INTESTINAL OBSTRUCTION.

IV. THE MECHANISM OF ABSORPTION FROM THE MUCOSA OF CLOSED DUODENAL LOOPS.*

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In an earlier paper (1) we have shown that the poison of closed duodenal loops, which is responsible for the intoxication in that condition, is not absorbed by the mucosa of the unobstructed gut. We also tested the absorption of the same toxic fluid when introduced into recently isolated duodenal loops, and found that the dogs whose closed loops contain a double lethal dose of duodenal loop poison show no more intoxication than control dogs with empty closed loops, and die in about the same period, from which it is concluded that absorption from the lumen of the closed loop may be a secondary factor of intoxication and the important fraction is absorbed from the mucosa and not from the lumen of the loop. The observation of drained-loop dogs showing fatal intoxication confirms the conclusion that the greater part of the poison is absorbed from the mucosa itself, regardless of the amount of toxic material present in the lumen.

Similar experiments made by Davis (2) in this laboratory show that a closed duodenal loop is just as toxic when left washed and empty at operation or distended with a lethal dose of duodenal loop fluid from another animal. Davis also showed that repeated washing out of the stomach and duodenum, after ligating the bile and pancreatic ducts and establishing a low duodenal fistula, yields a certain amount of the toxic substance, a fact which may be interpreted to mean that the substance is excreted normally by the duodenal mucosa; and yet such a statement may exceed the facts. It

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has been shown by the writers that the toxic body is not present in demonstrable amounts in normal digested mucosa, but this does not preclude the possibility of its normal excretion in small amounts by the duodenum. It may be objected that the animal in the above experiment is not normal in that the bile and pancreatic juice are absent, the mucosa is constantly washed by water, and the animal is suffering from a certain amount of shock following extensive operative manipulations. The weight of evidence, however, seems to favor the possibility that the toxic substance may be excreted in small amounts by the normal mucous membrane of the small intestine. The formation of this toxic substance under abnormal conditions is rapid and abundant, as it can be demonstrated easily in the small amount of mucosa found in a closed or drained duodenal loop.

The essential point is, after all, the secretion of the toxic substance into the blood, which does not happen normally, but does occur in closed or drained duodenal loops and in intestinal obstruction. The important questions then are: What causes this changed function of the mucosa? Why does it form this poison and allow its passage into the blood? How does the mucosa readjust its equilibrium, and what may bring this about?

EXPERIMENTAL OBSERVATIONS.

CLOSED DUODENAL LOOP FILLED WITH TOXIC LOOP FLUID AT OPERATION. KILLED AFTER FOUR DAYS.

Dog O-100.—Young adult, male; weight 19 pounds.

July 16, 2 P. M. Ether anesthesia and operation. Closed duodenal loop with gastro-enterostomy made as usual. At the end of the operation the closed duodenal loop was filled with duodenal loop fluid, 50 c.c., obtained from dog O-86. This fluid had been standardized and 50 c.c. was fatal to a normal dog weighing 17½ pounds. 5 P. M. Dog recovering from operation; walks about and seems normal. 8 P. M. Some vomiting and diarrhea.

July 17. Dog appears like the usual closed-loop dog, and remains curled up quietly. Temperature 38.6° C. Weight 18½ pounds. 5 P. M. Dog appears better. Temperature 38.6° C.

July 18, 10 A. M. Dog appears fairly well. Pulse is fair. Temperature 38.5° C. Weight 17½ pounds.

July 19, 9 A. M. Condition remains the same. Pulse rather weak. Temperature 38.4° C. Weight 17½ pounds.

July 20, 11 A. M. Temperature 38.4° C. Weight 16½ pounds. Pulse is fair and dog does not seem gravely intoxicated. Etherized and killed.
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Autopsy.—Performed at once. Thorax, heart, and lungs normal. The peritoneum shows beginning purulent peritonitis with about 5 c.c. of thick, fibrino-purulent exudate in each flank. The surface is moist, injected, and shows fine grains of fibrin. The loop is distended tightly. The omentum is adherent about it. There are purplish patches showing through the wall. The ends are tightly closed and it contains 80 c.c. of thin slaty fluid having a very offensive odor. The mucosa of the loop is swollen and pinkish. There are purplish areas of inflammation with submucous hemorrhage and some superficial ulcers with obvious necrosis of the mucosa. Intestines and abdominal viscera are negative except for congestion. Liver shows cloudy swelling.

