and Vincent, B., *Boston Med. and Surg. Jour.*, 1911, cxlv, 684.
Stone, H. B., Bernheim, B. M., and Whipple, G. H., *Bull. Johns Hopkins Hosp.*, 1912, xxiii, 159.

## EXPLANATION OF PLATE 55.

FIG. 1. Stomach and duodenum of a dog acutely poisoned with fluid obtained from a closed duodenal loop (dog S–37). The purplish red color is due to extreme engorgement of the villi in the duodenum. The mucosa is covered with fluid and bile-stained mucus.

FIG. 1. (Whipple, Stone and Bernheim : Intestinal Obstruction.)