Closed Loop Distended with Toxic Fluid at Operation. Killed after Five Days.

Dog O-II1.—Strong, white bulldog, male; weight 32 pounds.

July 24, 3 P. M. Ether anesthesia and operation. Closed duodenal loop with gastro-enterostomy was done as usual. At the end of the operation the closed duodenal loop was filled with 100 c.c. of duodenal loop fluid. The loop in this instance was somewhat longer than normally, but this amount of fluid distended it tightly. This fluid had undergone autolysis for weeks and filtered readily. 50 c.c. of the fluid was a lethal dose for a normal dog 20 pounds in weight.

July 25, 10 A. M. Temperature 39.1° C. Weight 31½ pounds. Dog appears intoxicated to about the usual degree noted in control dogs with simple closed loops.

July 26, 10 A. M. Temperature 39.2° C. Weight 30½ pounds. Dog in fair condition and looks exactly like control dog. There is no evidence of increased intoxication from the fluid introduced into the loop.

July 27, 11 A. M. Dog has been vomiting a good deal. Temperature 38.8° C. Weight 28 pounds.

July 28, 10 A. M. Condition about the same. Temperature 39.2° C. Weight 27½ pounds.

July 29, 10 A. M. Dog looks very weak and will probably succumb during the day. Temperature 39.2° C. Weight 26½ pounds. Etherized and killed.

Autopsy.—Thorax, lungs, heart, and kidneys are normal. Liver is pale and shows evidence of fatty degeneration. The loop contains a good deal of fluid and is dilated with thickened walls. The ligatures at both ends have cut nearly through the wall, allowing the escape of fluid and entrance of a small amount of bile-stained material from the stomach. The mucosa is intact everywhere except at the site of ligation. There is a slight congestion of the mucosa of the loop and of the jejunum. It is possible that with the cutting through of these ligatures and beginning of the flow of normal secretion through the loop the intoxication in this animal would be overcome and recovery would take place, but it is obvious that the introduction of a large amount of duodenal loop fluid did not intensify the intoxication noted in the first few days when the loop was closed tightly.

Closed Duodenal Loop Distended with Toxic Fluid. Recovery.

Dog O-II2.—Strong bulldog, female; weight 24 pounds.

July 24, 4 P. M. Ether anesthesia and operation. Closed duodenal loop with gastro-enterostomy formed as usual. At the end of the operation the closed loop
was distended with 75 c.c. of duodenal loop fluid obtained from dog O-95. This fluid had undergone autolysis for three days, followed by filtration but not heating. 60 c.c. had poisoned rapidly a normal dog weighing 13 pounds, causing death in two hours.

July 25, 10 a.m. Temperature 38.9° C. Weight 22 1/2 pounds. Pulse is fair and dog curled up quietly.

July 26, 11 a.m. Condition about the same. Temperature 37.8° C. Weight 21 1/2 pounds.

July 27, 11 a.m. Dog looks much better, and is rather active. Temperature 38.1° C. Weight 21 1/2 pounds.

July 28, 10 a.m. Dog is fairly well. Pulse is of good tension. Temperature 38.8° C. Weight 21 1/2 pounds.

July 29, 10 a.m. Dog is rather sick, but not much shocked. Temperature 38.9° C. Weight 21 1/2 pounds.

July 30, 10 a.m. Dog is much better. Temperature 38.3° C. Weight 23 pounds. Dog does not vomit and is eating food. It is evident that the ligatures have cut through and the intoxication is diminishing. Condition improved until Aug. 5, when the dog is etherized and killed. Weight 23 1/2 pounds.

Autopsy.—Thoracic and abdominal organs normal. The loop shows both ligatures cut through, lying embedded in the mucosa on one side of the lumen. The lumen of the lower end is dilated to almost normal, whereas the upper end still shows some constriction. The wall of the loop is thickened and is somewhat dilated. The mucosa everywhere except at the site of ligation is intact and normal.

The three preceding experiments (dogs O-100, O-111, and O-112) indicate that the presence of large amounts of toxic, standardized duodenal loop fluid in a recently established closed loop will not modify the picture of intoxication. The control dog with an empty closed loop appears to be just as much intoxicated during the first forty-eight hours following the operation as the dogs whose closed loop is distended to its maximum capacity with old or fresh loop fluid.

The distended loops may show an early cutting through of the ligatures, with return to normal. We believe that pressure and distension are important factors in this result. A similar reaction is seen in the common bile duct when a ligature producing icterus cuts through in about five days and allows the free flow of bile, the ligature lying in the side of the duct wall. In the empty closed loop the fluid accumulates slowly and may be considerable after twenty-four to forty-eight hours, whereupon there will be violent peristalsis and a tendency for the ligatures at the ends of the loop to cut through the wall. Perforation or fatal intoxication almost always
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supervene before this has taken place. But with a distended loop at the start, there will be violent peristalsis with increased tension on the end ligatures. This causes more or less pressure necrosis in the tissues below the ligatures, and the ligatures slowly cut and press into the tissue while the wall adheres behind the ligature and obliterates its track. Finally the ligature cuts through the soft mucosa and lies in the lumen adherent to a segment of the mucosa which is not cut through. The linear cut or ulcer of the mucosa heals over rapidly and the gut slowly comes back to its normal diameter and thickness. Shortly after a free flow through the loop is established the toxic symptoms vanish and the dog begins to eat and put on weight.

DRAINED DUODENAL LOOP. DEATH IN FIVE DAYS.

Dog O-21.—Black mongrel, male; weight 23½ pounds.
Jan. 9. Good drainage from tube and loop washed out with water. Dog is in good condition and eats.
Jan. 10. Dog is active. Drainage has taken place and loop is washed out again with water.
Jan. 11. Dog seems well. Drainage tube has come out of the loop, but the loop is washed as usual.

Autopsy.—The ligature below the pancreatic duct had cut through, allowing bile and pancreatic juice in small amounts to escape into the loop. The other ligature is tight. The loop contains 1 to 2 c.c. of thick buttery material. Its mucosa is reddened, but everywhere normal except for congestion. The small intestine shows a diffuse injection with a red velvety mucosa and contains abundant fluid feces. The duodenum above the ligature shows a congested, reddish purple, velvety mucosa. The gastro-enterostomy is normal. Stomach shows congestion in the cardiac portion. The peritoneum is everywhere clean, but the mesenteric vessels are injected and widely distended. Spleen and liver are definitely engorged and tense. Thorax, heart, and lungs are normal. There is evidence in this case that the characteristic toxic agent was present, causing fatal intoxication associated with a great deal of splanchnic congestion. The escape of pancreatic juice and bile in small amounts did not modify the reaction in the loop.

DRAINED DUODENAL LOOP. DEATH IN SIX DAYS.

Dog O-2.—Weight 17½ pounds.
Oct. 22. Loop had been rinsed out with water daily by inserting a catheter and using a liter or more of fluid. 9 A.M. Dog found dead.

_Autopsy._—The peritoneal cavity is clean. The duodenal loop is normal and the lower end firmly fixed by granulation in the abdominal wound. The loop is collapsed and contains about 2 c.c. of pasty material. The mucosa close to the opening exteriorly shows a small ulcer involving the mucosa, measuring only 6 mm. in length. Elsewhere the mucosa is normal and intact, having a pale, pinkish mottled color. The other abdominal viscera are normal. The heart contains blood clots. The lungs show a few small purplish patches of consolidation not over 0.5 cm. in diameter.

_DRAINED DUODENAL LOOP. DEATH IN TWENTY-FOUR HOURS._

_Dog O-24._—Strong mongrel, male; weight 20 pounds.

-Jan. 15, 3 P.M. Ether anesthesia and operation as usual. Drained duodenal loop of the usual length isolated, but both ends drained through the abdominal wound and drainage tubes sewed into the open ends. Gastro-enterostomy.

-Jan. 16, 3 P.M. Dog appears very much intoxicated. Temperature is subnormal. Loop washed out thoroughly with warm water. 4 P.M. Death.

_Autopsy._—Performed at once. The peritoneum is clean. Thorax is normal. The blood is fluid and clotted slowly only when in contact with the body tissues, indicating the presence of antithrombin. The spleen and liver are moderately congested. The jejunum shows a mottled mucosa, reddish areas alternating with paler pink areas. The loop shows a good deal of edema and hemorrhage in the distal portions which were sewed into the abdominal wall. This was probably due to constriction and interference with the blood supply. Elsewhere the loop mucosa shows a moderate grade of congestion and is intact. It is possible that a part of this acute intoxication was due to the obvious interference with the blood supply to the ends of the drained loop.

_DRAINED DUODENAL LOOP. DEATH IN THREE DAYS._

_Dog O-36._—Large mongrel, male; weight 30½ pounds.

-Feb. 5, 4 P.M. Ether anesthesia and operation. Drained loop made as usual and gastro-enterostomy established. Tubes sewed in both ends. One was brought out through a puncture wound in the right rectus, and the other through the abdominal wound.

-Feb. 6, 10 A.M. Dog shows considerable drainage from the duodenal loop which is washed out thoroughly with water and a very dilute solution of permanganate. Temperature 37.7° C. 4 P.M. Dog appears intoxicated. Temperature 38.9° C.

-Feb. 7, 10 A.M. Temperature 38.5° C. Dog looks better and loop is washed out thoroughly with a large amount of dilute permanganate solution. 2 P.M. Dog appears gravely intoxicated.

-Feb. 8, 12 M. Much vomiting. Death.

_Autopsy._—Performed at once. The peritoneum is clean. The stomach is full of bile-stained fluid similar to that found in intestinal obstruction. The intestine everywhere is full of a similar fluid. The mucosa of the small intestine has a patchy, injected appearance. Gastro-enterostomy is clean. Drainage tube ex-
tended well into the loop, and the mucosa in contact with the tubes is red and swollen, and there is evidence of some inflammation. There is some mucus and fluid accumulated in the dependent portion of the loop. Between the ligature just below the pancreatic duct and the upper drainage tube is a portion of intestine about two inches in length which was not drained and in which material had accumulated. Other organs are negative except for a few very small patches of hemorrhagic bronchopneumonia in one lung.

The loop showed incomplete drainage in spite of large amounts of wash fluid (permanganate), because a small bit of intestine between the upper tube and the ligature below the pancreatic duct did not open freely into the loop, the drainage tube being too large and long. The accumulation of the characteristic fluid in this small portion of the duodenum may have hastened the fatal intoxication which was acute and characteristic.

The group of dogs (O-21, O-2, O-24, and O-36) with drained and washed loops shows that intoxication may develop under such conditions, and the only possible source for the poison is the mucosa. Moreover, the toxin can be demonstrated in the mucosa of the loop and in the loop washings. In an earlier publication (3) similar cases were cited and we have now a series of experiments that prove this point beyond doubt. It will be recalled that under favorable conditions a dog with a drained loop may live in good health for many weeks, and it may now be assumed that such a dog has developed a strong immunity that protects it against the intoxication. An experiment cited below gives evidence of an immunity demonstrable in the mucosa of a drained-loop dog. The immune mucosa can destroy a lethal dose of duodenal loop fluid after incubation for a few days, while normal mucosa has no such activity.

Conditions do not seem to be as abnormal in a drained loop as in a closed loop where we may have accumulation of much toxic fluid under tension with enormous multiplication of bacteria and often some injury and ulceration of the loop wall. The drained loop is rinsed out carefully each day with much fluid, and little or no material accumulates. Yet the intoxication develops and is usually fatal in the majority of cases. We can eliminate great numbers of bacteria by the repeated washings, although, of course, bacteria are still present but probably in less numbers than in the normal gut. It is clear that the bacterial flora will be much modified in a drained loop even if not greatly lessened in amount. The normal flow of the products of digestion and excretion is obliterated and
we are inclined toward the view that it is this essential deviation from normal which causes the perverted activity of the mucosa.

DUODENAL LOOP DRAINING INTO THE JEJUNUM. INTOXICATION AND IMMUNITY.

Dog O-40.—Strong bulldog, male; weight 25 pounds.
Feb. 14, 4 P.M. Ether anesthesia and operation. Gastro-enterostomy as usual. The duodenum just below the pancreatic duct is cut across and ligated with inversion of ends and closure. This partially closed duodenal loop can drain freely into the jejunum.
Feb. 15, 10 A.M. Dog looks well. 4 P.M. Dog appears toxic, but there is no vomiting.
Feb. 16–19. Dog appears well.
Mar. 1. Dog is losing weight but appetite is good; weight 21 pounds.
Mar. 7. Animal continues to lose weight. Temperature 38.9° C. Weight 18 pounds. There is some vomiting. 4 P.M. Dog killed.

Autopsy.—Beginning peritonitis with abscesses forming about the duodenal section. Thorax, heart, and lungs normal. Spleen and liver swollen and grayish. Duodenal loop is empty except for a little mucus. Other organs are relatively negative. The mucosa from the duodenum, jejunum, and ileum are washed, scraped off carefully, and combined with the duodenal loop fluid (dog O-33), 30 c.c. in amount. The fluid had been standardized and shown to be toxic, 25 c.c. poisoning fatally in four hours a normal dog (No. O-46), weighing 26 pounds.
The mixture of mucosa (dog O-41) and duodenal loop fluid (dog O-33) was allowed to undergo autolysis at 38° C. for eight days, and was then heated at 60° C. for one hour, centrifugalized, and filtered. This gave a clear, odorless broth, 115 c.c. in amount, which was injected intravenously into a normal dog (No. O-51), weighing 15½ pounds. It caused an initial drop in blood pressure followed by a rise (kymograph) with return to normal in thirty minutes. After six hours the dog appeared fairly well. Pulse good. There has been no vomiting and only one soft stool. The next day the dog is normal in every way. The experiment indicates that this loop dog (No. O-41) had been immunized by the presence of his partially drained loop, causing more or less intoxication. The immune mucosa in vitro completely destroyed with considerable rapidity a standard toxic dose of duodenal loop fluid.

DUODENAL LOOP DRAINING INTO THE JEJUNUM. DEATH IN FOUR DAYS.

Dog O-19.—Active young female; weight 17 pounds.
Dec. 14, 3 P.M. Ether anesthesia and operation. Gastro-enterostomy was done at the usual place and a single ligature placed at the site of the usual upper ligature of the closed duodenal loop. The lower ligature was not placed, so that a part of the duodenum is isolated which can drain freely into the jejunum. The gastric contents, bile, and pancreatic juice escape through the gastro-enterostomy.
Dec. 15. Dog appears normal. Temperature 38.6° C.
Dec. 16. Temperature 37.9° C. Dog seems well.
Dec. 17. Temperature 38° C. Dog has lost weight. Weight 15 pounds. At this time the dog had a violent convolution.
Dec. 18. Temperature 36.6° C. Dog appears sick. 3 P. M. Temperature 32.4° C. Animal desperately ill and died shortly after this observation.

Autopsy.—The peritoneum is normal. The partially closed loop contains about 10 c.c. of bile-stained, alkaline fluid. Its mucosa is normal, except for a slight congestion which is present as well in the jejunum. There is free communication between the duodenum and the upper portion of the jejunum. The small intestine shows a mottled, pink and red mucosa and contains a large amount of fluid fecal material. Stomach contains bile-stained fluid with alkaline reaction. Gastro-enterostomy is perfect. Liver, spleen, and kidneys show some congestion. Heart contains fluid blood. The lungs show small patches of hemorrhagic bronchopneumonia in the lower lobe.

**Duodenal Loop Draining into the Jejunum. Intoxication.**

Dog O-20.—Mongrel bulldog, male; weight 22½ pounds.

Jan. 3, 3 P. M. Dog is in poor condition. Ether anesthesia and operation. A partially isolated duodenal loop, similar to that described in the preceding experiment, was made with gastro-enterostomy in the usual location.

A single ligature was placed just below the pancreatic duct, completely occluding the lumen of the duodenum.

Jan. 4, 4 P. M. Temperature 38.1° C. Dog is sick and has diarrhea.

Jan. 5, 10 A. M. Temperature 38.7° C. Diarrhea continues.

Jan. 6, 10 A. M. Temperature 38° C. Diarrhea still more marked. Dog is very quiet and refuses food.

Jan. 7. Found dead.

Autopsy.—General peritonitis with a good deal of purulent exudate due to leakage at the site of gastro-enterostomy. This is a recent peritonitis, and the symptoms of intoxication which preceded its development associated with diarrhea, etc., were probably due to the intoxication from the partially closed duodenal loop.

This group of experiments (dogs O-41, O-19, and O-20) brings out two points. Ligation or section across the duodenum below the pancreatic duct together with a gastro-enterostomy just beyond the duodenjejunal junction produces a condition which we may call a partially or half closed loop. This half closed loop drains freely into the upper jejunum, and can be washed incompletely by a back flow of fluids, passing from the stomach through the gastro-enterostomy. The presence of such a partially isolated duodenal loop may be associated with intoxication, more or less severe, which will bring about an immunity reaction in the body cells. The intestinal mucosa from such a dog has the characteristic property of immune tissue; it can destroy with some rapidity the duodenal loop fluid in vitro and render the mixture harmless when given intravenously to a normal dog. The normal mucosa does not possess this activity.
CLOSED DUODENAL LOOP PLUS BILE. DEATH ON SECOND DAY.

Dog O-10.—Fox-terrier, male; weight 19 pounds.
Nov. 6, 3 P.M. Ether anesthesia and operation. The pancreatic duct is isolated by ligature and cut. The lower ligature of the closed loop is placed in the usual situation. The upper ligature is placed between the bile duct and the pylorus. The common bile duct was left open and drained freely into the closed loop.
Nov. 7, 12 M. Dog appears sick. Temperature 36.9° C.
Nov. 8, 9 A.M. Dog found dead.

Autopsy.—Performed at once. Numerous fat necroses throughout the peritoneal cavity, indicating the escape of pancreatic juice at the site of operation. The duodenal loop had ruptured with the escape of bile-stained fluid and obvious peritonitis. The loop shows necrosis with ulceration of the mucosa and submucous hemorrhage and the mucosa is very soft and easily separated. The fluid is slimy, thick, and deeply bile-stained. The lungs show some edema and areas of purplish pneumonia. Other viscera are normal except for engorgement.

CLOSED DUODENAL LOOP PLUS BILE. DEATH IN TWENTY-FOUR HOURS.

Dog O-12.—Mongrel, female; weight 21½ pounds.
Nov. 21, 4 P.M. Ether anesthesia and operation. The isolated duodenal loop included about six inches of jejunum, being somewhat longer than usual. The upper ligature is placed between the bile papilla and the pylorus. Gastroenterostomy as usual. The pancreatic duct is ligated and cut.
Nov. 22, 9 A.M. Temperature 38.9° C. 1 P.M. Death.

Autopsy.—Performed shortly after death. The peritoneum contains a few cubic centimeters of blood-stained fluid with delicate grains of fibrin over the intestinal coils in the region of the liver. The pancreas shows a few fat necroses around the head of the organ. The loop is greatly dilated with fluid. Its wall is thin and shows subserous hemorrhages. The mucosa is intact, but obviously inflamed and swollen and scrapes off easily. The liver and spleen show a good deal of congestion. The small intestine shows a reddish congested mucosa. The other organs are negative. The duodenal loop fluid in this case was tested on a normal dog (No. O-28), and 70 c.c. given intravenously caused rapid and fatal intoxication, with death in two and one half hours. Weight 11½ pounds.

CLOSED DUODENAL LOOP PLUS PANCREATIC JUICE. DEATH ON FOURTH DAY.

Dog O-6.—Black mongrel, male; weight 19 pounds.
Oct. 30, 3 P.M. Ether anesthesia and operation. Duodenal loop made with the lower ligature in the usual situation. The upper ligature is placed above the pancreatic duct, which opens freely into the closed loop. The common bile duct is isolated between the ligatures and cut.
Oct. 31. Dog does not appear intoxicated to a grave degree and takes a little food.
Nov. 1. Dog seems fairly well. Temperature 38.1° C.
Nov. 2, 9 A.M. Found dead, but quite warm.

Autopsy.—The peritoneal cavity is filled with turbid, yellow, bile-stained fluid.
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Thorax negative except for a few patches of bronchopneumonia. Spleen and liver slightly congested. The loop shows a rupture in the middle third where the wall shows extensive ulceration and softening. On cutting open the loop the ends are found to be tightly closed and the mucosa shows extensive ulceration and necrosis with submucous hemorrhage and a great deal of ecchymotic reaction, edema, and exudation. The small intestine shows a purple, mottled mucosa with evident engorgement of the mesenteric vessels.

CLOSED DUODENAL LOOP PLUS PANCREATIC JUICE. DEATH ON THIRD DAY.

Dog O-7.—Black and tan mongrel, male; weight 15 pounds.

Oct. 31, 4 P.M. Ether anesthesia and operation. The closed duodenal loop is made as in the preceding experiment, the lower ligature being in the usual location, but the upper ligature well above the bile and pancreatic papillae. The common bile duct is doubly ligated and cut.

Nov. 1, 9 A.M. Dog curled up quietly. Temperature 38.9° C.

Nov. 2, 9 A.M. Death.

Autopsy.—Performed at once. The peritoneum contains about 100 c.c. of blood-stained, turbid fluid. The serous surfaces are specked with small hemorhages, and the reaction is like that following the injection of duodenal fluid into the peritoneal cavity. The duodenal loop shows areas of hemorrhage, necrosis, and ulceration with perforation in the middle third. The mucosa everywhere is coated with mucus, deeply injected, and swollen, with extensive inflammatory reaction. There are deep ulcers with hemorrhages in the submucous tissue. The upper ligature is not quite tight and a little exchange of fluid may have been possible. Thorax, heart, and lungs negative. Spleen, liver, and kidneys are engorged. The jejunum shows a congested and velvety mucosa with deeper purplish patches. The lower portion of the small intestine is also congested. The picture is practically identical with that which may be found following intraperitoneal injection of heated, filtered duodenal loop fluid.

DUODENAL LOOP PLUS THE PYLORIC HALF OF THE STOMACH. DEATH ON FOURTH DAY.

Dog O-15.—Strong mongrel, male; weight 45 pounds.

Nov. 30, 2 P.M. Ether anesthesia and operation. Common bile duct and pancreatic duct ligated and cut. Stomach bisected. Gastro-enterostomy made by mistake into the pyloric half of the stomach, and the upper or cardiac portion completely isolated. The partially closed loop then contained the normal amount of duodenum plus the pyloric portion of the stomach which opened into the jejunum through a gastro-enterostomy.

Dec. 1. Condition as usual. Temperature 38.3° C.

Dec. 2, 3 P.M. Condition about the same. Temperature 38.8° C.

Dec. 3, 9 A.M. Temperature 37.5° C. There is some diarrhea and much vomiting. 12:30 P.M. Temperature 38.5° C. Dog seems very sick.

Dec. 4, 9 A.M. Found dead.

Autopsy.—There is some fresh peritonitis about the pyloric portion of the loop, and a few fat necroses around the head of the pancreas. The loop mucosa is intact and the duodenum contains about 100 c.c. of the usual brown soupy fluid. This material is shown to contain the usual toxic material. The lungs show a few patches of bronchopneumonia in the lower lobes.
CLOSED DUODENAL LOOP PLUS THE PYLORIC HALF OF THE STOMACH. DEATH ON THIRD DAY.

Dog O-17.—Large male; weight 43 pounds.

Dec. 7, 3 P. M. Ether anesthesia and operation. Stomach is bisected and gastro-enterostomy is made between the cardiac portion and the jejunum. Bile duct and pancreatic duct ligated and cut. The closed loop included the pyloric portion of the stomach with the entire duodenum and about three inches of the jejunum, with a simple ligature at the lower end of the loop.

Dec. 8, 10 A. M. Dog seems fairly well. Temperature 37.7° C.

Dec. 9, 9 A. M. Temperature 37.9° C. Dog is vomiting repeatedly.

Dec. 10, 9 A. M. Found dead, but quite warm.

Autopsy.—The peritoneal cavity contains blood-tinged, turbid fluid, about 150 c.c. There has been a rupture of the loop in the descending arm of the duodenum, where there are extensive areas of hemorrhage and ulceration. The pyloric portion of the stomach included in the loop is somewhat reddened but intact. The small intestine shows a congested velvety mucosa. The pancreas shows a few fat necroses around the head. The lungs are normal. The heart shows several adult specimens of *Filaria imitis*.

The preceding group of experiments shows that a closed duodenal loop is quite as toxic when the pancreatic juice or bile flows into it or when it includes the pyloric portion of the stomach. In the latter instance the dogs survived slightly longer, but this may be explained partly by the fact that the dogs in these experiments were unusually large and strong. These animals may survive a simple closed loop for a period of four or even five days.

DISCUSSION.

It will be recalled that a closed duodenal loop is isolated between two ligatures, and the continuity of the intestinal tract is established by means of a gastro-enterostomy. The intoxication under such conditions is very acute. If the lower ligature is omitted we form a partially closed loop which drains freely into the jejunum. Under the latter conditions the intoxication is less marked but obvious; immunity may result and be clearly demonstrated. With a simple obstruction of the upper jejunum a dog may live four to eight days, which is considerably longer than in the case of a simple closed loop. The intoxication is clearly of the same type; but why does the simple obstruction cause less acute symptoms?

Does the bile or pancreatic juice have the power of neutralizing or destroying the poison? This question is answered in the negative
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by the last group of experiments. Moreover, the gastric juice is unable in any way to neutralize the poison formed in the loop or to lengthen the life of the animal. The drained duodenal loops give rise to the same type of intoxication, yet the lumen here is free from any fluid toxic accumulation. There is good evidence that the poison is not absorbed by the normal mucosa. Furthermore, absorption is not appreciably more rapid from a closed loop recently filled with the toxic fluid than from a simple closed loop.

This again emphasizes the fact that the mucosa is the source of the toxic absorption rather than the material accumulated in the lumen of the gut. The bile and pancreatic and gastric juices have no power to destroy the poison or check its production in a closed loop. Removal of the fluid by vomiting is not an essential feature, as the poison will not be absorbed from the lumen.

The essential feature perhaps is the flow of intestinal contents which provides the normal environment of the cells of the mucous membrane. When this flow is completely stopped, as in a closed loop, we note the most acute type of intoxication. It is probable that the abnormal fluid accumulation and perhaps bacterial growth may stimulate the mucosa to produce greater amounts of toxin. When simple obstruction is present there is an interchange of fluids, the current in the main being the reverse of normal, resulting in accumulation of fluid in the stomach and vomiting. Intoxication develops, but it is not as intense as in a closed loop, the reason for this being perhaps that fluids are still passing over the mucosa and tend to check the accumulation of the toxic substance within the mucosa which is most evident in the simple closed loops.

Our work with the toxic substance within the closed loops has brought out several points of interest bearing on its nature. It is clear that the poison is resistant to ordinary digestion or autolysis (pancreas or intestinal mucosa), and it can be boiled over a free flame, when in a non-coagulable fluid, without destruction. When the toxic substance is digested for weeks and months with normal intestinal mucosa it may be completely or partially destroyed. For this reason the duodenal loop fluid may deteriorate slowly, as in collection of the material it is easy to include a little of the mucosa. It can be shown that the mucosa of a closed loop, where the dog was
resistant and perhaps survived four days, can destroy the loop poison much more rapidly than normal mucosa. This fact must be kept in mind when making digestion extracts of the mucosa of closed loops, as prolonged digestion is apt to destroy some or all of the contained poison.

Normal organ extracts can destroy the duodenal loop poison when incubated for many weeks and the liver extract is most active, but their activity is far inferior to the same materials derived from immune dogs. When a sublethal dose of poison is introduced intravenously in a normal animal, it is probably fixed and destroyed by the tissue cells, and the capacity of destruction is greatly increased by this procedure, resulting subsequently in more or less immunity. The cell digestion and destruction of the poison is shown crudely by the incubation of mixtures of organ juices and loop poison. This suggests some ferment as the active factor.

Another point comes out clearly in our series of experiments. There seems to be a slight but definite seasonal fluctuation in the resistance of dogs to a duodenal loop, whether closed or drained. The operations have been done by the same persons and a great variety of animals have been included in the experiments. Dogs have a slightly greater resistance in the spring and summer than in the fall and winter. We believe that food, type of animal, and operative technique can be ruled out. The only possible factor is the temperature, and we believe that this is concerned in the slightly greater resistance of the dogs during the warm season.

The intoxication is associated with much loss of body heat and lowering of temperature. When the room temperature is between 80 and 90° F, it is obvious that there will be much less loss of body heat than with a room temperature of 60 to 70° F. This point is recognized in the treatment of operative shock, but perhaps is not sufficiently emphasized in connection with the treatment of intestinal obstruction and intoxication, which, when uncomplicated, may be associated with a subnormal temperature.

CONCLUSIONS.

Intoxication is evident in a drained duodenal loop whether it opens externally or into the jejunum and may be associated with
more or less immunity which can be demonstrated after a period of days.

Intoxication with a closed duodenal loop is identical whether the loop is left empty at operation or filled with a lethal dose of loop fluid. This again emphasizes the fact that absorption of the poison is essentially from the mucous membrane rather than from the contents of the closed loop.

The intoxication of a closed duodenal loop is not modified by the presence of bile, pancreatic juice, or gastric secretion.

Cessation of the normal flow of intestinal fluids which bathe the mucous membrane may be essentially responsible for the perverted activity of the mucosa and secretion of a poisonous material into the blood.

Animals may be slightly more resistant to closed or drained loops during the warm months, which may be explained by the increased loss of body heat in the colder months. This indicates that cases of acute intestinal intoxication with subnormal temperature may be benefited by a generous supply of artificial heat.

BIBLIOGRAPHY.